National Institute for Health and Care Excellence

Draft

Head injury: assessment and management (update)

[K] Evidence review for hospital admission in people with small intracranial injuries

NICE guideline <number>

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

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Draft for Consultation

These evidence reviews were developed by The National Guideline Centre]

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1.1 Review question

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

1.1.1 Introduction

In people who suffer a head injury, structural damage to the brain is found on CT scanning, including for example a depressed fracture, haematoma, or contusion. Some of these intracranial injuries are significant, and require close observation or neurosurgery, due to the risk of ongoing damage to the brain. However, in some patients, small intracranial injuries are identified which do not require immediate neurosurgical intervention. Most people with small intracranial injuries are admitted to hospital to ensure any clinical deterioration can be immediately acted upon. However, there is likely to be a cohort of patients with small intracranial injuries, in whom the likelihood of injury progression or further damage to the brain is very small. If it were deemed possible to accurately identify this low-risk patient group, it would be possible to provide guidance for clinicians on which patients could be safely discharged home, and which would require admission. Being able to discharge some patients with stable small intracranial injuries would benefit the patient by reducing the morbidity associated with hospital infection, and the healthcare system through reduced use of inpatient beds.

1.1.2 Summary of the protocol

For full details see the review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Inclusion: Infants, children and adult with all intracranial injuries positive CT scan and GCS 13-15 • Adults (aged ≥16 years) • Children (aged ≥1 to <16 years) • Infants (aged <1 year) Mixed population studies will be included but downgraded for indirectness. Cut-off of 60% will be used for all age groups Exclusion: Adults, and children (including infants under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury. Studies will be downgraded for indirectness as we will be including people with all intracranial injuries
Prognostic variables under consideration	Risk factors for clinical deterioration in people with small intracranial injuries: • Severity of anatomical injury on CT (scales as defined in the study) different scales are used– Marshall scale or AIS (Abbreviated injury scale - gives size and site of injury) - some papers report large or small contusion/extradural haemorhahge

	[there has to be some description of anatomical injury on CT in the studies and adjust for GCS] Size of injury is included as part of anatomical injury • Severity of injury based on GCS (mild/moderate/severe) • Anticoagulant therapy • Anti-platelet therapy • Age • Blood measurements such as clotting, haemoglobin, blood glucose • Abnormal pupillary responses and neurological deficits (pupils measured by shining light whether pupils constrict, neurological deficit – examination finding) • Pre-existing co-morbidity and frailty • Significant extracranial injuries
Confounding factors	Key confounders: • Severity of injury (based on GCS) Studies will only be included if key confounder of severity of injury have been accounted for in a multivariate analysis Other confounders: • Severity of anatomical injury on CT • Anticoagulant therapy • Anti-platelet therapy • Age • Blood measurements such as clotting, haemoglobin, blood glucose • Abnormal pupillary responses and neurological deficits (pupils measured by shining light whether pupils constrict, neurological deficit – examination finding) • Pre-existing co-morbidity and frailty • Significant extracranial injuries Studies will not be excluded if not adjusted for other confounders but will be downgraded for risk of bias.
Outcomes	Clinical deterioration, which includes: • Death or neurosurgery within 30 days of injury • Need for critical care admission • Reduction in GCS (drop of of 2 or more) • Seizures • Unplanned hospital re-admission at 30 days This is not an exhaustive list Results may be reported in the form of adjusted RR or OR *(post-hoc protocol deviation made to allow sensitivity/specificity data to be included for clinical decision rules, see 'Methods and process' section below)*
Study design	Cohort studies (prospective and retrospective) Systematic reviews and meta-analyses of the above Case-control studies will be excluded.

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.

Note that after the review had been completed and presented, it became clear that for clinical decision rules it was important to include prognostic accuracy data (sensitivity/specificity) as these are the most important measures for interpreting how useful decision rules are. A post-hoc deviation to the protocol was therefore made to allow inclusion of sensitivity/specificity data for clinical decision rules. Thresholds used for assessing imprecision were 0.9 and 0.7 for sensitivity and 0.6 and 0.4 for specificity, in line with those used for another review looking at clinical decision rules in this guideline.

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 prospective or retrospective cohort studies (or systematic reviews including these study types) investigating the association of risk factors with outcomes in those with confirmed small intracranial injury and GCS 13-15. As it was noted that it would be difficult to identify evidence in the small intracranial injury population and the definition of this varies, studies involving populations with any confirmed intracranial injury, regardless of size, and GCS 13-15 were included but downgraded for indirectness. Following a post-hoc deviation to the protocol, sensitivity/specificity data (prognostic accuracy) was included for studies reporting the performance of clinical decision rules as it was noted these are the most important measures for assessing the performance of decision rules.

Seventeen observational studies (one prospective and sixteen retrospective studies) were included in the review; [1-7, 9-18]these are summarised in below. Evidence from these studies is summarised in the clinical evidence summary below (Tables 3 to 35). Summary matrix tables are provided in Tables 36 to 46.

All but one of the included studies were in the adult population. Although the number of studies and risk factor definitions varied, there was at least one study reporting multivariate results for each of the nine risk factor groupings listed in the protocol; therefore, for studies reporting odds ratios/risk ratios, studies reporting only univariate results were not included for any of the risk factors. For studies reporting clinical decision rules, multivariate adjustment was not required given they consist of multiple variables themselves and it is not possible to adjust sensitivity/specificity results.

Even where multiple studies reported data for the same risk factor, differences between studies in how the risk factor was analysed (for example as a continuous variable or as a dichotomous variable divided into categories based on thresholds), outcome reported and variables included in the multivariate analysis meant that pooling across studies was not appropriate.

Only one study in children[2] was identified for inclusion in the review.

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.

Population

The population of included studies was generally similar across studies, though some of the exclusion criteria differed between studies (for example, some allowed inclusion of people using anticoagulant therapy while others specifically excluded this).

For most included studies, the population was not specifically limited to those with small intracranial injuries and there was therefore population indirectness relative to the review protocol. Only studies that limited the population to people with mild head injury (GCS 13-15, with some limiting further to those with GCS 14-15) were however included, as it was noted that people with GCS ≤12 would never usually be discharged home.

Two studies[4, 10] were the exception as they did appear to limit to smaller intracranial injuries: one[10] only included people with an intracranial haemorrhage of 1 cm or less and a GCS score of 13 or greater and the other[4] described 'relatively small volume of subdural haematoma' as one of the inclusion criteria in the study flow chart and although this is an unclear definition does suggests that smaller injuries only may have been included.

Risk factors

Although for many risk factors there was data from multiple studies, the definition of the risk factor or way in which it was analysed as part of the multivariate analysis varied.

For example, a number of different injury severity scales were reported, such as the Fisher scale and Marshall scale. Also, even when the same scale or measure was reported across studies, different studies analysed this data differently; for example it could be analysed as a continuous variable (for example, where the OR is reported for every 1-unit increase on the scale) or as a categorical/dichotomous variable (for example, those that were above or below a specific value on the scale).

Risk factors analysed as dichotomous variables (for example those ≥65 years vs. <65 years) were generally well defined but where risk factors were analysed as continuous variables (for example increasing age) this was often not as well defined, with many studies not clearly stating whether the OR was for a 1-unit increase or 10-unit increase in that continuous variable, for example.

Three papers[6, 7, 9] provided raw data available to calculate ORs for those meeting vs. not meeting at least one criterion included in potential or established decision rules. In addition, following a post-hoc deviation from the protocol, sensitivity and specificity results reported in these papers were also included and presented.

Outcome

In general, most outcomes reported and included in this review were indirect relative to the protocol. Many studies only reported outcomes within the same admission, meaning time-points were much shorter than the ideal 30 days specified in the protocol.

In addition, studies often reported the outcome of 'progression on repeat CT', which again was within the same admission at a short time-point but was also indirect to the protocol as it may be less indicative of clinical deterioration as it is a radiological observation rather than a clinical outcome as defined in the protocol (examples including death, seizures or need for readmission). Studies where progression on repeat CT was included as an outcome were only included if it was clear that repeat CT was routine for all people with an injury on CT and that the study had not selected for a specific population receiving repeat CT, as often repeat CT is only performed when there is some indication of clinical deterioration and this would bias the population.

Confounders

All studies included in the review had performed some form of multivariate analysis, though the variables included and number of variables included varied across studies.

Only studies that limited the population to people with GCS 13-15 were included. No studies were excluded based on the variables they had included in the multivariate analysis as any multivariate analysis was considered acceptable. Instead, the confounders specified in the protocol were considered when assessing risk of bias for these studies.

In general, most studies had at least moderate concerns about confounding in the risk of bias assessment, though there were three studies[7, 9,14] where this was low given they had included a larger number of factors in the multivariate analysis and covered most or all of those listed for consideration in the review protocol.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix J.

1.1.5 Summary of studies included in the prognostic evidence

Table 2: Summary of studies included in the evidence review

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
Adults						
Borczuk 2019[1] N=1079 Retrospective	Inclusion: aged ≥16 years with blunt head trauma; and isolated cranial trauma Exclusion: GCS ≤12; trauma to other organ systems (those requiring consultation with a service other than neurosurgery)	Multivariate logistic regression analysis performed using variables that were significant in univariate analyses at P≤0.02	• GCS 15 vs. GCS 13-13 • Subdural haematoma ≤6 mm vs. >6 mm	Full list included unclear but following significant variables identified: GCS of 15, isolated traumatic subarachnoid haemorrhage and subdural haematoma with thickness ≤6 mm	**Discharge within 24 h**	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – indirect relevant to review protocol as could be other factors contributing to length of stay other than clinical deterioration
Joseph 2015[3] N=876 Retrospective	Inclusion: aged ≥18 years; isolated traumatic brain injury (head Abbreviated Injury	Multivariate logistic regression analysis including those that had	• Age ≥65 years vs. <65 years	**Progression on repeat CT:** Loss of consciousness;	**Progression on repeat CT** Defined as development of	Risk of bias: high Indirectness: • Population – not specific to those

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	Score [AIS] ≥3 and other body region AIS score <3); GCS 13-15 on presentation (mild TBI); intracranial injury (skull fracture or intracranial haemorrhage) on initial head CT scan; and routine repeat head CT scan. Exclusion: patients on antiplatelet (aspirin or clopidogrel) or anticoagulation therapy (warfarin); patients transferred from other institutions; and those undergoing emergency neurosurgical intervention	P≤0.2 on univariate analyses	• Subdural haemorrhage >10 mm vs. ≤10 mm • Epidural haemorrhage >10 mm vs. ≤10 mm • Platelet ≤100,000 mm^{-3} vs. >100,000 mm^{-3} • Lactate ≤2.5 vs. >2.5 • Base deficit >4 vs. ≤4	displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4 **Neurosurgical intervention:** Age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4	new intracranial haemorrhage or increase in the size of the initial haemorrhage. All patients had routine repeat head CT within 6 h of initial CT scan. Scan was reviewed by single trauma surgeon for type of skull fracture and size and type of intracranial haemorrhage. Findings of repeat CT scan categorised as progressed or unchanged. **Neurosurgical intervention** Defined as need for neurosurgical intervention, which included craniectomy or craniotomy.	with small intracranial injuries • Outcome: ○ Positive repeat CT – lesion progression is radiological outcome not specifically clinical deterioration ○ Neurosurgical intervention – time-point unclear and possibly within same admission

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
Kim 2014[4] N=98 Retrospective	Inclusion: acute trauma-related subdural haematoma diagnosed on CT; mild head injury (GCS 13-15); no focal neurological deficits; no significant mass effect; no significant midline shift; **relatively small volume of subdural haematoma**; and medically managed at time of admission Exclusion: urgent craniotomy performed and evacuation of haematoma within 24 h of admission; neurological deterioration within first 48 h following admission; moderate-severe head injury (GCS <13) at admission; vascular abnormality;	Multivariate logistic regression models built to control for potential compounding variables	• Initial volume of lesion (ml) as continuous variable • Degree of midline shift (mm) as continuous variable • Maximum thickness of lesion (mm) as continuous variable Note that increments unclear for all three variables	Full list included unclear but following significant variables identified: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present	**Haematoma enlargement leading to surgery – ~1 week following injury** Repeat follow-up CTs performed routinely in all patients. Those with stable neurological status without significant increase in haematoma volume were maintained with conservative management. Those with progressive neurological symptoms/signs unresponsive to medical treatment with pathological radiographic features (including haematoma enlargement leading to mass effect, midline shift and/or herniation) underwent surgery	Risk of bias: high Indirectness: • Risk factor – possibly uses values on latest CT scan for those that had a worse measure on second scan (does not limit to values on initial CT scan) • Outcome – short time-point of ~1-week post-injury

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	subdural haemorrhage localised only to falx or tentorium cerebelli; bilateral acute subdural haematoma; <15 years old; other significant organ injury; and those refusing surgical treatment.					
Lewis 2017[5] N=500 Retrospective	Inclusion: age ≥15 years; blunt mild TBI; GCS ≥13; and intracranial haemorrhage Exclusion: no documentation of intracranial haemorrhage according to ICD (9th revision) diagnosis codes 852.0, 852.1, 852.3, 852.4, 852.5, 853.1.	Multivariable logistic regression analysis (backward stepwise)	• Head Abbreviated Injury Scale (AIS) as a continuous variable – unclear if analysed per 1-unit increment or alternative	Hospital length of stay, ICU length of stay, days of mechanical ventilation, head-AIS score, Injury Severity Score, skull fracture, abnormal initial neurological examination, subdural haemorrhage, subarachnoid haemorrhage.	**Neurosurgical intervention at unclear time-point, possibly within same admission** Definition unclear but events included craniotomy, craniectomy, intracranial pressure monitor placement and ventriculostomy.	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – neurosurgical intervention at unclear time-point and possibly part of initial management decision rather than assessing at a longer time-point and including possible

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
						delayed interventions
Marincowitz 2020[7] N=1699 (n=1569 for clinical decision rules) Retrospective	Inclusion: ≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage Exclusion: non-traumatic cause of intracranial haemorrhage; pre-existing CT	Multivariate backward elimination with statistical significance threshold of 0.1 used for model selection. All candidate predictors initially included and imputed datasets combined using Rubin's rules at each stage of model selection. Prognostic model developed was subsequently used to derive a risk score using optimism-adjusted coefficients. Individual patient risk scores were calculated. A risk score for ED	• Hull Salford Cambridge Decision Rule (rule developed in the paper) – score >0 for admission and score of 0 for discharge • BIG criteria – score >1 for admission and score of 1 for discharge Various risk factors separately: • Age as continuous variable (per 1-unit increase) • GCS 13 and GCS 14 vs. GCS 15 (separately for each group) • Preinjury anticoagulation/ antiplatelets vs. none	Note that for clinical decision rules, multivariate analysis was not performed as ORs calculated were based on raw data reported in the paper. Sensitivity and specificity data reported in paper also presented. For individual risk factors, the following variables were included in multivariate analyses: **Deterioration outcome:** GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT	**Deterioration up to 30 days after ED attendance** Defined as composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI. Where reason for death, ICU admission or readmission was unknown it was attributed to TBI deterioration. **Need for neurosurgical specialist admission up to 30 days after ED attendance**	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	abnormalities preventing determination of whether acute injury had occurred; and patients transferred from other hospitals	discharge was proposed based on the trade-off between risk of deterioration in a discharged patient and number of patients admitted for observation. BIG criteria also assessed.	• Abnormal vs. normal first neurological examination • Injury severity on CT (various groups compared to simple skull fracture group) • Extracranial injury (body regions excluding head) as continuous variable (per 1-unit increment on ISS) • Rockwood Frailty score groupings (1-3, 4-6 and 7-9) vs. <50 year group	(categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase) **Neurological admission outcome:** age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty	Defined as composite of neurosurgery, ICU admission for TBI or intubation.	

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
				Scale score (categories described above under prognostic factors, versus people <50 years)		
Marincowitz 2022[6] N=1047 (n=961 and n=921 analysed for two decision rules) Retrospective	CENTER-TBI population was used to validate decision rules Inclusion: 16 years old; presenting with GCS 13-15 attending ED following and either skull fracture, intracranial haemorrhage or cerebral contusion identified on first CT scan (regardless of care pathway) Exclusion: initial GCS in the ED unknown; diffuse axonal injury sole injury on initial CT scan	Retrospectively applied two decision rules described above in Marincowitz 2020 paper to the CENTER-TBI population to validate the rules in an external population	• Hull Salford Cambridge Decision Rule (rule developed in the paper) – score >0 for admission and score of 0 for discharge • BIG criteria – score >1 for admission and score of 1 for discharge	Note that for clinical decision rules, multivariate analysis was not performed as ORs calculated were based on raw data reported in the paper. Sensitivity and specificity data reported in paper also presented.	**Need for hospital admission** Defined as composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration (new deficit or drop in GCS of more than 1 point).	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
Nishijima 2014[9] N=600 Prospective	Inclusion: adult patients (≥18 years) with mild tICH on initial CT and initial GCS 13-15 presenting to a Level 1 trauma centre Exclusion: patients with documented pre-existing "Do-Not-Resuscitate" (DNR) orders and patients with pre-injury anticoagulation use	Multivariate analysis with binary recursive partitioning Decision rule developed in paper assessed	• Decision rule consisting of following four variables: admission GCS <15, non-isolated head injury, age 65 years or older and the presence of swelling or shift on initial cranial CT vs. none <u>Individual risk factors separately:</u> • Admission GCS <15 vs. 15 • Non-isolated vs. isolated head injury • Age ≥65 years vs. <65 years • Presence vs. absence of swelling or shift on initial CT • Presence vs. absence of any high-risk comorbidity • Preinjury antiplatelet use vs. no use • Hypoxia prior to admission vs. no hypoxia	Note that for the clinical decision rule, multivariate analysis was not performed as OR calculated were based on raw data reported in the paper. Sensitivity and specificity data reported in paper also presented. For individual risk factors, the following variables were included in multivariate analyses: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial	**Patient need for ICU admission** Defined as the presence of an acute critical care intervention within 48 hours of emergency department arrival	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – 48 h time-point much shorter than 30 days

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
				fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.		
Overton 2014[10] N=171	Inclusion: patients with mild TBI (defined as an **intracranial**	Multivariate analysis was undertaken using backward-	• GCS motor scores on admission as a	Trauma surgeon only vs. neurosurgical consultation, age as a continuous variable	**Good outcome according to Glasgow Outcome Scale**	Risk of bias: high Indirectness:

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
Retrospective	**haemorrhage of 1 cm or less** and a GCS score of 13 or greater) at the time of arrival. Exclusion: additional intracranial injuries (i.e. intraparenchymal haemorrhages, diffuse axonal injuries with white matter shearing) and patients transferred to another acute care facility or those who left against medical advice.	stepwise binary logistic regression analyses	• continuous measure • Age as a continuous measure • ISS as a continuous measure Note that increments unclear for all three variables	(increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).	**(GOS) – unclear time-point, possibly same admission?** GOS ranges from 1 to 4, with higher scores reflecting better outcomes. Patients were classified into 2 categories based on their GOS. Scores equal to or less than 3 suggest moderate to severe outcomes and scores greater than 3 suggest good outcomes.	• Outcome – GOS may not be a good representation of clinical deterioration and the time-point at which it is reported is unclear, possibly within the same admission
Pruitt 2017[11] N=340 in derivation set and N=304 in validation set Retrospective	Inclusion: isolated subdural haemorrhage (SDH) (included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions); GCS 13-15; and age ≥16 years	Multivariable logistic regression analysis model including variables significant in univariate analysis at 0.2 level. Binary version of final model created	• Decision rule consisting of following six variables (high-risk predictors from the study): >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin	Note that for the clinical decision rule, multivariate analysis was not performed as OR calculated were based on raw data reported in the paper. Sensitivity and specificity data reported in paper also presented.	**Composite outcome** - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – follow-up duration

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	Exclusion: penetrating mechanism of injury; GCS <13; those with lesions other than SDH; and aged <16 years	using same predictors. Decision rule developed in the paper assessed	use or clopidogrel use <u>Individual risk factors separately:</u> • Presence of any midline shift vs. no midline shift • Maximum SDH thickness >5 mm vs. ≤5 mm • GCS 13 vs. GCS 14-15 • Warfarin use vs. no warfarin use • Clopidogrel use vs. no clopidogrel use	For individual risk factors, the following variables were included in multivariate analyses: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel	procedure (intracranial pressure monitoring or operations) during admission **AND** **Each of three outcomes mentioned above also reported separately** for sensitivity/specificity data in terms of clinical decision rule Worsening repeat CT scan was defined as an increase in lesion size ≥ 2 mm, new midline shift, or the presence of a new area of haemorrhage. Patients who required burr-hole drainage for sub-acute or acute-on-chronic SDH were included in the	unclear, though ~90% had >30 days; for composite outcome and worsening on CT outcome, also indirectness as radiological outcome included rather than specifically clinical deterioration

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
					neurosurgical intervention group, although these procedures were frequently performed on an elective basis. Patients deemed inoperable and transitioned to "comfort measures only" were included in the neurologic decline group	
Schwed 2016[12] N=201 Retrospective	Inclusion: admitted with blunt head trauma to level 1 trauma centre; mild TBI (GCS 13-15) at arrival in ED; and intracranial haemorrhage of any variety confirmed on CT scan. Exclusion: death within 24 h of admission; transferred from a different facility; required	Multivariate regression analysis where factors that were statistically significant on univariate analysis were included, as well as clinically important factors	• GCS 15 vs. <15 at admission to ICU • Age <55 years vs. ≥55 years	GCS of 15 at admission to ICU, isolated subarachnoid haemorrhage, age <55 years, ED blood pressure, Marshall score, head AIS, and ISS <25	**Favourable outcome – time-point unclear, appears to be within hospital admission (mean hospital length of stay 7.6 days)** Composite including the following: alive at discharge, required ICU admission for a maximum of 24 h, had no in-hospital complications (e.g. pneumonia, urinary tract infection or seizures) and did	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – not at time-point of 30 days and limits to in-hospital outcome

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	emergency surgical intervention within 24 h of presentation; who were not admitted to ICU; <18 years old; had missing records; left against medical advice; penetrating injuries; pregnancy; and being in police custody				not require neurosurgical intervention during their hospital stay. Patients not considered to have favourable outcome if ICU-level care required for another indication (ventilator management for respiratory failure, vasopressor or inotrope therapy for cardiac failure, etc.) that would have precluded them from a 24 h admission solely for neuromonitoring.	
Shih 2016[13] N=340 Retrospective	Inclusion: adult patients (15–75 years) with acute TBI and traumatic intracranial haemorrhage on initial brain CT admitted within 24 h after onset of acute TBI to single hospital in Taiwan; and initial	Multivariate stepwise logistic regression analysis was used to evaluate the relationship between significant variables and therapeutic outcomes	• EDH volume as a continuous variable (per 1 cubic centimetre increase)	Has performed multivariate analysis but does not list those variables included other than EDH volume which was the only significant predictor	**Delayed neurosurgical intervention (indicating failure of initial non-operative management)** Median time of surgical intervention after injury was 67.7 (IQR 11.7, 130.9) h	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – unclear time-point and

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	management was non-operative – included EDH, subdural haemorrhage (SDH), intraparenchymal haemorrhage (IPH), and subarachnoid haemorrhage (SAH). Exclusion: penetrating head injury or gunshot wound; moderate-to-severe TBI (Glasgow Coma Score <13); no traumatic intracranial haemorrhage found on initial brain CT; immediate neurosurgical intervention on admission; and only chronic intracranial haemorrhage in the initial brain CT.				(median hospital stay whole cohort was 8 days). Neurosurgical intervention was defined as placement of craniotomy or craniectomy with or without an intracranial pressure monitor. Patients with intracranial pressure monitor placed were excluded in the neurosurgical group.	possibly within same admission rather than close to 30 days in protocol

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
Sweeney 2015[14] N=33,327 Retrospective	Inclusion: aged ≥18 years; diagnosis of intracranial injury (851.0-854.9 based on ICD-9-CM); admitted to the hospital; and GCS of 14-15 in the ED Exclusion: skull fracture diagnoses (800-801.9 and 803-804.9) not included as ICD-9-CM codes don't distinguish between type of intracranial lesions that are present and open fractures are an indication for operative intervention meaning it is difficult to assess intracranial injury progression; penetrating mechanism of injury; Abbreviated Injury Scale (AIS)	Multiple logistic regression	• Age as a continuous variable (unclear increments) • Anticoagulation disorder vs. no anticoagulation disorder • ED GCS possibly as GCS 15 vs. GCS 14 • ISS categories of 7-11, 12-18, 19-27 and >27 vs. category 0-6	Age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).	**Neurosurgical intervention – unclear time-point, possibly within same admission?** Defined as having either an operative neurosurgical procedure or placement of neuromonitoring device (e.g. Camino bolt or endoventricular drainage catheter). Surgery and placement of catheters identified using ICD-9-CM procedure codes of 01-02.	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – unclear time-point and possibly within same admission rather than close to 30 days in protocol

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	score >1 in any body region other than head; and missing data about ED vital signs.					
Thorson 2013[15] N=360 Retrospective	Inclusion: adults arriving with GCS 13-15; head Abbreviated Injury Scale (AIS) score of at least 1; repeat CT scan within 24 h; and no associated injuries (AIS score 0 for chest, abdomen, extremity and external). Exclusion: penetrating trauma; pregnant; <18 years; incarcerated; and transferred from outside hospitals	Multivariate stepwise logistic regression used to identify predictors, variables with P<0.2 entered into model	• GCS 13 and GCS 14 vs. GCS 15 (separately) • ISS as a continuous variable (increment unclear) • Mass effect vs. no mass effect on CT	Full list not provided but provides list of those that were significant independent predictors: **Head CT progression:** GCS score 13 or 14 vs. GCS score 15; ISS as a continuous variable (increments unclear) and mass effect vs. no mass effect on CT **Craniotomy:** Initial mass effect, new/worse epidural haemorrhage on repeat CT, new/worse mass effect on repeat CT and new/worse herniation on repeat CT	**Head CT progression on repeat CT – within 24 h** Worsening of repeat CT finding defined as any of following: 1. Increase in size, progression or worsening of a previously identified lesion; 2. Increased oedema, mass effect, midline shift, herniation; and/or 3. Development of a new intracranial lesion **Operative intervention performed at unclear time-point**	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome: ○ Progression on CT – lesion progression is radiological outcome not specifically clinical deterioration ○ Operative intervention – time-point unclear and possibly within same admission rather than close to 30 days

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
					No definition provided but possibly includes craniotomy, craniectomy or haematoma evacuation mentioned in another section of the paper	
Tourigny 2021[16] N=478 Retrospective	Inclusion: aged ≥16 years; directly or transferred to one of participating centres between September 2016 and December 2017; diagnosed with complicated mild TBI (GCS 13-15 and either one of four following criteria: altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24, focal neurological deficit; and a complication including	Multivariate models performed using multiple logistic regression models. Predictors significant at 10% level in univariate logistic models were considered for inclusion in the multiple logistic regression model.	• Subdural haemorrhage width ≥4 mm vs. <4 mm • Midline shift vs. no midline shift • Unilateral weakness vs. no unilateral weakness on neurological assessment	Full list not provided but following list of those that were independent predictors was given: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.	**Neurosurgical intervention performed – median time between admission to ED and surgery was 16.1 h (IQR, 6.1-48.2 h)** Neurosurgical intervention according to attending neurosurgeon. Intracranial pressure monitor was not considered to be neurosurgery. Interventions performed included: craniotomy, evacuation of	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – events only within index hospitalisation rather than longer time-frame up to 30 days

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	intracranial haemorrhage or skull fracture on initial head CT) Exclusion: penetrating injury; cerebral tumour; and cerebral aneurysm.				haematoma, burr holes, fracture fixation, ventricular bypass and debridement	
Van Ornam 2019[17] N=1126 Retrospective	Inclusion: CT-confirmed mild traumatic intracranial haemorrhage GCS≥13 presenting to academic emergency department (urban level 1 trauma centre) Exclusion: patients <16 years of age or GCS <13 and those with penetrating head trauma	Multivariable logistic regression (stepwise forward model)	• GCS 13 vs. GCS 14-15 • Age ≥60 vs. <60 years	Not clearly stated which confounders were included in the final multivariable analysis but the following were considered in the study: Age, hospital length of stay, sex, past medical history (e.g. anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion	**Composite outcome of CT progression, change in neurologic status, need for neurosurgery or death/comfort measures only – unclear time-point but likely within admission as said data not collected following discharge** Mean length of stay was 3.6 or 8.3 days in those without and with composite outcome	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – measured up to discharge which is much shorter than 30 days, also includes components that may not present as clinical deterioration (e.g. CT progression)

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
Velmahos 2006[18] N=179 Retrospective	Inclusion: patients admitted with mild head injury after blunt trauma (GCS 13-15 with loss of consciousness, short-term amnesia, headache, emesis or dizziness) – all of these patients had head CT shortly after ED arrival and neurosurgical consultation requested. Exclusion: not reported	Multivariate stepwise logistic regression performed using variables that reached P≤0.2 on univariate analyses	• Age >65 years vs. ≤65 years • GCS <15 vs. GCS 15	Full list not provided but following list of those that were independent predictors was given: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT	**Worsening of brain lesion on repeat head CT – average of 13 h after first CT** Defined as worse brain lesion on repeat head CT, though more detail about how this was defined is not provided. If initially CT indicated traumatic pathology, routine repeat head CT was ordered. Pre-existing diseases or treatments predisposing them to bleeding, rather than a positive first head CT, was the reason for some undergoing a repeat head CT (14.0% reported above in characteristics to have no lesion on initial CT).	Risk of bias: high Indirectness: • Population: ○ Not limited to those with positive CT as includes 14.0% with no finding on initial CT ○ Not specific to those with small intracranial injuries • Outcome – lesion progression is radiological outcome not specifically clinical deterioration

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
Children						
Greenberg 2017[2] N=839 Retrospective secondary analysis of PECARN dataset	Inclusion: <18 years; mild TBI; non-penetrating head trauma; and ED CT scan showing intracranial injury (intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis). Exclusion: trivial injury history or presentation (e.g. running into stationary objects); penetrating TBI;	Multivariate logistic regression model used, including variables that had P<0.20 on univariate analysis into the multivariate model Decision rule developed in the paper assessed	• Decision rule (CHIIDA) consisting of following four variables: depressed skull fracture; midline shift; epidural haematoma; GCS 13 and GCS 14: ▪ Score >0 (anyone with any of the risk factors to be admitted to ICU) ▪ Score >2 (anyone with any of the risk factors to be admitted, apart from those where only risk factor is GCS 14) CHIIDA: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from	Note that for the clinical decision rule, multivariate analysis was not performed as OR calculated were based on raw data reported in the paper. Sensitivity and specificity data reported in paper also presented. For individual risk factors, the following variables were included in multivariate analyses: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15	**Composite outcome –** neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients) Patients were followed up with standardized telephone surveys of guardians and/or medical record review 7 to 90 days post-ED visit to ensure no outcomes were missed. Events in composite outcome chosen because they indicated a significant objective	Risk of bias: high Indirectness: • Population – not specific to those with small intracranial injuries • Outcome – follow-up duration varies between patients (7-90 days) meaning much longer/shorter follow-up than 30 days in some patients

Study	Population	Analysis	Prognostic variables	Confounders	Outcomes	Limitations
	pre-existing comorbid neurological disease; and bleeding disorders.		2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points). <u>Individual risk factors separately:</u> • Presence of any midline shift vs. no midline shift • GCS 13 vs. GCS 15 • GCS 14 vs. GCS 15		worsening in a patient who initially appeared to have a minor head injury and indicated a strong need for critical care observation.	

1 See Appendix D for full evidence tables.

1.1.6 Summary of the prognostic evidence

Adults/children – clinical decision rules – sensitivity/specificity results

Table 3: Adults – Clinical evidence summary: diagnostic test accuracy of Hull Salford Cambridge Decision Rule

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI)											
Hull Salford Cambridge Decision Rule – score >0 Marincowitz 2020[7]	1	1569	Any of events included in composite outcome occurring	Up to 30 days post-ED admission	1.00 (0.98 to 1.00)	0.07 (0.06 to 0.09)	Sensitivity				
							Very serious[a]	Serious[b]	None	None	VERY LOW
							Specificity				
									None	None	

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Rule included multiple variables, with following required for discharge: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination – **not meeting at least one of these criteria meant admission was indicated with score >0**							Very serious[a]	Serious[b]			VERY LOW
Need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point)											

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Hull Salford Cambridge Decision Rule – score >0	1	961	Any of events included in composite	Up to 30 days post-ED admission	1.00 (0.98 to 1.00)	0.05 (0.03 to 0.06)	Sensitivity				
							Very serious[a]	Serious[b]	None	None	VERY LOW
							Specificity				

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Marincowitz 2022[6] Rule included multiple variables, with following required for discharge: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination – **not meeting at least one of these criteria meant admission was indicated with score >0**			outcome occurring				Very serious[a]	Serious[b]	None	None	VERY LOW

[a] *Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Reasons for downgrading included it being unclear if index test and reference standard*

were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, people that did not have data for both decision rules were excluded (missing data) and unclear if follow-up/reference standard for all patients consisted of the same components

[b] *Downgraded by 1 increment for indirectness as the population was not limited to those with small injuries*

Table 4: Adults – Clinical evidence summary: diagnostic test accuracy of BIG criteria

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI)											
BIG criteria – score >1 Marincowitz 2020[7]	1	1569	Any of events included in composite outcome occurring	Up to 30 days post-ED admission	1.00 (0.98 to 1.00)	0.05 (0.04 to 0.06)	Sensitivity				
							Very serious[a]	Serious[b]	None	None	VERY LOW
							Specificity				
									None	None	

Rule included multiple variables, with following required for discharge: with following required for discharge: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated – **not meeting at least one of these criteria meant admission was indicated with score >1**							Very serious[a]	Serious[b]			VERY LOW
Need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point)											
	1	961					Sensitivity				

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
BIG criteria – score >1			Any of events included in composite	Up to 30 days post-ED admission	0.95 (0.91 to 0.97)	0.13 (0.11 to 0.16)	Very serious[a]	Serious[b]	None	None	VERY LOW
							Specificity				

Marincowitz 2022[6] Rule included multiple variables, with following required for discharge: with following required for discharge: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated – **not meeting at least one of these criteria meant admission was indicated with score >1**			outcome occurring				Very serious[a]	Serious[b]	None	None	VERY LOW

[a] *Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Reasons for downgrading included it being unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, people that did not have data for both decision rules were excluded (missing data) and unclear if follow-up/reference standard for all patients consisted of the same components*

[b] *Downgraded by 1 increment for indirectness as the population was not limited to those with small injuries*

Table 5: Adults – Clinical evidence summary: diagnostic test accuracy of Nishijima 2014 rule – at least one risk factor

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Need for ICU admission (acute critical care intervention within 48 h of ED arrival)											
Nishijima 2014 rule – ≥1 four variables (GCS <15, non-isolated head injury, ≥65 years and presence of swelling or shift on initial	1	600	Need for ICU admission (acute critical care intervention)	Within 48 h of ED arrival	0.98 (0.94 to 1.00)	0.40 (0.35 to 0.44)	Sensitivity				
							Very serious[a]	Very serious[b]	None	None	VERY LOW
							Specificity				
									None	Serious[c]	

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
cranial CT) indicated positive on the rule Nishijima 2014[9] Decision rule included following four variables, with those with at least one of the criteria being considered to be positive as per the decision rule: admission GCS <15, non-isolated head injury, age 65 years or older and the presence of swelling or shift on initial cranial CT							Very serious[a]	Very serious[b]			VERY LOW

[a] *Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Reasons for downgrading included it being unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given decision rule was retrospectively applied and no mention of blinding, 20% of eligible patients were not included in analysis and unclear if follow-up/reference standard for all patients consisted of the same components*

[b] *Downgraded by 2 increments for indirectness as the population was not limited to those with small injuries and the time-point of 48 h was much shorter than 30 days in the review protocol*

[c] *Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.6 and 0.4, respectively, which were the thresholds used for specificity to determine if a decision rule should be recommended or was of no clinical use*

Table 6: Adults – Clinical evidence summary: diagnostic test accuracy of Pruitt 2017 rule – at least one high-risk predictor

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Composite of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission											
Pruitt 2017 rule – at least one high-risk predictor Pruitt 2017[11]	1	N=340 derivation and N=304 validation	Any of events included in composite outcome occurring	Ninety percent of follow-up included clinical visits occurring greater than	Derivation: 0.99 (0.93 to 1.00) Validation: 0.96 (0.90 to 0.99)	Derivation: 0.37 (0.31 to 0.43) Validation: 0.32 (0.25 to 0.38)	Sensitivity				
							Very serious[a]	Very serious[b]	None	None	VERY LOW
							Specificity				
									None		

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use				30 days after initial presentation			Very serious[a]	Very serious[b]		Serious[c] for derivation AND none for validation	VERY LOW
Neurologic decline (decreasing mental status, regardless of cause)											
Pruitt 2017 rule – at least one high-risk predictor Pruitt 2017[11] Decision rule included following six variables, with those with at least one of the criteria being	1	N=340 derivation and N=304 validation	Any of events included in composite outcome occurring	Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation	Derivation: 0.96 (0.79 to 1.00) Validation: 0.89 (0.67 to 0.99)	Derivation: 0.31 (0.26 to 0.37) Validation: 0.25 (0.20 to 0.30)	Sensitivity				
							Very serious[a]	Very serious[d]	None	Serious[e] for derivation and very serious[e] for validation	VERY LOW
							Specificity				

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use							Very serious[a]	Very serious[d]	None	None	VERY LOW
Worsening repeat CT scan											
Pruitt 2017 rule – at least one high-risk predictor Pruitt 2017[11]	1	N=340 derivation and N=304	Any of events included in composite	Ninety percent of follow-up included clinical visits	Derivation: 1.00 (0.85 to 1.00) Validation: 0.96 (0.78 to 1.00)	Derivation: 0.31 (0.26 to 0.37) Validation: 0.26 (0.21 to 0.31)	Sensitivity				
							Very serious[a]	Very serious[b]	None	Serious[e] for both sets	VERY LOW
							Specificity				

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use		validation	outcome occurring	occurring greater than 30 days after initial presentation			Very serious[a]	Very serious[b]	None	None	VERY LOW
Neurosurgical procedure (intracranial pressure monitoring or operations) during admission											
Pruitt 2017 rule – at least one high-risk predictor Pruitt 2017[11]	1	N=340 derivation and N=304	Any of events included in composite	Ninety percent of follow-up included clinical visits	Derivation: 1.00 (0.91 to 1.00) Validation: 0.98 (0.91 to 1.00)	Derivation: 0.33 (0.28 to 0.39) Validation: 0.29 (0.24 to 0.35)	Sensitivity				
							Very serious[a]	Very serious[d]	None	None	VERY LOW
							Specificity				

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use		validation	outcome occurring	occurring greater than 30 days after initial presentation			Very serious[a]	Very serious[d]	None	None	VERY LOW

[a] *Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Reasons for downgrading included it being if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, >10% reported not to have follow-up data, unclear time interval between index test and reference standard and unclear if reference standard/follow-up may have had different components for each patient*

[b] *Downgraded by 2 increments for indirectness as the population was not limited to those with small injuries and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.*

[c] *Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.6 and 0.4, respectively, which were the thresholds used for specificity to determine if a decision rule should be recommended or was of no clinical use*

[d] *Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days.*

[e] *Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if a decision rule should be recommended or was of no clinical use*

1

2 **Table 7: Children – Clinical evidence summary: diagnostic test accuracy of CHIIDA score >0 (Greenberg 2017)**

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death)											
CHIIDA score >0 (Greenberg 2017 rule) Greenberg 2017[2]	1	839	Any of events included in composite outcome occurring	Follow-up 7-90 days post-ED visit (varies between patients)	0.93 (0.85 to 0.98)	0.55 (0.52 to 0.59)	Sensitivity				
							Very serious[a]	Very serious[b]	None	Serious[c]	VERY LOW
							Specificity				
									None	None	

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).							Very serious[a]	Very serious[b]			VERY LOW

[a] *Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Reasons for downgrading included it being unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, unclear if there was missing data/all patients were analysed, unclear time interval between index test and reference standard likely different between patients (e.g. length of follow-up varied)*

[b] *Downgraded by 2 increments for indirectness as the population was not limited to those with small injuries and outcome time-point indirectness as was much shorter/longer than*

1 *30 days in some patients (ranged from 7 to 90 days)*
2 *[c] Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if a*
3 *decision rule should be recommended or was of no clinical use*

4 **Table 8: Children – Clinical evidence summary: diagnostic test accuracy of CHIIDA score >2 (Greenberg 2017)**

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death)											
CHIIDA score >2 (Greenberg 2017 rule) Greenberg 2017[2]	1	839	Any of events included in composite outcome occurring	Follow-up 7-90 days post-ED visit (varies between patients)	0.86 (0.76 to 0.93)	0.70 (0.67 to 0.74)	Sensitivity				
							Very serious[a]	Very serious[b]	None	Serious[c]	VERY LOW
							Specificity				
									None	None	

Index Test/study	No. of studies	n	Ref. standard	Follow-up	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).							Very serious[a]	Very serious[b]			VERY LOW

[a] *Risk of bias was assessed using the QUADAS-2 checklist. The evidence was downgraded by 1 increment if the majority of studies were rated at high risk of bias, and downgraded by 2 increments if the majority of studies were rated at very high risk of bias. Reasons for downgrading included it being unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, unclear if there was missing data/all patients were analysed, unclear time interval between index test and reference standard likely different between patients (e.g. length of follow-up varied)*

[b] *Downgraded by 2 increments for indirectness as the population was not limited to those with small injuries and outcome time-point indirectness as was much shorter/longer than*

30 days in some patients (ranged from 7 to 90 days)
[c] Downgraded by 1 or 2 increments if the confidence intervals crossed one or both of 0.9 and 0.7, respectively, which were the thresholds used for sensitivity to determine if a decision rule should be recommended or was of no clinical use

Adults/children – clinical decision rules – odds ratio results

Table 9: Adults – Clinical evidence summary: Hull Salford Cambridge Decision Rule

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Score >0 vs. score 0 on decision rule developed in the paper for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) (≥15 years with blunt mild TBI, GCS ≥13 and intracranial haemorrhage on CT) Decision rule included multiple variables, with following required for discharge: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination – not meeting at least one of these criteria meant admission was indicated with score >0	1569 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	OR: 16.98 (4.16 to 69.30)
Score >0 vs. score 0 on decision rule (validation in an existing cohort) for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point)	961 (1) 30 days post-ED admission Marincowitz 20226	VERY LOWa,c,d Due to risk of bias, indirectness	OR: 23.33 (1.42 to 382.05)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(≥16 years with GCS ≥13 attending ED, with either skull fracture, intracranial haemorrhage or cerebral contusion on first CT scan – excluded those with GCS unknown in ED and where diffuse axonal injury was sole injury on CT) – CENTER TBI population Decision rule included multiple variables, with following required for discharge: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination – not meeting at least one of these criteria meant admission was indicated with score >0			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(d) Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding domains

Table 10: Adults – Clinical evidence summary: BIG criteria

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
BIG score >1 vs. BIG 1 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) (≥15 years with blunt mild TBI, GCS ≥13 and intracranial haemorrhage on CT)	1569 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	OR: 10.68 (2.59 to 43.99)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Decision rule included multiple variables, with following required for discharge: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated – not meeting at least one of these criteria meant admission was indicated with score >1			
BIG score >1 vs. BIG 1 for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point) (≥16 years with GCS ≥13 attending ED, with either skull fracture, intracranial haemorrhage or cerebral contusion on first CT scan – excluded those with GCS unknown in ED and where diffuse axonal injury was sole injury on CT) – CENTER TBI population Decision rule included multiple variables, with following required for discharge: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated – not meeting at least one of these criteria meant admission was indicated with score >1	921 (1) 30 days post-ED admission Marincowitz 20226	VERY LOWa,c,d Due to risk of bias, indirectness	OR: 2.69 (1.44 to 5.00)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(d) Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding domains

Table 11: Adults – Clinical evidence summary: Nishijima 2014 decision rule

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
≥1 four variables (GCS <15, non-isolated head injury, ≥65 years and presence of swelling or shift on initial cranial CT) vs. none for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) Decision rule included following four variables, with those with at least one of the criteria being considered to be positive as per the decision rule: admission GCS <15, non-isolated head injury, age 65 years or older and the presence of swelling or shift on initial cranial CT	600 (1) Within 48 h of ED arrival Nishijima 20149	VERY LOWa,b,c Due to risk of bias, indirectness	OR: 37.49 (9.15 to 153.49)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study participation and outcome measurement domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome time-point was at 48 h which is shorter than that specified as ideal in the protocol

Table 12: Adults – Clinical evidence summary: Pruitt 2017 decision rule – at least one high-risk predictor

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or	N=340 in derivation set and N=304 in validation set (1) Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation	VERY LOWa,b,c Due to risk of bias, indirectness	OR: Derivation set: 41.84 (5.72 to 305.86) Validation set: 12.13 (3.70 to 39.75)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
neurosurgical procedure (intracranial pressure monitoring or operations) during admission (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use	Pruitt 201711		
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death) (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use	N=340 in derivation set and N=304 in validation set (1) Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOWa,b,d,e Due to risk of bias, imprecision (validation group only), indirectness Note that imprecision was for validation group only. Overall risk of bias (very low) applied for both datasets	OR: Derivation set: 10.49 (1.40 to 78.80) Validation set: 2.82 (0.64 to 12.51)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting worsening repeat CT scan (defined as an increase in lesion size ≥ 2 mm, new midline shift, or the presence of a new area of haemorrhage) (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use	N=340 in derivation set and N=304 in validation set (1) Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOWa,b,c Due to risk of bias, indirectness	OR: Derivation set: 20.70 (1.24 to 344.61) Validation set: 7.58 (1.00 to 57.24)
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting neurosurgical procedure (intracranial pressure monitoring or operations) during admission (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision	Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOWa,b,e Due to risk of bias, indirectness	OR: Derivation set: 41.81 (2.55 to 686.72) Validation set: 23.59 (3.20 to 173.60)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, outcome measurement and study confounding domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.
(d) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days.

Table 13: Children – Clinical evidence summary: Greenberg 2017 decision rule – CHIIDA score >0 or >2

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Score >0 on CHIIDA rule for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders)	839 (1) Follow-up 7-90 days post-ED visit (varies between patients) Greenberg 20172	VERY LOWa,b,c Due to risk of bias, indirectness	OR: 16.95 (6.76 to 42.50)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).			
Score >2 on CHIIDA rule for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders) CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).	839 (1) Follow-up 7-90 days post-ED visit (varies between patients) Greenberg 20172	VERY LOWa,b,c Due to risk of bias, indirectness	OR: 14.96 (7.54 to 29.67)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding

(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

Adults – injury severity scales

Table 14: Clinical evidence summary: Head AIS score (unclear how analysed)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Increasing head AIS score (increments analysed unclear) for predicting neurosurgical intervention (≥15 years with blunt mild TBI, GCS ≥13 and intracranial haemorrhage on CT) MV analysis included: hospital length of stay, ICU length of stay, days of mechanical ventilation, head-AIS score, Injury Severity Score, skull fracture, abnormal initial neurological examination, subdural haemorrhage, subarachnoid haemorrhage.	500 (1) Unclear time-point, possibly within same admission Lewis 20175	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 12.87 (6.47 to 25.58)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome time-point was unclear and possibly an initial management decision rather than also including any delayed interventions

Table 15: Clinical evidence summary: Injury Severity Scale (ISS)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
As a continuous variable (increments analysed unclear)			
Increasing ISS score (increments analysed unclear) for predicting head CT progression on repeat CT	360 (1) Repeat CT performed within 24 h of initial CT	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 1.07 (1.02 to 1.12)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT	Thorson 201315		
Increasing ISS score (increments analysed unclear) for predicting good outcome (GOS >4) (median age 48-49 years, patients with mild TBI defined as intracranial haemorrhage of 1 cm or less and GCS of at least 13 at time of arrival – excluded those with additional intracranial injuries, patients transferred to another acute care facility and those leaving against medical advice) MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).	171 (1) Unclear time-point, possibly within same admission Overton 201410	VERY LOW[a,d,e] Due to risk of bias, indirectness	Adjusted OR: 0.87 (0.81 to 0.94)
Various ISS categories vs. the ISS 0-6 score category			
The following ISS categories were compared with ISS 0-6 category for predicting neurosurgical intervention: ISS 7-11 ISS 12-18 ISS 19-27 ISS >27	33,327 across all groups (1) Unclear time-point, possibly within same admission Sweeney 201514	VERY LOW[a,f,g] Due to risk of bias, indirectness (applicable to all groups vs. ISS 0-6 group)	Adjusted OR for individual groups vs. ISS 0-6 group: OR 2.35 (1.35 to 4.09) for ISS 7-11 OR 3.37 (1.94 to 5.86) for ISS 12-18 OR 18.90 (10.82 to 33.00) for ISS 19-27

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded) MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).			OR 7.01 (3.67 to 13.40) for ISS >27

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(d) Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
(e) Downgraded by 1 increment for indirectness as GOS may not be a good representation of clinical deterioration and the time-point it is reported at is unclear, possibly within the same admission which is much shorter than 30 days specified in the protocol
(f) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(g) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

Adults/children – specific features/measurements of lesions

Table 16: Clinical evidence summary: Subdural haemorrhage/haematoma measurements

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Variables using thresholds/categories			
Adults – Subdural haemorrhage ≤6 mm vs. >6 mm for predicting discharge within 24 h	1079 (1) Discharge within 24 h of arrival	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 3.10 (2.14 to 4.50)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(≥16 years with blunt head trauma, isolated cranial trauma – excluded those with GCS <13 or trauma to other organ systems requiring service other than neurosurgery) MV analysis: full list of variables included not given but included at least the following three variables that were significantly associated with the outcome: GCS, isolated traumatic subarachnoid haemorrhage and subdural haematoma thickness ≤6 mm	Borczuk 20191		
Adults – Subdural haemorrhage >10 mm vs. ≤10 mm for predicting progression on repeat CT (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	876 (1) Repeat head CT performed within 6 h Joseph 20153	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 4.80 (1.90 to 12.13)
Adults – Subdural haemorrhage >10 mm vs. ≤10 mm for predicting neurosurgical intervention (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT –	876 (1) Time-point unclear, possibly within same admission Joseph 20153	VERY LOWa,d,f Due to risk of bias, indirectness	Adjusted OR: 3.40 (2.10 to 5.50)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.			
Adults – Subdural haemorrhage width ≥4 mm vs. <4 mm for predicting neurosurgical intervention (aged ≥16 years, diagnosed complicated mild TBI with either altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24 h or focal neurological deficit, and a complication including intracranial haemorrhage or skull fracture on initial CT – excluded penetrating injury, cerebral tumour and cerebral aneurysm) MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.	478 (1) Median time from admission to surgery was 16.1 h Tourigny 202116	VERY LOW[a,g,h] Due to risk of bias, indirectness	Adjusted OR: 3.76 (1.29 to 10.93)
Adults – max SDH thickness >5 mm vs. ≤5 mm for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with	N=340 (1) – derivation set only Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOW[a,i,j] Due to risk of bias, indirectness	Adjusted OR: 5.10 (2.42 to 10.75)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel			
Variables analysed as a continuous variable			
Adults – Increasing initial volume of subdural haematoma lesion (ml) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery (aged ≥15 years, acute trauma-related subdural haematoma diagnosed on CT, mild head injury with GCS 13-15, no focal neurological deficits, no significant mass effect, no significant midline shift, relatively small volume of subdural haematoma and medically managed at time of admission – excluded those where surgery performed within 24 h, neurological deterioration within 48 h, vascular abnormality, haemorrhage localised only to falx or tentorium cerebelli, bilateral acute subdural haematoma, other significant organ injury and those refusing surgical treatment) MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present	98 (1) Assessed at ~1 week post-injury Kim 20144	VERY LOWa,k,l,m Due to risk of bias, imprecision, indirectness	Adjusted OR: 2.52 (0.15 to 41.10)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – Increasing maximum thickness of subdural haematoma lesion (mm) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery (aged ≥15 years, acute trauma-related subdural haematoma diagnosed on CT, mild head injury with GCS 13-15, no focal neurological deficits, no significant mass effect, no significant midline shift, relatively small volume of subdural haematoma and medically managed at time of admission – excluded those where surgery performed within 24 h, neurological deterioration within 48 h, vascular abnormality, haemorrhage localised only to falx or tentorium cerebelli, bilateral acute subdural haematoma, other significant organ injury and those refusing surgical treatment) MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present	98 (1) Assessed at ~1 week post-injury Kim 20144	VERY LOWa,k,m Due to risk of bias, indirectness	Adjusted OR: 1.43 (1.09 to 1.89)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for outcome measurement, study confounding and statistical analysis/reporting domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome is indirect relevant to review protocol as there could be other factors contributing to length of stay other than clinical deterioration
(d) Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(f) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol
(g) Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains

(h) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol (might represent initial decision to perform surgery in some cases rather than delayed events due to clinical deterioration)
(i) Risk of bias was identified for study attrition, outcome measurement and study confounding domains
(j) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.
(k) Risk of bias was identified for study participation, prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
(l) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(m) Downgraded by 2 increments for indirectness as although there is some suggestion from the flow chart that only those with smaller injuries were included, this is not consistently clear within the paper; in addition, there is possible risk factor indirectness as measurements from up to three CT scans were included rather than only including those on the first CT scan and outcome is limited to a time period of 1 week, which is shorter than the 30 days in the protocol

Table 17: Clinical evidence summary: Epidural haemorrhage measurements

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Variables using thresholds/categories			
Adults – Epidural haemorrhage >10 mm vs. ≤10 mm for predicting progression on repeat CT (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	876 (1) Repeat head CT performed within 6 h Joseph 20153	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 7.90 (2.40 to 26.01)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – Epidural haemorrhage >10 mm vs. ≤10 mm for predicting neurosurgical intervention (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	876 (1) Time-point unclear, possibly within same admission Joseph 20153	VERY LOWa,b,d Due to risk of bias, indirectness	Adjusted OR: 3.50 (1.40 to 8.75)
Variables analysed as a continuous variable			
Adults – Increasing epidural haemorrhage volume as a continuous variable (per 1 cubic centimetre increase) for predicting delayed neurosurgical intervention (indicating failed non-operative management) (aged 15-75 years, acute TBI and traumatic intracranial haemorrhage on CT, admitted within 24 h of TBI, initial non-operative management – excluded penetrating injuries, moderate-severe TBI with GCS <13, negative CT for intracranial haemorrhage, immediate neurosurgical intervention and chronic/pre-existing intracranial haemorrhages only on initial CT) MV analysis: has performed adjustment but does not provide details of those included in the final model	340 (1) Within same admission, median hospital stay was 8 days for whole cohort Shih 201613	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 1.19 (1.04 to 1.36)

1 *(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias*

(b) Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(d) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol
(e) Risk of bias was identified for study participation, prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains

Table 18: Clinical evidence summary: Specific features on CT

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Variables analysed as a continuous variable			
Adults – Degree of midline shift (mm) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery (aged ≥15 years, acute trauma-related subdural haematoma diagnosed on CT, mild head injury with GCS 13-15, no focal neurological deficits, no significant mass effect, no significant midline shift, relatively small volume of subdural haematoma and medically managed at time of admission – excluded those where surgery performed within 24 h, neurological deterioration within 48 h, vascular abnormality, haemorrhage localised only to falx or tentorium cerebelli, bilateral acute subdural haematoma, other significant organ injury and those refusing surgical treatment) MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present	98 (1) Assessed at ~1 week post-injury Kim 20144	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 1.09 (1.02 to 1.17)
Variables using thresholds/categories			

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – Midline shift vs. no midline shift for predicting neurosurgical intervention (aged ≥16 years, diagnosed complicated mild TBI with either altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24 h or focal neurological deficit, and a complication including intracranial haemorrhage or skull fracture on initial CT – excluded penetrating injury, cerebral tumour and cerebral aneurysm) MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.	478 (1) Median time from admission to surgery was 16.1 h Tourigny 202116	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 7.51 (3.32 to 16.99)
Adults – Midline shift vs. no midline shift for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel	N=340 (1) – derivation set only Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOWa,f,g Due to risk of bias, indirectness	Adjusted OR: 4.73 (2.42 to 9.24)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – Presence vs. absence of swelling or shift on admission CT for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.	600 (1) Within 48 h of ED arrival Nishijima 20149	VERY LOWa,h,i Due to risk of bias, indirectness	Adjusted RR: 4.11 (3.08 to 5.48)
Adults – The following CT injury severity categories were compared with simple skull fracture category for predicting need for neurosurgical specialist admission: Complex skull fracture 1-2 bleeds <5 mm (total) No or minimal mass effect Significant midline shift	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,j,k,l Due to risk of bias, imprecision (first 3 groups only), indirectness	Adjusted OR for individual groups vs. simple skull fracture group: OR 0.90 (0.17 to 4.90) for complex skull fracture group

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
High/mixed density lesion Cerebellar/brain stem injury (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)		(note: imprecision for first three groups but not remaining risk factor groups)	OR 0.80 (0.16 to 4.10) for 1-2 bleeds <5 mm (total) group OR 2.30 (0.55 to 9.70) for no/minimal mass effect group OR 7.40 (1.62 to 33.90) for significant midline shift group OR 37.10 (8.14 to 168.99) for high/mixed density lesion group OR 8.50 (1.29 to 56.20) for cerebellar/brainstem injury group
Adults – The following CT injury severity categories were compared with simple skull fracture category for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI): Complex skull fracture 1-2 bleeds <5 mm (total) No or minimal mass effect Significant midline shift High/mixed density lesion Cerebellar/brain stem injury	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,j,k,l Due to risk of bias, imprecision (first 3 groups only), indirectness (note: imprecision for first three groups but not remaining risk factor groups)	Adjusted OR for individual groups vs. simple skull fracture group: OR 1.40 (0.46 to 4.30) for complex skull fracture group OR 1.10 (0.39 to 3.10) for 1-2 bleeds <5 mm (total) group

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)			OR 2.30 (0.90 to 5.88) for no/minimal mass effect group OR 6.80 (2.50 to 18.49) for significant midline shift group OR 21.60 (7.69 to 60.70) for high/mixed density lesion group OR 7.00 (1.91 to 25.70) for cerebellar/brainstem injury group
Adults – Mass effect vs. no mass effect on CT for predicting head CT progression on repeat CT (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT	360 (1) Repeat CT performed within 24 h of initial CT Thorson 201315	VERY LOWa,m,n Due to risk of bias, indirectness	Adjusted OR: 2.02 (1.08 to 3.78)
Adults – Mass effect vs. no mass effect on CT for predicting craniotomy being performed (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external)	360 (1) Unclear time-point, possibly within same admission Thorson 201315	VERY LOWa,d,o Due to risk of bias, indirectness	Adjusted OR: 5.24 (1.96 to 14.01)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
MV analysis: full list not provided but those that were significant and were included were initial mass effect, new/worse epidural haemorrhage on repeat CT, new/worse mass effect on repeat CT and new/worse herniation on repeat CT			
Children – Any midline shift vs. no midline shift for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders) MV analysis: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15	839 (1) Follow-up 7-90 days post-ED visit (varies between patients) Greenberg 20172	VERY LOWa,p,q Due to risk of bias, indirectness	OR: 6.50 (3.70 to 11.42)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study participation, prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
(c) Downgraded by 2 increments for indirectness as although there is some suggestion from the flow chart that only those with smaller injuries were included, this is not consistently clear within the paper; in addition, there is possible risk factor indirectness as measurements from up to three CT scans were included rather than only including those on the first CT scan and outcome is limited to a time period of 1 week, which is shorter than the 30 days in the protocol
(d) Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol (might represent initial decision to perform surgery in some cases rather than delayed events due to clinical deterioration)
(f) Risk of bias was identified for study attrition, outcome measurement and study confounding domains

(g) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.
(h) Risk of bias was identified for study participation and outcome measurement domains
(i) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol
(j) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(k) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(l) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(m) Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
(n) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(o) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of craniotomy, the time-point is unclear and possibly only captures events during same hospital admission rather than within 30 days
(p) Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding
(q) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

Adults/children – GCS

Table 19: Clinical evidence summary: GCS 15 vs. GCS 13-14

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – GCS 15 vs. GCS 13-14 for predicting discharge within 24 h (≥16 years with blunt head trauma, isolated cranial trauma – excluded those with GCS <13 or trauma to other organ systems requiring service other than neurosurgery) MV analysis: full list of variables included not given but included at least the following three variables that were significantly associated	1079 (1) Discharge within 24 h of arrival Borczuk 20191	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 2.90 (1.90 to 4.43)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
with the outcome: GCS, isolated traumatic subarachnoid haemorrhage and subdural haematoma thickness ≤6 mm			
Adults – GCS 15 vs. GCS 13-14 for predicting worsening of brain lesion on repeat head CT (mean age 51 years, patients admitted with mild head injury following blunt trauma with GCS 13-15 and loss of consciousness, short-term amnesia, headache, emesis or dizziness, all with head CT shortly after ED arrival and neurosurgical consultation requested) MV analysis: only those that were significant were reported and a full list of variables included not given: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT	179 (1) Average 13 h following initial CT Velmahos 200618	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 0.32 (0.12 to 0.82)
Adults – GCS 15 vs. GCS 13-14 for predicting favourable outcome (alive, admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention) (aged ≥18 years, admitted with blunt head trauma to trauma centre and ICU, mild TBI with GCS 13-15 at arrival in ED and intracranial haemorrhage confirmed on CT scan – excluded those dying within 24 h of admission, transferred from another facility, requiring emergency surgical intervention within 24 h, those not admitted to the ICU, left against advice, penetrating injuries, pregnancy and being in police custody) MV analysis: GCS of 15 at admission to ICU, isolated subarachnoid haemorrhage, age <55 years, ED blood pressure, Marshall score, head AIS, and ISS <25	201 (1) Unclear time-point, possibly within same admission Schwed 201612	VERY LOWa,f,g Due to risk of bias, indirectness	Adjusted OR: 5.50 (1.61 to 18.80)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – GCS 15 vs. GCS 13-14 for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.	600 (1) Within 48 h of ED arrival Nishijima 20149	VERY LOWa,h,i Due to risk of bias, indirectness	Adjusted RR: 0.34 (0.24 to 0.47)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for outcome measurement, study confounding and statistical analysis/reporting domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome is indirect relevant to review protocol as there could be other factors contributing to length of stay other than clinical deterioration
(d) Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with a positive CT (14.0% had no finding on initial CT) and it is also not specific to those with small intracranial injuries; for outcome, lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(f) Risk of bias was identified for study attrition, outcome measurement, study confounding and statistical analysis/reporting domains
(g) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the composite outcome was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

(h) Risk of bias was identified for study participation and outcome measurement domains
(i) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

Table 20: Clinical evidence summary: GCS 14 vs. GCS 15

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – GCS 14 vs. GCS 15 for predicting need for neurosurgical specialist admission (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 2.30 (1.60 to 3.31)
Adults – GCS 14 vs. GCS 15 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures,	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 1.60 (1.22 to 2.10)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)			
Adults – GCS 14 vs. GCS 15 for predicting head CT progression on repeat CT (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT	360 (1) Repeat CT performed within 24 h of initial CT Thorson 201315	VERY LOW[a,d,e] Due to risk of bias, indirectness	Adjusted OR: 3.11 (1.77 to 5.48)
Adults – GCS 14 vs. GCS 15 for predicting neurosurgical intervention: (age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded) MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various	33,327 (1) Unclear time-point, possibly within same admission Sweeney 201514	VERY LOW[a,b,f,g] Due to risk of bias, imprecision, indirectness	Adjusted OR: 1.12 (0.97 to 1.29)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).			
Children – GCS 14 vs. GCS 15 for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders) MV analysis: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15	839 (1) Follow-up 7-90 days post-ED visit (varies between patients) Greenberg 20172	VERY LOWa,f,h,i Due to risk of bias, imprecision, indirectness	OR: 1.60 (0.82 to 3.12)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(d) Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(f) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(g) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol
(h) Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding
(i) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

1 **Table 21: Clinical evidence summary: GCS 13 vs. GCS 15**

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – GCS 13 vs. GCS 15 for predicting need for neurosurgical specialist admission (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 3.70 (2.32 to 5.90)
Adults – GCS 13 vs. GCS 15 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 2.30 (1.60 to 3.31)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)			
Adults – GCS 13 vs. GCS 15 for predicting head CT progression on repeat CT (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT	360 (1) Repeat CT performed within 24 h of initial CT Thorson 201315	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 4.00 (2.02 to 7.93)
Children – GCS 13 vs. GCS 15 for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders)	839 (1) Follow-up 7-90 days post-ED visit (varies between patients) Greenberg 20172	VERY LOWa,f,g Due to risk of bias, indirectness	OR: 3.40 (1.50 to 7.71)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
MV analysis: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(d) Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(f) Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding
(g) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

Table 22: Clinical evidence summary: GCS 13 vs. GCS 14-15

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – GCS 13 vs. GCS 14-15 for predicting composite outcome of CT progression, change in neurologic status, need for surgery or death/comfort measures only (≥16 years, CT-confirmed mild traumatic intracranial haemorrhage with GCS 13-15 presenting to ED – excluded those with penetrating head trauma) MV analysis: final list unclear but following were considered for inclusion: age, hospital length of stay, sex, past medical history (such as anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion	1126 (1) Unclear time-point, possibly within same admission – mean length of stay was 3.6 and 8.3 days in those without and with outcome Van Ornam 201917	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 4.50 (2.47 to 8.20)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – GCS 13 vs. GCS 13-15 for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel	N=340 (1) – derivation set only Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 4.09 (1.18 to 14.22)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome was measured up to discharge which is a much shorter period than the 30 days in the protocol and also includes components that may not present as clinical deterioration (e.g. progression on CT only)
(d) Risk of bias was identified for study attrition, outcome measurement and study confounding domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.

Table 23: Clinical evidence summary: GCS as a continuous measure/unclear increments

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – GCS motor scores on admission (unclear increments, possibly per 1-unit increase between 13 and 15?) for predicting good outcome (GOS >4)	171 (1) Unclear time-point, possibly within same admission	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 13.96 (2.23 to 87.30)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(median age 48-49 years, patients with mild TBI defined as intracranial haemorrhage of 1 cm or less and GCS of at least 13 at time of arrival – excluded those with additional intracranial injuries, patients transferred to another acute care facility and those leaving against medical advice) MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).	Overton 201410		

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
(c) Downgraded by 1 increment for indirectness as GOS may not be a good representation of clinical deterioration and the time-point it is reported at is unclear, possibly within the same admission which is much shorter than 30 days specified in the protocol

Adults – anticoagulation/antiplatelet treatments

Table 24: Clinical evidence summary: Anticoagulation/antiplatelet use vs. no use

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Anticoagulant/antiplatelet use vs. no use for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 1.40 (1.03 to 1.90)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries

Table 25: Clinical evidence summary: Antiplatelet therapy vs. no antiplatelet therapy

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Antiplatelet therapy vs. no antiplatelet therapy for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-	600 (1) Within 48 h of ED arrival Nishijima 20149	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted RR: 1.54 (1.03 to 2.30)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study participation and outcome measurement domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

Table 26: Clinical evidence summary: Anticoagulation disorder vs. no anticoagulation disorder

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Anticoagulation disorder (any condition increasing risk of bleeding e.g. vitamin K deficiency, haemophilia, thrombocytopenia, chronic anticoagulation therapy) vs. no anticoagulation disorder for predicting neurosurgical intervention (age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded) MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural	33,327 Unclear time-point, possibly within same admission Sweeney 201514	VERY LOWa,b,c,d Due to risk of bias, imprecision, indirectness	Adjusted OR: 0.85 (0.67 to 1.09)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(d) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

Table 27: Clinical evidence summary: Warfarin use vs. no warfarin use

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – Warfarin use vs. no warfarin use for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel	N=340 (1) – derivation set only Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOWa,b,c,d Due to risk of bias, imprecision, indirectness	Adjusted OR: 2.21 (0.97 to 5.01)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, outcome measurement and study confounding domains
(c) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)

(d) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.

Table 28: Clinical evidence summary: Clopidogrel use vs. no clopidogrel use

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Adults – Clopidogrel use vs. no clopidogrel use for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel	N=340 (1) – derivation set only Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation Pruitt 201711	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 2.70 (1.00 to 7.31)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, outcome measurement and study confounding domains
(c) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.

1 **Adults – age**

2 **Table 29: Clinical evidence summary: Age as a continuous variable (increments unclear)**

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Increasing age as a continuous variable (increments unclear) for predicting good outcome (GOS >4) (median age 48-49 years, patients with mild TBI defined as intracranial haemorrhage of 1 cm or less and GCS of at least 13 at time of arrival – excluded those with additional intracranial injuries, patients transferred to another acute care facility and those leaving against medical advice) MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).	171 (1) Unclear time-point, possibly within same admission Overton 201410	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 0.94 (0.91 to 0.97)
Increasing age as a continuous variable (increments unclear) for predicting neurosurgical intervention (age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded) MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).	33,327 Unclear time-point, possibly within same admission Sweeney 201514	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 1.00 (1.00 to 1.00)

3 *(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias*
4 *(b) Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains*

(c) Downgraded by 1 increment for indirectness as GOS may not be a good representation of clinical deterioration and the time-point it is reported at is unclear, possibly within the same admission which is much shorter than 30 days specified in the protocol
(d) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

Table 30: Clinical evidence summary: Age as a continuous variable (per 1-unit increase)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Increasing age as a continuous variable (per 1-unit increase) for predicting need for neurosurgical specialist admission (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 1.00 (1.00 to 1.00)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries

Table 31: Clinical evidence summary: Age – specific thresholds used as risk factors

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
65 years as threshold			
Age ≥65 vs. <65 years for predicting progression on repeat CT (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	876 (1) Repeat head CT performed within 6 h Joseph 20153	VERY LOWa,b,c,d Due to risk of bias, imprecision, indirectness	Adjusted OR: 1.40 (0.73 to 2.70)
Age >65 vs. ≤65 years for predicting worsening of brain lesion on repeat head CT (mean age 51 years, patients admitted with mild head injury following blunt trauma with GCS 13-15 and loss of consciousness, short-term amnesia, headache, emesis or dizziness, all with head CT shortly after ED arrival and neurosurgical consultation requested) MV analysis: only those that were significant were reported and a full list of variables included not given: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT	179 (1) Average 13 h following initial CT Velmahos 200618	VERY LOWa,e,f Due to risk of bias, indirectness	Adjusted OR: 3.33 (1.29 to 8.60)
Age ≥65 vs. <65 years for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival)	600 (1) Within 48 h of ED arrival	VERY LOWa,g,h	Adjusted RR: 1.46 (1.05 to 2.03)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.	Nishijima 20149	Due to risk of bias, indirectness	
60 years as threshold			
Age ≥60 vs. <60 years for predicting composite outcome of CT progression, change in neurologic status, need for surgery or death/comfort measures only (≥16 years, CT-confirmed mild traumatic intracranial haemorrhage with GCS 13-15 presenting to ED – excluded those with penetrating head trauma)	1126 (1) Unclear time-point, possibly within same admission – mean length of stay was 3.6 and 8.3 days in those without and with outcome Van Ornam 201917	VERY LOWa,e,i Due to risk of bias, indirectness	Adjusted OR: 1.60 (1.10 to 2.33)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
MV analysis: final list unclear but following were considered for inclusion: age, hospital length of stay, sex, past medical history (such as anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion			
55 years as threshold			
Age <55 vs. ≥55 years for predicting favourable outcome (alive, admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention) (aged ≥18 years, admitted with blunt head trauma to trauma centre and ICU, mild TBI with GCS 13-15 at arrival in ED and intracranial haemorrhage confirmed on CT scan – excluded those dying within 24 h of admission, transferred from another facility, requiring emergency surgical intervention within 24 h, those not admitted to the ICU, left against advice, penetrating injuries, pregnancy and being in police custody) MV analysis: GCS of 15 at admission to ICU, isolated subarachnoid haemorrhage, age <55 years, ED blood pressure, Marshall score, head AIS, and ISS <25	201 (1) Unclear time-point, possibly within same admission Schwed 201612	VERY LOWa,j,k Due to risk of bias, indirectness	Adjusted OR: 3.50 (1.09 to 11.20)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
(c) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(d) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(e) Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
(f) Downgraded by 2 increments for indirectness as the population was not specific to those with a positive CT (14.0% had no finding on initial CT) and it is also not specific to those with small intracranial injuries; for outcome, lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(g) Risk of bias was identified for study participation and outcome measurement domains

(h) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol
(i) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome was measured up to discharge which is a much shorter period than the 30 days in the protocol and also includes components that may not present as clinical deterioration (e.g. progression on CT only)
(j) Risk of bias was identified for study attrition, outcome measurement, study confounding and statistical analysis/reporting domains
(k) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the composite outcome was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

Adults – blood measurements

able 32: Clinical evidence summary: Blood measurements

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Platelets			
Platelet ≤100,000 mm-3 vs. >100,000 mm-3 for predicting progression on repeat CT (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	876 (1) Repeat head CT performed within 6 h Joseph 20153	VERY LOWa,b,c,d Due to risk of bias, imprecision, indirectness	Adjusted OR: 1.30 (0.47 to 3.60)
Platelet ≤100,000 mm-3 vs. >100,000 mm-3 for predicting neurosurgical intervention	876 (1) Time-point unclear, possibly within same admission	VERY LOWa,b,c,e	Adjusted OR: 1.60 (0.53 to 4.80)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	Joseph 20153	Due to risk of bias, imprecision, indirectness	
Lactate			
Lactate ≤2.5 vs. >2.5 for predicting progression on repeat CT (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	876 (1) Repeat head CT performed within 6 h Joseph 20153	VERY LOWa,b,c,d Due to risk of bias, imprecision, indirectness	Adjusted OR: 2.10 (0.89 to 4.95)
Lactate ≤2.5 vs. >2.5 for predicting neurosurgical intervention (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT –	876 (1) Time-point unclear, possibly within same admission Joseph 20153	VERY LOWa,b,c,e Due to risk of bias, imprecision, indirectness	Adjusted OR: 1.90 (0.62 to 5.82)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.			
Base deficit			
Base deficit >4 vs. ≤4 for predicting progression on repeat CT (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.	876 (1) Repeat head CT performed within 6 h Joseph 20153	VERY LOWa,b,d Due to risk of bias, indirectness	Adjusted OR: 2.80 (1.60 to 4.90)
Base deficit >4 vs. ≤4 for predicting neurosurgical intervention (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery)	876 (1) Time-point unclear, possibly within same admission Joseph 20153	VERY LOWa,b,e Due to risk of bias, indirectness	Adjusted OR: 21.00 (1.60 to 275.64)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.			
Haemoglobin			
Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L) for predicting need for neurosurgical specialist admission (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,c,f,g Due to risk of bias, imprecision, indirectness	Adjusted OR: 0.99 (0.98 to 1.00)
Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L) for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,c,f,g Due to risk of bias, imprecision, indirectness	Adjusted OR: 0.99 (0.98 to 1.00)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
(c) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(d) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol
(f) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(g) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries

1 Adults – abnormal neurological exam findings

2 Table 33: Clinical evidence summary: abnormal neurological symptoms/examination findings

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Abnormal vs. normal neurological examination			
Abnormal vs. normal neurological examination for predicting need for neurosurgical specialist admission (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOW[a,b,c] Due to risk of bias, indirectness	Adjusted OR: 1.90 (1.20 to 3.00)
Abnormal vs. normal neurological examination for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures,	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOW[a,b,c] Due to risk of bias, indirectness	Adjusted OR: 1.70 (1.20 to 2.41)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)			
Unilateral weakness			
Unilateral weakness vs. no unilateral weakness on neurological assessment for predicting neurosurgical intervention (aged ≥16 years, diagnosed complicated mild TBI with either altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24 h or focal neurological deficit, and a complication including intracranial haemorrhage or skull fracture on initial CT – excluded penetrating injury, cerebral tumour and cerebral aneurysm) MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.	478 (1) Median time from admission to surgery was 16.1 h Tourigny 202116	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted OR: 3.76 (1.29 to 10.93)

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(d) Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains

(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol (might represent initial decision to perform surgery in some cases rather than delayed events due to clinical deterioration)

Adults – frailty/comorbidities

Table 34: Clinical evidence summary: Frailty/comorbidities

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Frailty score			
The following categories on Rockwood Frailty Score were individually compared to a group of people <50 years (frailty score not assessed/applicable) for predicting need for neurosurgical specialist admission: Frailty score 1-3 Frailty score 4-6 Frailty score 7-9 (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not),	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c,d Due to risk of bias, imprecision (for second comparison only), indirectness (overall risk of bias applicable for all groups vs. <50 years group) note: imprecision only present for second comparison, frailty score 4-6, but not remaining risk factor groups	Adjusted OR: Frailty score 1-3, 1.90 (1.16 to 3.10) Frailty score 4-6, 0.70 (0.27 to 1.80) Frailty score 7-9, 0.09 (0.01 to 0.70)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)			
Hypoxia			
Hypoxia vs. no hypoxia prior to admission for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.	600 (1) Within 48 h of ED arrival Nishijima 20149	VERY LOWa,e,f Due to risk of bias, indirectness	Adjusted RR: 1.52 (1.03 to 2.24)
Any high-risk comorbidity			
Presence vs. absence of any high-risk comorbidity (atrial fibrillation or flutter, bleeding disorder, congestive heart failure, coronary artery disease, end-stage liver disease, pulmonary disease requiring oxygen at home or end-stage renal disease requiring dialysis) for	600 (1) Within 48 h of ED arrival	VERY LOWa,e,f Due to risk of bias, indirectness	Adjusted RR: 1.58 (1.07 to 2.33)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.	Nishijima 20149		

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
(d) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(e) Risk of bias was identified for study participation and outcome measurement domains
(f) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

1 Adults – extracranial injury

2 Table 35: Clinical evidence summary: Extracranial injury/non-isolated head injury

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
Extracranial injury severity – continuous variable			
Increasing severity of extracranial injury (measured on ISS, per 1-unit increase) for predicting need for neurosurgical specialist admission (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 1.06 (1.03 to 1.09)
Increasing severity of extracranial injury (measured on ISS, per 1-unit increase) for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI)	1699 (1) 30 days post-ED admission Marincowitz 20207	VERY LOWa,b,c Due to risk of bias, indirectness	Adjusted OR: 1.03 (1.01 to 1.05)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
(≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)			
Non-isolated head injury			
Non-isolated head injury vs. isolated head injury for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease,	600 (1) Within 48 h of ED arrival Nishijima 20149	VERY LOWa,d,e Due to risk of bias, indirectness	Adjusted RR: 2.74 (1.99 to 3.78)

Risk factor and outcome (population)	Number of participants (studies) Follow up	Quality of the evidence (GRADE)	Effect (95% CI)
end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.			

(a) Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
(b) Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
(c) Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
(d) Risk of bias was identified for study participation and outcome measurement domains
(e) Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

Summary matrix tables – odds ratios/risk ratios

Worse outcome in risk factor group Better outcome in risk factor group **Bold = no imprecision**

Table 36: Clinical decision rules – odds ratio results

Deterioration composite outcome[a]– 30 days post-ED admission	Need for hospital admission composite outcome[b] – 30 days post-ED admission	Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival	**Composite outcome** - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission - ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation **AND each outcome individually**	**Composite outcome** – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – follow-up 7-90 days post-ED visit (varies between patients)

Score >0 Hull Salford Cambridge Decision Rule - adults: **OR 16.98 (4.16-69.30)** BIG score >1: **OR 10.68 (2.59-43.99)**	Score >0 Hull Salford Cambridge Decision Rule - adults: **OR 23.33 (1.42-382.05)** BIG score >1: **OR 2.69 (1.44-5.00)**	Nishijima 2014 decision rule[c] - adults: **OR 37.49 (9.15-153.49)**	Pruitt 2017 decision rule (at least one high-risk predictor)[d] – adults: *Composite outcome:* **OR 41.84 (5.72 to 305.86)** – derivation set **OR 12.13 (3.70 to 39.75)** – validation set *Neurologic decline outcome:* **OR 10.49 (1.40 to 78.80)** – derivation set OR 2.82 (0.64 to 12.51) – validation set *Worsening repeat CT outcome:* **OR 20.70 (1.24 to 344.61)** – derivation set **OR 7.58 (1.00 to 57.24)** – validation set *Neurosurgical procedure (intracranial pressure monitoring or operations) during admission outcome:* **OR 41.81 (2.55 to 686.72)** – derivation set **OR 23.59 (3.20 to 173.60)** – validation set	CHIIDA score >0 (Greenberg 2017)[e] – children: **OR 16.95 (6.76 to 42.50)** CHIIDA score >2 (Greenberg 2017)[e] – children: **OR 14.96 (7.54 to 29.67)**

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI
[b] Composite of seizure as inpatient or at 2 week follow-up, death attributable to TBI within 30 days, intubation within 30 days, ICU admission for reasons other than close monitoring, neurosurgical intervention and neurological deterioration indicated by new deficit or drop in GCS of >1 point
[c] One or more of following: GCS <15, non-isolated head injury, ≥65 years and presence of swelling or shift on initial cranial CT
[d] Those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use
[e] CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).

1 **Table 37: GCS score**

Deterioration composite outcome[a]– 30 days post-ED admission	Need for neurosurgical specialist admission – 30 days post-ED admission	Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival	Composite of CT progression, change in neurologic status, need for surgery or death/comfort measures only – unclear time-point, possibly within same admission	Composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission - ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation	Composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) - follow-up 7-90 days post-ED visit (varies between patients)	Head CT progression on repeat CT – within 24 h	Worsening of brain lesion on repeat head CT – average 13 h post-initial CT	Neurosurgical intervention – unclear, possibly within same admission	Favourable outcome[b] – unclear, possibly within same admission	Good outcome (GOS >4)	Discharge within 24 h
Adults GCS 14 vs. GCS 15: **OR 1.60 (1.22-2.10)** GCS 13 vs. GCS 15: **OR 2.30 (1.60-3.31)**	*Adults* GCS 14 vs. GCS 15: **OR 2.30 (1.60-3.31)** GCS 13 vs. GCS 15: **OR 3.70 (2.32-5.90)**	*Adults* GCS 15 vs. GCS 13-14: **RR 0.34 (0.24-0.47)**	*Adults* GCS 13 vs. GCS 14-15: **OR 4.50 (2.47-8.20)**	*Adults* GCS 13 vs. GCS 14-15: **OR 4.09 (1.18 to 14.22)**	*Children* GCS 14 vs. GCS 15: OR 1.60 (0.82 to 3.12) GCS 13 vs. GCS 15: **OR 3.40 (1.50 to 7.71)**	*Adults* GCS 14 vs. GCS 15: **OR 3.11 (1.77-5.48)** GCS 13 vs. GCS 15: **OR 4.00 (2.02-7.93)**	*Adults* GCS 15 vs. GCS 13-14: **OR 0.32 (0.12-0.82)**	*Adults* GCS 14 vs. GCS 15: OR 1.12 (0.97-1.29)	*Adults* GCS 15 vs. GCS 13-14: **OR 5.50 (1.61-18.80)**	*Adults* GCS motor scores on admission (possibly per 1-unit increase between 13 and 15): **OR: 13.96 (2.23 to 87.30)**	*Adults* GCS 15 vs. GCS 13-14: **OR 2.90 (1.90-4.43)**

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI
[b] Defined as being alive, having admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention

Table 38: CT measures/findings

Deterioration composite outcome[a]– 30 days post-ED admission	Need for neurosurgical specialist admission – 30 days post-ED admission	Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival	Composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission - ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation	Composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) - follow-up 7-90 days post-ED visit (varies between patients)	Head CT progression on repeat CT – within 24 h	Progression on repeat CT – within 6 h	Neurosurgical intervention – unclear, possibly within same admission	Delayed neurosurgical intervention (indicating failed non-operative management) – unclear, possibly within same admission	Haematoma enlargement leading to surgery - ~1-week post-injury	Discharge within 24 h

Adults Following vs. simple skull fracture: • Complex skull fracture: OR 1.40 (0.46 to 4.30) • 1-2 bleeds <5 mm (total): OR 1.10 (0.39 to 3.10) • No/minimal mass effect: ORR 2.30 (0.90 to 5.88) • Significant midline shift: **OR 6.80 (2.50 to 18.49)** • High/mixed density lesion: **OR 21.60 (7.69 to 60.70)** • Cerebellar/brainstem injury:	*Adults* Following vs. simple skull fracture: • Complex skull fracture: OR 0.90 (0.17 to 4.90) • 1-2 bleeds <5 mm (total): OR 0.80 (0.16 to 4.10) • No/minimal mass effect: OR 2.30 (0.55 to 9.70) • Significant midline shift: **OR 7.40 (1.62 to 33.90)** • High/mixed density lesion: **OR 37.10 (8.14 to 168.99)** • Cerebellar/brainstem injury:	*Adults* Presence vs. absence of swelling or shift on admission CT: **RR: 4.11 (3.08 to 5.48)**	*Adults* Max subdural haemorrhage thickness >5 mm vs. ≤5 mm: **OR 5.10 (2.42 to 10.75)** Any midline shift vs. no midline shift: **OR 4.73 (2.42 to 9.24)**	*Children* Any midline shift vs. no midline shift: **OR 6.50 (3.70 to 11.42)**	*Adults* Mass effect vs. no mass effect on CT: **OR: 2.02 (1.08 to 3.78)**	*Adults* Subdural haemorrhage >10 mm vs. ≤10 mm: **OR: 4.80 (1.90 to 12.13)** Epidural haemorrhage >10 mm vs. ≤10 mm: **OR: 7.90 (2.40 to 26.01)**	*Adults* Subdural haemorrhage >10 mm vs. ≤10 mm: **OR: 3.40 (2.10 to 5.50)** Subdural haemorrhage width ≥4 mm vs. <4 mm: **OR: 3.76 (1.29 to 10.93)** Epidural haemorrhage >10 mm vs. ≤10 mm: **OR: 3.50 (1.40 to 8.75)** Midline shift vs. no midline shift: **OR: 7.51 (3.32 to 16.99)**	*Adults* Increasing epidural haemorrhage volume as a continuous variable (per 1 cubic centimetre increase): **OR: 1.19 (1.04 to 1.36)**	*Adults* Increasing initial volume of subdural haematoma lesion (ml) (increments unclear): OR: 2.52 (0.15 to 41.10) Increasing maximum thickness of subdural haematoma lesion (mm) (increments unclear): **OR: 1.43 (1.09 to 1.89)** Degree of midline shift (mm) as a continuous variable (increments unclear): **OR: 1.09 (1.02 to 1.17)**	*Adults* Subdural haemorrhage ≤6 mm vs. >6 mm: **OR: 3.10 (2.14 to 4.50)**

OR 7.00 (1.91 to 25.70)	**OR 8.50 (1.29 to 56.20)**						Mass effect vs. no mass effect on CT: **OR: 5.24 (1.96 to 14.01)**			

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI

Table 39: Injury severity scales

Head CT progression on repeat CT – within 24 h	Neurosurgical intervention – unclear, possibly within same admission	Good outcome (GOS >4)
Adults Increasing ISS score (increments analysed unclear): **OR: 1.07 (1.02 to 1.12)**	*Adults* Increasing head AIS score (increments analysed unclear): **OR: 12.87 (6.47 to 25.58)** Following vs. ISS 0-6 group: • ISS 7-11: **OR 2.35 (1.35 to 4.09)** • ISS 12-18: **OR 3.37 (1.94 to 5.86)** • ISS 19-27: **OR 18.90 (10.82 to 33.00)** • ISS >27: **OR 7.01 (3.67 to 13.40)**	*Adults* Increasing ISS score (increments analysed unclear): **OR: 0.87 (0.81 to 0.94)**

Table 40: Anticoagulation/antiplatelet treatments

Deterioration composite outcome[a]– 30 days post-ED admission	Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival	Composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission - ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation	Neurosurgical intervention – unclear, possibly within same admission
Adults Anticoagulant/antiplatelet use (either or both) vs. no use: **OR: 1.40 (1.03 to 1.90)**	*Adults* Antiplatelet therapy (aspirin or clopidogrel) vs. no antiplatelet therapy: **RR: 1.54 (1.03 to 2.30)**	*Adults* Warfarin use vs. no warfarin use: OR: 2.21 (0.97 to 5.01) Clopidogrel use vs. no clopidogrel use: **OR: 2.70 (1.00 to 7.31)**	*Adults* Anticoagulation disorder vs. no anticoagulation disorder: OR: 0.85 (0.67 to 1.09)

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI

Table 41: Age

Need for neurosurgical specialist admission – 30 days post-ED admission	Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival	Composite of CT progression, change in neurologic status, need for surgery or death/comfort measures only – unclear time-point, possibly within same admission	Worsening of brain lesion on repeat head CT – average 13 h post-initial CT	Progression on repeat CT – within 6 h	Neurosurgical intervention – unclear, possibly within same admission	Favourable outcome[a] – unclear, possibly within same admission	Good outcome (GOS >4)
Adults Increasing age as a continuous variable (per 1-unit increase): **OR: 1.00 (1.00 to 1.00)**	*Adults* Age ≥65 vs. <65 years: **RR: 1.46 (1.05 to 2.03)**	*Adults* Age ≥60 vs. <60 years: **OR: 1.60 (1.10 to 2.33)**	*Adults* Age >65 vs. ≤65 years: **OR: 3.33 (1.29 to 8.60)**	*Adults* Age ≥65 vs. <65 years: OR: 1.40 (0.73 to 2.70)	*Adults* Increasing age as a continuous variable (increments unclear): **OR: 1.00 (1.00 to 1.00)**	*Adults* Age <55 vs. ≥55 years: **OR: 3.50 (1.09 to 11.20)**	*Adults* Increasing age continuous (increment unclear): **OR: 0.94 (0.91 to 0.97)**

[a] Defined as being alive, having admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention

Table 42: Blood measurements

Deterioration composite outcome[a]– 30 days post-ED admission	Need for neurosurgical specialist admission – 30 days post-ED admission	Progression on repeat CT – within 6 h	Neurosurgical intervention – unclear, possibly within same admission
Adults Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L): OR: 0.99 (0.98 to 1.00)	*Adults* Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L): OR: 0.99 (0.98 to 1.00)	*Adults* Platelet ≤100,000 mm^{-3} vs. >100,000 mm^{-3}: OR: 1.30 (0.47 to 3.60) Lactate ≤2.5 vs. >2.5: OR 2.10 (0.89 to 4.95) Base deficit >4 vs. ≤4: **OR: 2.80 (1.60 to 4.90)**	*Adults* Platelet ≤100,000 mm^{-3} vs. >100,000 mm^{-3}: OR 1.60 (0.53 to 4.80) Lactate ≤2.5 vs. >2.5: OR: 1.90 (0.62 to 5.82) Base deficit >4 vs. ≤4: **OR: 21.00 (1.60 to 275.64)**

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI

Table 43: Abnormal neurological exam findings

Deterioration composite outcome[a]– 30 days post-ED admission	Need for neurosurgical specialist admission – 30 days post-ED admission	Neurosurgical intervention – unclear, possibly within same admission
Adults Abnormal vs. normal neurological examination: **OR: 1.70 (1.20 to 2.41)**	*Adults* Abnormal vs. normal neurological examination: **OR: 1.90 (1.20 to 3.00)**	*Adults* Unilateral weakness vs. no unilateral weakness on neurological assessment: **OR: 3.76 (1.29 to 10.93)**

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI

Table 44: Frailty/comorbidity

Need for neurosurgical specialist admission – 30 days post-ED admission	Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival
Adults Following vs. group <50 years: • Frailty score 1-3: **OR 1.90 (1.16 to 3.10)** • Frailty score 4-6: OR 0.70 (0.27 to 1.80) • Frailty score 7-9: **OR 0.09 (0.01 to 0.70)**	*Adults* Hypoxia vs. no hypoxia prior to admission: **RR: 1.52 (1.03 to 2.24)** Presence vs. absence of any high-risk comorbidity: **RR: 1.58 (1.07 to 2.33)**

Table 45: Extracranial injury

Deterioration composite outcome[a]– 30 days post-ED admission	Need for neurosurgical specialist admission – 30 days post-ED admission	Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival
Adults Increasing severity of extracranial injury (measured on ISS, per 1-unit increase): **OR: 1.03 (1.01 to 1.05)**	*Adults* Increasing severity of extracranial injury (measured on ISS, per 1-unit increase): **OR: 1.06 (1.03 to 1.09)**	*Adults* Non-isolated head injury vs. isolated head injury: **RR: 2.74 (1.99 to 3.78)**

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI

Summary matrix tables – sensitivity/specificity results for clinical decision rules

Bold = no imprecision Sensitivity ≥90% Specificity ≥60%

Table 46: Clinical decision rules – sensitivity/specify results

	Outcome/reference standard									
	Deterioration composite outcome[a]– 30 days post-ED admission		**Need for hospital admission composite outcome[b] – 30 days post-ED admission**		**Need for ICU admission (acute critical care intervention) – within 48 h of ED arrival**		**Composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission - ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation AND each outcome individually**		**Composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – follow-up 7-90 days post-ED visit (varies between patients)**	
Adults – Score >0 Hull Salford Cambridge Decision Rule	**Sens 1.00 N=1569**	**Spec 0.07 N=1569**	**Sens 1.00 N=961**	**Spec 0.05 N=961**	-	-	-	-	-	-

Adults – BIG criteria score >1	**Sens** **1.00** **N=1569**	**Spec** **0.05** **N=1569**	**Sens** **0.95** **N=961**	**Spec** **0.13** **N=961**	-	-	-	-	-	-
Adults – Nishijima 2014 decision rule (at least one risk factor)[c]	-	-	-	-	**Sens** **0.98** **N=600**	Spec 0.40 N=600	-	-	-	-
Adults – Pruitt 2017 decision rule (at least one high-risk predictor)[d]	-	-	-	-	-	-	*Composite outcome* ***Sens:*** • ***0.99 derivation*** • ***0.96 validation*** *Neurologic decline outcome* *Sens:* • *0.96 derivation* • *0.89 validation*	*Composite outcome* *Spec:* • *0.37 derivation* • ***0.32 validation*** *Neurologic decline outcome* ***Spec:*** • ***0.31 derivation*** • ***0.25 validation***	-	-

							Worsening on repeat CT outcome *Sens:* • *1.00 derivation* • *0.96 validation* *Neurosurgical procedure during admission outcome* ***Sens:*** • ***1.00 derivation*** • ***0.98 validation*** *N=340 derivation and N=304 validation set*	*Worsening on repeat CT outcome* ***Spec:*** • ***0.31 derivation*** • ***0.26 validation*** *Neurosurgical procedure during admission outcome* ***Spec:*** • ***0.33 derivation*** • ***0.29 validation*** *N=340 derivation and N=304 validation set*		
Children – CHIIDA score >0 (Greenberg 2017)[e]	-	-	-	-	-	-	-	-	***Sens*** ***0.93*** ***N=839***	Spec 0.55 N=839

Children – CHIIDA score >2 (Greenberg 2017)[e]	-	-	-	-	-	-	-	-	Sens 0.86 N=839	**Spec** **0.70** **N=839**

[a] Composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI
[b] Composite of seizure as inpatient or at 2 week follow-up, death attributable to TBI within 30 days, intubation within 30 days, ICU admission for reasons other than close monitoring, neurosurgical intervention and neurological deterioration indicated by new deficit or drop in GCS of >1 point
[c] One or more of following: GCS <15, non-isolated head injury, ≥65 years and presence of swelling or shift on initial cranial CT
[d] Those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use
[e] CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).

Sens, sensitivity; spec, specificity.

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

Modelling was not conducted for this review.

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			
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

- No relevant economic evaluations were identified.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

Only one outcome was listed in the review protocol (clinical deterioration). A set definition of clinical deterioration was not specified but examples of what this might include were provided: death or neurosurgery within 30 days of injury, need for critical care admission, reduction in GCS (drop of 2 or more), seizures or unplanned hospital readmission at 30 days. This was not an exhaustive list and any other outcomes in studies possibly indicating clinical deterioration were accepted and included.

The outcome definition varied widely across studies meaning pooling between studies was not possible.

1.1.12.2 The quality of the evidence

Seventeen observational studies (one prospective and sixteen retrospective studies) were included in the review. All evidence included in the review was graded very low quality based on GRADE. This was most often because of risk of bias associated with studies (all but one were retrospective and had associated limitations such as blinding in terms of outcome assessment and concerns about prognostic factor measurement. In addition, despite multivariate analysis being performed there were concerns that remained about the variables included for all but three studies relative to those mentioned as important in the protocol) and indirectness. Indirectness was common across studies as outcomes were indirect relevant to the protocol, either because it was reported at a much shorter or longer time-point than specified and/or because it may not be as representative of clinical deterioration as examples given in the protocol (for example, many studies only reported progression or worsening of lesion on repeat CT, which is a radiological outcome rather than a clinical presentation such as death, readmission or seizures listed in the review protocol as examples of clinical deterioration). All but two studies were also downgraded for population indirectness as they included a general GCS 13-15 population with confirmed injury on CT and they were not specific to those with smaller injuries.

It was also noted that for certain outcomes, particularly neurosurgical intervention, effects of risk factors on the outcome could be driven in part by the risk factor itself for retrospective studies. For example, those with higher frailty may have had less neurosurgical intervention but this will partly be because frailty increases the likelihood that surgery is thought to be of increased risk.

Only one study specifically in children was reported.

In terms of making recommendations, the committee agreed that the limitations and very low quality evidence identified were a limitation particularly for risk factors with fewer studies or that were not already covered by existing recommendations. For example, there was clear and consistent evidence across eleven studies (including one in children) that a GCS 13 or 14 was associated with worse outcome compared to GCS 15, which was interpreted as strong given the consistency across many studies even with the limitations described. However, a GCS <15 was already included as an indication for admission and therefore did not need to be added.

1.1.12.3 Benefits and harms

Evidence for risk factors

Across all risk factor types included in the review (clinical decision rules, GCS, specific CT findings and measurements, injury severity scales, anticoagulation/antiplatelet use, age blood measurements, abnormal neurological exam findings, frailty/comorbidity and extracranial injury), there was evidence for worse outcome with the risk factor or as the risk factor increased/decreased. For risk factors that were analysed as both dichotomous variables and continuous variables (for example age ≥65 years vs. <65 years and age as a continuous variable per 1-unit increment), it was noted that effect sizes were larger when analysed as a dichotomous variable, and those analysed continuously were smaller. For continuously analysed variables, these were also difficult to interpret in terms of thresholds that could be used in any recommendations for admission or discharge. The number of studies and consistency of results for risk factors varied, with evidence being stronger for some than others.

The committee noted that the effect sizes for the clinical decision rules appeared overall to be larger than those for individual risk factors and agreed that clinical decision rules were likely to be the way forward in terms of identifying those that should be admitted. However, the currently reported decision rules are all retrospective even for validation studies. Prospective studies are preferred over retrospective studies as there are less potential for

bias and confounding. The committee therefore did not feel there was sufficient evidence to recommend a specific clinical decision rule until prospective validation studies have been done, particularly as these would be new to clinical practice. A research recommendation for prospective validation studies of clinical decision rules in those with GCS 13-15 (mild head injury) and a confirmed abnormality on CT was therefore made.

In terms of individual risk factors, it was noted that there was consistent evidence across eleven studies (including one in children) that GCS 13 and GCS 14 were associated with worse outcome compared to GCS 15; however, this is already an existing indication for admission in recommendation 1.8.1. Evidence for specific thresholds and findings on CT (including thresholds for subdural or epidural haemorrhage size or findings such as midline shift or mass effect on CT) also indicated larger effect sizes than for some other risk factors; however, for factors such as midline shift it was noted that any midline shift seen on imaging would be clinically important. The varying thresholds used for subdural and epidural haemorrhage across the different studies and the inconsistency in results made the ideal threshold to use unclear. Thresholds for age also showed that they could be associated with worse outcome in the higher age groups, but the committee noted that age is not something that would currently be used in practice solely to make decisions about admission based on and further highlighted that admission in older age groups can also be associated with harms such as the risk of hospital-acquired infections. They noted that age and/or frailty may be a concern but should not be a sole indicator for admission; whether or not a person is admitted should be about whether the person could benefit from admission which may not always be the case for some groups particularly with increasing age or frailty. Overall, the committee agreed a research recommendation for the GCS 13-15 group with an injury confirmed on CT (of any size) should be prospective validation of existing clinical decision rules for predicting deterioration in order to be able to refine indications for admission in this group.

Discussion of existing recommendation on indications for admission and current practice

The committee discussed current practice in terms of people with confirmed head injury on imaging that are admitted to hospital. Practice varied but in general the committee agreed that most people, even those with small injuries, would be admitted for a period of time as although the existing recommendation in 1.8.1 specifies clinically significant injuries on imaging, this is not defined due to lack of evidence and in current practice a cautious approach is taken. The committee discussed whether the included evidence would allow a definition of clinically significant injury to be added to the recommendation, but this was difficult as although the evidence shows some lesions or features of lesions may be associated with increased risk of worse outcome, this does not mean that those without those lesions or a different type are without risk. A further review was conducted, specifically looking at isolated skull fracture evidence (see review 3.3), which identified that simple, linear non-displaced fractures are not likely to be clinically significant. Therefore, the committee included explanatory text that isolated simple linear non-displaced skull fracture is unlikely to be a clinically significant abnormality, to clarify this recommendation.

1.1.12.4 Cost effectiveness and resource use

In current practice patients who have an intracranial injury of any size are admitted for observation and then treated as required. Therefore, if a prognostic factor or clinical decision rule was used to discharge some of these patients then there would be a cost saving. However, unless the rule is 100% sensitive then there is a risk that some patients that are discharged would deteriorate and consequently receive treatment later with potentially worse long-term outcomes.

There were no published economic evaluations found and so the committee were presented with unit costs for them to consider cost effectiveness in the context of the clinical evidence.

As noted above, the guideline's clinical review found various prognostic variables to be associated with a higher/lower risk of deterioration. The strongest indication was GCS score of less than 15 but this is already an indication for admission. The accuracy of clinical decision rules was better than for individual risk factors but given there is a risk of harm compared to the existing recommendations, the committee decided that stronger evidence of accuracy was required. A research recommendation for prospective validation studies of clinical decision rules in those with GCS 13-15 (mild head injury) and a confirmed abnormality on CT was therefore made. Such a study could form the basis of an economic evaluation that works out the trade-off between the resource use savings and other benefits with any increase in the number of patients deteriorating.

1.1.12.5 Other factors the committee took into account

The committee discussed whether or not a suspicion of post-traumatic amnesia should be added to the 'other sources of concern to the clinician' bullet point in recommendation 1.8.1 as an example. It was noted that even people with GCS 15 when assessed for post-traumatic amnesia by an occupational therapist may be found to have deficits remaining that may benefit from admission. The committee were aware that assessment of post-traumatic amnesia is actively done in other countries. However, variation in how this is done in the UK was discussed, with it not being used routinely and often qualitatively rather than a formal assessment by an occupational therapist. Including this in the recommendation was therefore not thought to be appropriate as it could represent a resource impact and particularly because it was not something specifically identified in the review.

The committee noted that the existing recommendation 1.8.1 did not make any reference to considering whether appropriate supervision is available at home before deciding whether to admit or discharge people and made a cross-reference to the 'Discharge and Follow-up' section of the guideline to ensure this is clear.

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Appendices

Appendix A – Review protocols

Review protocol for hospital admission in people with small intracranial injuries

Note that there was a post-hoc deviation from the below protocol to allow inclusion of sensitivity/specificity data for clinical decision rules.

ID	Field	Content
1.	Review title	Indications for hospital admission in people with small intracranial injuries. Definition of small intracranial injuries: Various scoring/coding systems are used to define type/size of intracranial injury. Hence GC wants us to include definitions as reported in the studies. Some studies define as Small intracranial bleeds (<5 mm) This group will include people with GCS 13-15. Some people with small intracranial injuries are admitted for 24-48 hours but there is a risk of hospital acquired complications. Some people can be discharged safely to the community when there are no indications for admission. People with GCS less than or equal to12, are never discharged. Current recommendations are to discuss all patients with intracranial injuries with neurosurgeons and admit all

2.	Review question	3.3 What are the indications for hospital admission in people with small intracranial injuries?
3.	Objective	To determine which patients with small intracranial injuries should be admitted to hospital
4.	Searches	The following databases (from inception) will be searched: • MEDLINE • Embase • Cochrane Database of Systematic Reviews (CDSR) • Epistemonikos Searches will be restricted by: • English language studies • Human studies 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 and Embase search strategies to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details). Key papers: Marincowitz C, Paton L, Lecky F, et al Predicting need for hospital admission in patients with traumatic brain injury or skull fractures identified on CT imaging: a

		machine learning approachEmergency Medicine Journal Published Online First: 08 April 2021. doi: 10.1136/emermed-2020-210776 Marincowitz C, Lecky FE, Townend W, Borakati A, Fabbri A, Sheldon TA. The Risk of Deterioration in GCS13-15 Patients with Traumatic Brain Injury Identified by Computed Tomography Imaging: A Systematic Review and Meta-Analysis. J Neurotrauma. 2018 Mar 1;35(5):703-718. doi: 10.1089/neu.2017.5259. Marincowitz C, Gravesteijn B, Sheldon T, et alPerformance of the Hull Salford Cambridge Decision Rule (HSC DR) for early discharge of patients with findings on CT scan of the brain: a CENTER-TBI validation studyEmergency Medicine Journal Published Online First: 27 July 2021. doi: 10.1136/emermed-2020-210975 Marincowitz C, Lecky FE, Allgar V, Hutchinson P, Elbeltagi H, Johnson F, Quinn E, Tarantino S, Townend W, Kolias AG, Sheldon TA. 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. J Neurotrauma. 2020 Jan 15;37(2):324-333. doi: 10.1089/neu.2019.6652.
5.	Condition or domain being studied	Head Injury
6.	Population	Inclusion: Infants, children and adult with all intracranial injuries positive CT scan and GCS 13-15 • Adults (aged ≥16 years) • Children (aged ≥1 to <16 years) • Infants (aged <1 year) . Mixed population studies will be included but downgraded for indirectness. Cut-off of 60% will be used for all age groups

		Exclusion: Adults, and children (including infants under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury. Studies will be downgraded for indirectness as we will be including people with all intracranial injuries
7.	Eligibility criteria –risk factors	1. Clinical decision rules (post-hoc edit) 2. Risk factors for clinical deterioration in people with small intracranial injuries: • Severity of anatomical injury on CT (scales as defined in the study) different scales are used– marshall scale or AIS (Abrrevatied injury scale- gives size and site of injury)- some papers report large or small contusion/extradural haemorhahge [there has to be some decription of anatomical injury on CT in the studies and adjust for GCS] Size of injury is inlcuded as part of anatomical injury • Severity of injury based on GCS (mild/moderate/severe)Anticoalgulant therapy • Anti-platelet therapy • Age • Blood measurements such as clotting, haemoglogin, blood glucose • Abnormal Pupilllary responses and neurological deficits (pupils measured by shining light whether pupils constrict, neurological deficit – examination finding) • Pre-existing co-morbidity and fraility

		• Significant extracranial injuries Key confounders: • Severity of injury (based on GCS) Studies will only be included if key confounder of severity of injury have been accounted for in a multivariate analysis Other confounders: • Severity of anatomical injury on CT • Anticoagulant therapy Anti-platelet therapy • Age • Blood measurements such as clotting, haemoglobin, blood glucose • Abnormal Pupillary responses and neurological deficits (pupils measured by shining light whether pupils constrict, neurological deficit – examination finding) • Pre-existing co-morbidity and fraility • Significant extracranial injuries Studies will not be excluded if not adjusted for other confounders but will be downgraded for high risk of bias. Note from studies: if they are on anti-coagulant therapy
	Eligibility criteria – comparator(s)	Absence of risk factors
9.	Types of study to be included	Cohort studies (prospective and retrospective) Systematic reviews and meta-analyses of the above Case-control studies will be excluded.

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. Studies not adjusted for pre-specified key confounder of severity of injury Univariate analysis will be excluded
11.	Context	Risk factors for hospital admission in people with small intracranial injuries
12.	Primary outcomes (critical outcomes)	Clinical deterioration Which includes: • Death or neurosurgery within 30 days of injury • Need for critical care admission • Reduction in GCS (drop of of 2 or more) • Seizures • Unplanned hospital re-admission at 30 days This is not an exhaustive list Association data • Adjusted RR or OR Accuracy data: • Sensitivity and specificity (post-hoc edit)

13.	Data extraction (selection and coding)	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. This review will make use of the priority screening functionality within the EPPI-reviewer software. 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	The methodological quality of each study will be assessed using the QUIPS checklist for risk factor data and QUADAS-2 for clinical decision rules where sensitivity and specificity data is reported (post-hoc edit). The risk of bias across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/
15.	Strategy for data synthesis	

		• meta-analyses will be performed if possible using Cochrane Review Manager (RevMan5) depending on the appropriateness of data. • Studies will be pooled if they have adjusted for the same confounders. • If meta-analysis is not possible, data will be presented as individual values in adapted GRADE profile tables and plots of un-pooled prognostic odds/risk ratios or sensitivity and specificity from RevMan software for clinical decision rule data (post-hoc edit).	
16.	Analysis of sub-groups	NA	
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	[For the purposes of PROSPERO, the date of commencement for the systematic review can be defined as any point after completion of a protocol but before formal screening of the identified studies against the eligibility criteria begins. A protocol can be deemed complete after sign-off by the NICE team with responsibility for quality assurance.]	

<table>
<tr><td>21.</td><td>Anticipated completion date</td><td colspan="3">[Give the date by which the guideline is expected to be published. This field may be edited at any time. All edits will appear in the record audit trail. A brief explanation of the reason for changes should be given in the Revision Notes facility.]</td></tr>
<tr><td rowspan="7">22.</td><td rowspan="7">Stage of review at time of this submission</td><td>Review stage</td><td>Started</td><td>Completed</td></tr>
<tr><td>Preliminary searches</td><td>☐</td><td>☐</td></tr>
<tr><td>Piloting of the study selection process</td><td>☐</td><td>☐</td></tr>
<tr><td>Formal screening of search results against eligibility criteria</td><td>☐</td><td>☐</td></tr>
<tr><td>Data extraction</td><td>☐</td><td>☐</td></tr>
<tr><td>Risk of bias (quality) assessment</td><td>☐</td><td>☐</td></tr>
<tr><td>Data analysis</td><td>☐</td><td>☐</td></tr>
<tr><td>23.</td><td>Named contact</td><td colspan="3">5a. Named contact
National Guideline Centre

5b Named contact e-mail
[Guideline email]@nice.org.uk
[Developer to check with Guideline Coordinator for email address]

5e Organisational affiliation of the review
National Institute for Health and Care Excellence (NICE) and [National Guideline Alliance / National Guideline Centre / NICE Guideline Updates Team / NICE</td></tr>
</table>

		Public Health Guideline Development Team] [Note it is essential to use the template text here and one of the centre options to enable PROSPERO to recognise this as a NICE protocol]
24.	Review team members	[Give the title, first name, last name and the organisational affiliations of each member of the review team. Affiliation refers to groups or organisations to which review team members belong.] From the National Guideline Centre: [Guideline lead] [Senior systematic reviewer] Systematic reviewer [Health economist] [Information specialist] [Others]
25.	Funding sources/sponsor	This systematic review is being completed by the National Guideline Centre which receives funding from NICE.
26.	Conflicts of interest	All guideline committee members and anyone who has direct input into NICE guidelines (including the evidence review team and expert witnesses) must declare any potential conflicts of interest in line with NICE's code of practice for declaring and dealing with conflicts of interest. Any relevant interests, or changes to interests, will also be declared publicly at the start of each guideline committee meeting. Before each meeting, any potential conflicts of interest will be considered by the guideline committee Chair and a senior member of the development team. Any decisions to exclude a person from all or part of a meeting will be documented. Any changes to a member's declaration of interests will be recorded in the minutes of the meeting. Declarations of interests will be published with the final guideline.
27.	Collaborators	Development of this systematic review will be overseen by an advisory committee who will use the review to inform the development of evidence-based

		recommendations in line with section 3 of Developing NICE guidelines: the manual. Members of the guideline committee are available on the NICE website: [NICE guideline webpage].	
28.	Other registration details	[Give the name of any organisation where the systematic review title or protocol is registered (such as with The Campbell Collaboration, or The Joanna Briggs Institute) together with any unique identification number assigned. If extracted data will be stored and made available through a repository such as the Systematic Review Data Repository (SRDR), details and a link should be included here. If none, leave blank.]	
29.	Reference/URL for published protocol	[Give the citation and link for the published protocol, if there is one.]	
30.	Dissemination plans	NICE may use a range of different methods to raise awareness of the guideline. These include standard approaches such as: • notifying registered stakeholders of publication • publicising the guideline through NICE's newsletter and alerts • issuing a press release or briefing as appropriate, posting news articles on the NICE website, using social media channels, and publicising the guideline within NICE. [Add in any additional agree dissemination plans.]	
31.	Keywords	Diagnosis, head injury, selection for CT/MRI	
32.	Details of existing review of same topic by same authors	[Give details of earlier versions of the systematic review if an update of an existing review is being registered, including full bibliographic reference if possible. NOTE: most NICE reviews will not constitute an update in PROSPERO language. To be an update it needs to be the same review question/search/methodology. If anything has changed it is a new review]	
33.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published

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

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2 **Health economic review protocol**

3

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).[8]

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.

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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.[8]

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

Table 47: Database parameters, filters and limits applied

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

Medline (Ovid) search terms

1.	craniocerebral trauma/ or exp brain injuries/ or exp head injuries, closed/ or exp intracranial hemorrhage, traumatic/ or exp skull fractures/
2.	((skull or cranial) adj3 fracture*).ti,ab,kf.
3.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab,kf.
4.	(((trauma* or injur*) and (subdural or intracranial or epidural or subarachnoid)) adj2 (h?ematoma* or h?emorrhage* or bleed*)).ti,ab,kf.
5.	or/1-4
6.	letter/
7.	editorial/

8.	news/
9.	exp historical article/
10.	Anecdotes as Topic/
11.	comment/
12.	case report/
13.	(letter or comment*).ti.
14.	or/6-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animals/ not humans/
18.	exp Animals, Laboratory/
19.	exp Animal Experimentation/
20.	exp Models, Animal/
21.	exp Rodentia/
22.	(rat or rats or mouse or mice or rodent*).ti.
23.	or/16-22
24.	5 not 23
25.	limit 24 to English language
26.	Clinical Deterioration/
27.	*Hospitalization/
28.	*Patient Admission/
29.	*Patient discharge/
30.	(deteriorat* or hospitali?* or admission* or admit* or discharg* or monitor* or observ*).ti,ab,kf.
31.	or/26-30
32.	(Brain Injury Guideline* or Marshall or HSC DR or HSCDR).ti,ab,kf.
33.	abbreviated injury scale.ti,ab,kf.
34.	(risk adj2 (tool* or tree or rule* or assess* or factor* or scale*)).ti,ab,kf.
35.	((single or small) adj2 (bleed* or h?emorrhage*)).ti,ab,kf.
36.	(GCS or Glasgow coma scale).ti,ab,kf.
37.	((CT or CAT or compute* tomograph*) adj4 (positive* or finding* or confirm* or identif* or injur* or sever* or scale* or result* or outcome* or reading*)).ti,ab,kf.
38.	(blood* adj test*).ti,ab,kf.
39.	(pupillary adj2 (respons* or deficit* or abnormal or defect* or constrict* or reflex*)).ti,ab,kf.
40.	or/32-39
41.	25 and 31 and 40
42.	predict.ti.
43.	(validat* or rule*).ti,ab.
44.	(predict* and (outcome* or risk* or model*)).ti,ab.
45.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
46.	decision*.ti,ab. and Logistic models/
47.	(decision* and (model* or clinical*)).ti,ab.
48.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.

49.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
50.	ROC curve/
51.	or/42-50
52.	Epidemiologic studies/
53.	Observational study/
54.	exp Cohort studies/
55.	(cohort adj (study or studies or analys* or data)).ti,ab.
56.	((follow up or observational or uncontrolled or non randomi#ed or epidemiologic*) adj (study or studies or data)).ti,ab.
57.	((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort* or data)).ti,ab.
58.	Controlled Before-After Studies/
59.	Historically Controlled Study/
60.	Interrupted Time Series Analysis/
61.	(before adj2 after adj2 (study or studies or data)).ti,ab.
62.	Cross-sectional studies/
63.	(cross sectional and (study or studies or review or analys* or cohort* or data)).ti,ab.
64.	or/52-63
65.	Meta-Analysis/
66.	exp Meta-Analysis as Topic/
67.	(meta analy* or metanaly* or metaanaly* or meta regression).ti,ab.
68.	((systematic* or evidence*) adj3 (review* or overview*)).ti,ab.
69.	(reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab.
70.	(search strategy or search criteria or systematic search or study selection or data extraction).ab.
71.	(search* adj4 literature).ab.
72.	(medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab.
73.	cochrane.jw.
74.	((multiple treatment* or indirect or mixed) adj2 comparison*).ti,ab.
75.	or/65-74
76.	41 and (51 or 64 or 75)

1 **Embase (Ovid) search terms**

1.	*head injury/ or *brain injury/ or exp *brain hemorrhage/ or *skull injury/ or exp *skull fracture/
2.	((skull or cranial) adj3 fracture*).ti,ab,kf.
3.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab,kf.
4.	(((trauma* or injur*) and (subdural or intracranial or epidural or subarachnoid)) adj2 (h?ematoma* or h?emorrhage* or bleed*)).ti,ab,kf.
5.	or/1-4
6.	letter.pt. or letter/
7.	note.pt.
8.	editorial.pt.
9.	(conference abstract or conference paper).pt.

10.	case report/ or case study/
11.	(letter or comment*).ti.
12.	or/6-11
13.	randomized controlled trial/ or random*.ti,ab.
14.	12 not 13
15.	animal/ not human/
16.	nonhuman/
17.	exp Animal Experiment/
18.	exp Experimental Animal/
19.	animal model/
20.	exp Rodent/
21.	(rat or rats or mouse or mice or rodent*).ti.
22.	or/14-21
23.	5 not 22
24.	limit 23 to English language
25.	*Deterioration/
26.	*Hospitalization/
27.	*Hospital Admission/
28.	*Hospital Discharge/
29.	(deteriorat* or hospitali?* or admission* or admit* or discharg* or monitor* or observ*).ti,ab,kf.
30.	or/25-29
31.	(Brain Injury Guideline* or Marshall or HSC DR or HSCDR).ti,ab,kf.
32.	abbreviated injury scale.ti,ab,kf.
33.	(risk adj2 (tool* or tree or rule* or assess* or factor* or scale*)).ti,ab,kf.
34.	((single or small) adj2 (bleed* or h?emorrhage*)).ti,ab,kf.
35.	(GCS or Glasgow coma scale).ti,ab,kf.
36.	((CT or CAT or compute* tomograph*) adj4 (positive* or finding* or confirm* or identif* or injur* or sever* or scale* or result* or outcome* or reading*)).ti,ab,kf.
37.	(blood* adj test*).ti,ab,kf.
38.	(pupillary adj2 (respons* or deficit* or abnormal or defect* or constrict* or reflex*)).ti,ab,kf.
39.	or/31-38
40.	24 and 30 and 39
41.	predict.ti.
42.	(validat* or rule*).ti,ab.
43.	(predict* and (outcome* or risk* or model*)).ti,ab.
44.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
45.	decision*.ti,ab. and Statistical model/
46.	(decision* and (model* or clinical*)).ti,ab.
47.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
48.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
49.	Receiver operating characteristic/
50.	or/41-49

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

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

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

2 **Epistemonikos search terms**

1.	(title:((title:((trauma* OR injur*)) OR abstract:((trauma* OR injur*))) AND (title:((subdural OR intracranial OR epidural OR subarachnoid)) OR abstract:((subdural OR intracranial OR epidural OR subarachnoid))) AND (title:((haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*)) OR abstract:((haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*)))) OR abstract:((title:((trauma* OR injur*)) OR abstract:((trauma* OR injur*))) AND (title:((subdural OR intracranial OR epidural OR subarachnoid)) OR abstract:((subdural OR intracranial OR epidural OR subarachnoid))) AND (title:((haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*)) OR abstract:((haematoma* OR hematoma* OR haemorrhage* OR hemorrhage OR bleed*)))))

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 48: Database parameters, filters and limits applied

Database	Dates searched	Search filters and limits applied
Medline (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments, editorials, case studies/reports) English language
	Quality of Life 1946 – 22 June 2022	
Embase (OVID)	Health Economics 1 January 2014 – 22 June 2022	Health economics studies Quality of life studies Exclusions (animal studies, letters, comments, editorials, case studies/reports, conference abstracts) English language
	Quality of Life 1974 – 22 June 2022	
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

1 **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)

1 **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)

1 **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

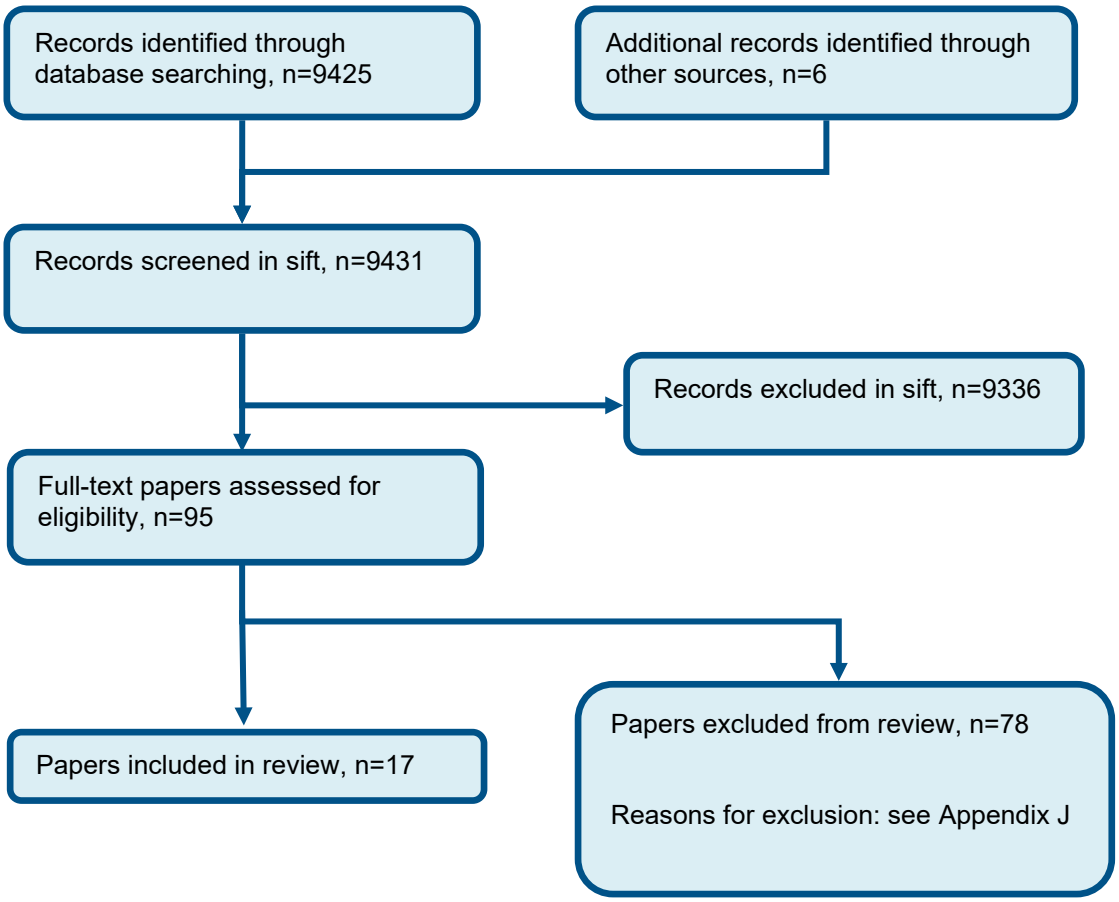
2 **INAHTA search terms**

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])

3

Appendix C –Prognostic evidence study selection

Figure 1: Flow chart of clinical study selection for the review of hospital admission in people with small intracranial injuries



Appendix D –Prognostic evidence

Reference	Borczuk 2019[1]
Study type and analysis	Retrospective observational study Multivariate logistic regression analysis performed using variables that were significant in univariate analyses at P≤0.02. Variables removed in forward stepwise fashion within multivariate analysis.
Number of participants and characteristics	N=1079 • GCS 15, n=890 • GCS 13-14, n=189 • Subdural haematoma ≤6 mm, n= 850 • Subdural haematoma >6 mm, n= 229 (note: n=662 had a subdural haematoma on CT, unclear if only this group included for this risk factor or those without subdural haematoma included in ≤6 mm group) **Inclusion criteria:** aged ≥16 years with blunt head trauma; and isolated cranial trauma **Exclusion criteria:** GCS ≤12; trauma to other organ systems (those requiring consultation with a service other than neurosurgery) **Population characteristics:** given separately for those with discharge within 24 h (n=386) and ≥24 h (n=693) • Age ≥60 years, 54.1 vs. 72.6% • Male sex, 55.2 vs. 56.1% • CT lesions: ○ Any subarachnoid haemorrhage, 45.6 vs. 48.2% ○ Any subdural haemorrhage, 52.6 vs. 66.2% ○ Any epidural haemorrhage, 2.9 vs. 3.9% ○ Any contusion, 22.0 vs. 28.0% ○ Any skull fracture, 14.3 vs. 15.3%

Reference	Borczuk 2019[1]
	• CT lesions isolated: ○ Isolated subarachnoid haemorrhage, 25.9 vs. 17.0% ○ Isolated subdural haemorrhage, 34.5 vs. 36.2% ○ Isolated epidural haemorrhage, 0.5 vs. 0.0% ○ Isolated contusion, 9.1 vs. 7.7% ○ Isolated skull fracture, 4.2 vs. 2.2% ○ Depressed skull fracture, 0.5 vs. 0.6% ○ Subdural haemorrhage ≥6 mm, 12.7 vs. 26.0% ○ Subdural haemorrhage ≥10 mm, 5.4 vs. 16.7% • Antithrombotic treatment: ○ Aspirin use, 17.1 vs. 28.7% ○ Warfarin use, 4.2 vs. 12.4% ○ Other antiplatelet use, 2.6 vs. 4.8% ○ Novel oral anticoagulant use, 0.3 vs. 0.1% • Hypertension, 40.2 vs. 48.1% • Intoxicant, 17.6 vs. 14.1% • Mechanism of injury: ○ Fall, 72.3 vs. 83.1% ○ Motor vehicle collision, 7.3 vs. 4.3% ○ Assault, 13.2 vs. 6.2% ○ Pedestrian struck, 0.8 vs. 1.4% ○ Cyclist struck, 4.2 vs. 1.6% ○ Motorcycle collision, 1.6 vs. 1.6% • GCS score: ○ 15, 91.5 vs. 77.5% ○ 14, 7.5 vs. 16.2% ○ 13, 1.1 vs. 6.4% • Clinical outcomes:

Reference	Borczuk 2019[1]
	○ Neurologic event, 1.0 vs. 8.9% ○ Repeat CT worse, 2.9 vs. 10.1% ○ Neurosurgical intervention, 0.0 vs. 11.8% ○ Death, 0.5 vs. 2.9% **Population source:** retrospective observational study performed at single urban, academic level I trauma centre with annual ED volume of >100,000 visits. Patients identified by running query in electronic health record using International Statistical Classification of Diseases and Related Health Problems (9th edition) codes for traumatic intracranial haemorrhage between 1st January 2009 and 31st December 2015.
Prognostic variables	**Subdural haematoma ≤6 mm** **Subdural haematoma >6 mm (referent)** *Note: for this risk factor, it is unclear whether only those with subdural haematoma were analysed or whether those without were included but grouped into the ≤6 mm group* **GCS 15** **GCS 13-14 (referent)** Chart data abstracted from physician notes, radiology reports, laboratory data and discharge summaries. Trained emergency physician reviewers who were not blinded to study hypothesis abstracted clinical data. Output reviewed after first 100 charts and again at intervals throughout the process. Periodically met to review abstraction process and to review ambiguous charts. Conflicting abstraction resolved by consensus of primary investigators after in-depth chart review. For those discharged from ED, records were reviewed for any subsequent traumatic intracranial haemorrhage-related admissions. No data was missing for any key clinical variables. Cranial CT results abstracted from finalised attending radiologist reports, including number, location and size of haematomas and presence of midline shift. Confluent haematomas counted as single lesion. All received neurosurgical consultation, with repeat neuroimaging performed routinely at 6 h and subsequently as indicated by the treating team. Patient and scheduling factors used to separate out patients with isolated mild head injury that are stable for monitoring in an ED observation unit, patients could also be placed in observation at discretion of physicians. Patients with multisystem traumatic injuries admitted to trauma surgery service while those with isolated nonoperative head trauma were admitted on rotating basis to neurosurgery, trauma surgery or neurology services.
Confounders	Multivariate logistic regression identified three variables associated with the outcome: GCS of 15, isolated traumatic subarachnoid haemorrhage and subdural haematoma with thickness ≤6 mm

Reference	Borczuk 2019[1]
	Unclear if other variables may have been included in the final multivariate analysis and only significant ones discussed **Accounts for key confounder of GCS as in our protocol**
Outcomes and effect sizes	**Length of stay <24 h/discharge within 24 h** **OR 2.9 (95% CI 1.9 to 4.4) for GCS 15 vs. GCS 13-14** **OR 3.1 (95% CI 2.2 to 4.5) for subdural haemorrhage ≤6 mm vs. >6 mm** Hospital length of stay was collected retrospectively from records.
Comments	**Risk of bias (applies to both risk factors):** 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — MODERATE OVERALL RISK OF BIAS — HIGH **Indirectness (applies to both risk factors):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome – length of stay/discharge within 24 h is indirect relevant to review protocol as could be other factors contributing to length of stay other than clinical deterioration

1

Reference	Greenberg 2017[2]
Study type and analysis	Secondary analysis of prospective PECARN cohort study of children Multivariate logistic regression model used, including variables that had P<0.20 on univariate analysis into the multivariate model
Number of participants and characteristics	N=839 • Presence of any midline shift, n=58 • No midline shift, n=781 • GCS 13, n=63 • GCS 14, n=165 • GCS15, n=611 • Score >0 on Children's Intracranial Injury Decision Aid (CHIIDA), n=NR • Score 0 on CHIIDA, n=NR • Score >2 on CHIIDA, n=NR • Score ≤2 on CHIIDA, n=NR **Inclusion criteria:** <18 years; mild TBI; non-penetrating head trauma; and ED CT scan showing intracranial injury (intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis). **Exclusion criteria:** trivial injury history or presentation (e.g. running into stationary objects); penetrating TBI; pre-existing comorbid neurological disease; and bleeding disorders. **Population characteristics:** given separately for those without (n=73) and with (n=766) the composite outcome • Median age: 5 vs. 7 years

Reference	Greenberg 2017[2]
	• Age <2 years, 35.1% vs. 28.8% • Age ≥2 years, 64.9% vs. 71.2% • Male sex, 64.5% vs. 63.0% • Race/ethnicity: ○ White, 61.2% vs. 63.0% ○ Black, 24.0% vs. 21.9% ○ Asian, 2.9% vs. 2.7% ○ Other, 11.9% vs. 12.3% • GCS score: ○ 15, 74.2% vs. 58.9% ○ 14, 19.1% vs. 26.0% ○ 13, 6.8% vs. 15.1% • Neurological deficit, 2.5% vs. 6.9% • Altered mental status, 50.4% vs. 61.6% • Acting normally, 54.4% vs. 38.4% • Amnesia: ○ No, 25.1% vs. 37.0% ○ Yes, 27.2% vs. 17.8% ○ Preverbal, 47.8% vs. 45.2% • Headache: ○ No, 18.0% vs. 11.0% ○ Mild, 9.9% vs. 8.2% ○ Moderate, 20.5% vs. 23.3% ○ Severe, 6.1% vs. 9.6% ○ Preverbal, 45.4% vs. 48.0%

Reference	Greenberg 2017[2]
	• Vomiting: ○ <2 times, 90.3% vs. 80.8% ○ ≥2 times, 9.7% vs. 19.2% • CT findings: ○ Epidural haematoma, 10.6% vs. 37.0% ○ Subarachnoid haemorrhage, 20.4% vs. 9.6% ○ Subdural haematoma, 25.3% vs. 17.8% ○ Midline shift, 4.7% vs. 30.1% ○ Cerebral oedema, 5.1% vs. 9.6% ○ Pneumocephalus, 18.7% vs. 27.4% ○ Depressed skull fracture, 13.3% vs. 46.6% ○ Non-depressed skull fracture, 44.0% vs. 34.3% • ED disposition: ○ Home, 8.9% vs. 0.0% ○ Operating room, 0.65% vs. 32.9% ○ General ward, 40.6% vs. 15.1% ○ Intensive care unit, 35.8% vs. 48.0% ○ Observation unit/short-stay, 9.3% vs. 1.4% ○ Other, 4.8% vs. 2.7% **Population source:** secondary, retrospective analysis of prospective PECARN cohort study. Observational study enrolled children and presenting to 1 of 25 North American EDs from 2004 to 2006. Data analysed from de-identified public-use dataset. Data analysis conducted between May 2015 and October 2016.
Prognostic variables	**Presence of any midline shift** **No midline shift (referent)**

Reference	Greenberg 2017[2]
	GCS 13 **GCS 14** **GCS 15 (referent)** **Score >0 on Children's Intracranial Injury Decision Aid (CHIIDA) – anyone with any of the variables would be admitted: depressed skull fracture; midline shift; epidural haematoma; GCS 13 and GCS 14.** **Score 0 on CHIIDA (referent)** **Score >2 on CHIIDA – anyone would be admitted apart from those with GCS 14 and no other risk factor, who would not be admitted to ICU as they would only have 2 points: depressed skull fracture; midline shift; epidural haematoma; GCS 13 and GCS 14.** **Score ≤2 on CHIIDA (referent)** Imaging variables abstracted from radiology reports with investigators able to add additional findings if relevant. Because primary CT images were not available for review, depressed skull fracture was defined by reviewing radiologist impressions from CT scan reports for any mention of fracture depression or displacement in patients with known skull fracture. GCS scores recorded at time first evaluated by ED team as part of routine standard care. Missing data described for several variables and imputation performed. For dichotomous measures with 5% or less missing data, assumed not present for missing values. For categorical variables with missing data and all variables with at least 6% missing data, multiple imputation performed with 5 imputed datasets. CHIIDA: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).
Confounders	Multivariate model for odds ratio results included: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15 **Model for odds ratio results accounts for key confounder of GCS as in our protocol**

Reference	Greenberg 2017[2]
	Clinical decision rule results Note that for results for the decision rule developed in the paper, ORs were based on raw data of those having or not having the composite outcome and being above or below the respective threshold (0 or 2 points). There were no multivariate results as results were reported as prognostic accuracy (sensitivity/specificity) in the paper. As the decision rules are based on consideration of multiple factors rather than a single risk factor, the results were considered suitable to include despite the fact there is no adjustment. ORs were calculated and sensitivity/specificity data was also extracted and presented.
Outcomes and effect sizes	**Composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)** Odds ratios **OR 6.50 (95% CI 3.70 to 11.4) for any midline shift vs. no midline shift** **OR 1.6 (95% CI 0.82 to 3.1) for GCS 14 vs. GCS 15** **OR 3.40 (95% CI 1.50 to 7.40) for GCS 13 vs. GCS 15** **OR 16.95 (95% CI 6.76 to 42.50) for CHIIDA score >0 vs. CHIIDA score 0 –** calculated based on 68/409 of those with score >0 having the composite outcome and 5/430 of those with score 0 having the composite outcome **OR 14.96 (95% CI 7.54 to 29.67) for CHIIDA score >2 vs. CHIIDA score ≤2 –** calculated based on 63/290 of those with score >2 having the composite outcome and 10/549 of those with score ≤2 having the composite outcome Sensitivity/specificity – for CHIIDA score >0 or >2 only *CHIIDA score >0 vs. score 0* **Sensitivity: 0.932 (95% CI 0.847 to 0.977)** **Specificity: 0.555 (95% CI 0.519 to 0.590)** **PPV: 0.166 (95% CI 0.132 to 0.206)**

Reference	Greenberg 2017[2]
	NPV: 0.988 (95% CI 0.973 to 0.996) Raw data reported in paper/calculated from measures reported in paper: TP, 68; FP, 341; TN, 425; FN, 5 *CHIIDA score >2 vs. score ≤2* **Sensitivity: 0.863 (95% CI 0.763 to 0.932)** **Specificity: 0.704 (95% CI 0.670 to 0.736)** **PPV: 0.217 (95% CI 0.171 to 0.269)** **NPV: 0.982 (95% CI 0.967 to 0.991)** Raw data reported in paper/calculated from measures reported in paper: TP, 63; FP, 227; TN, 539; FN, 10 Patients were followed up with standardized telephone surveys of guardians and/or medical record review 7 to 90 days post-ED visit to ensure no outcomes were missed. Events in composite outcome chosen because they indicated a significant objective worsening in a patient who initially appeared to have a minor head injury and indicated a strong need for critical care observation.
Comments	***Odds ratio results*** **Risk of bias (applies to all risk factors):** 1. Study participation — LOW 2. Study attrition — MODERATE 3. Prognostic factor measurement — MODERATE 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — LOW OVERALL RISK OF BIAS — HIGH **Indirectness (applies to all risk factors):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15

Reference	Greenberg 2017[2]
	• Outcome – follow-up duration varies between patients (7 days to 90 days), meaning some much longer and some much shorter follow-up than 30 days in protocol ***Sensitivity/specificity results*** **Risk of bias (QUADAS 2 – risk of bias):** very serious. Unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, unclear if there was missing data/all patients were analysed, unclear time interval between index test and reference standard likely different between patients (e.g. length of follow-up varied) **Indirectness (QUADAS 2 – applicability):** very serious: Population not limited to those with small intracranial injuries and outcome time-point indirectness as was much shorter/longer than 30 days in some patients (ranged from 7 to 90 days)

1

2

Reference	Joseph 2015[3]
Study type and analysis	Retrospective cohort study Multivariate logistic regression analysis including those that had P≤0.2 on univariate analyses
Number of participants and characteristics	N=876 • Age ≥65 years, n= not reported • Age <65 years, n= not reported • Subdural haemorrhage >10 mm, n= not reported • No subdural haemorrhage >10 mm, n= not reported • Epidural haemorrhage >10 mm, n= not reported • No epidural haemorrhage >10 mm, n= not reported

Reference	Joseph 2015[3]
	• Platelet ≤100,000 mm^{-3}, n= not reported • Platelet >100,000 mm^{-3}, n= not reported • Lactate ≤2.5 (units unclear), n= not reported • Lactate >2.5 (units unclear), n= not reported • Base deficit >4 (units unclear) – blood measure related to pH, n=36 • Base deficit ≤4 (units unclear) – blood measure related to pH, n=840 *Note that not all risk factors were included in the multivariate models for both outcomes* **Inclusion criteria:** aged ≥18 years; isolated traumatic brain injury (head Abbreviated Injury Score [AIS] ≥3 and other body region AIS score <3); GCS 13-15 on presentation (mild TBI); intracranial injury (skull fracture or intracranial haemorrhage) on initial head CT scan; and routine repeat head CT scan. **Exclusion criteria:** patients on antiplatelet (aspirin or clopidogrel) or anticoagulation therapy (warfarin); patients transferred from other institutions; and those undergoing emergency neurosurgical intervention. **Population characteristics:** given for whole cohort – continuous values are mean (SD) unless otherwise indicated • Age: 54.3 (21.5) years • Males, 65.5% • White, 83.0% • Injury type: ○ Falls, 42.0% ○ Motor vehicle accident, 30.0% • GCS, median (IQR): 15 (14-15) • Injury Severity Score (ISS), median (IQR): 15 (10-17)

Reference	Joseph 2015[3]
	• Head AIS, median (IQR): 2 (2-3) • ED systolic blood pressure: 141.8 (25.1) mmHg • ED heart rate: 88 (18.7) min^{-1} • Haemoglobin: 13.5 (6.2) g/dL^{-1} • Platelet count x 10^3: 182 (61) • Lactate: 2.2 (1.4), units unclear • Base deficit >4, 4.1% (units unclear) • Hospital length of stay: 3.6 (4.6) days • Intensive care unit length of stay: 1.2 (2.2) days • Mortality, 8.2% • Initial CT findings: ○ Skull fracture, 33.3% ○ Displaced skull fracture, 16.3% ○ Intracranial haemorrhage, 91.3% ○ Subdural haematoma, 41.0% ▪ ≥10 mm, 15.0% ○ Epidural haematoma, 6.7% ▪ ≥10 mm, 2.4% ○ Subarachnoid haemorrhage, 2.8% ○ Intraventricular haemorrhage, 4.0% ○ Intraparenchymal haemorrhage, 34.1% **Population source:** 3-year retrospective cohort (2009-2012) of patients presenting to a single level 1 trauma centre.
Prognostic variables	• **Age ≥65 years** • **Age <65 years (referent)** • **Subdural haemorrhage >10 mm**

Reference	Joseph 2015[3]
	• **No subdural haemorrhage >10 mm (referent)** • **Epidural haemorrhage >10 mm** • **No epidural haemorrhage >10 mm (referent)** • **Platelet ≤100,000 mm^{-3}** • **Platelet >100,000 mm^{-3} (referent)** • **Lactate ≤2.5 (units unclear)** • **Lactate >2.5 (units unclear) (referent)** • **Base deficit >4 (units unclear) – blood measure related to pH** • **Base deficit ≤4 (units unclear) – blood measure related to pH (referent)** Electronic medical records reviewed and information about demographics, vitals on presentation, laboratory data on presentation, initial and repeat head CT scan findings, neurosurgical intervention as well as other outcome information was obtained. Base deficit and lactate assess perfusion which when elevated can be associated with mortality. Low platelet may be associated with progression on routine repeat head CT. Initial and repeat head CT reviewed by single trauma surgeon for type of fracture, size and type of intracranial haemorrhage.
Confounders	Full list of factors included in multivariate analysis provided for each outcome: <u>Progression on repeat head CT</u> Loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4. <u>Neurosurgical intervention</u> Age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

Reference	Joseph 2015[3]
	Does not account for key confounder of GCS as in our protocol
Outcomes and effect sizes	**<u>Progression on repeat head CT – within 6 h</u>** **OR 1.4 (95% CI 0.7 to 2.7) for age ≥65 vs. <65 years** **OR 4.8 (95% CI 1.9 to 9.6) for subdural haemorrhage >10 mm vs. ≤10 mm** **OR 7.9 (95% CI 2.4 to 12.6) for epidural haemorrhage >10 mm vs. ≤10 mm** **OR 1.3 (95% CI 0.98 to 3.6) for platelet ≤100,000 vs. >100,000** **OR 2.1 (95% CI 0.89 to 2.50) for lactate ≤2.5 vs. >2.5** **OR 2.8 (95% CI 1.6 to 4.1) for base deficit >4 vs. ≤4** Outcome defined as development of new intracranial haemorrhage or increase in the size of the initial haemorrhage. All patients had routine repeat head CT within 6 h of initial CT scan. Scan was reviewed by single trauma surgeon for type of skull fracture and size and type of intracranial haemorrhage. Findings of repeat CT scan categorised as progressed or unchanged. N=115 had progression on repeat CT. **<u>Neurosurgical intervention – unclear time-point</u>** **OR 3.4 (95% CI 2.1 to 4.46) for subdural haemorrhage >10 mm vs. ≤10 mm** **OR 3.5 (95% CI 1.4 to 5.5) for epidural haemorrhage >10 mm vs. ≤10 mm** **OR 1.6 (95% CI 0.98 to 4.8) for platelet ≤100,000 vs. >100,000** **OR 1.9 (95% CI 0.62 to 3.1) for lactate ≤2.5 vs. >2.5** **OR 21.0 (95% CI 1.6 to 27.0) for base deficit >4 vs. ≤4** Outcome was defined as need for neurosurgical intervention, which included craniectomy or craniotomy. N=47 had neurosurgical intervention.
Comments	**Risk of bias (applies for all risk factors within each outcome): - <u>progression on repeat CT outcome</u>** 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — MODERATE

Reference	Joseph 2015[3]
	4. Outcome Measurement MODERATE 5. Study confounding HIGH 6. Statistical analysis LOW OVERALL RISK OF BIAS HIGH **Risk of bias (applies for all risk factors within each outcome): - <u>neurosurgical intervention outcome</u>** 1. Study participation LOW 2. Study attrition LOW 3. Prognostic factor measurement MODERATE 4. Outcome Measurement HIGH 5. Study confounding HIGH 6. Statistical analysis LOW OVERALL RISK OF BIAS HIGH **Indirectness (applies to both risk factors):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome: o For positive repeat CT, lesion progression on CT may not always lead to clinical deterioration – indirect relative to examples of outcomes in protocol which involve clinical effects such as death, readmission or seizures o For neurosurgical intervention, time-point unclear and possibly within same admission

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Reference	Kim 2014[4]
Study type and analysis	Retrospective study Multivariate logistic regression models built to control for potential compounding variables

Reference	Kim 2014[4]
Number of participants and characteristics	N=98 • Initial volume of lesion (ml) as a continuous variable (increments unclear), n=98 • Degree of midline shift (mm) as a continuous variable (increments unclear), n=98 • Maximum thickness of lesion (mm) as a continuous variable (increments unclear), n=98 **Inclusion criteria:** acute trauma-related subdural haematoma diagnosed on CT; mild head injury (GCS 13-15); no focal neurological deficits; no significant mass effect; no significant midline shift; relatively small volume of subdural haematoma; and medically managed at time of admission **Exclusion criteria:** urgent craniotomy performed and evacuation of haematoma within 24 h of admission; neurological deterioration within first 48 h following admission; moderate-severe head injury (GCS <13) at admission; vascular abnormality; subdural haemorrhage localised only to falx or tentorium cerebelli; bilateral acute subdural haematoma; <15 years old; other significant organ injury; and those refusing surgical treatment. **Population characteristics:** given for whole cohort – continuous values are mean (range) • Age: 65 (16-95) years • Male, 64.3% • GCS: o 13, 13.3% o 14, 21.4% o 15, 65.3% • Prior medical history: o Hypertension, 51.0% o Diabetes, 30.6% o Smoking, 20.4%

Reference	Kim 2014[4]
	○ Alcohol abuse, 33.7% ○ Use of anticoagulant, 5.1% ○ Use of antiplatelet, 28.65% • Laboratory finding: ○ Thrombocytopenia (<50,000), 10.2% ○ Prolonged prothrombin time (INR >1.4), 5.1% • Cause of head trauma ○ Fall from standing, 45.9% ○ Motor vehicle accident, 28.6% ○ Fall from a height, 12.2% ○ Assault, 6.1% ○ Bicycle accident, 7.1% • Subdural haematoma maximal thickness: 7.8 (2.0-19.0) mm • Subdural haematoma volume: 7.8 (3.5-119.7) • Midline shift degree: 3.0 (0.0-10.0) mm • Presence of cerebral contusion, 40.8% • Presence of subarachnoid haemorrhage, 37.8% **Population source:** retrospective review of inpatient database between January 2002 and December 2012. Likely single centre.
Prognostic variables	**Initial volume of lesion (ml) as a continuous variable (increments unclear)** **Degree of midline shift (mm) as a continuous variable (increments unclear)**

Reference	Kim 2014[4]
	Maximum thickness of lesion (mm) as a continuous variable (increments unclear) Patient charts reviewed for age, gender, cause of trauma, presence of other brain injury, GCS at admission and other clinical/medical history. Laboratory test data included for coagulation parameters. All patients had CT without contrast enhancement at time of diagnosis. All patients also had second CT within 8 h of initial CT scan and a third CT scan was obtained within 24 h in a subset of patients that had shown increase in volume of trauma-associated haemorrhage on second CT (there was no change in volume and no other intracranial pathology on this third scan). Radiological parameters including thickness of haematoma, midline shift etc. were reviewed on the final CT that had been acquired within the initial 24 h period following head trauma. Volume of haematoma calculated as follows: length x width x depth/2.
Confounders	Only reports variables included that were demonstrated to be independently significant so full list of variables in model is unclear: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present **Does not account for key confounder of GCS as in our protocol or is unclear if this was included**
Outcomes and effect sizes	**Haematoma enlargement leading to surgery – ~1 week following injury** **OR 2.519 (95% CI 0.154 to 41.104) for initial volume of lesion (ml) as a continuous variable (increments unclear)** **OR 1.094 (95% CI 1.021 to 1.173) for degree of midline shift (mm) as a continuous variable (increments unclear)** **OR 1.433 (95% CI 1.088 to 1.888) for maximum thickness of lesion (mm) as a continuous variable (increments unclear)** Repeat follow-up CT scans routinely performed in all patients at ~1 week after injury. Emergency scans performed for those presenting with unexpected neurological signs or symptoms. Patients were divided into those treated with operative management and those maintaining non-operative treatment based on neurological examinations, imaging findings, patient-advanced directives and other relevant clinical features. Those with stable neurological status without significant increase in haematoma volume were maintained with conservative management. Those with progressive neurological symptoms/signs unresponsive to medical treatment with pathological radiographic features (including haematoma enlargement leading to mass effect, midline shift and/or herniation) underwent surgery. Operations were performed as soon as possible by burr-hole drainage. Drainage maintained with standard silicone drains connected to collection bags placed for a minimum of 24 h.

Reference	Kim 2014[4]
Comments	**Risk of bias (applies to all risk factors):** 1. Study participation MODERATE 2. Study attrition LOW 3. Prognostic factor measurement MODERATE 4. Outcome Measurement MODERATE 5. Study confounding HIGH 6. Statistical analysis MODERATE OVERALL RISK OF BIAS HIGH **Indirectness (applies to all risk factors):** • Population – unclear if limits only to smaller injuries but some suggestion of this from patient flow chart; also limits only to those with GCS 13-15 • Risk factor – not on initial CT scan, all had two or three CT scans within 24 h period and suggests values on latest CT was used in the analysis, which may be indirect relative to current practice if usually/most of this group of patients only receive an initial CT. • Outcome – limited to period of 1 week since injury rather than ideal 30 days in protocol

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Reference	Lewis 2017[5]
Study type and analysis	Retrospective cohort study Multivariable logistic regression analysis (backward stepwise)
Number of participants and characteristics	N=500 consecutive patients (≥15 years) with bunt mild traumatic brain injury (TBI), GCS ≥ 13 and intracranial haemorrhage (ICH) admitted during a 28-month period from November 2010 to February 2013 at a Level I trauma centre (USA). Data source: Scripps Mercy Hospital trauma registry Exclusion criteria: no documentation of ICH according to ICD (9th revision) diagnosis codes 852.0, 852.1, 852.3, 852.4, 852.5, 853.1.

Reference	**Lewis 2017[5]**		
	Characteristics	No Neurosurgical intervention (n=451)	Neurosurgical intervention (n=49)
	Age, median (IQR)	62 (43-79)	59 (34-76)
	Male (%)	61.2	75.5
	Injury Severity Score, median (IQR)	17 (16-21)	25 (25-26)
	Head-AIS score, median (IQR)	4 (4-5)	5 (4-5)
	Loss of consciousness	59.2	51
	Abnormal neurological examination (%)	12.6	30.6
	Preinjury antiplatelet or anticoagulation (%)	30.4	30.6
	Skull fracture (%)	16	28.6
	Open skull fracture (%)	0.4	12.2
	ICH progression (new or larger on repeat CT) (%)	27.3	18.4
	Documented neurosurgical consultation (%)	92.5	100
	Mortality (%)	2	8.2
Prognostic variables	Head-Abbreviated Injury Scale (AIS) – unclear how analysed (e.g. per increment?)		
Confounders OR Stratification strategy	Factors that were statistically significant at P<0.05 were included in the final mode. These were: hospital length of stay, ICU length of stay, days of mechanical ventilation, head-AIS score, Injury Severity Score, skull fracture, abnormal initial neurological examination, subdural haemorrhage, subarachnoid haemorrhage.		
Outcomes and effect sizes	Outcome: Neurosurgical intervention – unclear time-point, possibly within initial admission Adjusted OR (95% CI) for each prognostic factor and p value: Head-AIS 12.87 (6.48-25.58) p <0.001 Secondary outcomes included ICU length of stay, hospital length of stay and in-hospital mortality but no adjusted effect sizes were calculated for these.		
Comments	**Risk of bias:**		

Reference	Lewis 2017[5]
	1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — MODERATE 4. Outcome Measurement — MODERATE 5. Study confounding — HIGH 6. Statistical analysis — MODERATE OVERALL RISK OF BIAS — HIGH **Indirectness:** • Population – not specific to those with small intracranial injuries, however does limit to GCS 13-15 • Outcome – neurosurgical intervention reported at unclear time-point, possibly initial management decision rather than assessing for longer time-point and including possible delayed interventions

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Reference	Marincowitz 2020[7]
Study type and analysis	Retrospective cohort study Multivariate backward elimination with statistical significance threshold of 0.1 used for model selection. All candidate predictors initially included and imputed datasets combined using Rubin's rules at each stage of model selection. Prognostic model developed was subsequently used to derive a risk score using optimism-adjusted coefficients. Individual patient risk scores were calculated. A risk score for ED discharge was proposed based on the trade-off between risk of deterioration in a discharged patient and number of patients admitted for observation. BIG criteria also assessed.
Number of participants and characteristics	N=1699 (n=1569 for clinical decision rules) • Score >0 on risk score developed in paper (admission), n=1482 – Hull Salford Cambridge Decision Rule • Score ≤0 on risk score developed in paper (discharge), n=87 – Hull Salford Cambridge Decision Rule

Reference	Marincowitz 2020[7]
	• BIG criteria, not BIG1 group (admission), n=1512 • BIG criteria, BIG1 group, n=57 • Age as continuous variable (per 1-unit increase), n=1699 • GCS 13, n=185 • GCS 14, n=533 • GCS 15, n=976 *Note: n=5 with missing data (0.3%), imputed* • Pre-injury anticoagulation or antiplatelets, n= 457 • No preinjury anticoagulation or antiplatelets, n=1242 • Abnormal first neurological examination, n=233 • Normal first neurological examination, n=1377 *Note: n=89 with missing data (5.2%), imputed* • Injury severity on CT (each versus simple skull fracture, n=66) – based on Marshall classification system ○ Complex skull fractures, n=123 ○ 1-2 bleeds <5 mm total, n=208 ○ No or minimal mass effect, n=1001 ○ Significant midline shift, n=159 ○ High/mixed density lesion (volume >25 ml, Marshall classification VI), n=122 ○ Cerebellar/brainstem injury, n=22 • Extracranial injury (body regions excluding head) as a continuous variable (per 1-unit increase on Injury Severity Scale; ISS), n=1699

Reference	Marincowitz 2020[7]
	• Rockwood Frailty Score (all compared to those <50 years old, n=649) ○ Scores 1-3, n=642 ○ Scores 4-6, n=308 ○ Scores 7-9, n=72 *Note: missing data for n=28 (1.6%), imputed* Note that not all of the risk factors listed above were included in the models for both outcomes. **Inclusion criteria:** ≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded) **Exclusion criteria:** non-traumatic cause of intracranial haemorrhage; pre-existing CT abnormalities preventing determination of whether acute injury had occurred; and patients transferred from other hospitals **Population characteristics:** given for whole cohort with missing data for some characteristics – continuous values are mean (SD) and range • Age: 58.2 (23.3) years, 16-101 years • Males, 67% • GCS: ○ 13, 11.0% ○ 14, 31.0% ○ 15, 58.0% • Mechanism of injury: ○ Assault, 13.0% ○ Fall, 64.0% ○ Fall from height, 21.0%

Reference	Marincowitz 2020[7]
	○ Road traffic collision, 18.0% ○ Sport, 1.0% ○ Other, 2.0% • Intoxicated, 29.0% • Seizure pre-hospital or in ED, 4.0% • Vomiting pre-hospital or in ED, 18.0% • Pre-injury anticoagulation or antiplatelets: ○ Anticoagulation, 9.0% ○ Antiplatelets, 17.3% ○ Both, 0.5% • Abnormal first neurological examination, 14.5% • Number of injuries on CT: ○ 1, 48.5% ○ 2, 23.6% ○ 3, 12.7% ○ 4, 8.4% ○ 5, 6.1% • Injury severity on CT – based on Marshall classification ○ Simple skull fractures, 3.9% ○ Complex skull fractures, 7.2% ○ 1-2 bleeds <5 mm (total), 12.2% ○ No or minimal mass effect, 58.9% ○ Significant midline shift, 9.4% ○ High/mixed density lesion, 7.2% ○ Cerebellar/brainstem injury, 1.2%

Reference	Marincowitz 2020[7]
	• Skull fracture (simple), 19.0% • Skull fracture (complex), 21.0% • Contusion, 34.0% • Extradural bleed, 8.0% • Intraparenchymal haemorrhage, 14.0% • Subdural bleed, 41.0% • Intraventricular bleed, 3.0% • Subarachnoid bleed, 32.0% • Rockwood Clinical Frailty Scale ○ Patients under 50 years old, 39.0% ○ Scores 1-3, 38.0% ○ Scores 4-6, 18.5% ○ Scores 7-9, 4.5% • Charlson Comorbidity Index: 1.4 (2.9), 0.0-28.0 • ISS (body regions excluding head): 5.2 (5.2), 0.0-75.0 **Population source:** case notes of patients presenting to ED of three major trauma centres between 2010 and 2017: Hull University Teaching Hospital NHS Trust, Salford Royal NHS Foundation Trust and Addenbrooke's Hospital. CT brain scan requests and reports screened to identify patients with traumatic findings and were subsequently matched to case records.
Prognostic variables	**Score >0 on decision rule developed in the paper – Hull Salford Cambridge Decision Rule** **Score ≤0 on decision rule developed in the paper – Hull Salford Cambridge Decision Rule** **Not BIG1 on BIG criteria** **BIG1 on BIG criteria** **Age as continuous variable (per 1-unit increase)**

Reference	Marincowitz 2020[7]
	GCS 13 **GCS 14** **GCS 15 (referent)** **Pre-injury anticoagulation or antiplatelets** **No pre-injury anticoagulation or antiplatelets (referent)** **Abnormal first neurological examination** **Normal first neurological examination (referent)** **Injury severity on CT – based on Marshall classification system** • **Complex skull fractures** • **1-2 bleeds <5 mm total** • **No or minimal mass effect** • **Significant midline shift** • **High/mixed density lesion (volume >25 ml, Marshall classification VI)** • **Cerebellar/brainstem injury** • **Simple skull fractures (referent)** **Extracranial injury (body regions excluding head) as a continuous variable (per 1-unit increase on ISS)** **Rockwood Frailty Score** • **Scores 1-3** • **Scores 4-6** • **Scores 7-9** • **Age <50 years (referent)**

Reference	Marincowitz 2020[7]
	For the decision rule developed in the paper (Hull Salford Cambridge Decision Rule), this was based on the multivariate model for clinical deterioration. Despite haemoglobin being a significant predictor of outcome in the multivariate model, it was not included as based on the small effect size and range of abnormal values, inclusion did not improve performance. Based on the trade-off between sensitivity and specificity, a patient risk score of 0 was used as a threshold for ED discharge. Patients at this cut-off had the following characteristics: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination. BIG criteria also assessed. Details of this rule obtained elsewhere: BIG 1 (minor head injury) had normal findings on neurological examination, were not taking any antiplatelet or anticoagulation medications, and had minuscule findings on an initial CT scan of the head; BIG2, moderately injured patients with a nondisplaced skull fracture and/or a localized ICH of 5 to 7 mm; BIG3, at least 1 of the following high-risk features: an abnormal neurological examination finding, intoxication, antiplatelet or anticoagulation medication use, concerning CT scan findings (displaced skull fractures, diffused subarachnoid haemorrhage, multiple types of bleeding, or an ICH ≥8 mm). Patients who could not be examined and those who were intubated were also categorized as BIG 3. Records were used to obtain data on variables including pre-injury anticoagulant therapy. Rockwood Frailty Scale scores assigned to patients >50 years of age using information in case notes and data collapsed into established categories. Injury severity coded using AIS, injury size and presence of midline shift or mass effect. AIS codes mapped to Marshall classification using method described by Lesko and colleagues and description of midline shift. An additional category of severity up to two injuries with combined maximal diameter <5 mm was added.
Confounders	<u>Model for outcome of deterioration</u> Multivariate analysis included: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase) <u>Model for outcome of neurological admission</u> Multivariate analysis included: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (categories described above under prognostic factors, versus people <50 years)

Reference	Marincowitz 2020[7]
	Models for both outcomes account for key confounder of GCS as in our protocol Clinical decision rule results Note that for results for the decision rule developed in the paper (Hull Salford Cambridge Decision Rule) and the BIG criteria, ORs were those based on raw data of those deteriorating/not deteriorating and either meeting or not meeting criteria for admission. There were no multivariate results as results were reported as prognostic accuracy (sensitivity/specificity) in the paper. As the decision rules are based on consideration of multiple factors rather than a single risk factor, the results were considered suitable to include despite the fact there is no adjustment. ORs were calculated from the paper and sensitivity/specificity data reported in the paper was also presented.
Outcomes and effect sizes	**Deterioration up to 30 days after ED attendance** *Decision rule developed in the paper* – Hull Salford Cambridge Decision Rule **OR 16.98 (95% CI 4.16 to 69.30)** – calculated from following data: 423/1482 deteriorating in score >0 group and 2/87 deteriorating in score ≤0 group **Sensitivity: 0.995 (95% CI 0.981 to 0.999)** **Specificity: 0.074 (95% CI 0.060 to 0.091)** **PPV: 0.285 (95% CI not reported)** **NPV: 0.977 (95% CI not reported)** Raw data reported in the paper were: TP, 423; FP, 1059; TN, 85; FN, 2 *BIG criteria* **OR 10.68 (95% CI 2.59 to 43.99)** – calculated from following data: 423/1512 deteriorating in BIG score >1 group and 2/57 deteriorating in BIG score 1 group **Sensitivity: 0.995 (95% CI 0.981 to 0.999)** **Specificity: 0.048 (95% CI 0.037 to 0.063)** **PPV: 0.280 (95% CI not reported)** **NPV: 0.965 (95% CI not reported)**

Reference	Marincowitz 2020[7]
	Raw data reported in the paper were: TP, 423; FP, 1089; TN, 55; FN, 2 *GCS* **OR 1.6 (95% CI 1.2 to 2.1) for GCS 14 vs. GCS 15** **OR 2.3 (95% CI 1.6 to 3.3) for GCS 13 vs. GCS 15** *Pre-injury anticoagulation or antiplatelets* **OR 1.4 (95% CI 1.03 to 1.80) for use vs. no use** *Abnormal neurological examination* **OR 1.7 (95% CI 1.2 to 2.3) for abnormal vs. normal neurological examination** *Haemoglobin* **OR 0.99 (95% CI 0.98 to 1.00) as a continuous variable per 1-unit increase (g/L)** *Injury severity on CT* **OR 1.4 (95% CI 0.5 to 4.3) for complex skull fractures vs. simple skull fracture** **OR 1.1 (95% CI 0.4 to 3.1) for 1-2 bleeds <5 mm (total) vs. simple skull fracture** **OR 2.3 (95% CI 0.9 to 5.9) for no or minimal mass effect vs. simple skull fracture** **OR 6.8 (95% CI 2.5 to 18.5) for significant midline shift vs. simple skull fracture** **OR 21.6 (95% CI 7.7 to 60.7) for high/mixed density lesion vs. simple skull fracture** **OR 7.0 (95% CI 1.9 to 25.7) for cerebellar/brainstem injury vs. simple skull fracture** *Extracranial injury* **OR 1.03 (95% CI 1.002 to 1.050) for ISS per 1-unit increase**

Reference	Marincowitz 2020[7]
	Outcome defined as composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI. Where reason for death, ICU admission or readmission was unknown it was attributed to TBI deterioration. **<u>Need for neurosurgical specialist admission up to 30 days after ED attendance</u>** *Age* **OR 0.997 (95% CI 0.9960 to 0.9989) as a continuous variable per 1-unit increase (years)** *GCS* **OR 2.3 (95% CI 1.6 to 3.3) for GCS 14 vs. GCS 15** **OR 3.7 (95% CI 2.3 to 5.9) for GCS 13 vs. GCS 15** *Abnormal neurological examination* **OR 1.9 (95% CI 1.3 to 3.0) for abnormal vs. normal neurological examination** *Haemoglobin* **OR 0.99 (95% CI 0.98 to 1.00) as a continuous variable per 1-unit increase (g/L)** *Injury severity on CT* **OR 0.9 (95% CI 0.5 to 4.9) for complex skull fractures vs. simple skull fracture** **OR 0.8 (95% CI 0.1 to 4.1) for 1-2 bleeds <5 mm (total) vs. simple skull fracture** **OR 2.3 (95% CI 0.5 to 9.7) for no or minimal mass effect vs. simple skull fracture** **OR 7.4 (95% CI 1.6 to 33.9) for significant midline shift vs. simple skull fracture** **OR 37.1 (95% CI 8.1 to 169.0) for high/mixed density lesion vs. simple skull fracture** **OR 8.5 (95% CI 1.3 to 56.2) for cerebellar/brainstem injury vs. simple skull fracture** *Extracranial injury* **OR 1.06 (95% CI 1.03 to 1.09) for ISS per 1-unit increase**

Reference	Marincowitz 2020[7]
	Rockwood Frailty Scale score **OR 1.9 (95% CI 1.1 to 3.1) for scores 1-3 vs. people <50 years** **OR 0.7 (95% CI 0.3 to 1.8) for scores 4-6 vs. people <50 years** **OR 0.09 (95% CI 0.01 to 0.70) for scores 7-9 vs. people <50 years** Outcome defined as composite of neurosurgery, ICU admission for TBI or intubation.
Comments	***Odds ratio results*** **Risk of bias – QUIPS (applies to all risk factors/outcome combinations): - differences for individual subdomains across risk factors indicated** 1. Study participation — LOW 2. Study attrition — MODERATE 3. Prognostic factor measurement — MODERATE OR HIGH *(abnormal neurological examination and haemoglobin had high rating, others moderate – same for both outcomes)* 4. Outcome Measurement — MODERATE 5. Study confounding — LOW 6. Statistical analysis — LOW OVERALL RISK OF BIAS — HIGH **Indirectness (applies to all risk factors/outcome combinations):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 ***Sensitivity/specificity results:*** **Risk of bias (QUADAS 2 – risk of bias):** very serious. Unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, people that did not have data for both

Reference	Marincowitz 2020[7]
	decision rules were excluded (missing data) and unclear if follow-up/reference standard for all patients consisted of the same components **Indirectness (QUADAS 2 – applicability):** serious: Population not limited to those with small intracranial injuries.

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Reference	Marincowitz 2022[6]
Study type and analysis	Retrospective – used Center-TBI data to validate two existing clinical decision rules (Hull Salford Cambridge Decision Rule and BIG criteria)
Number of participants and characteristics	N=1047 (N=961 for Hull Salford Cambridge decision rule and n=921 for BIG criteria) **Inclusion criteria:** ≥16 years old; presenting with GCS 13-15 attending ED following and either skull fracture, intracranial haemorrhage or cerebral contusion identified on first CT scan (regardless of care pathway) – said to reflect population used in derivation study. **Exclusion criteria:** initial GCS in the ED unknown; diffuse axonal injury sole injury on initial CT scan **Population characteristics:** given for whole cohort (missing data for some variables) – continuous values are mean (SD) and range • Age: 54.8 (19.7), 16-96 years • Age ≥65 years, 36.7% • Males, 66% • GCS: ○ 13, 10.6% ○ 14, 24.7% ○ 15, 64.7% • Admission/care pathway stratum: ○ ED, 8.3% ○ Admission, 56.0%

Reference	Marincowitz 2022[6]
	○ ICU, 35.6% • Mechanism of injury: ○ High velocity trauma, 20.1% ○ Blow to head/struck by object, 17.5% ○ Ground level fall, 36.7% ○ Fall from >1 m or 5 stairs, 20.8% ○ Other, 1.8% • Intoxicated, 23.1% • Preinjury anticoagulation/antiplatelets: ○ Anticoagulation, 6.9% ○ Antiplatelets, 12.8% ○ Both, 0.7% • Pre-injury anticoagulation or antiplatelets: ○ Anticoagulation, 9.0% ○ Antiplatelets, 17.3% ○ Both, 0.5% • Abnormal first neurological examination, 14.5% • Number of injuries on CT: ○ 1, 44.7% ○ 2, 23.2% ○ 3, 12.9% ○ 4, 7.7% ○ 5, 5.4% ○ Multiple diffuse injury/>5, 6.1%

Reference	Marincowitz 2022[6]
	• Injury severity on CT – based on Marshall classification ○ Simple skull fractures, 1.8% ○ Complex skull fractures, 6.4% ○ 1-2 bleeds <5 mm (total), 40.7% ○ No or minimal mass effect, 31.0% ○ Significant midline shift, 2.8% ○ High/mixed density lesion, 10.9% ○ Cerebellar/brainstem injury, 6.5% • ISS (body regions excluding head): 17.3 (20.6), 1-75 **Population source:** CENTER-TBI data collected between December 2014 and 2017 at 63 centres across Europe and Israel (all TBI severity. All patients initially managed in ED. Prospectively collected data by trained research staff. Follow-up data collected at 2-3 weeks, 3 months and 6 months with 83.4% having data collected at 6 months.
Prognostic variables	**Hull Salford Cambridge Decision Rule:** includes pre-injury anticoagulation or antiplatelets, first neurological examination, injury severity on CT and intoxication • **No indication to discharge vs. indication to discharge** ○ Following this rule, people would be discharged if: no anticoagulation or antiplatelets, GCS 15, normal first neurological examination, 1 injury only on initial CT, injury severity on CT was simple skull fracture or 1-2 bleeds <5 mm total and Injury Severity Score (body regions excluding head) was up to 2 non-significant extracranial injuries (not requiring inpatient care e.g. closed fracture humerus) **BIG criteria:** includes pre-injury anticoagulation or antiplatelets, first neurological examination, number of injuries on CT (1-5 or diffuse), injury severity on CT, and Injury Severity Score • **No indication to discharge vs. indication to discharge** ○ Following this rule, people would be discharged if: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated

Reference	Marincowitz 2022[6]
	To be recommended for discharge all components of Hull Salford Cambridge Decision Rule or BIG criteria must be fulfilled. Missing data (12.1% for Hull Salford Cambridge Decision Rule and not reported for BIG criteria) multiply imputed assuming they were missing at random. Performance averaged across imputed datasets.
Confounders	ORs were those based on raw data of those deteriorating/not deteriorating and either meeting or not meeting criteria for admission. There were no multivariate results as results were reported as prognostic accuracy (sensitivity/specificity) in the paper. As the decision rules are based on consideration of multiple factors rather than a single risk factor, the results were considered suitable to include despite the fact there is no adjustment. ORs were calculated from the paper and sensitivity/specificity data reported in the paper was also presented.
Outcomes and effect sizes	**Need for hospital admission – composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration (new deficit or drop in GCS of more than 1 point).** *Hull Salford Cambridge Decision Rule* **OR 23.33 (95% CI 1.42 to 382.05)** – calculated from following data: 234/927 with outcome in score >0 group and 0/34 with outcome in score 0 group **Sensitivity: 1.000 (95% CI 0.988 to 1.000)** **Specificity: 0.047 (95% CI 0.033 to 0.065)** **PPV: 0.252 (95% CI 0.225 to 0.282)** **NPV: 1.000 (95% CI 0.874 to 1.000)** Raw data reported in the paper were: TP, 234; FP, 693; TN, 34; FN, 0 *BIG criteria* **OR 2.69 (95% CI 1.44 to 5.00)** – calculated from following data: 210/816 with outcome in BIG score >1 group and 12/105 with outcome in BIG score 1 group **Sensitivity: 0.946 (95% CI 0.905 to 0.970)** **Specificity: 0.133 (95% CI 0.109 to 0.161)** **PPV: 0.257 (95% CI 0.228 to 0.289)**

Reference	Marincowitz 2022[6]
	NPV: 0.886 (95% CI 0.805 to 0.937) Raw data reported in the paper were: TP, 210; FP, 606; TN, 93; FN, 12
Comments	***Odds ratio results*** **Risk of bias: applies for both decision rules - QUIPS** 1. Study participation — LOW 2. Study attrition — MODERATE 3. Prognostic factor measurement — MODERATE 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — LOW OVERALL RISK OF BIAS — HIGH **Indirectness (applies to all risk factors/outcome combinations):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 ***Sensitivity/specificity results:*** **Risk of bias (QUADAS 2 – risk of bias):** very serious. Unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, people that did not have data for both decision rules were excluded (missing data) and unclear if follow-up/reference standard for all patients consisted of the same components **Indirectness (QUADAS 2 – applicability):** serious: Population not limited to those with small intracranial injuries.

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Reference	Nishijima 2014[9]
Study type and analysis	Prospective observational using binary recursive partitioning
Number of participants and characteristics	N=600 consecutive adult patients (≥18 years) with mild tICH on initial CT and initial GCS 13-15 presenting to a Level 1 trauma centre from July 2009 to February 2013 (USA) Exclusion criteria: patients with documented pre-existing “Do-Not-Resuscitate” (DNR) orders and patients with pre-injury anticoagulation use Characteristic n (%) Mean age (SD) 52 (22) Gender: Male 425 (70.8%) History of antiplatelet use 79 (13.2%) Injury severity Initial ED GCS score 13 32 (5.3%) Initial ED GCS score 14 162 (27.0%) Initial ED GCS score 15 406 (67.7%) Admission GCS score 15 396 (66.0%) Abbreviated injury score for head and neck, median (IQR) 4 (IQR 3–4) Injury severity score, median (IQR) 16 (IQR 10–20) Mortality at 48 hours 3 (0.5%)
Prognostic variable(s)	**Decision rule developed in paper, one or more of following: admission GCS <15, non-isolated head injury, age 65 years or older and the presence of swelling or shift on initial cranial CT vs. none** **Admission GCS <15 vs. 15 (referent)** **Non-isolated head injury vs. isolated head injury (referent)** **Age 65 years or older vs <65 years (referent)** **Presence of swelling or shift on initial cranial CT vs. none of these on CT (referent)**

Reference	Nishijima 2014[9]
	Presence of any high-risk comorbidity vs. presence of no high risk comorbidity (referent) **Preinjury antiplatelet use vs. no preinjury platelet use (referent)** **Hypoxia prior to admission vs. no hypoxia prior to admission (referent)** Demographic data from medical records and clinical data from emergency physicians.
Confounders OR Stratification strategy	Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury. <u>Clinical decision rule</u> OR was based on raw data of those with/without outcome and having at least one or none of the four variables included. There were no multivariate results as results were reported as prognostic accuracy (sensitivity/specificity) in the paper. As the decision rule is based on consideration of multiple factors rather than a single risk factor, the results were considered suitable to include despite the fact there is no adjustment. ORs were calculated from the paper and sensitivity/specificity data reported in the paper was also presented.
Outcomes and effect sizes	**Patient need for ICU admission (defined as the presence of an acute critical care intervention within 48 hours of emergency department arrival)** Binary recursive partitioning derived a decision instrument with the following four predictor variables for requiring an acute critical care intervention: **Admission GCS less than 15, RR (95% CI) 2.95 (2.12–4.12)** **Non-isolated head injury, RR (95% CI) 2.74 (1.99–3.78)** **Age 65 years or older, RR (95% CI) 1.46 (1.05–2.03)**

Reference	Nishijima 2014[9]
	Presence of swelling or shift on initial cranial CT, RR (95% CI) 4.11 (3.08–5.48) Also reports results for the following which appears to be multivariate results: **Presence of any high-risk comorbidity, 1.58 (1.07 to 2.33)** **Preinjury antiplatelet use, 1.54 (1.04 to 2.30)** **Hypoxia prior to admission, 1.52 (1.03 to 2.24)** <u>Clinical decision rule</u> **RR 37.48 (95% CI 9.15 to 153.49) for one or more risk factor in rule vs. none** – calculated from following data: 114/406 with outcome in group with at least 1 risk factor and 2/194 with outcome in group with no risk factors **Sensitivity: 0.983 (95% CI 0.939 to 0.995)** **Specificity: 0.397 (95% CI 0.354 to 0.441)** **PPV: 0.281 (95% CI 0.239 to 0.326)** **NPV: 0.990 (95% CI 0.963 to 0.997)** Raw data reported in the paper were: TP, 114; FP, 292; TN, 192; FN, 2
Comments	***Risk ratio results*** **Risk of bias (relevant for all risk factors) - QUIPS:** 1. Study participation — MODERATE 2. Study attrition — LOW 3. Prognostic factor measurement — LOW 4. Outcome Measurement — MODERATE 5. Study confounding — LOW 6. Statistical analysis — LOW OVERALL RISK OF BIAS — HIGH **Indirectness:**

Reference	Nishijima 2014[9]
	• Population – not specific to those with small intracranial injuries, but did limit to GCS 13-15 • Outcome – 48 h time-point is much shorter than 30 day time-point in the protocol ***Sensitivity/specificity results:*** **Risk of bias (QUADAS 2 – risk of bias):** very serious. Unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given decision rule was retrospectively applied and no mention of blinding, 20% of eligible patients were not included in analysis and unclear if follow-up/reference standard for all patients consisted of the same components **Indirectness (QUADAS 2 – applicability):** very serious: Population not limited to those with small intracranial injuries and outcome reported at 48 h time-point which is much shorter than 30 days in protocol

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Reference	Overton 2014[10]
Study type and analysis	Retrospective study Multivariate analysis was undertaken using backward-stepwise binary logistic regression analyses to measure the association of trauma versus neurosurgical management on outcome, while controlling for confounding effects such as age and GCS motor scores upon arrival to the emergency department
Number of participants and characteristics	N=171 • GCS motor scores on admission, possibly as a continuous measure (increments unclear), n=171 • Age as a continuous measure (increments unclear), n=171 • Injury Severity Score (ISS) as a continuous measure (increments unclear), n=171 **Inclusion criteria:** patients with mild TBI (defined as an intracranial haemorrhage of 1 cm or less and a GCS score of 13 or greater) at the time of arrival.

Reference	Overton 2014[10]
	Exclusion criteria: additional intracranial injuries (i.e. intraparenchymal haemorrhages, diffuse axonal injuries with white matter shearing) and patients transferred to another acute care facility or those who left against medical advice. **Population characteristics:** given separately for groups managed by trauma surgeons alone (n=51) vs. those managed by neurosurgeons (n=120) – continuous values are median (IQR): • Age: 48 (34-64) vs. 49 (29-71) years • 71% vs. 68% male • 58% vs. 65% white non-Hispanic • ISS: 17 (16-25) vs. 17 (16-21) • First ED systolic blood pressure: 132 (122-154) vs. 134 (120-146) mmHg • GCS: ○ 13, 6% vs. 6% ○ 14, 31% vs. 14% ○ 15, 63% vs. 80% • GCS motor: 6 (6-6) vs. 6 (6-6) • Mechanism of injury: ○ Fall, 42% vs. 48% ○ Motor vehicle, 31% vs. 23% ○ Assault, 15% vs. 13% ○ Motorcycle, 10% vs. 4% ○ Auto-pedestrian, 0% vs. 3% ○ Other, 2% vs. 8% • Glasgow Outcome Score: ○ Good recovery, 82% vs. 78% ○ Moderate disability, 14% vs. 14%

Reference	Overton 2014[10]
	○ Severe disability, 4% vs. 2% ○ Death, 0% vs. 7% • Discharge location: ○ Home, 82% vs. 79% ○ Facility, 18% vs. 13% ○ Other, 0% vs. 1% • Length of stay: 2 (1-5) vs. 3 (2-6) days • ICU length of stay: 1 (1-3) vs. 2 (1-5) days **Population source:** retrospective analysis of patients treated at a major urban level 1 trauma centre at a public institution over a period of 7 years (January 2006 to June 2012). Patients were monitored before (2006 to 2008) and after (2008 to 2012) the implementation of the protocol described in the paper (a protocol of selective neurosurgical consultation in 2008 that enabled trauma surgeons to manage patients with mild TBI without neurosurgical consultations).
Prognostic variables	**GCS motor scores on admission, possibly as a continuous measure (increments unclear)** **Age as a continuous measure (increments unclear)** **ISS as a continuous measure (increments unclear)** Data from trauma registry retrospectively analysed. Management by a trauma surgeon was defined by whether or not a neurosurgeon was consulted. Neurosurgical consultations could occur at any point during the patients' admission, so patients with a shift and neurosurgical consultation after initial examination were included in the neurosurgical management group. The need for neurosurgery consultation was at the discretion of the trauma surgeons.
Confounders	Full list of variables included in the model provided: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).

Reference	Overton 2014[10]
	Also reports that race/ ethnicity, sex distribution, length of stay and mechanism of injury were similar between the trauma and neurosurgery consultation groups – possibly not included in multivariate analysis for this reason. **Accounts for key confounder of GCS as in our protocol**
Outcomes and effect sizes	**Good outcome according to Glasgow Outcome Scale (GOS) – unclear time-point, possibly same admission?** **OR 13.96 (95% CI 2.23 to 87.3) for increasing GCS motor scores on admission (increments unclear, per 1-unit increase?)** **OR 0.94 (95% CI 0.91 to 0.96) for increasing age (increments unclear, for example if per every 1-year increment)** **OR 0.87 (95% CI 0.81 to 0.94) for increasing ISS (increments unclear, for example if per every 1-unit increase?)** GOS ranges from 1 to 4, with higher scores reflecting better outcomes. Patients were classified into 2 categories based on their GOS. Scores equal to or less than 3 suggest moderate to severe outcomes and scores greater than 3 suggest good outcomes.
Comments	**Risk of bias (applies to all risk factors):** 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — MODERATE 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — LOW OVERALL RISK OF BIAS — HIGH **Indirectness (applies to all factors):** • Population – none: limits to those with intracranial haemorrhage of 1 cm or less – some attempt to limit size of lesion in population

Reference	Overton 2014[10]
	• Outcome – GOS may not be a good representation of clinical deterioration and the time-point at which it is reported is unclear, possibly within the same admission which is a few days after injury in terms of median length of stay and much shorter than 30 days in protocol

1

Reference	Pruitt 2017[11]
Study type and analysis	Retrospective cohort study Multivariable logistic regression analysis model including variables significant in univariate analysis at 0.2 level. Binary version of final model created using same predictors.
Number of participants and characteristics	N=340 in derivation set and n=304 in validation set • Presence of any midline shift, n=84 • No midline shift, n=256 • Maximum subdural haemorrhage (SDH) thickness >5 mm, n=167 • Maximum SDH thickness ≤5 mm, n=173 • GCS 13, n=15 • GCS 14-15, n=325 • Warfarin use, n=53 • No warfarin use, n=287 • Clopidogrel use, n=28 • No clopidogrel use, n=312

Reference	Pruitt 2017[11]
	• Having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use, n=NR • Having none of the above listed high-risk predictors, n=NR **Inclusion criteria:** isolated subdural haemorrhage (included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions); GCS 13-15; and age ≥16 years **Exclusion criteria:** penetrating mechanism of injury; GCS <13; those with lesions other than SDH; and aged <16 years **Population characteristics:** given separately for those in derivation (n=340) and validation (n=304) cohorts • Mean (range) age: 67.9 (17-98) vs. 72.9 (18-99) years • Age ≥65 years, 62.4% vs. 71.4% • Male sex, 54.1% vs. 58.0% • Warfarin use, 15.6% vs. 14.8% • Aspirin use, 38.8% vs. 37.0% • Clopidogrel use, 8.2% vs. 4.3% • Alcohol use, 30.6% vs. 30.3% • Novel oral anticoagulant use, 0.0% vs. 1.3% • Mechanism of injury: ○ Fall, 77.4% vs. 82.9% ○ Motor vehicle collision, 6.5% vs. 5.2% ○ Assault, 5.9% vs. 6.2% ○ Pedestrian struck, 2.9% vs. 2.0% ○ Motorcycle, 1.8% vs. 0.0% ○ Cyclist, 1.8% vs. 1.3% ○ Other/unknown, 3.8% vs. 2.3%

Reference	Pruitt 2017[11]
	• Mental status on presentation: ○ GCS 15, 86.2% vs. 81.5% ○ GCS 14, 9.4% vs. 14.8% ○ GCS 13, 4.4% vs. 3.6% • Haematoma characteristics: ○ Number of SDH, mean (range): 1.4 (1-5) vs. 1.6 (1-5) ○ Thickness of largest haematoma, mean (range): 7.3 (0-35) vs. 9.5 (1-35) mm ○ Midline shift degree, mean (range): 1.3 (0-15) vs. 2.25 (0-18) mm • Disposition: ○ ICU, 17.4% vs. 16.8% ○ Floor, 49.7% vs. 41.5% ○ ED observation unit, 21.2% vs. 24.0% ○ Home from ED, 11.8% vs. 17.8% • Admitting service: ○ Neurosurgery, 19.4% vs. 21.4% ○ Trauma, 22.7% vs. 14.8% ○ Neurology, 14.4% vs. 13.2% ○ Medicine, 10.6% vs. 8.9% **Population source:** retrospective review of data from single urban academic level 1 trauma centre with annual ED volume of >100,000 visits. Identified through querying electronic medical record using ICD codes and further narrowed down based on individual record review. Derivation group between 1st January 2009 and 31st December 2013 and validation group between 1st January 2014 and 31st December 2015.
Prognostic variables	**Presence of any midline shift** **No midline shift (referent)**

Reference	Pruitt 2017[11]
	Maximum SDH thickness >5 mm **Maximum SDH thickness ≤5 mm (referent)** **GCS 13** **GCS 14-15 (referent)** **Warfarin use** **No warfarin use (referent)** **Clopidogrel use** **No clopidogrel use (referent)** **Having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use** **Having none of the above listed high-risk predictors (referent)** There were no missing values in any of the key predictors, so imputation was not required. Data extracted from physician notes, radiology reports, laboratory data and discharge summaries. Two emergency medicine physicians not blinded to study hypothesis but blinded to possible inclusion variables extracted derivation data. Validation data extracted by separate emergency medicine physician who was blinded to study hypothesis. Clinical variables were gathered from the initial emergency medicine and neurosurgery notes. Cranial CT results were categorised based on the finalised attending radiologist reports.
Confounders	Multivariate model for odds ratio results included: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel **Model for odds ratio results accounts for key confounder of GCS as in our protocol**

Reference	Pruitt 2017[11]
	Clinical decision rule results Note that for results for the decision rule developed in the paper, ORs were those based on raw data of those deteriorating/not deteriorating and either having at least one or having none of the high-risk predictors identified in the paper. There were no multivariate results as results were reported as prognostic accuracy (sensitivity/specificity) in the paper. As the decision rules are based on consideration of multiple factors rather than a single risk factor, the results were considered suitable to include despite the fact there is no adjustment. ORs were calculated and sensitivity/specificity data was also extracted and presented.
Outcomes and effect sizes	**Note that time-point measured at varied depending on the outcome. Follow-up via medical record review was obtained for patients who were discharged directly from the ED or from the observation unit. Follow-up was obtained for 88.3% of patients in the derivation set and 82.7% of patients in the validation set. Ninety percent of follow-up included clinical visits occurring greater than 30 days after initial presentation.** **Composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission** *Derivation set (n=340)* Odds ratios **OR 4.73 (95% CI 2.42 to 9.24) for any midline shift vs. no midline shift** **OR 5.1 (95% CI 2.42 to 9.24) for any max SDH thickness >5 mm vs. max SDH thickness ≤5 mm** **OR 4.09 (95% CI 1.18 to 14.22) for GCS 13 vs. GCS 14-15** **OR 2.21 (95% CI 0.98 to 5.01) for use of warfarin vs. no use of warfarin** **OR 2.70 (95% CI 0.99 to 7.31) for use of clopidogrel vs. no use of clopidogrel** **OR 41.84 (95% CI 5.72 to 305.86) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 71/239 of those with at least one risk factor and 1/100 of those with no risk factors having the outcome

Reference	Pruitt 2017[11]
	Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 0.986 (95% CI 0.926 to 1.000)** **Specificity: 0.371 (95% CI 0.313 to 0.432)** **PPV: not reported, calculated to be 0.30** **NPV: not reported, calculated to be 0.99** Raw data reported in paper/calculated from measures reported in paper: TP, 71; FP, 168; TN, 99; FN, 1 *Validation set (n=304)* Odds ratios **OR 12.13 (95% CI 3.70 to 39.75) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 79/231 of those with at least one risk factor and 3/73 of those with no risk factors having the outcome Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 0.963 (95% CI 0.897 to 0.992)** **Specificity: 0.315 (95% CI 0.255 to 0.381)** **PPV: not reported, calculated to be 0.34** **NPV: not reported, calculated to be 0.96** Raw data reported in paper/calculated from measures reported in paper: TP, 79; FP, 152; TN, 70; FN, 3 **Individual outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death)** *Derivation set (n=340)* **OR 10.49 (95% CI 1.40 to 78.80) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 23/240 of those with at least one risk factor and 1/100 of those with no risk factors having the outcome

Reference	Pruitt 2017[11]
	Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 0.958 (95% CI 0.789 to 0.999)** **Specificity: 0.313 (95% CI 0.263 to 0.368)** **PPV: not reported, calculated to be 0.10** **NPV: not reported, calculated to be 0.99** Raw data reported in paper/calculated from measures reported in paper: TP, 23; FP, 217; TN, 99; FN, 1 *Validation set (n=304)* Odds ratios **OR 2.82 (95% CI 0.61 to 12.51) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 17/231 of those with at least one risk factor and 2/73 of those with no risk factors having the outcome Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 0.895 (95% CI 0.669 to 0.987)** **Specificity: 0.249 (95% CI 0.200 to 0.304)** **PPV: not reported, calculated to be 0.07** **NPV: not reported, calculated to be 0.97** Raw data reported in paper/calculated from measures reported in paper: TP, 17; FP, 214; TN, 71; FN, 2 **Individual outcome - worsening repeat CT scan** *Derivation set (n=340)* **OR 20.70 (95% CI 1.24 to 344.61) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 22/240 of those with at least one risk factor and 0/100 of those with no risk factors having the outcome

Reference	Pruitt 2017[11]
	Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 1.00 (95% CI 0.846 to 1.00)** **Specificity: 0.314 (95% CI 0.264 to 0.369)** **PPV: not reported, calculated to be 0.09** **NPV: not reported, calculated to be 1.00** Raw data reported in paper/calculated from measures reported in paper: TP, 22; FP, 218; TN, 100; FN, 0 *Validation set (n=304)* Odds ratios **OR 7.58 (95% CI 1.00 to 57.24) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 22/231 of those with at least one risk factor and 1/73 of those with no risk factors having the outcome Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 0.957 (95% CI 0.781 to 0.999)** **Specificity: 0.256 (95% CI 0.206 to 0.311)** **PPV: not reported, calculated to be 0.10** **NPV: not reported, calculated to be 0.99** Raw data reported in paper/calculated from measures reported in paper: TP, 22; FP, 209; TN, 72; FN, 1 **Individual outcome – neurosurgical procedure (intracranial pressure monitoring or operations) during admission** *Derivation set (n=340)* **OR 41.81 (95% CI 2.55 to 686.72) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 41/240 of those with at least one risk factor and 0/100 of those with no risk factors having the outcome

Reference	Pruitt 2017[11]
	Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 1.00 (95% CI 0.914 to 1.00)** **Specificity: 0.334 (95% CI 0.281 to 0.391)** **PPV: not reported, calculated to be 0.17** **NPV: not reported, calculated to be 1.00** Raw data reported in paper/calculated from measures reported in paper: TP, 41; FP, 199; TN, 100; FN, 0 *Validation set (n=304)* Odds ratios **OR 23.59 (95% CI 3.20 to 173.60) for those with at least one risk factor vs. those with no risk factors in decision model –** calculated based on 57/231 of those with at least one risk factor and 1/73 of those with no risk factors having the outcome Sensitivity/specificity – for decision rule having at least one of following high-risk predictors: more than SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use **Sensitivity: 0.983 (95% CI 0.909 to 1.000)** **Specificity: 0.294 (95% CI 0.238 to 0.355)** **PPV: not reported, calculated to be 0.25** **NPV: not reported, calculated to be 0.99** Raw data reported in paper/calculated from measures reported in paper: TP, 57; FP, 174; TN, 72; FN, 1 Per protocol at the study hospital, all patients with traumatic intracranial haemorrhage received a neurosurgical consultation. Patients routinely underwent repeat neuroimaging at 6 hours and subsequently as indicated by the treating team. Initial disposition of these patients was governed by an institutional head trauma guideline, which considers clinical and subspecialty on-call factors. For patients discharged from the ED or the observation unit, records were reviewed for any subsequent traumatic intracranial haemorrhage-related

Reference	Pruitt 2017[11]
	admissions. Clinical variables were gathered from the initial emergency medicine and neurosurgery notes. Cranial CT results were categorised based on the finalised attending radiologist reports. Worsening repeat CT scan was defined as an increase in lesion size ≥ 2 mm, new midline shift, or the presence of a new area of haemorrhage. Patients who required burr-hole drainage for sub-acute or acute-on-chronic SDH were included in the neurosurgical intervention group, although these procedures were frequently performed on an elective basis. Patients deemed inoperable and transitioned to "comfort measures only" were included in the neurologic decline group. Clinical outcome variables were abstracted from discharge summaries; radiographic outcome variables were gathered from subsequent CT reports.
Comments	***Odds ratio results*** **Risk of bias (applies to all risk factors):** 1. Study participation — LOW 2. Study attrition — MODERATE 3. Prognostic factor measurement — LOW 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — LOW OVERALL RISK OF BIAS — HIGH **Indirectness (applies to all risk factors):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome – follow-up duration unclear, though ~90% had >30 days ***Sensitivity/specificity results*** **Risk of bias (QUADAS 2 – risk of bias):** very serious. Unclear if index test and reference standard were interpreted without knowledge of the other and unlikely given it was a retrospective application of the decision rule, >10% reported not to have follow-up data, unclear time interval between index test and reference standard and unclear if reference standard/follow-up may have had different components for each patient.

Reference	Pruitt 2017[11]
	Indirectness (QUADAS 2 – applicability): very serious: • Composite outcome: population not limited to those with small intracranial injuries and outcome time-point unclear and possibly different for each patient, possibly much shorter/longer than 30 days in protocol in many cases. Outcome also includes some events of worsening on CT which is a radiological outcome rather than clinical outcome. • Neurological decline outcome: population not limited to those with small intracranial injuries and outcome time-point unclear and possibly different for each patient, possibly much shorter/longer than 30 days in protocol in many cases. • Worsening on CT outcome: population not limited to those with small intracranial injuries and outcome time-point unclear and possibly different for each patient, possibly much shorter/longer than 30 days in protocol in many cases. Outcome limited to events of worsening on CT which is a radiological outcome rather than clinical outcome. • Neurosurgery outcome: population not limited to those with small intracranial injuries and outcome time-point unclear and possibly different for each patient, possibly much shorter/longer than 30 days in protocol in many cases.

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Reference	Schwed 2016[12]
Study type and analysis	Retrospective cohort study Multivariate regression analysis where factors that were statistically significant on univariate analysis were included, as well as clinically important factors
Number of participants and characteristics	N=201 • GCS 15 at admission to intensive care unit (ICU), n=129 • GCS <15 at admission to ICU, n=72 • Age <55 years, n= not reported • Age ≥55 years, n= not reported

Reference	Schwed 2016[12]
	Inclusion criteria: admitted with blunt head trauma to level 1 trauma centre; mild TBI (GCS 13-15) at arrival in ED; and intracranial haemorrhage of any variety confirmed on CT scan. **Exclusion criteria:** death within 24 h of admission; transferred from a different facility; required emergency surgical intervention within 24 h of presentation; who were not admitted to ICU; <18 years old; had missing records; left against medical advice; penetrating injuries; pregnancy; and being in police custody **Population characteristics:** given for whole cohort – continuous values are mean (SD) unless otherwise stated • Age, median (IQR): 60 (41-75) years • Male, 75.0% • Type of haemorrhage: ○ Epidural, 0.5% ○ Intraventricular haemorrhage, 2.0% ○ Subdural haemorrhage, 17.9% ○ Subarachnoid haemorrhage, 28.4% ○ Intraparenchymal haemorrhage, 10.0% ○ Combination, 41.3% • GCS 15 at time of admission, 64.0% • Neurosurgical intervention >24 h post-admission, 3.0% • Length of ICU stay: 2.9 (4.1) days, range 1-25 days • Length of hospital stay: 7.6 (8.7) days, range 1-65 days • Complication rate, 21.4% • In-hospital complications: ○ Urinary tract infection, 6.0% ○ Pneumonia, 4.0% ○ Seizure, 1.5%

Reference	Schwed 2016[12]
	• Achieved positive outcome, 39.0% • Mortality, 2.0% *Additional characteristics reported for those with favourable outcome (n=78) vs. unfavourable outcome (n=123) and not for whole cohort* • Injury Severity Score (ISS), median (IQR): 14.0 (10-17) vs. 17 (13-25) • Head Abbreviated Injury Score (AIS), median (IQR): 4 (3-4) vs. 3 (3-4) • Time to first head CT: 0.7 (0.7) vs. 0.9 (1.1) h • ED systolic blood pressure: 137 (24) vs. 148 (30) • ED heart rate: 87.5 (19.0) vs. 90.0 (15.5) • Marshall score, median (IQR): 2 (2-2) vs. 2 (2-2) • GCS at time of ICU admission, median (IQR): 15 (15-15) vs. 15 (14-15) **Population source:** retrospective review of people admitted to a single level 1 trauma centre into the ICU. Reviewed using trauma registry and individual medical records. Reviewed records between 1st July 2012 and 30th June 2015.
Prognostic variables	**GCS 15 at admission to ICU** **GCS <15 at admission to ICU (referent)** **Age <55 years** **Age ≥55 years (referent)** Patient details were reviewed from trauma registry and individual medical records. This included demographics, admission vital signs, severity scores, timing and results of radiological imaging, outcomes such as intervention and length of stay.
Confounders	Appears to only provide results for those factors that were significant on multivariate analysis but describes full list that were included in the model: GCS of 15 at admission to ICU, isolated subarachnoid haemorrhage, age <55 years, ED blood pressure, Marshall score, head AIS, and ISS <25 **Accounts for key confounder of GCS as in our protocol**

Reference	Schwed 2016[12]
Outcomes and effect sizes	**<u>Favourable outcome – time-point unclear, appears to be within hospital admission (mean hospital length of stay 7.6 days)</u>** **OR 5.5 (95% CI 1.6 to 18.8) for GCS of 15 vs. <15 at admission to ICU** **OR 3.5 (95% CI 1.1 to 11.2) for age <55 vs ≥55 years** Outcome was a composite including the following: alive at discharge, required ICU admission for a maximum of 24 h, had no in-hospital complications (e.g. pneumonia, urinary tract infection or seizures) and did not require neurosurgical intervention during their hospital stay. Patients not considered to have favourable outcome if ICU-level care required for another indication (ventilator management for respiratory failure, vasopressor or inotrope therapy for cardiac failure, etc.) that would have precluded them from a 24 h admission solely for neuromonitoring. N=78 met criteria for favourable outcome.
Comments	**Risk of bias (applies to both risk factors):** 1. Study participation LOW 2. Study attrition MODERATE 3. Prognostic factor measurement LOW 4. Outcome Measurement MODERATE 5. Study confounding MODERATE 6. Statistical analysis MODERATE OVERALL RISK OF BIAS HIGH **Indirectness (applies to both risk factors):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome – not at time-point of 30 days but limits to in-hospital outcome

1

Reference	Shih 2016[13]
Study type and analysis	Retrospective study Multivariate stepwise logistic regression analysis was used to evaluate the relationship between significant variables and therapeutic outcomes, with adjustments made for other potential confounding factors. Variables with zero cell count in a 2-by-2 table were eliminated from logistic analysis and only variables with strong association with poor outcome (P<0.05) were included in the final model.
Number of participants and characteristics	N=340 • Epidural haemorrhage (EDH) volume as a continuous variable (per 1 cubic centimetre increase), n=340 **Inclusion criteria:** adult patients (15–75 years) with acute TBI and traumatic intracranial haemorrhage on initial brain CT admitted within 24 h after onset of acute TBI to single hospital in Taiwan; and initial management was non-operative – included EDH, subdural haemorrhage (SDH), intraparenchymal haemorrhage (IPH), and subarachnoid haemorrhage (SAH). **Exclusion criteria:** penetrating head injury or gunshot wound; moderate-to-severe TBI (Glasgow Coma Score <13); no traumatic intracranial haemorrhage found on initial brain CT; immediate neurosurgical intervention on admission; and only chronic intracranial haemorrhage in the initial brain CT. **Population characteristics:** given for whole cohort – continuous values are median (IQR) • Age, 50 (32-60.75) years • 40.3% female • GCS on admission: o 13, 5.3% o 14, 19.4% o 15, 74.6% • Mechanism of injury: o Assault, 2.0% o Fall, 21.5% o Traffic accident, 75.3%

Reference	Shih 2016[13]
	• ISS score on admission: 10 (9-16) • Antiplatelet and/or warfarin therapy, 3.8% • Underlying disease: ○ Hypertension, 26.8% ○ Diabetes mellitus, 15.0% ○ Previous cerebral vascular accident, 2.6% ○ Coronary artery disease, 2.4% ○ Arrhythmia, 1.8% ○ Liver cirrhosis, 1.5% ○ Chronic kidney disease, 2.1% ○ Renal failure, 1.5% • ICU length of stay: 1 (0-3) days • Hospital length of stay: 8 (5-12) days *Additional characteristics only reported for delayed neurosurgical intervention (n=13) vs. no delayed neurosurgical intervention (n=327) groups:* • Hypotension, 0.0 vs. 1.2% • Haemoglobin: 14.10 (12.85-14.90) vs. 13.60 (12.30-15.00) • Coagulopathy, 0.0 vs. 3.1% • Single intracranial haemorrhage, 46.2% vs. 66.1% • Multiple intracranial haemorrhages, 53.8% vs. 33.9% • Type of intracranial haemorrhage: ○ EDH, 46.2% vs. 8.0% ○ SDH, 46.2% vs. 48.6% ○ IPH, 46.2% vs. 32.1% ○ SAH, 23.1% vs. 54.4%

Reference	Shih 2016[13]
	○ IVH, 33.4% vs. 0.6% ○ Midline shift, 33.4% vs. 3.1% ○ Skull fracture, 14.3% vs. 20.2% ○ Pneumocranium, 0.0% vs. 9.8% • Volume of haemorrhage in initial CT: ○ Volume of EDH: 30.98 (9.68-46.86) vs. 2.20 (0.67-6.71) ○ Volume of SDH: 4.56 (1.13-17.83) vs. 1.32 (0.15-5.38) ○ Volume of IPH: 2.33 (0.11-7.3) vs. 0.59 (0.11-2.53) **Population source:** single-centre retrospective study. Kaohsiung Chang Gung Memorial Hospital, a 2715-bed acute-care teaching medical centre in southern Taiwan providing both primary and tertiary referral care.
Prognostic variables	**EDH volume as a continuous variable (per 1 cubic centimetre increase)** Demographic information, mechanism of injury, initial vital signs, GCS, complete physical and neurologic examination, laboratory data and ISS were all assessed. Brain CT performed shortly after arriving at the ED. Repeat CT scans performed upon clinical deterioration (e.g., acute-onset focal neurologic deficits, seizures, status epilepticus, or progressively disturbed consciousness) and as routine post-neurosurgical procedure. The principal investigator reviewed all of the initial and follow-up CT scans. In equivocal cases, a second observer made the review. Both were blinded to the laboratory results at the time of clinical and radiologic assessment.
Confounders	Has adjusted for certain factors but does not list those included, only states that results for risk factor of EDH volume was only significant predictor. **Unclear if accounts for key confounder of GCS as in our protocol**
Outcomes and effect sizes	**Delayed neurosurgical intervention (indicating failure of initial non-operative management) – median time of surgical intervention after injury was 67.7 (IQR 11.7, 130.9) h (median hospital stay whole cohort was 8 days)** **OR 1.190 (95% CI 1.041 to 1.362) for EDH volume as a continuous variable (per 1 cubic centimetre increase)**

Reference	Shih 2016[13]
	Criteria for non-operative management were primarily based on the clinical and radiographic findings upon admission, including alert mental status, absent lateralising signs, basal cistern effacement or obliteration, and midline shift <5 mm. Initial neuro-surgical intervention was defined as an operation done immediately while the patient was at the emergency department. Delayed neuro-surgical intervention was defined as an operation done after the failure of non-operative management. All patients received complete medical and neurologic examinations, and brain CT. Neurosurgeon would be consulted to assessment of neuro-surgical intervention in the ED. Neuro-radiologists correlated the neuro-imaging findings. A neurosurgeon evaluated the acute TBI patients and decided on initial neuro-surgical intervention or non-operative management. Neurosurgical intervention was defined as placement of craniotomy or craniectomy with or without an intracranial pressure monitor. Patients with intracranial pressure monitor placed were excluded in the neurosurgical group. N=13 with event of delayed neurosurgical intervention.
Comments	**Risk of bias:** 1. Study participation — MODERATE 2. Study attrition — LOW 3. Prognostic factor measurement — MODERATE 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — MODERATE OVERALL RISK OF BIAS — HIGH **Indirectness:** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome – unclear time-point, possibly within same admission rather than follow-up close to 30 days in protocol

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Reference	Sweeney 2015[14]
Study type and analysis	Retrospective study

Reference	Sweeney 2015[14]
	Multiple logistic regression, with independent variables including age, presence of coagulopathy, ED vital signs, Injury Severity Score (ISS) and head injury type. Also run as mixed-effects model with different hospital facilities as random-effects variable to control for centre effect.
Number of participants and characteristics	N=50,496 (n=33,327 analysed as part of the training set) • Age as a continuous variable (years, unclear if 1-unit increments), n=33,327 • Anticoagulation disorder, n= not reported for analysed subset • No anticoagulation disorder, n= not reported for analysed subset • ED GCS unclear how analysed, possibly as GCS 15 vs. 14, n=33,327 • ISS category *ISS 7-11, n= not reported for analysed subset* *ISS 12-18, n= not reported for analysed subset* *ISS 19-27, n= not reported for analysed subset* *ISS >27, n= not reported for analysed subset* *ISS 0-6, n= not reported for analysed subset* **Inclusion criteria:** aged ≥18 years; diagnosis of intracranial injury (851.0-854.9 based on ICD-9-CM); admitted to the hospital; and GCS of 14-15 in the ED **Exclusion criteria:** skull fracture diagnoses (800-801.9 and 803-804.9) not included as ICD-9-CM codes don't distinguish between type of intracranial lesions that are present and open fractures are an indication for operative intervention meaning it is difficult to assess intracranial injury progression; penetrating mechanism of injury; Abbreviated Injury Scale (AIS) score >1 in any body region other than head; and missing data about ED vital signs. **Population characteristics:** given for the whole cohort – continuous values are mean (SD)

Reference	Sweeney 2015[14]
	• Male, 60.2% • Age: 60.6 (20.5) years • ED GCS: 14.8 (0.4) • ED systolic blood pressure: 144.4 (26.4) • ED pulse: 85.3 (18.0) • ED respiratory rate: 18.1 (3.7) • ISS at discharge: 13.7 (6.5) • Brain injury pattern: ○ Isolated contusion, 11.2% ○ Isolated subarachnoid haemorrhage, 26.1% ○ Isolated subdural haemorrhage, 37.2% ○ Isolated epidural haemorrhage, 1.8% ○ Multiple injury types, 23.7% • Comorbidities: ○ Total comorbidities: 0.9 (1.1) ○ Presence of coagulopathy, 4.6% • ED disposition: ○ Observation unit, 1.6% ○ Floor bed, 26.4% ○ Telemetry/step-down unit, 10.5% ○ Intensive care unit, 57.5% ○ Operating room, 4.0% • Outcomes: ○ Length of stay: 5.4 (6.5) days ○ Death during admission, 3.2%

Reference	Sweeney 2015[14]
	Population source: data from National Trauma Data Bank (NTDB) used from 2007 to 2012, with 2012 being year with most recent data available. National database covering multiple centres.
Prognostic variables	**Age as a continuous variable (years, unclear if 1-unit increments)** **Anticoagulation disorder** **No anticoagulation disorder (referent)** **ED GCS – unclear how analysed, possibly as GCS 15 vs. 15** ***ISS category*** **ISS 7-11** **ISS 12-18** **ISS 19-27** **ISS >27** **ISS 0-6 (referent)** ISS calculated from AIS severity codes extracted with the assumption that increasing ISS is solely due to worsening severity of head injury. Coagulopathy defined as any condition placing patient at risk for bleeding where there is a problem with the body's blood clotting process (e.g. vitamin K deficiency, haemophilia, thrombocytopenia, chronic anticoagulation therapy with Coumadin/warfarin, Plavix or similar medications) – this did not include those taking chronic aspirin therapy.
Confounders	Appears to give full list of factors included in the multivariate analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion). **Accounts for key confounder of GCS as in our protocol**
Outcomes and effect sizes	**Neurosurgical intervention – unclear time-point, possibly within same admission?** **OR 1.002 (95% CI 0.999 to 1.01) for age as a continuous variable (years, unclear if 1-unit increments)**

Reference	Sweeney 2015[14]
	OR 0.853 (95% CI 0.66 to 1.09) for anticoagulation disorder vs. no anticoagulation disorder **OR 0.894 (95% CI 0.781 to 1.03) for ED GCS (unclear how analysed, possibly GCS 15 vs. 14)** ***ISS groupings*** **OR 2.35 (95% CI 1.44 to 4.09) for ISS 7-11 vs. ISS 0-6** **OR 3.37 (95% CI 2.06 to 5.86) for ISS 12-18 vs. ISS 0-6** **OR 18.9 (95% CI 11.6 to 33.0) for ISS 19-27 vs. ISS 0-6** **OR 7.01 (95% CI 3.79 to 13.4) for ISS >27 vs. ISS 0-6** Outcome defined as having either an operative neurosurgical procedure or placement of neuromonitoring device (e.g. Camino bolt or endoventricular drainage catheter). Surgery and placement of catheters identified using ICD-9-CM procedure codes of 01-02. Overall rate of intervention was 8.8% (n=4444 – not reported for analysed subset).
Comments	**Risk of bias (variations for each risk factor indicated below):** 1. Study participation — LOW 2. Study attrition — MODERATE 3. Prognostic factor measurement — MODERATE/HIGH (high for age and GCS, moderate for others) 4. Outcome Measurement — HIGH 5. Study confounding — LOW 6. Statistical analysis — LOW OVERALL RISK OF BIAS — HIGH **Indirectness (applies to all risk factors):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 14-15 • Outcome – unclear time-point, possibly shorter term/during same hospital admission rather than capturing events within 30 days

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Reference	Thorson 2013[15]
Study type and analysis	Retrospective study Multivariate stepwise logistic regression used to identify predictors, variables with P<0.2 entered into model
Number of participants and characteristics	N=360 • GCS 13, n=59 • GCS 14, n=108 • GCS 15, n=193 • ISS as a continuous variable (unclear increment in analysis), n=360 • Mass effect on CT, n=62 • No mass effect on CT, n=298 **Inclusion criteria:** Adults arriving with GCS 13-15; head Abbreviated Injury Scale (AIS) score of at least 1; repeat CT scan within 24 h; and no associated injuries (AIS score 0 for chest, abdomen, extremity and external). **Exclusion criteria:** penetrating trauma; pregnant; <18 years; incarcerated; and transferred from outside hospitals. **Population characteristics:** given for whole cohort – continuous values are mean (SD) • Age: 47 (21) years • Male, 73.0% • Arrival GCS score: ○ 13, 16.0% ○ 14, 30.0% ○ 15, 54.0%

Reference	Thorson 2013[15]
	• Head AIS score: ○ 1, 2.0% ○ 2, 5.0% ○ 3, 43.0% ○ 4, 39.0% ○ 5, 10.0% • CT findings ○ Time to CT: 78 (77) min ○ Subarachnoid haemorrhage, 64.0% ○ Subdural haemorrhage, 40.0% ○ Epidural haemorrhage, 7.0% ○ Intraparenchymal haemorrhage, 57.0% ○ Intraventricular haemorrhage, 5.0% ○ Fracture, 37.0% ○ Mass effect, 17.0% • Repeat head CT data: ○ Time from initial CT, 8 (6) h ○ Recalled, 11.0% ○ Stable, 59.0% ○ Worse, 30.0% • Outcomes: ○ Operative intervention, 8.0% ○ Mortality, 6.0% ○ Hospital length of stay: 5 (6) days

Reference	Thorson 2013[15]
	Additional characteristics given for those with no change (n=252) vs. those with progression (n=108) on repeat head CT and not for overall population • Intubated, 71% vs. 79% • ISS: 12 (5) vs. 15 (6) • Coagulation data: ○ Anticoagulant use, 7.0% vs. 10.0% (including aspirin, Plavix, Coumadin/warfarin, low-molecular weight heparin) • Number of CT findings: 2.3 (1.3) vs. 3.0 (1.4) • 2+ findings, 64% vs 85% • 3+ findings, 37% vs. 58% • Intensive care unit admission, 19% vs. 53% • Intensive care unit length of stay: 0 (0) vs. 2 (7.0) days **Population source:** registry of a single urban level 1 trauma centre queried for patients matching protocol between January 1996 and May 2010.
Prognostic variables	**GCS 13** **GCS 14** **GCS 15 (referent)** **ISS as a continuous variable (unclear increment in analysis)** **Mass effect on CT** **No mass effect on CT (referent)** Trauma registry, resuscitation flow sheets, operative/anaesthesia reports, physician progress notes, ICU records and medical examiner reports of people undergoing repeat CT were reviewed for details about demographics, clinical findings, operative intervention and outcomes.
Confounders	Appears to only report those that were significant in multivariate analysis so full list not provided:

Reference	Thorson 2013[15]
	• For head CT progression outcome: GCS score 13 or 14 vs. GCS score 15; ISS as a continuous variable (increments unclear) and mass effect vs. no mass effect on CT • For craniotomy outcome: initial mass effect, new/worse epidural haemorrhage on repeat CT, new/worse mass effect on repeat CT and new/worse herniation on repeat CT **Accounts for key confounder of GCS as in our protocol for <u>head CT progression outcome but not for the craniotomy outcome</u>**
Outcomes and effect sizes	**<u>Head CT progression on repeat CT – within 24 h</u>** **OR 4.00 (95% CI 2.02 to 7.93) for GCS 13 vs. GCS 15** **OR 3.11 (95% CI 1.77 to 5.48) for GCS 14 vs. GCS 15** **OR 1.07 (95% CI 1.02 to 1.12) for ISS as a continuous variable (unclear increment in analysis)** **OR 2.02 (95% CI 2.02 to 3.78) for mass effect vs. no mass effect on CT** Repeat head CTs judged as stable (no change), worse or recalled (negative repeat CT finding, initial finding no longer present). Worsening of repeat CT finding defined as any of following: 1. Increase in size, progression or worsening of a previously identified lesion; 2. Increased oedema, mass effect, midline shift, herniation; and/or 3. Development of a new intracranial lesion. N=108 had progression on repeat CT. Institutional protocol across 15-year period was for patients with initial positive head CT to have urgent neurosurgical consultation. Those with indications for immediate operation (craniotomy, craniectomy or haematoma evacuation), those with isolated skull fracture, clearly nonsurvivable injuries or minimal injuries did not undergo repeat radiological examination (and therefore not included in this study). Remaining patients had repeat head CT ordered for 4-6 h after initial CT. **<u>Craniotomy performed – time-point unclear</u>** **OR 5.24 (95% CI 1.96 to 14.1) for initial mass effect vs. no initial mass effect on CT** No definition provided but possibly includes craniotomy, craniectomy or haematoma evacuation mentioned in another section of the paper. N=30 had operative intervention.
Comments	**Risk of bias (variations between risk factors/outcomes noted):** 1. Study participation LOW

Reference	Thorson 2013[15]	
	2. Study attrition	LOW
	3. Prognostic factor measurement	MODERATE
	4. Outcome Measurement	LOW/MODERATE (low for progression on CT outcome and moderate for operative intervention outcome)
	5. Study confounding	MODERATE
	6. Statistical analysis	MODERATE
	OVERALL RISK OF BIAS	HIGH
	Indirectness (applies to both risk factors): • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome: ○ For progression on CT outcome: lesion progression on CT may not always lead to clinical deterioration – indirect relative to examples of outcomes in protocol which involve clinical effects such as death, readmission or seizures ○ For operative intervention outcome: unclear time-point, possibly shorter term/during same hospital admission rather than capturing events within 30 days	

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Reference	Tourigny 2021[16]
Study type and analysis	Retrospective cohort study Multivariate models performed using multiple logistic regression models. Predictors significant at 10% level in univariate logistic models were considered for inclusion in the multiple logistic regression model. Models further refined using backwards selection at 5% level.
Number of participants and characteristics	N=478 • Subdural haemorrhage width ≥4 mm, n=204 • No subdural haemorrhage ≥4 mm, n=274 • Midline shift, n=72

Reference	Tourigny 2021[16]
	• No midline shift, n=406 • Unilateral weakness on neurological assessment, n=19 • No unilateral weakness on neurological assessment, n=459 **Inclusion criteria:** aged ≥16 years; directly or transferred to one of participating centres between September 2016 and December 2017; diagnosed with complicated mild TBI (GCS 13-15 and either one of four following criteria: altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24, focal neurological deficit; and a complication including intracranial haemorrhage or skull fracture on initial head CT) **Exclusion criteria:** penetrating injury; cerebral tumour; and cerebral aneurysm. **Population characteristics:** given separately for those with no neurosurgical intervention (n=438) and those having neurosurgical intervention (n=40) – continuous variables given as mean (SD) • Age: 62.6 (21.2) vs. 66.4 (18.4) years • ≥65 years, 54.8% vs. 60.0% • ≥55 years, 69.2% vs. 77.5% • Male, 68.3% vs. 70.0% • Intoxication, 16.1% vs. 15.0% • Medical history: ○ Coagulopathy, 0.2% vs. 2.5% ○ Neoplasia, 3.9% vs. 5.0% ○ Hypertension, 44.1% vs. 62.5% ○ Pulmonary embolism or thrombophlebitis, 0.5% vs 0.0% ○ Diabetes, 17.4% vs. 25.0% ○ Coronary artery disease, 16.4% vs. 27.5% ○ Dyslipidaemia, 34.0% vs. 45.0% ○ Stroke, 4.6% vs. 5.0%

Reference	Tourigny 2021[16]
	○ Liver failure, 1.1% vs 0.0%1. • Initial symptoms: ○ Amnesia, 62.1% vs. 37.5% ○ Loss of consciousness, 45.2% vs. 20.0% ○ Confusion, 35.6% vs. 37.5% ○ Nausea and/or vomiting, 19.6% vs. 8.0% ○ Headache, 32.2% vs. 42.5% ○ Seizure, 2.5% vs. 2.5% ○ Paresthesia, 1.4% vs. 12.5% • Initial signs: ○ Scalp haematoma, 11.0% vs. 5.0% ○ Unilateral weakness, 2.5% vs. 20.0% ○ Unilateral sensory loss, 1.1% vs. 2.5% ○ Abnormal cranial nerve examination, 4.3% vs. 2.5% ○ Pronator drift, 0.2% vs. 0.0% ○ Pupillary asymmetry, 2.5% vs. 0.0% ○ Loss of balance, 0.5% vs. 2.5% ○ Aphasia, 3.4% vs. 2.5% ○ Hemispatial neglect, 0.2% vs. 0.0% • Vital signs: ○ Abnormal systolic blood pressure, 42.9% vs. 65.0% ○ Abnormal diastolic blood pressure, 19.0% vs. 35.0% ○ Abnormal heart rate, 13.5% vs. 17.5% ○ Abnormal respiratory rate, 23.1% vs. 16.2%

Reference	Tourigny 2021[16]
	• Initial GCS <15, 37.0% vs. 35.0% • Anticoagulant use: 11.1% vs. 10.0% • Antiplatelet use: 26.7% vs. 20.0% • Injury mechanism: ○ Fall from height, 41.6% vs. 69.2% ○ Fall from more than height, 23.5% vs. 10.3% ○ Motorised vehicle accident (passenger), 12.0% vs. 7.7% ○ Motorised vehicle accident (pedestrian), 8.1% vs. 5.1% ○ Sport, 2.1% vs. 7.7% ○ Recreational injury, 9.2% vs. 0.0% ○ Physical abuse, 3.7% vs. 0.0% • Other trauma: ○ Cervical, 8.6% vs. 0.0% ○ Thoracic, 41.1% vs. 0.0% ○ Abdominal, 0.6% vs. 0.0% ○ Lumbar, 9.1% vs. 0.0% ○ Facial, 40.6% vs. 8.0% • Head CT findings: ○ Fracture, 29.0% vs. 22.5% ○ Subarachnoid haematoma, 57.1% vs. 25.0% ○ Subdural haematoma, 58.0% vs. 95.0% ▪ ≥4 mm, 38.6% vs. 87.5% ○ Epidural haematoma, 8.9% vs. 2.5% ○ Intraparenchymal haemorrhage (intraparenchymal + contusion), 34.7% vs. 22.5% ○ Intraventricular haematoma, 7.5% vs. 2.5% ○ Multiple haemorrhages, 45.0% vs. 23.1%

Reference	Tourigny 2021[16]
	○ Hernia, 0.4% vs. 5.0% ○ Sub-facial hernia, 1.6% vs. 12.5% ○ Midline shift, 10.5% vs. 65.0% ○ Diffuse axonal injury, 0.5% vs. 0.0% ○ Radiological deterioration, 18.2% vs. 7.5% **Population source:** retrospective review of consecutive medical records of patients from three Canadian level 1 trauma centres between September 2016 and December 2017.
Prognostic variables	**Subdural haemorrhage width ≥4 mm** **No subdural haemorrhage ≥4 mm** **Midline shift** **No midline shift** **Unilateral weakness on neurological assessment** **No unilateral weakness on neurological assessment** Initial and repeat head CT imaging reports reviewed to extracted types of intracranial haemorrhage and sizes, as well as fracture types using initial radiologist reports. Reports where this information was not available were assessed and appropriately documented by another trained reviewer. Three trained research assistants reviewed patient medical records and collected sociodemographic and clinical data, including age, medication use, GCS, presenting signs and symptoms and outcomes within 3 months following ED visit.
Confounders	A full list of variables included in the multivariate model is not provided and only those that were significant are reported: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift. **Does not account for key confounder of GCS as in our protocol**
Outcomes and effect sizes	**Neurosurgical intervention performed – median time between admission to ED and surgery was 16.1 h (IQR, 6.1-48.2 h)** **OR 3.755 (95% CI 1.290 to 10.928) for subdural haemorrhage width ≥4 mm vs. no subdural haemorrhage width ≥4 mm** **OR 7.507 (95% CI 3.317 to 16.989) for midline shift vs. no midline shift**

Reference	Tourigny 2021[16]
	OR 3.755 (95% CI 1.290 to 10.928) for unilateral weakness vs. no unilateral weakness on neurological assessment Stated to be neurosurgical intervention according to attending neurosurgeon. Outcome assessed from medical records. Intracranial pressure monitor was not considered to be neurosurgery. Interventions performed included: craniotomy and evacuation of haematoma, n=14; burr holes alone, n=9; burr holes and evacuation of haematoma, n=6; craniotomy alone, n=2; craniotomy and burr holes, n=2; fracture fixation, n=1; ventricular bypass, n=1; debridement, n=1; burr holes and fracture fixation, n=1; craniotomy and fracture fixation, n=1; craniotomy, burr holes and evacuation of haematoma, n=1.
Comments	**Risk of bias (applies to all risk factors):** 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — MODERATE 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — MODERATE OVERALL RISK OF BIAS — HIGH **Indirectness (applies to all risk factors):** • Population – not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome – appears to be only events occurring within index hospitalisation, not aiming to capture events within a longer time-frame (30 days). Might represent at least in some cases initial decision to perform surgery rather than there being a deterioration leading to unplanned surgery.

1

Reference	Van Ornam 2019[17]
Study type and analysis	Retrospective cohort study Multivariable logistic regression (stepwise forward model)

Reference	**Van Ornam 2019[17]**		
Number of participants and characteristics	N= 1126 consecutive patients with CT confirmed mild traumatic intracranial haemorrhage GCS≥13 presenting to academic emergency department (urban level 1 trauma centre) from January 2009 to December 2013 (USA) Data source: Patients were identified by running a query of a proprietary electronic medical record using the International Statistical Classification of Diseases and Related Health Problems (ninth edition) codes for traumatic intracranial haemorrhage (852.00–853.10, 851.00–851.90, 800.00–801.9, 803.00–804.9). Exclusion criteria: patients <16 years of age or GCS <13 and those with penetrating head trauma.		
		Patients with repeat head CT (RHCT) n = 975 Number (%)	Patients without RHCT N=151 Number (%)
	Mean age (years)	60.5	49.1
	Sex (Male)	571 (58.56)	94 (62.25)
	Aspirin use	323 (33.13%)	21 (13.91)
	Warfarin use	115 (11.79)	1 (0.66)
	Clopidogrel/other antiplatelet	48 (4.92)	0
	GCS 15	807 (82.77)	134 (88.74)
	GCS 14	118 (12.10)	12 (7.95)
	Epidural hematoma	4 (0.69)	2 (1.69)
	Subdural hematoma	308 (52.92)	32 (27.12)
	Subarachnoid haemorrhage	194 (33.33)	51 (43.22)
	Contusion	58 (9.97)	16 (13.56)
	Skull fracture	18 (3.09)	17 (14.41)
Prognostic variable	**GCS 13 vs. GCS 14-15 (referent)** **Age ≥60 years vs. <60 years (referent)**		

Reference	Van Ornam 2019[17]
	Data for demographics and clinical factors obtained from database.
Confounders OR Stratification strategy	Not clearly stated which confounders were included in the final multivariable analysis but the following were considered in the study: Age, hospital length of stay, sex, past medical history (e.g. anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion
Outcomes and effect sizes	Composite outcome of CT progression, change in neurologic status, need for neurosurgery or death/comfort measures only (CMO) – unclear time-point but likely within admission as said data not collected following discharge – mean length of stay was 3.6 or 8.3 days in those without and with composite outcome Adjusted OR (95% CI) for each prognostic factor. P values not stated GCS 13 4.5 (2.5–8.2) Age ≥ 60 1.6 (1.1–2.3)
Comments	**Risk of bias (relevant for both risk factors):** 1. Study participation — LOW 2. Study attrition — LOW 3. Prognostic factor measurement — MODERATE 4. Outcome Measurement — MODERATE 5. Study confounding — MODERATE 6. Statistical analysis — MODERATE OVERALL RISK OF BIAS — HIGH **Indirectness:** • Population – not specific to those with small intracranial injuries, but did limit to GCS 13-15 • Outcome – measured up to discharge which is a much shorter period in this study than the 30 days in protocol, includes components that may not present as clinical deterioration e.g. progression on CT

1

Reference	Velmahos 2006[18]
Study type and analysis	Retrospective study Multivariate stepwise logistic regression performed using variables that reached P≤0.2 on univariate analyses
Number of participants and characteristics	N=179 • Age >65 years, n=66 • Age ≤65 years, n=113 • GCS <15 (13 or 14), n= 44 • GCS 15, n=135 **Inclusion criteria:** patients admitted with mild head injury after blunt trauma (GCS 13-15 with loss of consciousness, short-term amnesia, headache, emesis or dizziness) – all of these patients had head CT shortly after ED arrival and neurosurgical consultation requested. **Exclusion criteria:** not reported **Population characteristics:** given for whole cohort – continuous variables are mean (SD) unless otherwise indicated • Male, 65% • Age: 51 (26) years • Age >65 years, 37% • Mechanism of blunt trauma: ○ Fall, 52.5% ○ Road accident, 29.0% ○ Other, 18.0% • Injury Severity Score (ISS): 17 (8) • ISS >16, 44.0% • GCS on arrival:

Reference	Velmahos 2006[18]
	○ 13, 3.5% ○ 14, 21.0% ○ 15, 75.5% • Systolic blood pressure on arrival: 145 (25) mmHg • Anticoagulation therapy at time of admission, 20.0% • Time from arrival to CT: 94 (57) min • First head CT findings: ○ Solitary lesion, 54.0% ○ Multiple lesions, 32.0% ○ None, 14.0% • Action taken after first CT: ○ None, 20.0% ○ ICU admission, 42.0% ○ Intracranial pressure monitoring, 3.0% ○ Antiseizure medication, 88.0% ○ Vitamin K/FFP administration, 10.0% ○ Mannitol infusion, 1.0% • Time between first and repeat CT: 13 (6) h • Hospital length of stay: 7 (12) days • Disposition to: ○ Home/jail/nursing home: 65.0% ○ Other hospital/rehabilitation facility, 31.0% • Mortality, 4.0%

Reference	Velmahos 2006[18]
	Population source: trauma registry and medical records of patients admitted to single hospital from 1st October 2003 and 30th September 2004 were reviewed.
Prognostic variables	**Age >65 years** **Age ≤65 years (referent)** **GCS <15 (13 or 14)** **GCS 15 (referent)** Trauma registry and medical records reviewed. Data about demographics, ISS, vital signs on admission, GCS on admission, initial head CT and repeat head CT findings, time intervals between admission and CT scans, interventions, complications and final outcome were collected.
Confounders	Appears to only provide results for those that were found to be independent predictors of the outcome, not a full list of those included in the model: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT **Accounts for key confounder of GCS as in our protocol**
Outcomes and effect sizes	**Worsening of brain lesion on repeat head CT – average of 13 h after first CT** **OR 3.33 (95% CI 1.29 to 8.60) for age >65 vs. ≤65 years** **OR 3.13 (95% CI 1.23 to 8.01) for GCS <15 (13 or 14) vs. GCS 15** Outcome defined as worse brain lesion on repeat head CT, though more detail about how this was defined is not provided. All patients received head CT shortly after ED arrival and neurosurgical consultation requested. First responder to consultation was usually second-year neurosurgery resident who discussed findings with attending physician. Head CT performed without contrast using 16-slice CT scanner and findings continuously reviewed by in-house attending radiologist. If initially CT indicated traumatic pathology, routine repeat head CT was ordered. Order specified time to perform the repeat scan which varied for each case and ranged from 2-24 h after the initial CT. Also noted that pre-existing diseases or treatments predisposing them to bleeding, rather than a positive first head CT, was the reason for some undergoing a repeat head CT (14.0% reported above in characteristics to have no lesion on initial CT). N=10 showed improvement in lesion, n=132 showed no change and n=37 showed worsening.
Comments	**Risk of bias (applies to both risk factors):**

Reference	Velmahos 2006[18]	
	1. Study participation	LOW
	2. Study attrition	LOW
	3. Prognostic factor measurement	MODERATE
	4. Outcome Measurement	MODERATE
	5. Study confounding	MODERATE
	6. Statistical analysis	MODERATE
	OVERALL RISK OF BIAS	HIGH
	Indirectness (applies to both risk factors): • Population: ○ Not limited to those with positive CT, as includes 14.0% with no finding on initial CT ○ Not specific to those with small intracranial injuries, does however limit to GCS 13-15 • Outcome – lesion progression on CT may not always lead to clinical deterioration – indirect relative to examples of outcomes in protocol which involve clinical effects such as death, readmission or seizures	

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Appendix E – Forest plots

E.1 Adults/children – clinical decision rules

Sensitivity/specificity results

Figure 2: Adults – Hull Salford Cambridge Decision Rule >0 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission

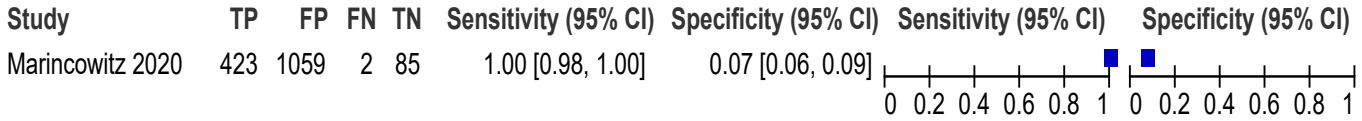

Figure 3: Adults – Hull Salford Cambridge Decision Rule >0 for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point)

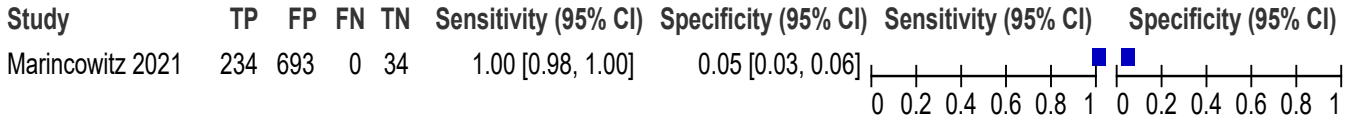

Figure 4: Adults – BIG score >1 vs. BIG 1 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission

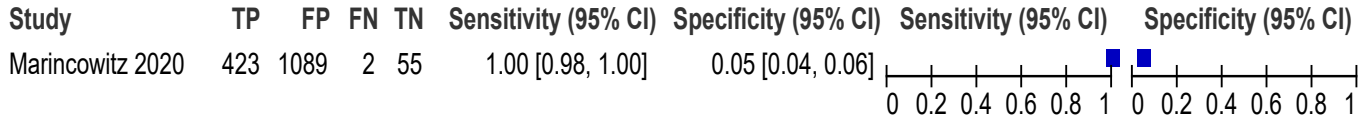

Figure 5: Adults – BIG score >1 vs. BIG 1 for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point)

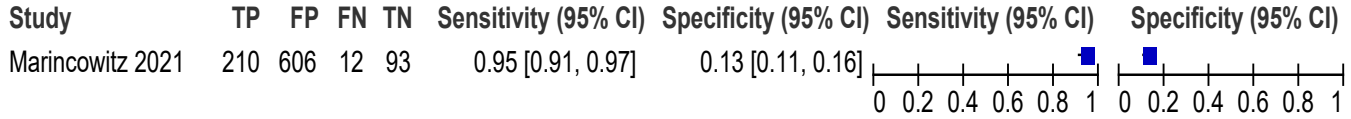

Figure 6: Adults – Nishijima 2014 – ≥1 four variables (GCS <15, non-isolated head injury, ≥65 years and presence of swelling or shift on initial cranial CT) vs. none for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival)

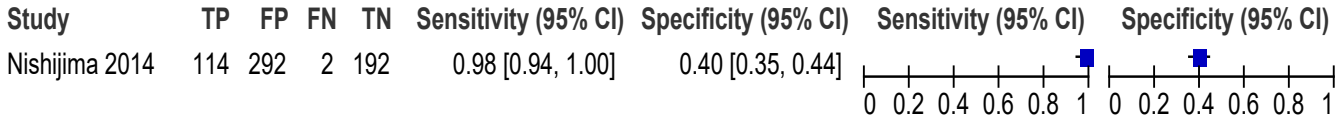

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Figure 7: Adults – Pruitt 2017 rule - at least one high-risk predictor - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission

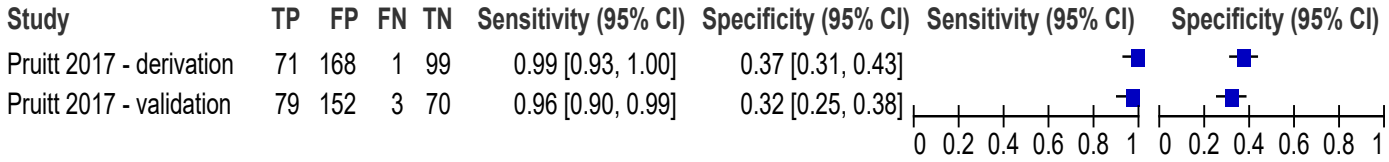

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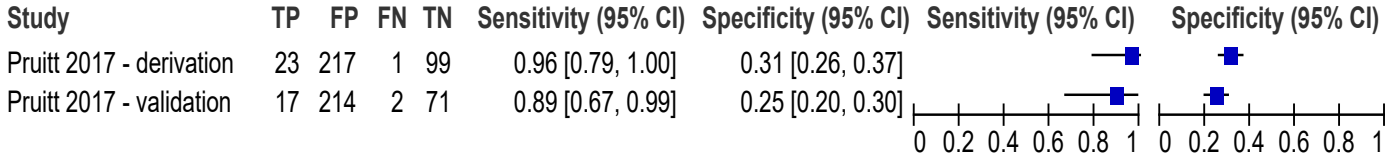
Figure 8: Adults – Pruitt 2017 rule - at least one high-risk predictor - neurologic decline (decreasing mental status, regardless of cause)



1

Figure 9: Adults – Pruitt 2017 rule - at least one high-risk predictor - worsening repeat CT scan

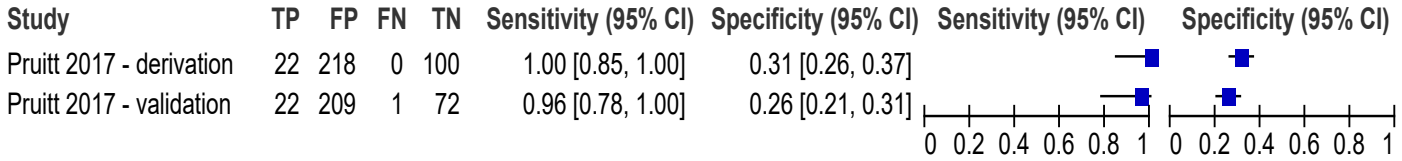


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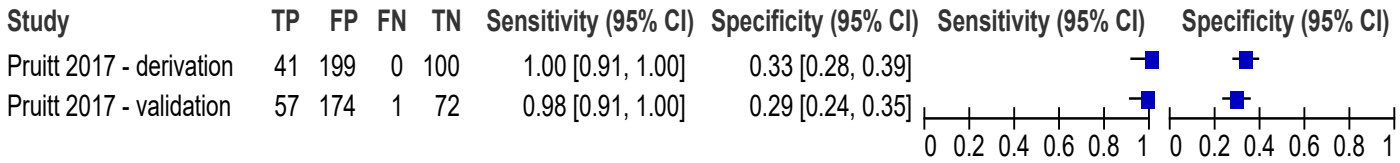
Figure 10: Adults – Pruitt 2017 rule - at least one high-risk predictor - neurosurgical procedure (intracranial pressure monitoring or operations) during admission



1

Figure 11: Children – CHIIDA score >0 - neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)

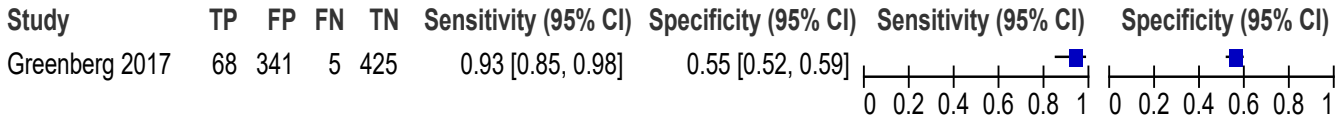


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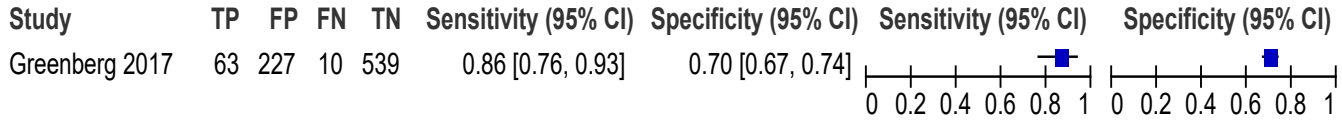
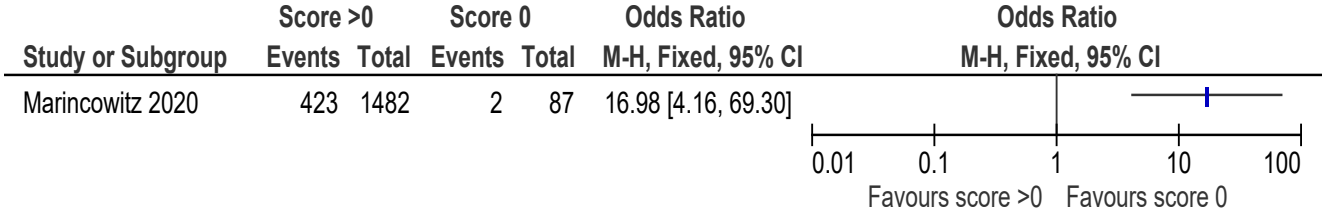
Figure 12: Children - CHIIDA score >2 - neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)



Odds ratio results

Figure 13: Adults – Hull Salford Cambridge Decision Rule >0 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission

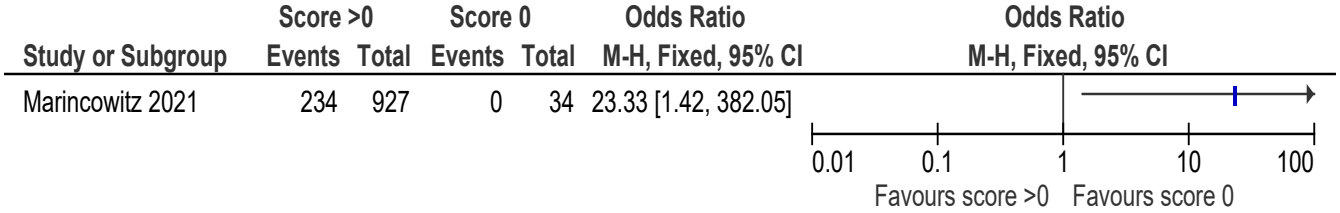


Decision rule included following for discharge – not meeting at least one meant score >0 and indication for admission: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination

1

2

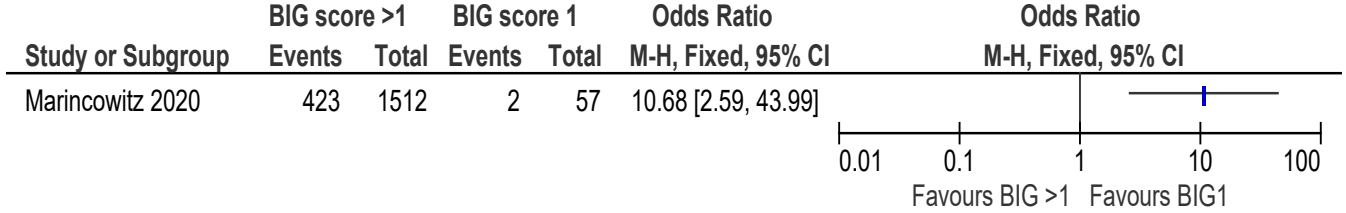
Figure 14: Adults – Hull Salford Cambridge Decision Rule >0 for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point)



Decision rule included following for discharge – not meeting at least one meant score >0 and indication for admission: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination

3

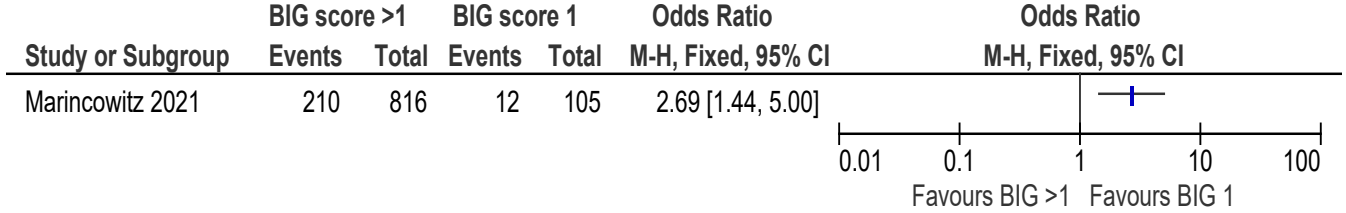
Figure 15: Adults – BIG score >1 vs. BIG 1 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



Decision rule included following for discharge – not meeting at least one meant score >1 and indication for admission: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated

1

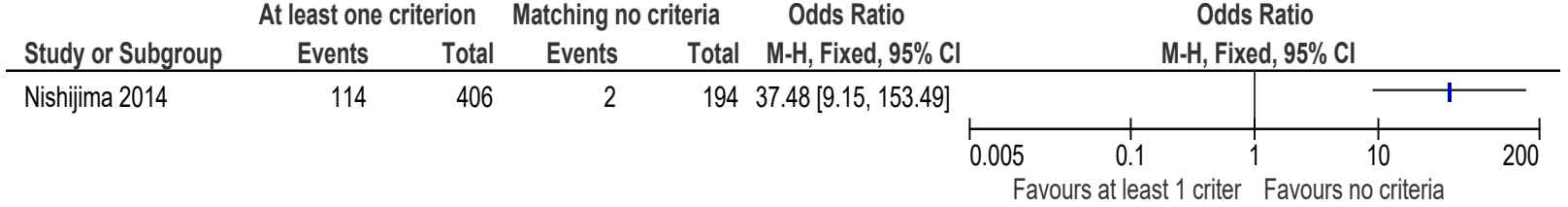
Figure 16: Adults – BIG score >1 vs. BIG 1 for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point)



Decision rule included following for discharge – not meeting at least one meant score >1 and indication for admission: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated

1

Figure 17: Adults – Nishijima 2014 – ≥1 four variables (GCS <15, non-isolated head injury, ≥65 years and presence of swelling or shift on initial cranial CT) vs. none for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival)



Having at least one of following four variables meant they were positive in terms of the decision rule: admission GCS <15, non-isolated head injury, age 65 years or older and the presence of swelling or shift on initial cranial CT

2

3

Figure 18: Adults – Pruitt 2017 rule - at least one high-risk predictor – composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission

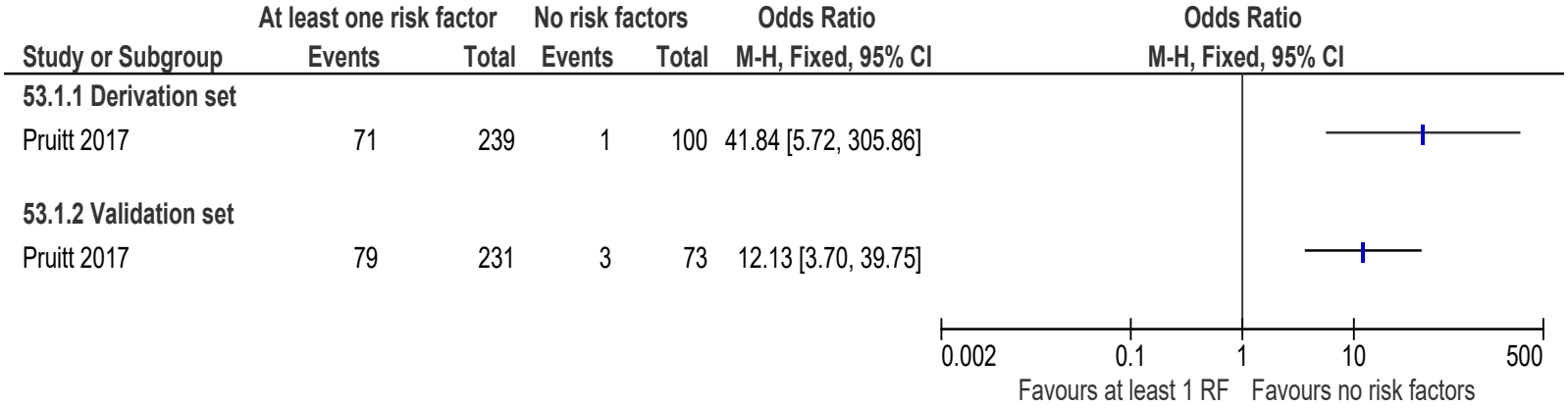


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Figure 19: Adults – Pruitt 2017 rule - at least one high-risk predictor – neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death)

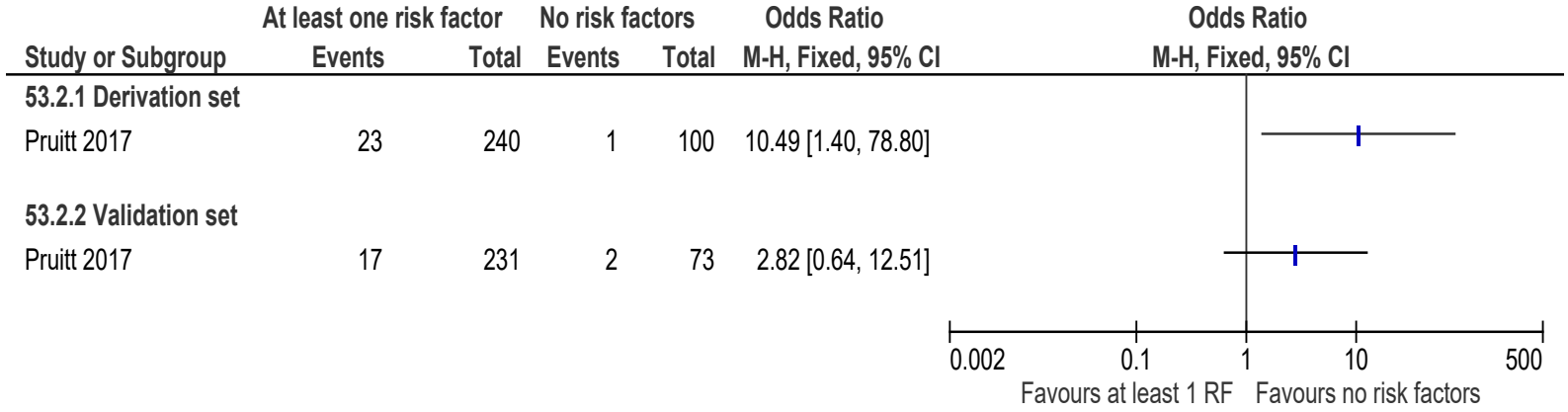

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Figure 20: Adults – Pruitt 2017 rule - at least one high-risk predictor – worsening on repeat CT

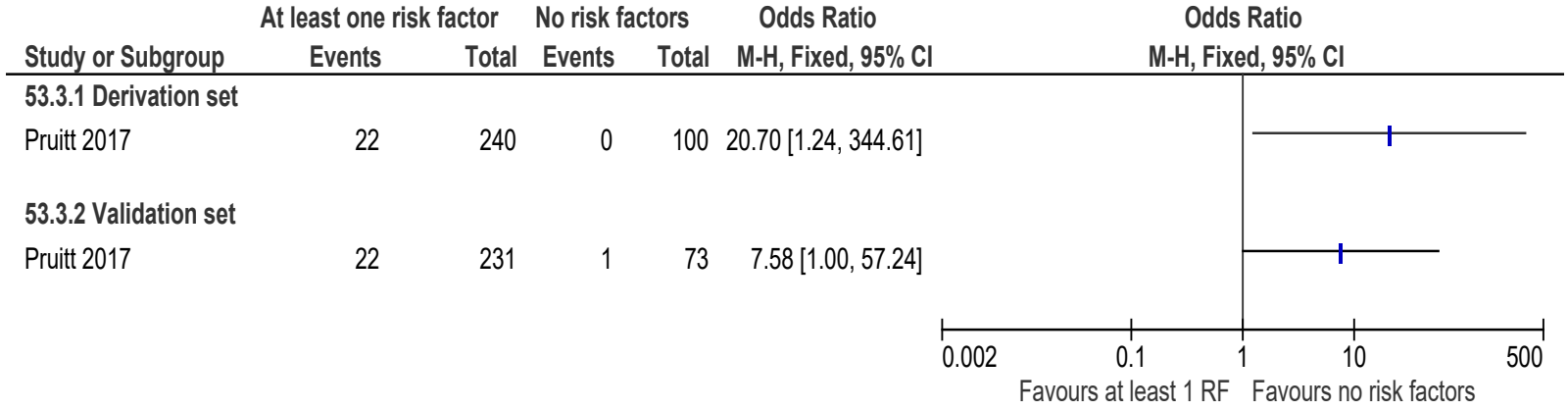

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Figure 21: Adults – Pruitt 2017 rule - at least one high-risk predictor – neurosurgery

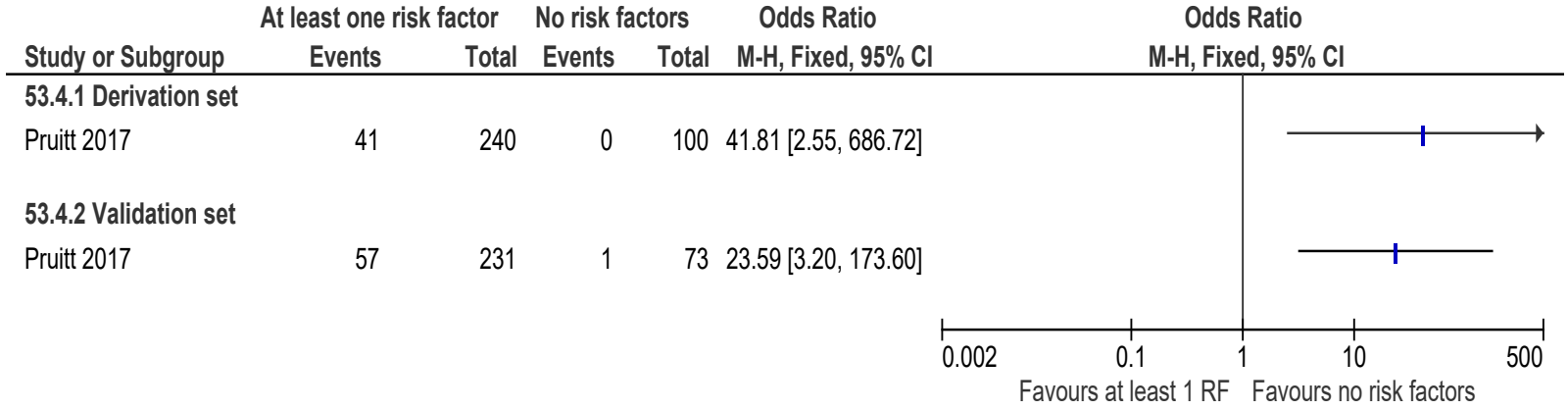

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Figure 22: Children – CHIIDA score >0 - neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)

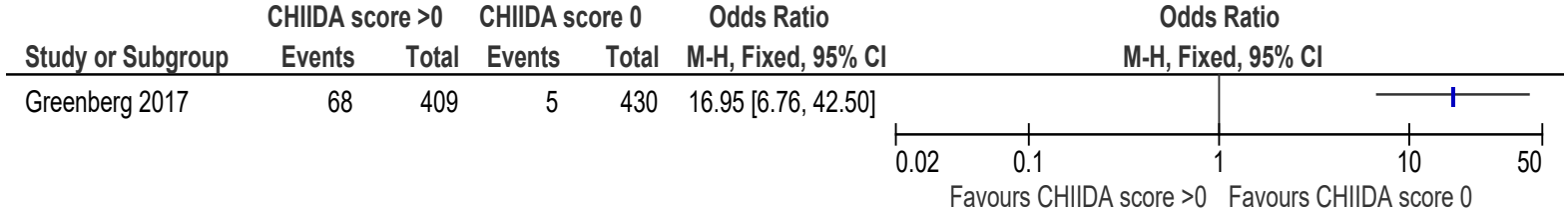
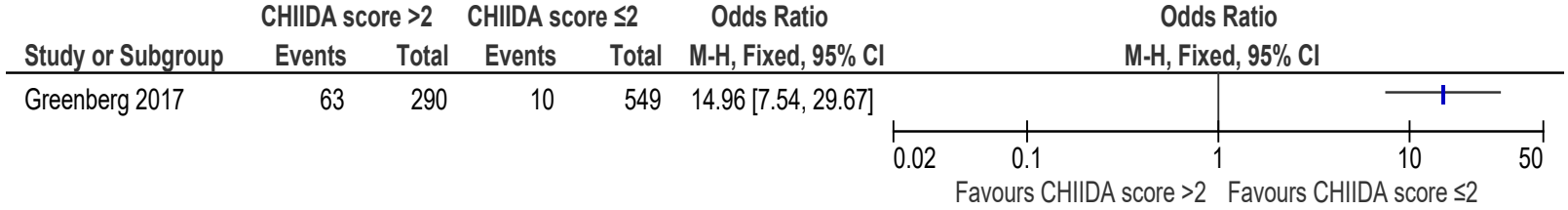
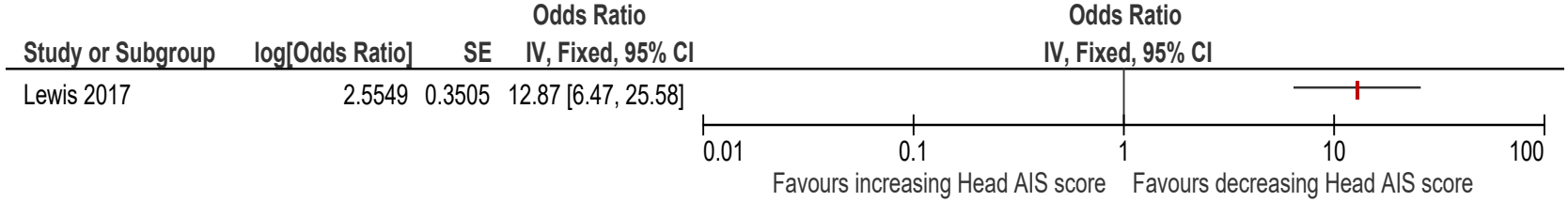


Figure 23: Children – CHIIDA score >2 - neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)



E.2 Adults – injury severity scales

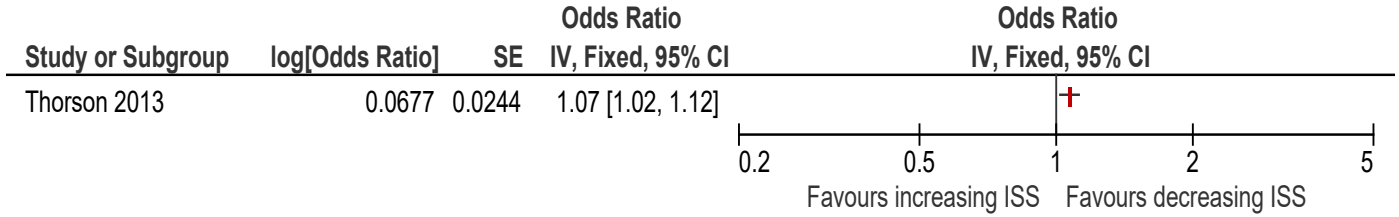
Figure 24: Increasing head AIS score (increments analysed unclear) for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: included hospital length of stay, ICU length of stay, days of mechanical ventilation, head-AIS score, Injury Severity Score, skull fracture, abnormal initial neurological examination, subdural haemorrhage, subarachnoid haemorrhage.

1

Figure 25: Increasing ISS score (increments analysed unclear) for predicting head CT progression on repeat CT, repeat CT performed within 24 h of initial CT



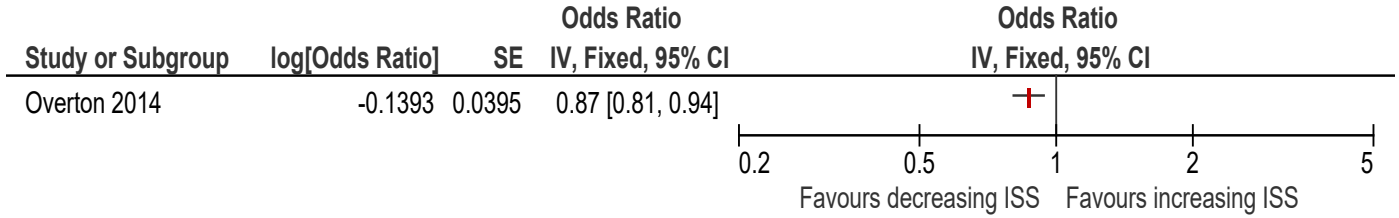
MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT

2

3

4

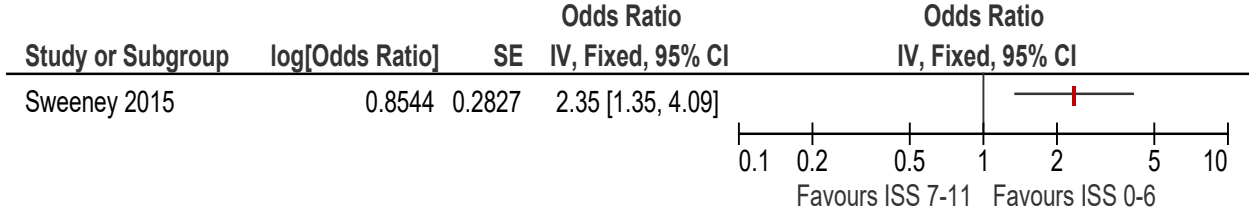
Figure 26: Increasing ISS score (increments analysed unclear) for predicting good outcome (GOS >4) at unclear time-point, possibly within same admission



MV analysis: included trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).

1

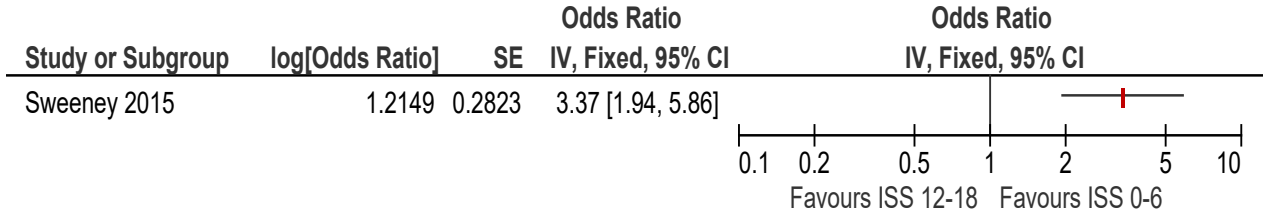
Figure 27: ISS score 7-11 vs. ISS score 0-6 for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).

2

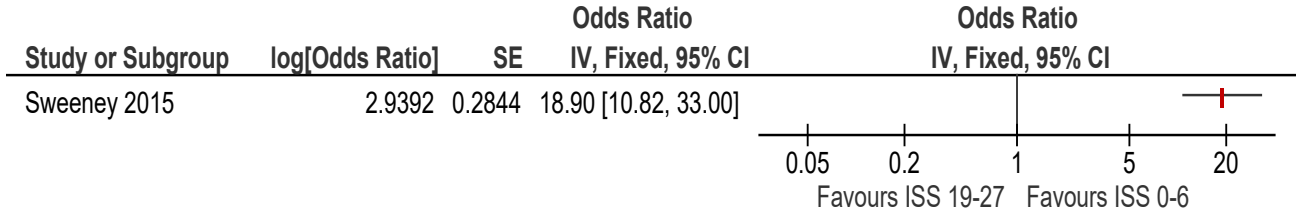
Figure 28: ISS score 12-18 vs. ISS score 0-6 for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).

1

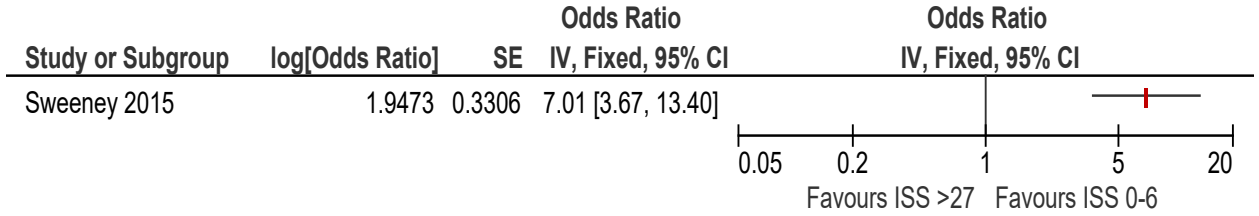
Figure 29: ISS score 19-27 vs. ISS score 0-6 for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).

2

Figure 30: ISS score >27 vs. ISS score 0-6 for predicting neurosurgical intervention at unclear time-point, possibly within same admission

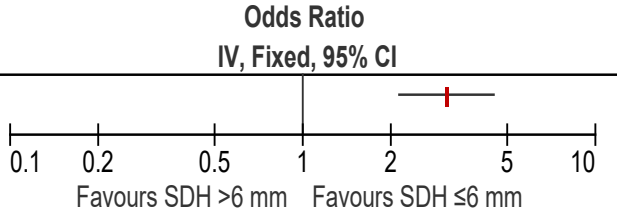


MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).

E.3 Adults/children – specific features/measurements of lesions

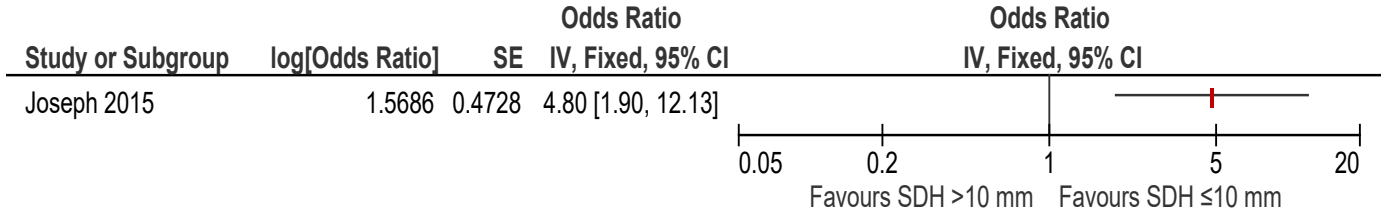
Figure 31: Adults – Subdural haemorrhage ≤6 mm vs. >6 mm for predicting discharge within 24 h

Study or Subgroup	log[Odds Ratio]	SE	SDH ≤6 mm Total	SDH >6 mm Total	Odds Ratio IV, Fixed, 95% CI
Borczuk 2019	1.1314	0.1901	850	229	3.10 [2.14, 4.50]



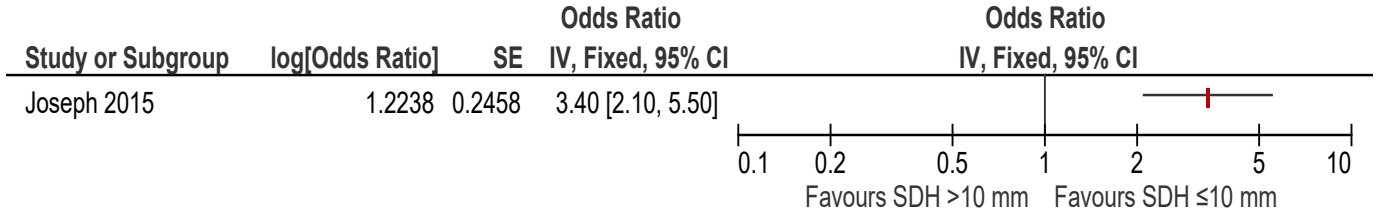
MV analysis: full list of variables included not given but included at least the following three variables that were significantly associated with the outcome: GCS, isolated traumatic subarachnoid haemorrhage and subdural haematoma thickness ≤6 mm

Figure 32: Adults – Subdural haemorrhage >10 mm vs. ≤10 mm for predicting progression on repeat CT, repeat head CT performed within 6 h



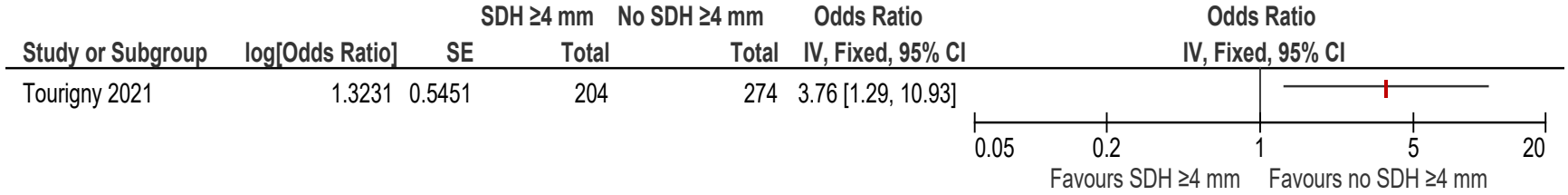
MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

Figure 33: Adults – Subdural haemorrhage >10 mm vs. ≤10 mm for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

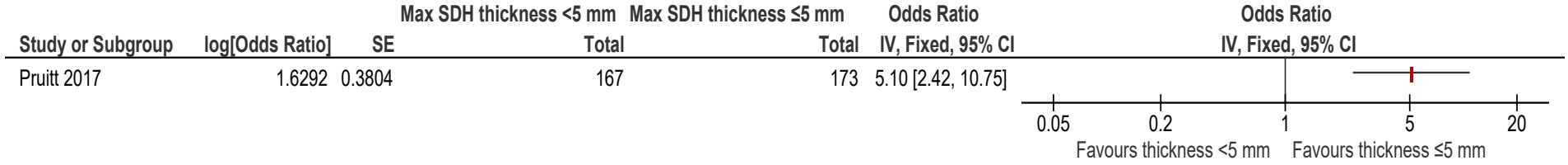
Figure 34: Adults – Subdural haemorrhage width ≥4 mm vs. <4 mm for predicting neurosurgical intervention, median time from admission to surgery was 16.1 h



MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.

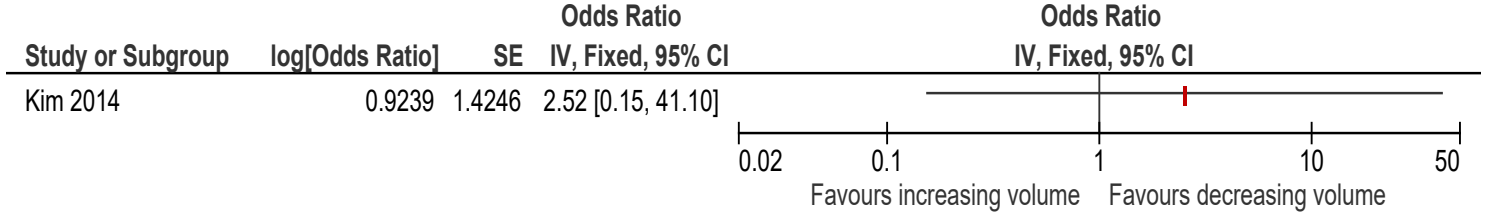
1

Figure 35: Adults – max subdural haemorrhage thickness >5 mm vs. ≤5 mm for predicting composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission



2

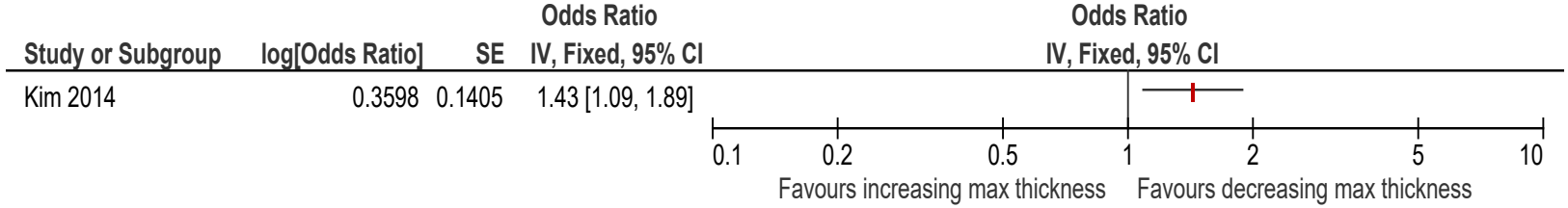
Figure 36: Adults – Increasing initial volume of subdural haematoma lesion (ml) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery at ~1 week post-injury



MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present

1

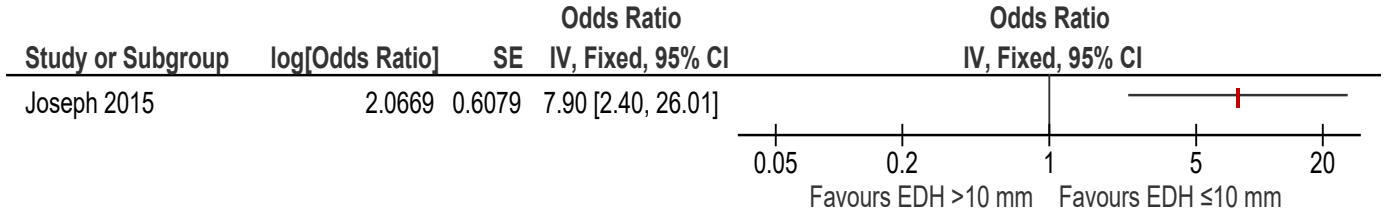
Figure 37: Adults – Increasing maximum thickness of subdural haematoma lesion (mm) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery at ~1 week post-injury



MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present

2

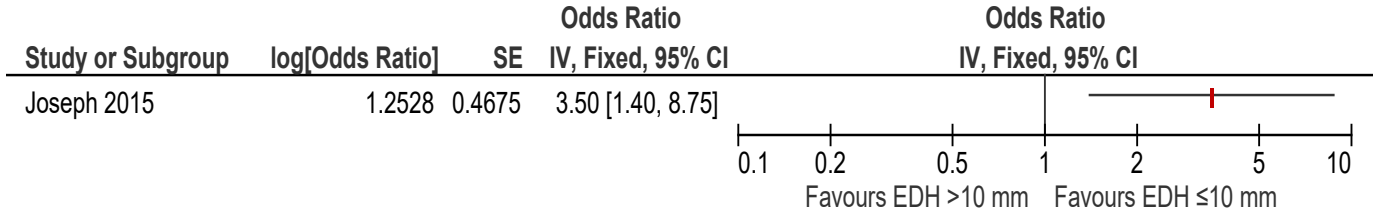
Figure 38: Adults – Epidural haemorrhage >10 mm vs. ≤10 mm for predicting progression on repeat CT, repeat CT performed within 6 h



MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

1

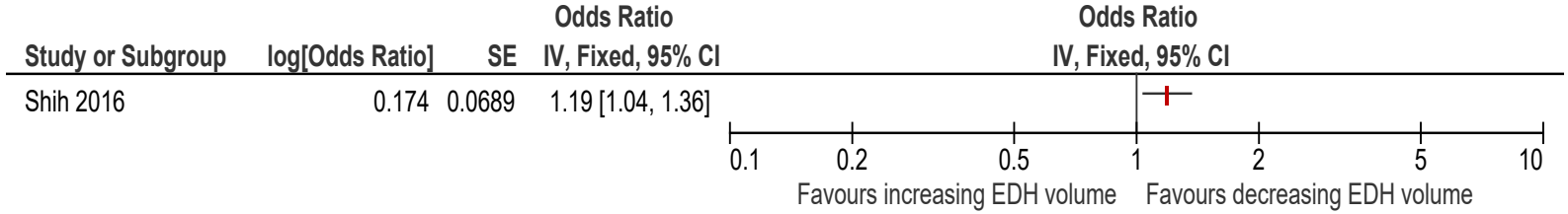
Figure 39: Adults – Epidural haemorrhage >10 mm vs. ≤10 mm for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

2

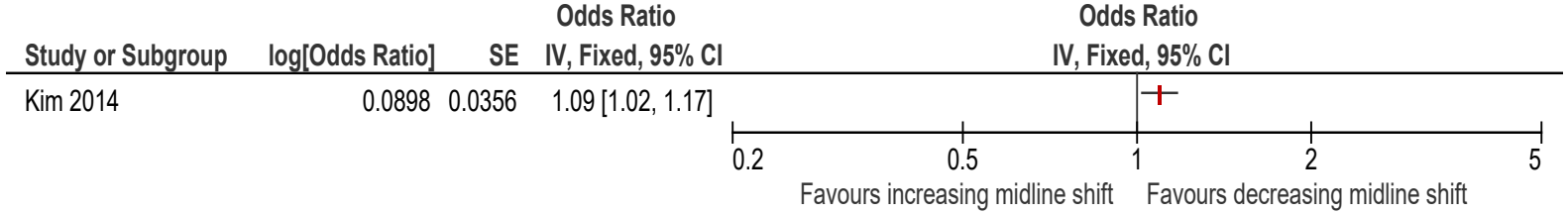
Figure 40: Adults – Increasing epidural haemorrhage volume as a continuous variable (per 1 cubic centimetre increase) for predicting delayed neurosurgical intervention (indicating failed non-operative management) within same admission (median hospital stay 8 days whole cohort)



MV analysis: has performed adjustment but does not provide details of those included in the final model

1

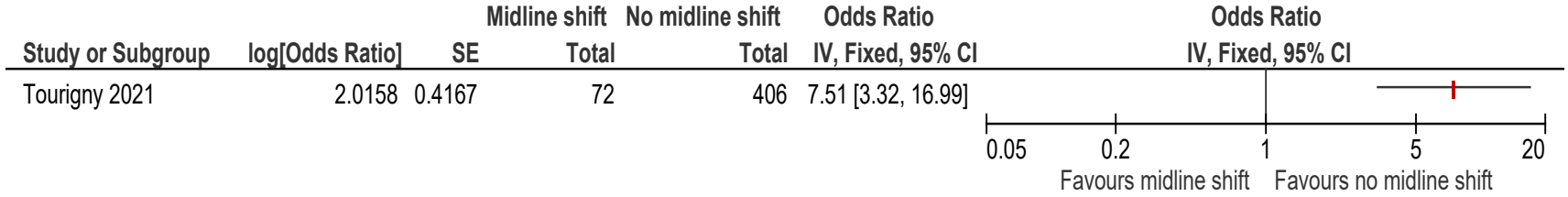
Figure 41: Adults – Degree of midline shift (mm) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery at ~1-week post-injury



MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present

2

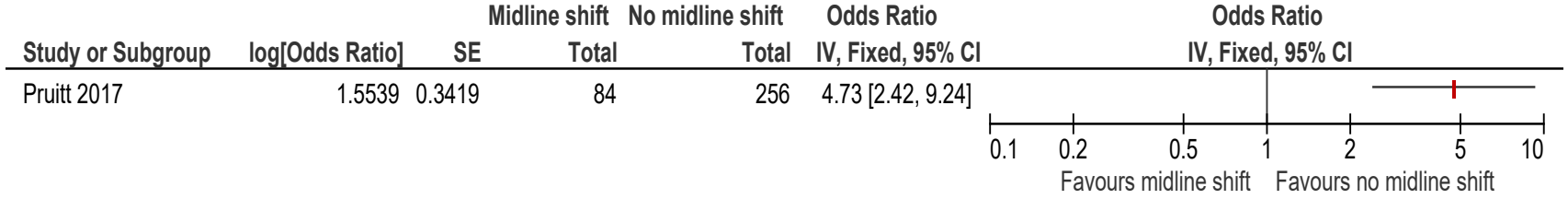
Figure 42: Adults – Midline shift vs. no midline shift for predicting neurosurgical intervention – median time from admission to surgery was 16.1 h



MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.

1

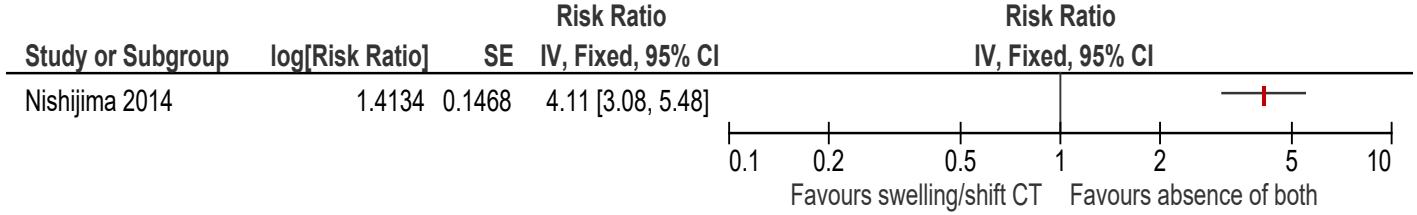
Figure 43: Adults – midline shift vs. no midline shift for predicting composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission



Source: <Insert Source text here>

2

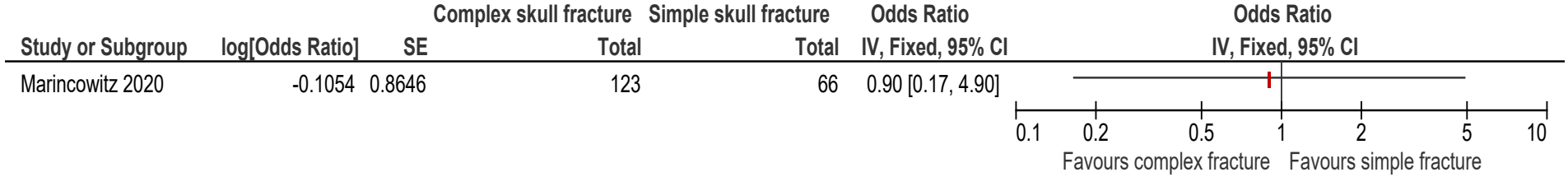
Figure 44: Adults – Presence vs. absence of swelling or shift on admission CT for predicting need for ICU admission (acute critical care intervention) within 48 h of ED arrival



MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.

1

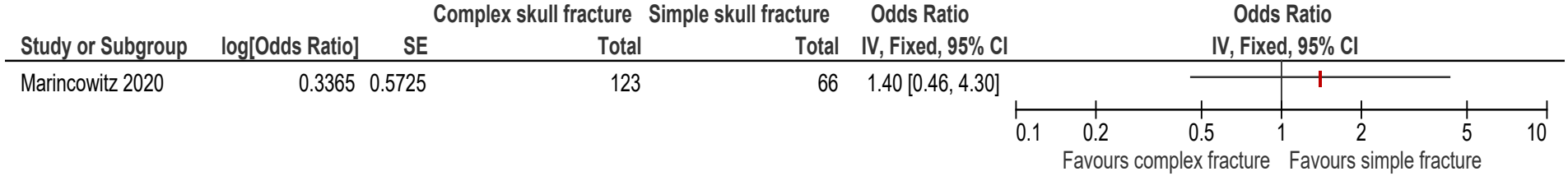
Figure 45: Adults – Complex skull fracture vs. simple skull fracture for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

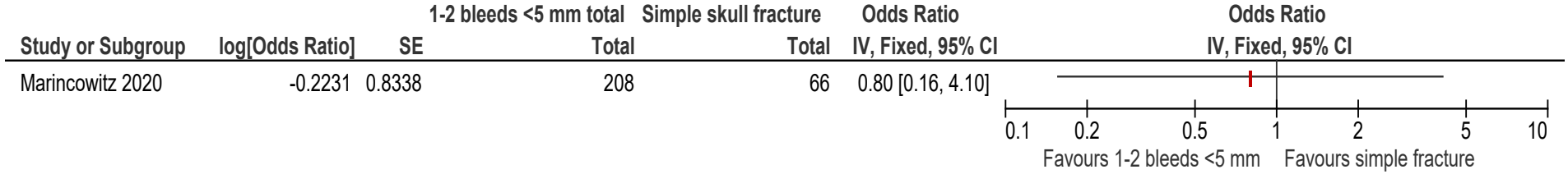
Figure 46: Adults – Complex skull fracture vs. simple skull fracture for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

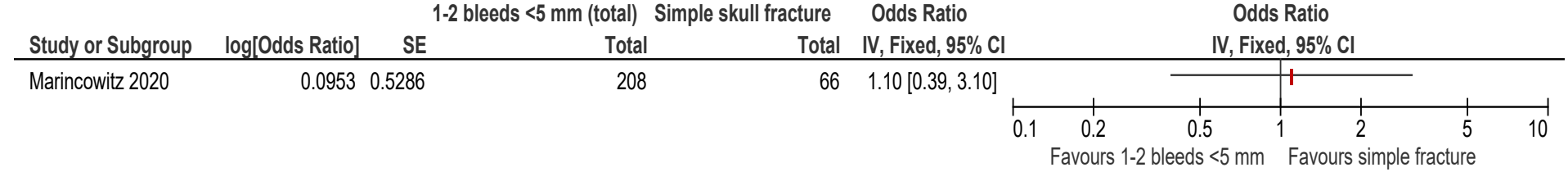
Figure 47: Adults – 1-2 bleeds <5 mm (total) vs. simple skull fracture for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

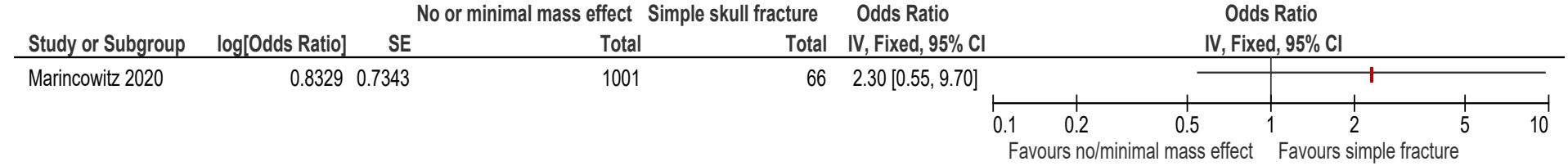
Figure 48: Adults – 1-2 bleeds <5 mm (total) vs. simple skull fracture for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

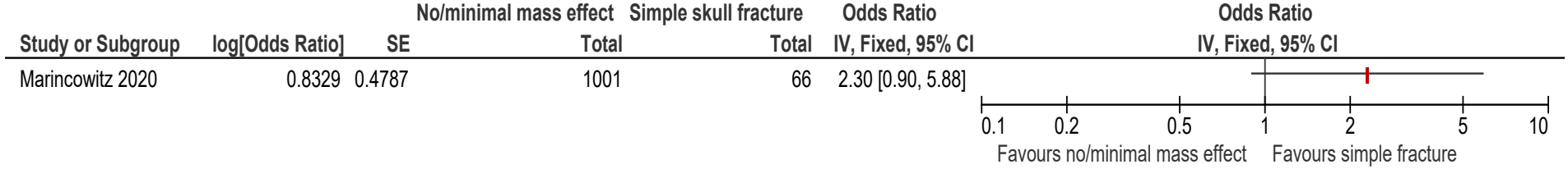
Figure 49: Adults – No or minimal mass effect vs. simple skull fracture for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

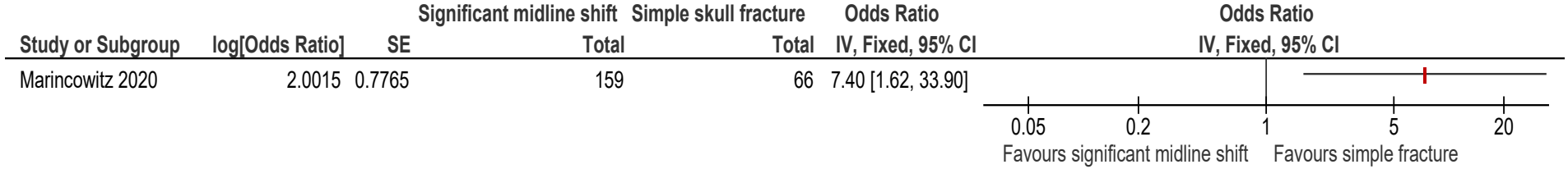
Figure 50: Adults – No or minimal mass effect vs. simple skull fracture for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

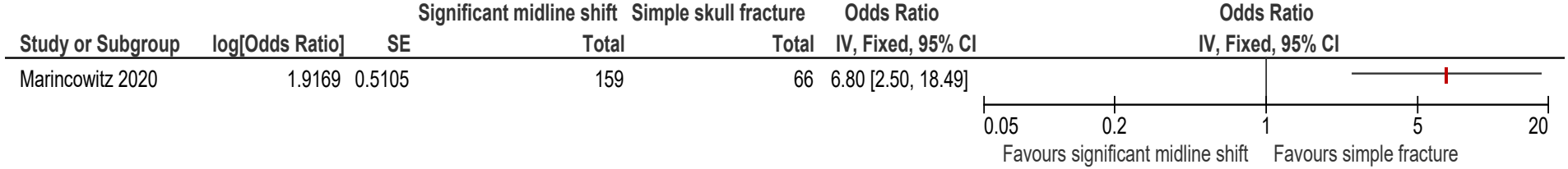
Figure 51: Adults – Significant midline shift vs. simple skull fracture for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

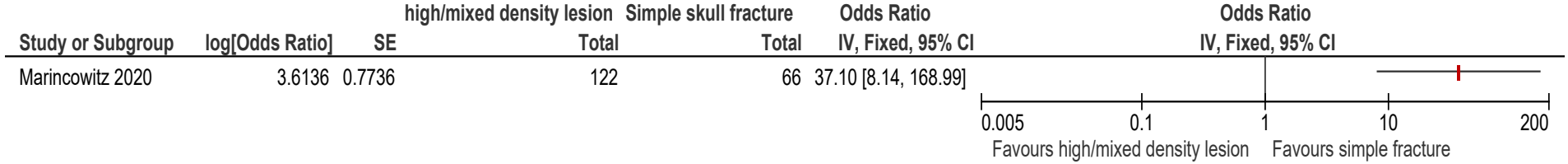
Figure 52: Adults – Significant midline shift vs. simple skull fracture for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

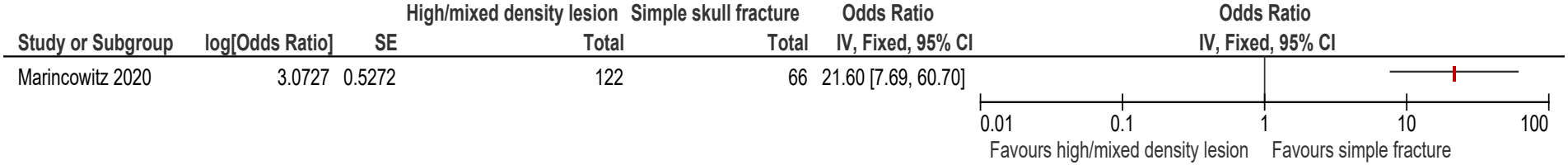
Figure 53: Adults – High/mixed density lesion vs. simple skull fracture for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

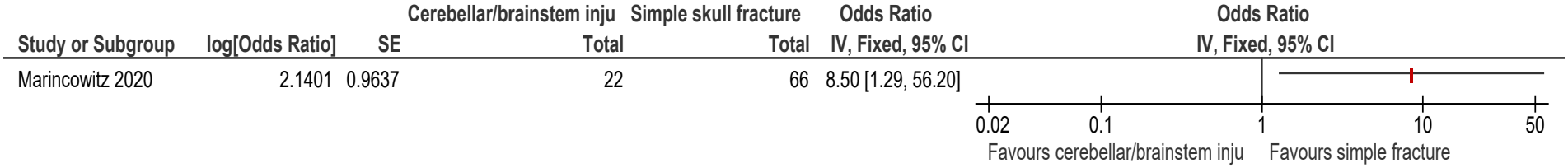
Figure 54: Adults – High/mixed density lesion vs. simple skull fracture for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

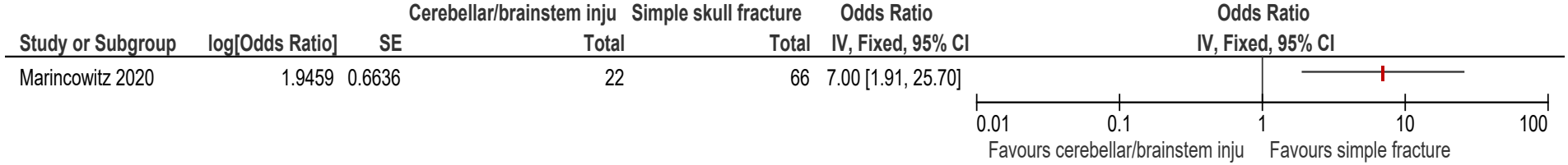
Figure 55: Adults – Cerebellar/brainstem injury vs. simple skull fracture for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

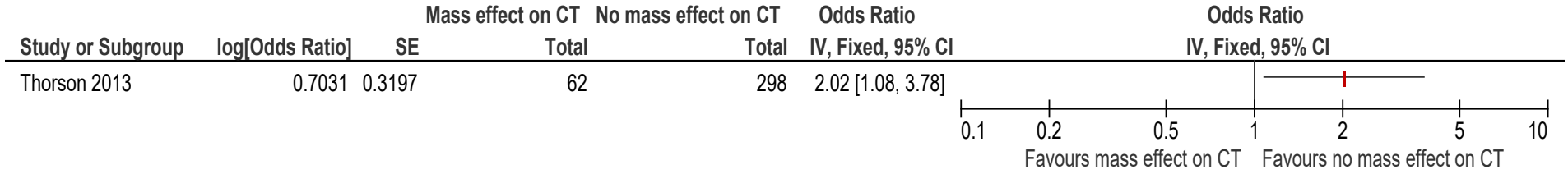
Figure 56: Adults – Cerebellar/brainstem injury vs. simple skull fracture for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

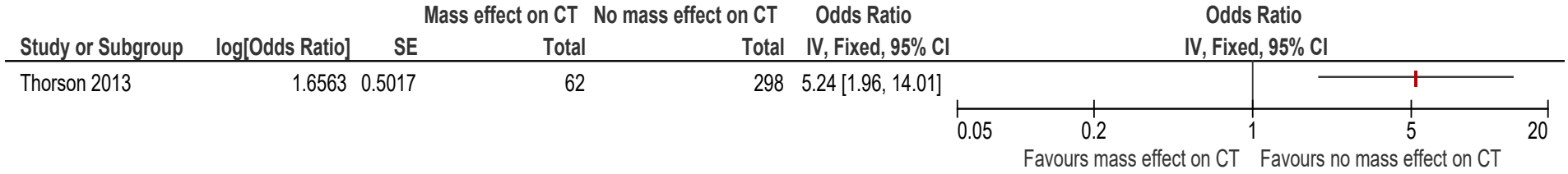
Figure 57: Adults – Mass effect vs. no mass effect on CT for predicting head CT progression on repeat CT, repeat CT performed within 24 h of initial CT



MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT

1

Figure 58: Adults – Mass effect vs. no mass effect on CT for predicting craniotomy being performed at unclear time-point, possibly within same admission

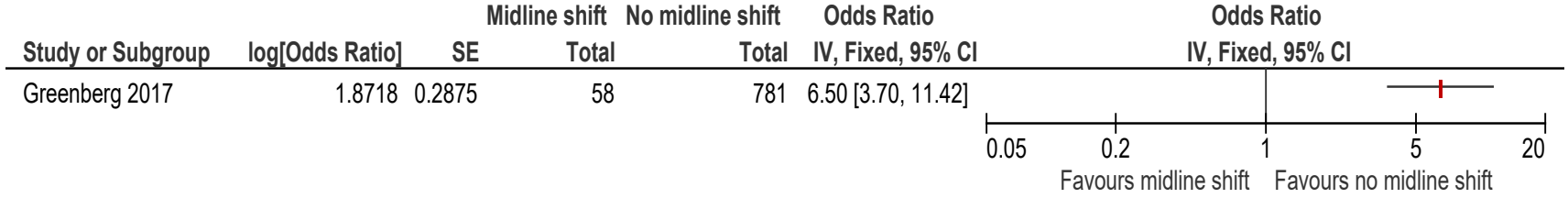


MV analysis: full list not provided but those that were significant and were included were initial mass effect, new/worse epidural haemorrhage on repeat CT, new/worse mass effect on repeat CT and new/worse herniation on repeat CT

2

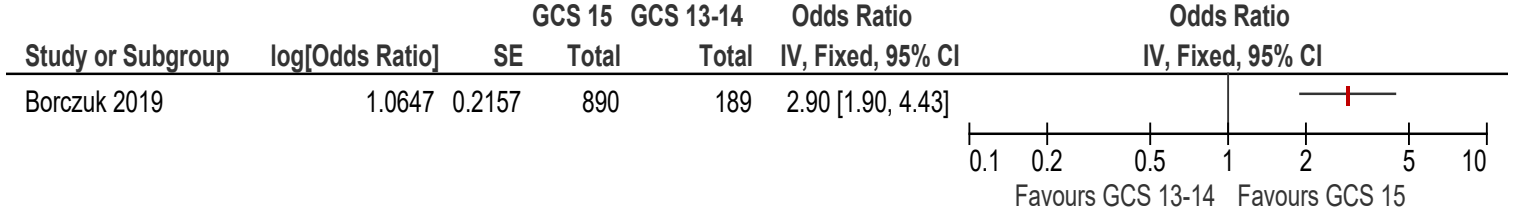
3

Figure 59: Children – midline shift vs. no midline shift for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)



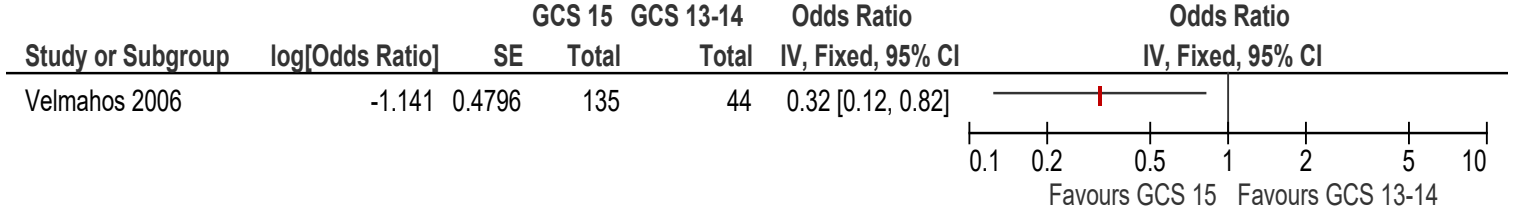
E.42 Adults/children – GCS

Figure 60: Adults – GCS 15 vs. GCS 13-14 for predicting discharge within 24 h



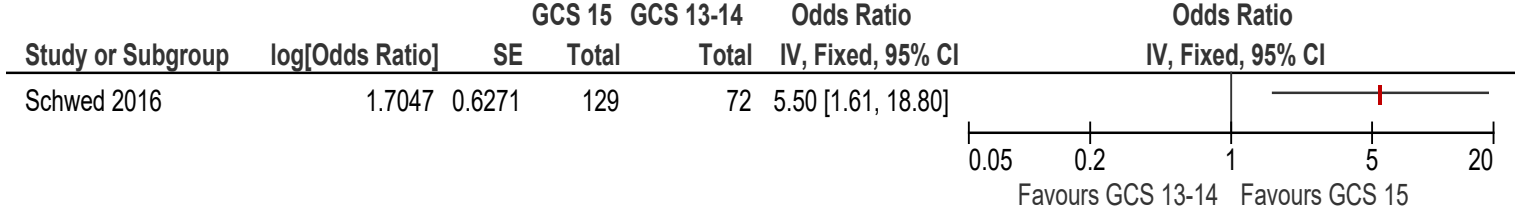
MV analysis: full list of variables included not given but included at least the following three variables that were significantly associated with the outcome: GCS, isolated traumatic subarachnoid haemorrhage and subdural haematoma thickness ≤6 mm

Figure 61: Adults – GCS 15 vs. GCS 13-14 for predicting worsening of brain lesion on repeat head CT, performed average 13 h following initial CT



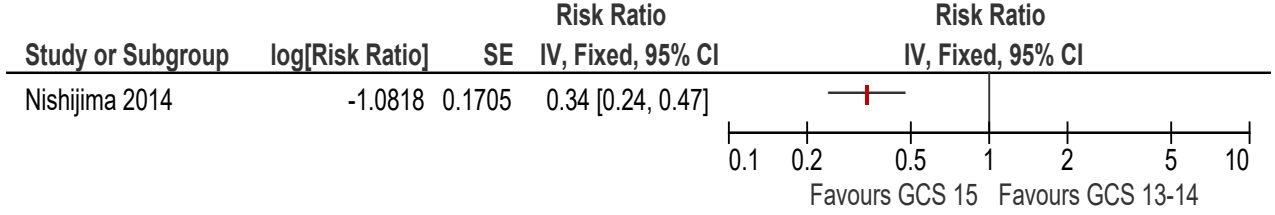
MV analysis: only those that were significant were reported and a full list of variables included not given: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT

Figure 62: Adults – GCS 15 vs. GCS 13-14 for predicting favourable outcome (alive, admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention) at unclear time-point, possibly within same admission



MV analysis: GCS of 15 at admission to ICU, isolated subarachnoid haemorrhage, age <55 years, ED blood pressure, Marshall score, head AIS, and ISS <25

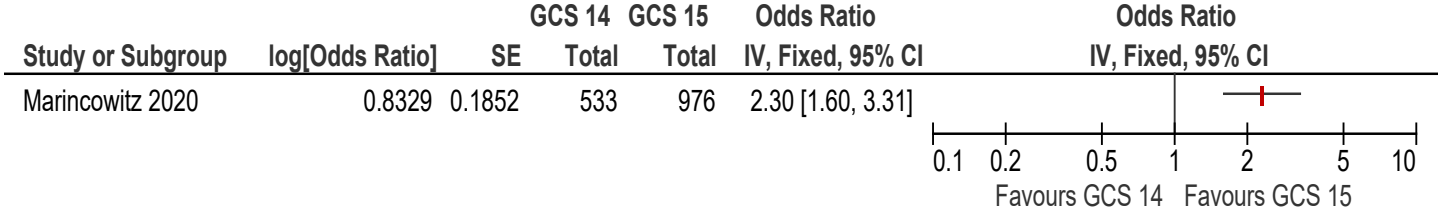
Figure 63: Adults – GCS 15 vs. GCS 13-14 for predicting need for ICU admission (acute critical care intervention) within 48 h of ED arrival



MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.

1

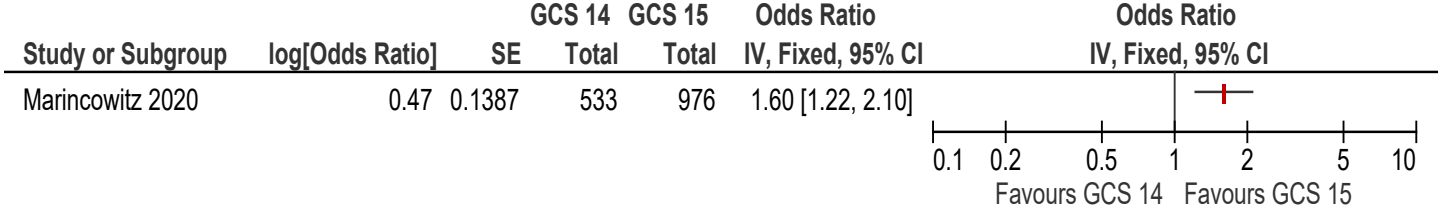
Figure 64: Adults – GCS 14 vs. GCS 15 for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

2

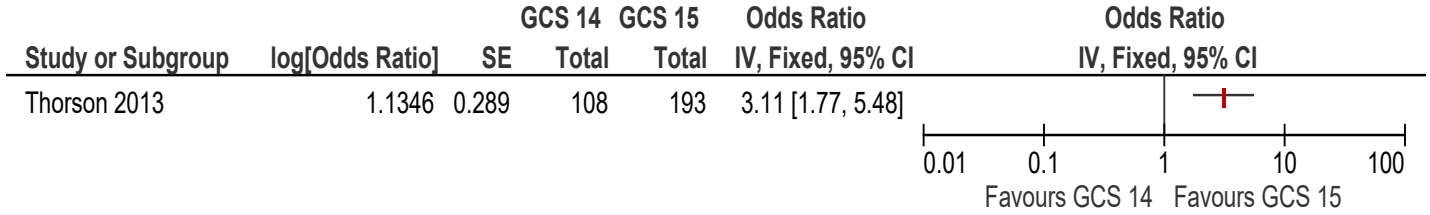
Figure 65: Adults – GCS 14 vs. GCS 15 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

1

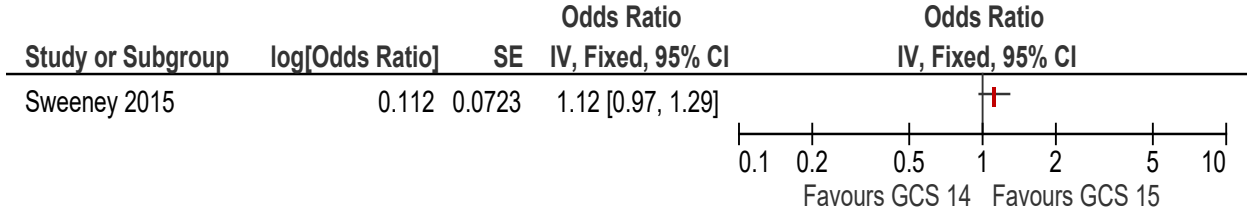
Figure 66: Adults – GCS 14 vs. GCS 15 for predicting head CT progression on repeat CT, repeat CT performed within 24 h of initial CT



MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT

2

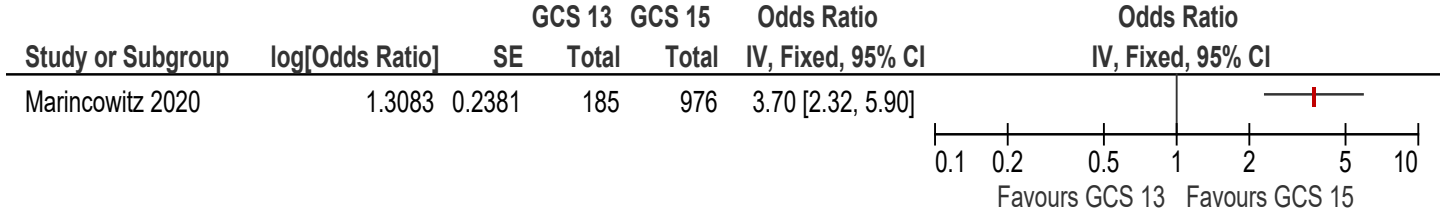
Figure 67: Adults – GCS 14 vs. GCS 15 for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).

1

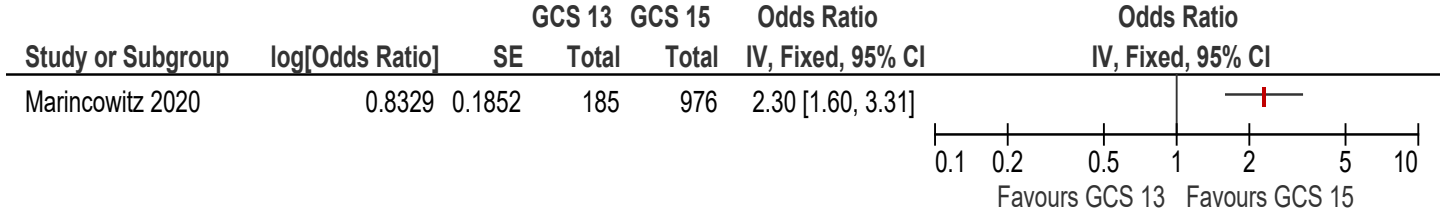
Figure 68: Adults – GCS 13 vs. GCS 15 for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

2

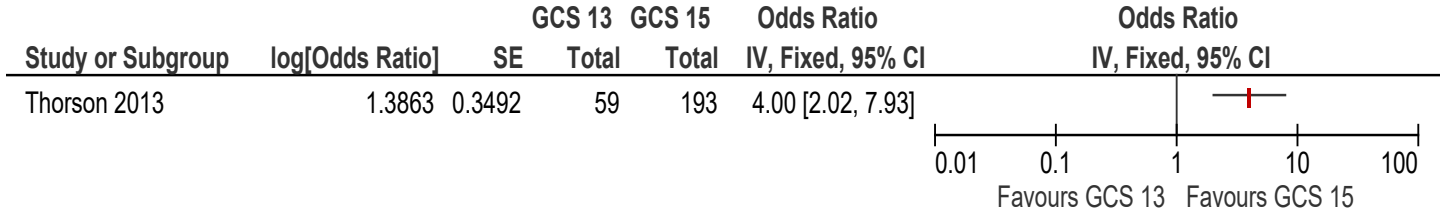
Figure 69: Adults – GCS 13 vs. GCS 15 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

1

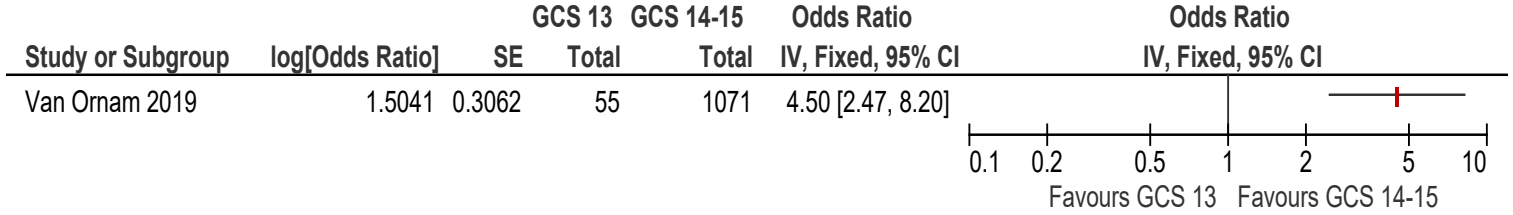
Figure 70: Adults – GCS 13 vs. GCS 15 for predicting head CT progression on repeat CT, repeat CT performed within 24 h of initial CT



MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT

2

Figure 71: Adults – GCS 13 vs. GCS 14-15 for predicting composite outcome of CT progression, change in neurologic status, need for surgery or death/comfort measures only at unclear time-point, possibly within same admission – mean length of stay was 3.6 and 8.3 days in those without and with outcome



MV analysis: final list unclear but following were considered for inclusion: age, hospital length of stay, sex, past medical history (such as anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion

Figure 72: Adults – GCS 13 vs. GCS 14-15 for predicting composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission

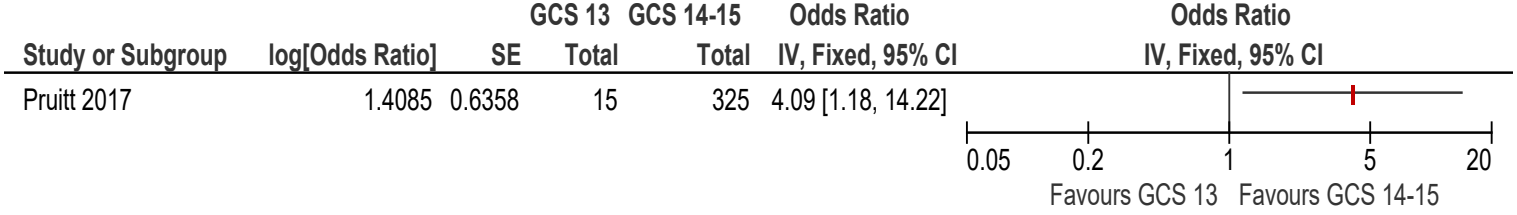
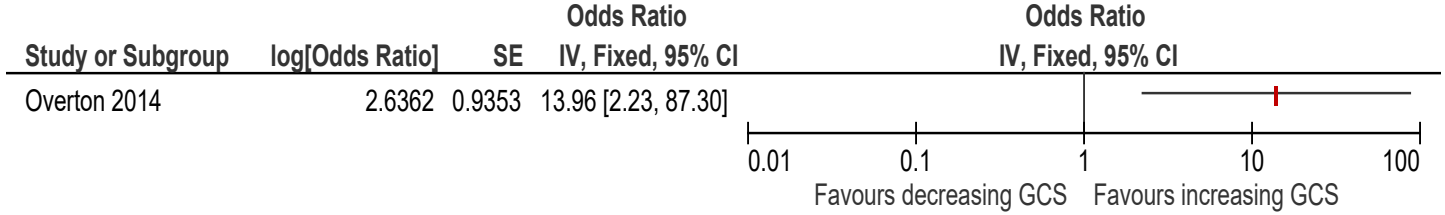


Figure 73: Adults – GCS motor scores on admission (unclear increments, possibly per 1-unit increase between 13 and 15?) for predicting good outcome (GOS >4) at unclear time-point, possibly within same admission



MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).

Figure 74: Children – GCS 14 vs. GCS 15 for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)

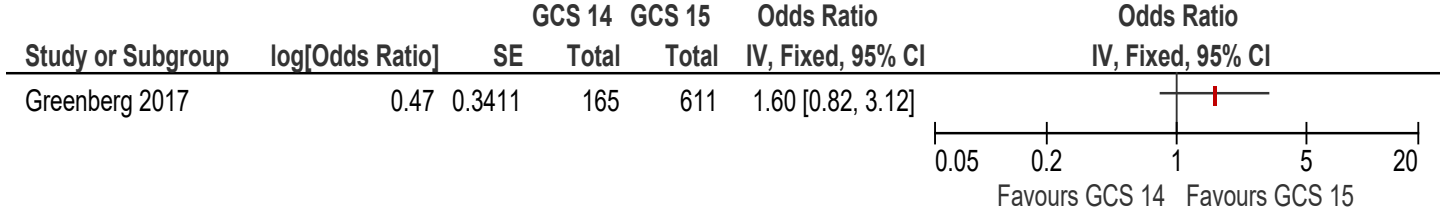
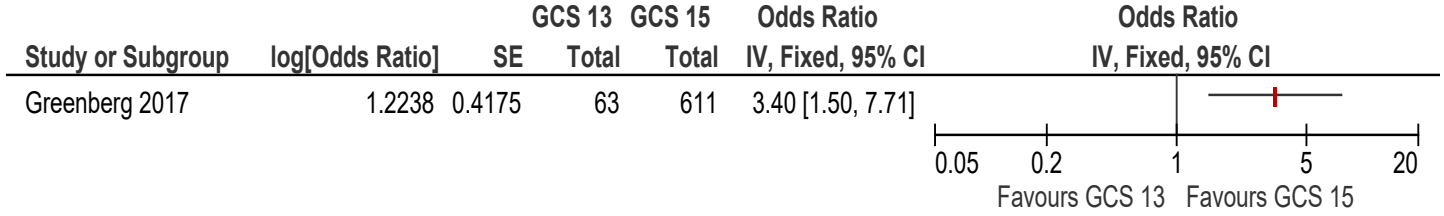


Figure 75: Children – GCS 13 vs. GCS 15 for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) – at 7-90 days post-ED visit (varies between patients)



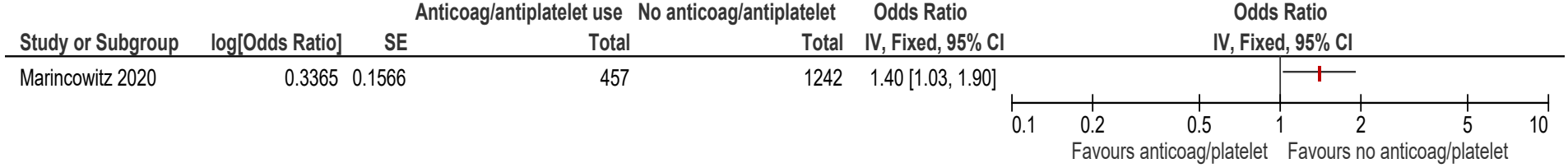
1

2

3

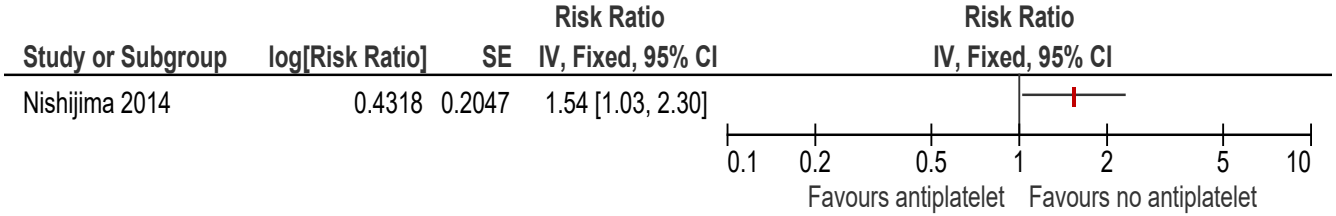
E.54 Adults – anticoagulation/antiplatelet treatments

Figure 76: Anticoagulant/antiplatelet use vs. no use for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



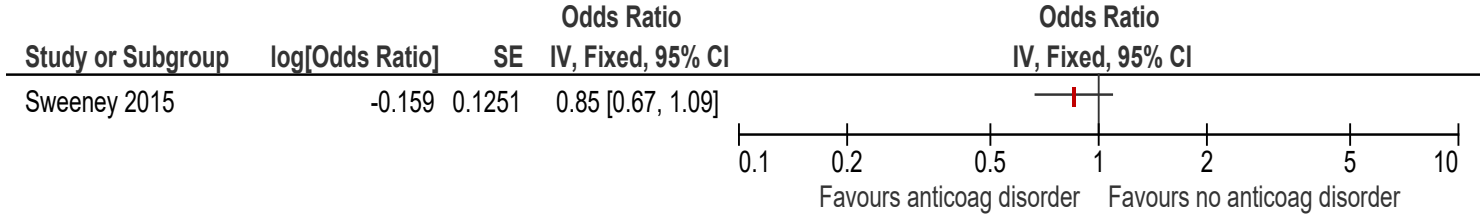
MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

Figure 77: Antiplatelet therapy vs. no antiplatelet therapy for predicting need for ICU admission (acute critical care intervention) within 48 h of ED arrival



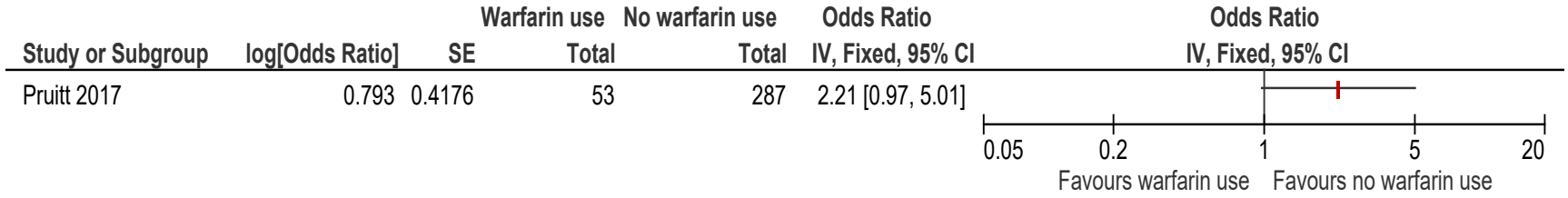
MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.

Figure 78: Anticoagulation disorder (any condition increasing risk of bleeding e.g. vitamin K deficiency, haemophilia, thrombocytopenia, chronic anticoagulation therapy) vs. no anticoagulation disorder for predicting neurosurgical intervention at unclear time-point, possibly within same admission



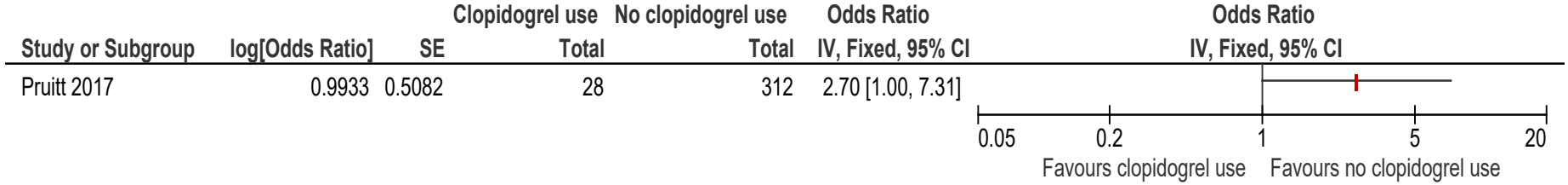
MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).

Figure 79: Warfarin use vs. no warfarin use for predicting composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission



1

Figure 80: Clopidogrel use vs. no clopidogrel use for predicting composite outcome - neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission

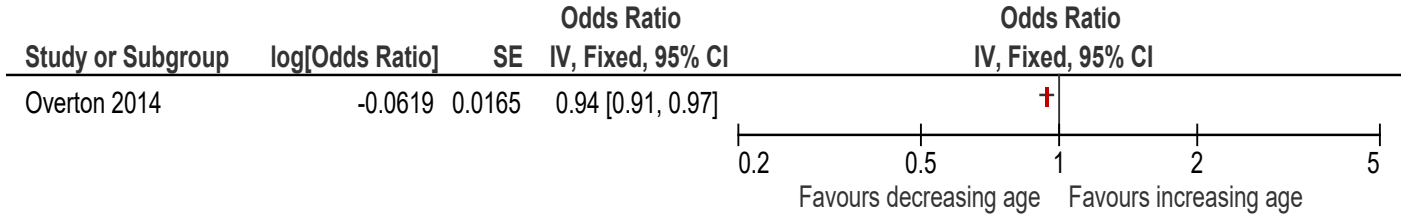


2

E.61 Adults – age

2

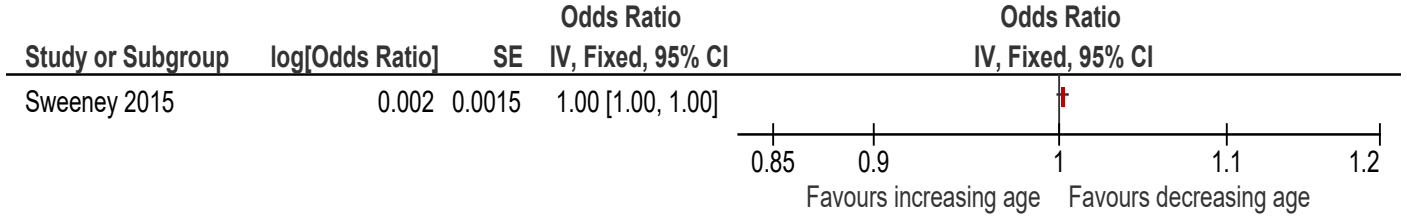
Figure 81: Increasing age as a continuous variable (increments unclear) for predicting good outcome (GOS >4) at unclear time-point, possibly within same admission



MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).

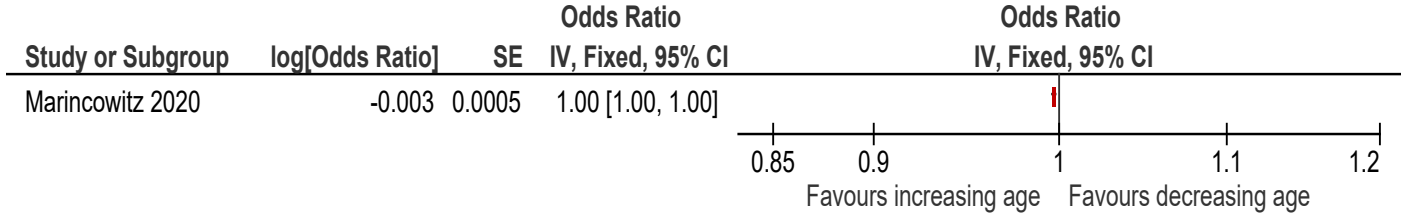
3

Figure 82: Increasing age as a continuous variable (increments unclear) for predicting neurosurgical intervention at unclear time-point, possibly within same admission



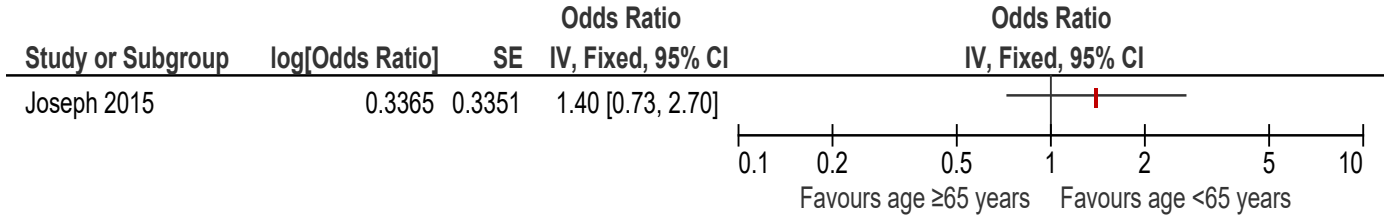
MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).

Figure 83: Increasing age as a continuous variable (per 1-unit increase) for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

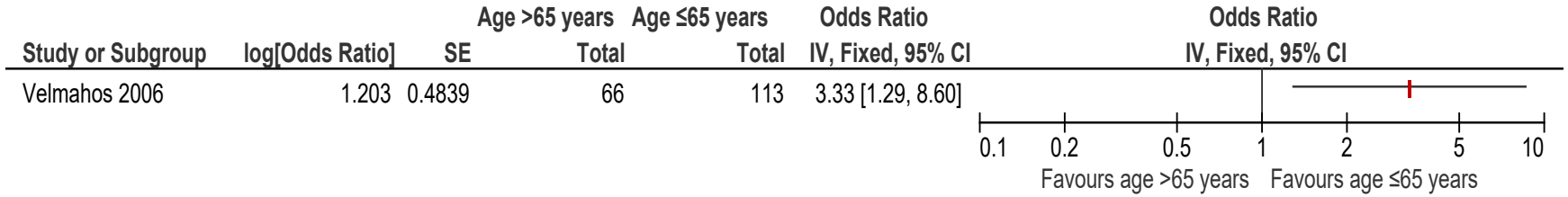
Figure 84: Age ≥65 vs. <65 years for predicting progression on repeat CT, repeat CT performed within 6 h



MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

1

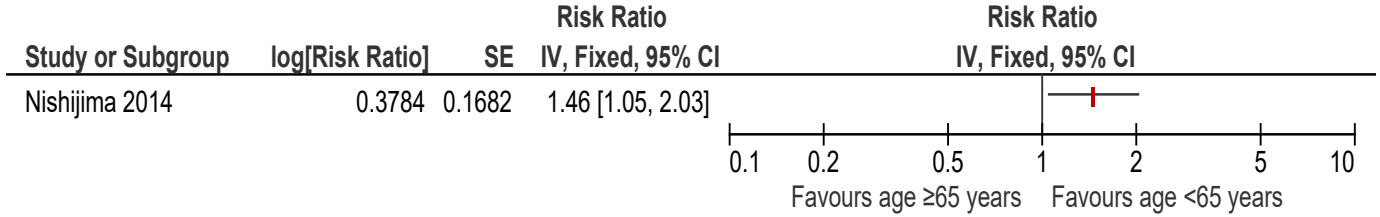
Figure 85: Age >65 vs. ≤65 years for predicting worsening of brain lesion on repeat head CT, repeat CT average 13 h following initial CT



MV analysis: only those that were significant were reported and a full list of variables included not given: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT

2

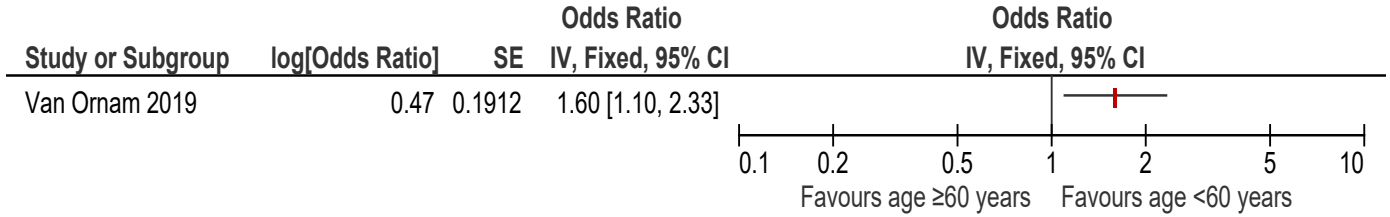
Figure 86: Age ≥65 vs. <65 years for predicting need for ICU admission (acute critical care intervention) within 48 h of ED arrival



MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.

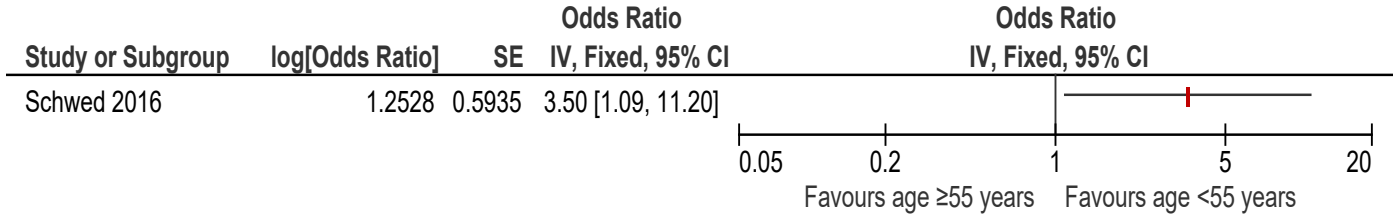
1

Figure 87: Age ≥60 vs. <60 years for predicting composite outcome of CT progression, change in neurologic status, need for surgery or death/comfort measures only at unclear time-point, possibly within same admission – mean length of stay was 3.6 and 8.3 days in those without and with outcome



MV analysis: final list unclear but following were considered for inclusion: age, hospital length of stay, sex, past medical history (such as anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion

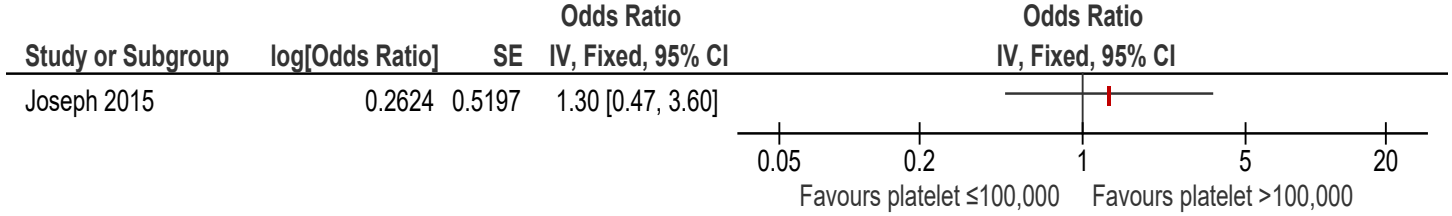
Figure 88: Age <55 vs. ≥55 years for predicting favourable outcome (alive, admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention) at unclear time-point, possibly within same admission



Age <55 vs. ≥55 years for predicting favourable outcome (alive, admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention)

E.7 Adults – blood measurements

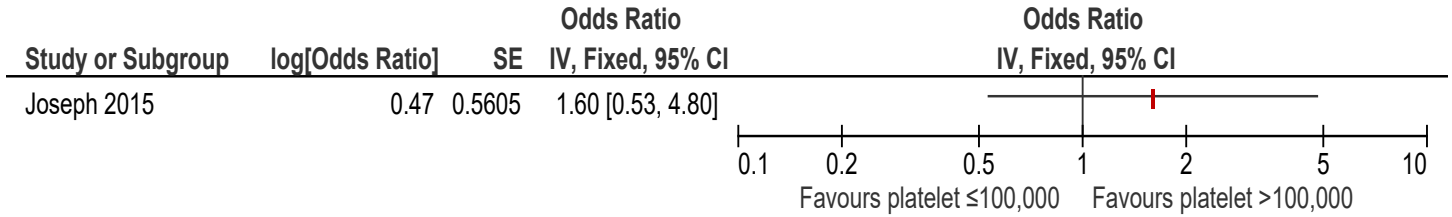
Figure 89: Platelet ≤100,000 mm^{-3} vs. >100,000 mm^{-3} for predicting progression on repeat CT, repeat head CT within 6 h



MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

1

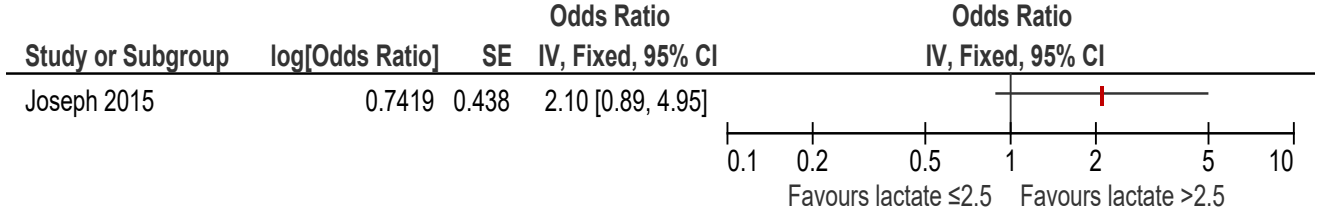
Figure 90: Platelet ≤100,000 mm-3 vs. >100,000 mm-3 for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

2

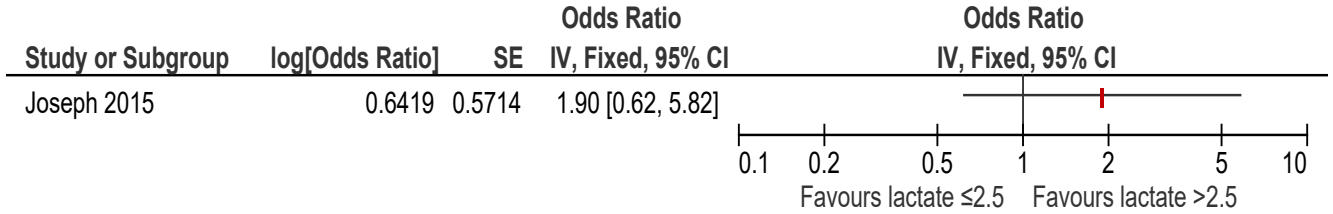
Figure 91: Lactate ≤2.5 vs. >2.5 for predicting progression on repeat CT, repeat head CT within 6 h



MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

3

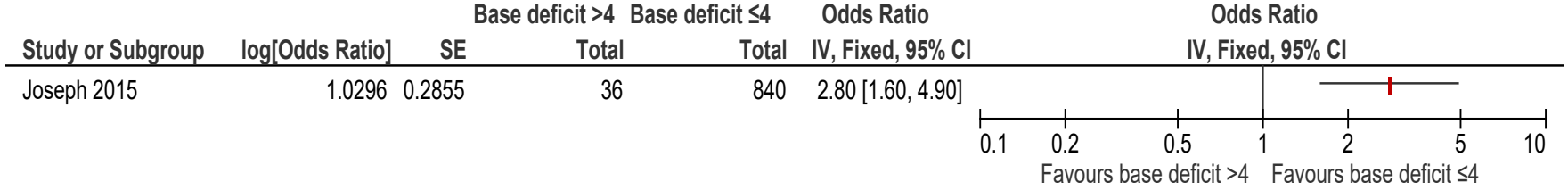
Figure 92: Lactate ≤2.5 vs. >2.5 for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

1

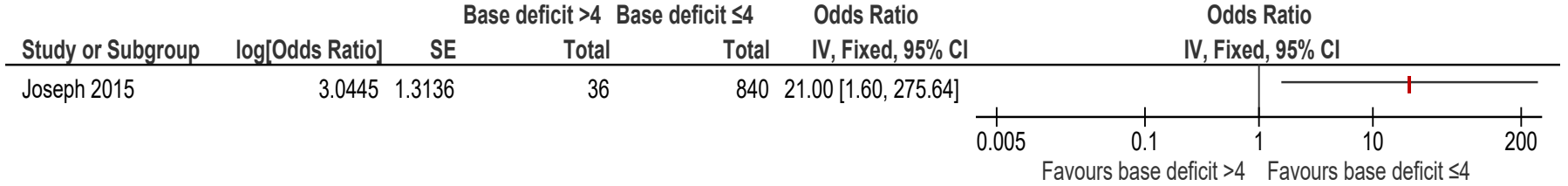
Figure 93: Base deficit >4 vs. ≤4 for predicting progression on repeat CT, repeat head CT within 6 h



MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

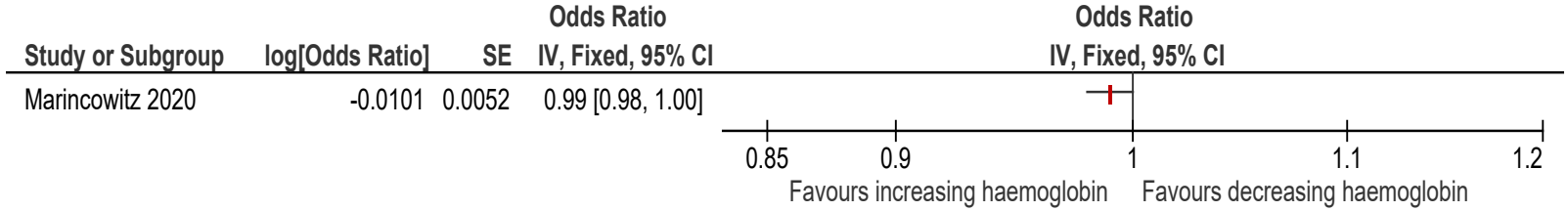
2

Figure 94: Base deficit >4 vs. ≤4 for predicting neurosurgical intervention at unclear time-point, possibly within same admission



MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.

Figure 95: Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L) for predicting need for neurosurgical specialist admission at 30 days post-ED admission



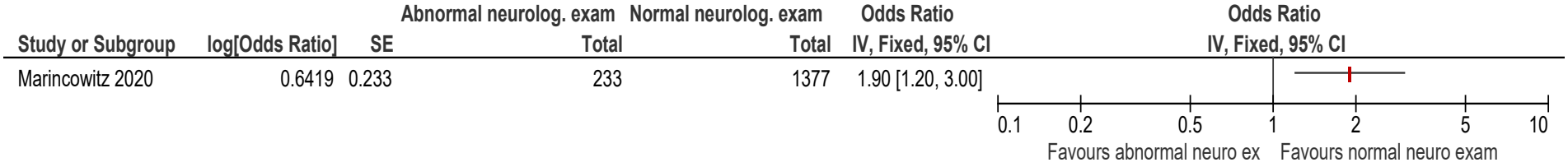
MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

Figure 96: Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L) for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission

MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

E.8 Adults – abnormal neurological exam findings

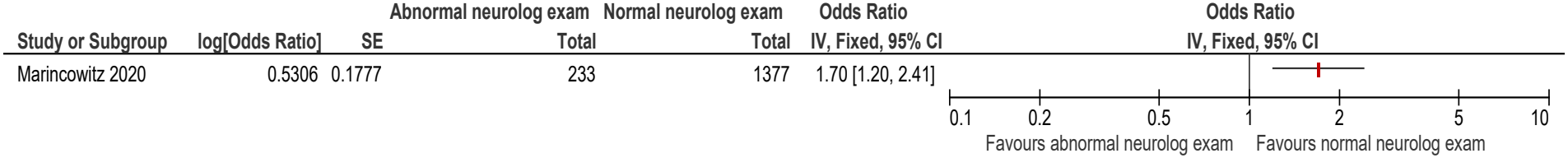
Figure 97: Abnormal vs. normal neurological examination for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

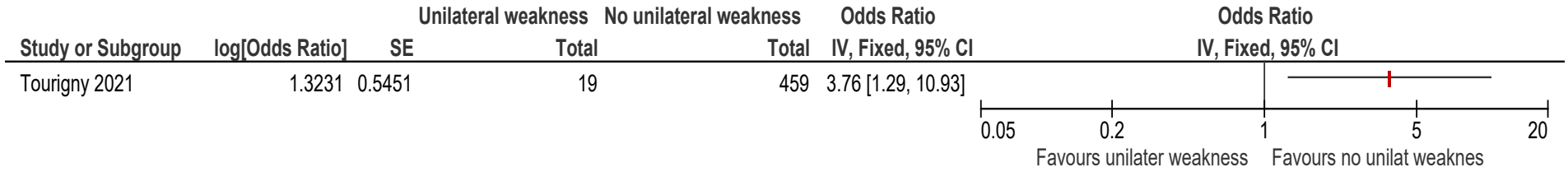
Figure 98: Abnormal vs. normal neurological examination for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

Figure 99: Unilateral weakness vs. no unilateral weakness on neurological assessment for predicting neurosurgical intervention – median time from admission to surgery was 16.1 h

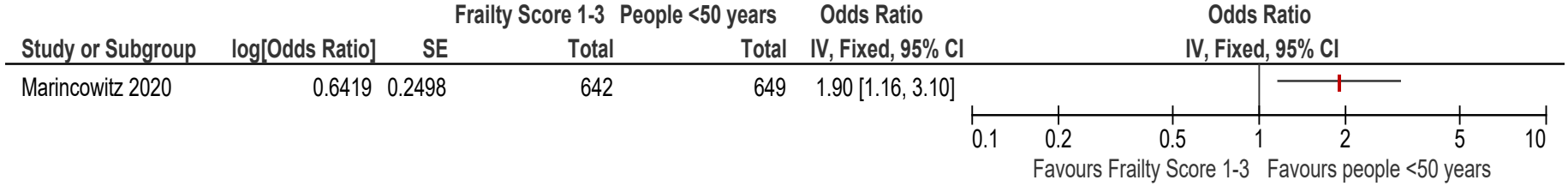


MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.

1

E.92 Adults – frailty/comorbidities

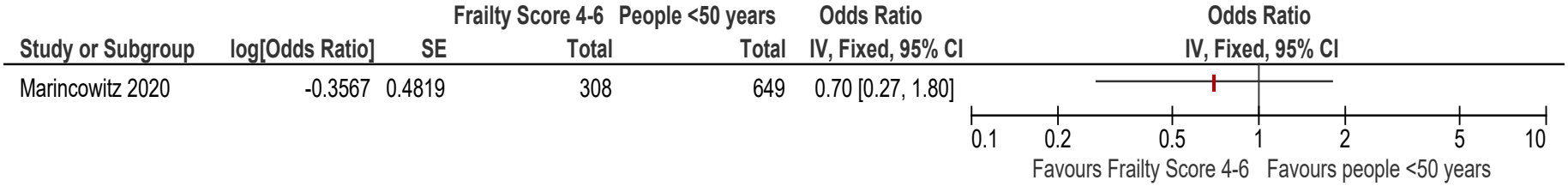
Figure 100: Rockwood Frailty Score 1-3 vs. people <50 years (frailty score not assessed/applicable) for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

3

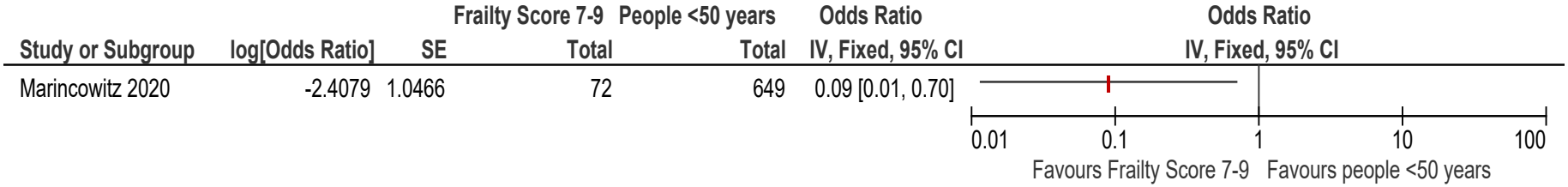
Figure 101: Rockwood Frailty Score 4-6 vs. people <50 years (frailty score not assessed/applicable) for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

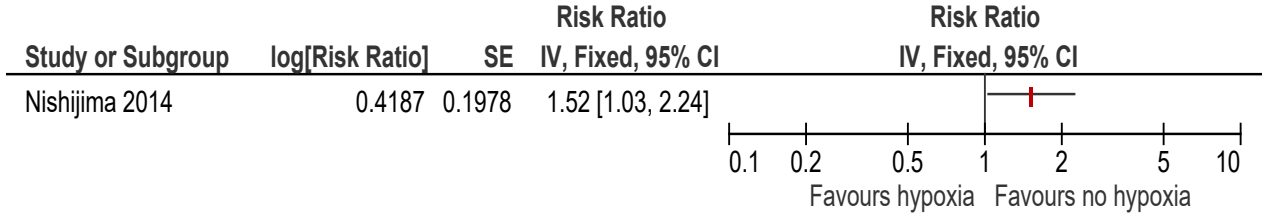
Figure 102: Rockwood Frailty Score 7-9 vs. people <50 years (frailty score not assessed/applicable) for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

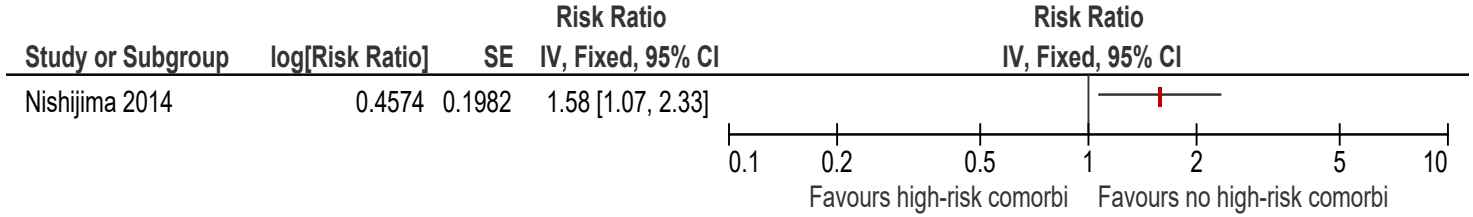
2

Figure 103: Hypoxia vs. no hypoxia prior to admission for predicting need for ICU admission (acute critical care intervention) within 48 h of ED arrival



MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.

Figure 104: Presence vs. absence of any high-risk comorbidity (atrial fibrillation or flutter, bleeding disorder, congestive heart failure, coronary artery disease, end-stage liver disease, pulmonary disease requiring oxygen at home or end-stage renal disease requiring dialysis) for predicting need for ICU admission (acute critical care intervention) within 48 h of ED arrival

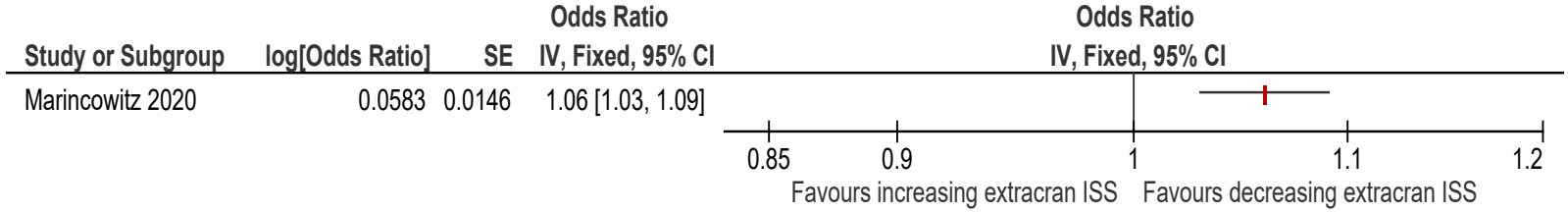


MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.

1

E.102 Adults – extracranial injury

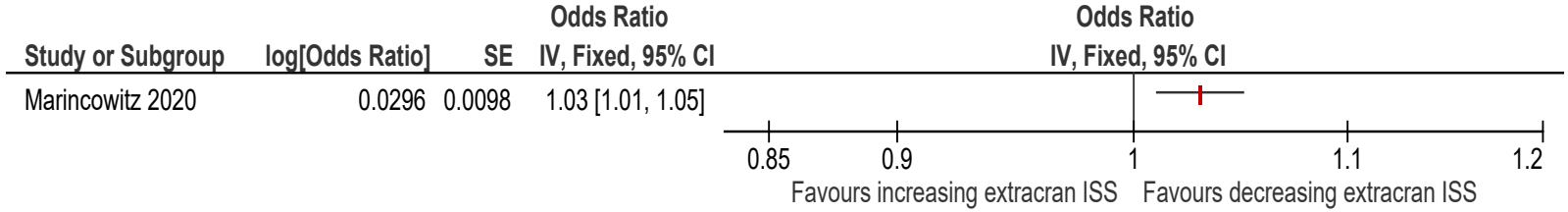
Figure 105: Increasing severity of extracranial injury (measured on ISS, per 1-unit increase) for predicting need for neurosurgical specialist admission at 30 days post-ED admission



MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)

1

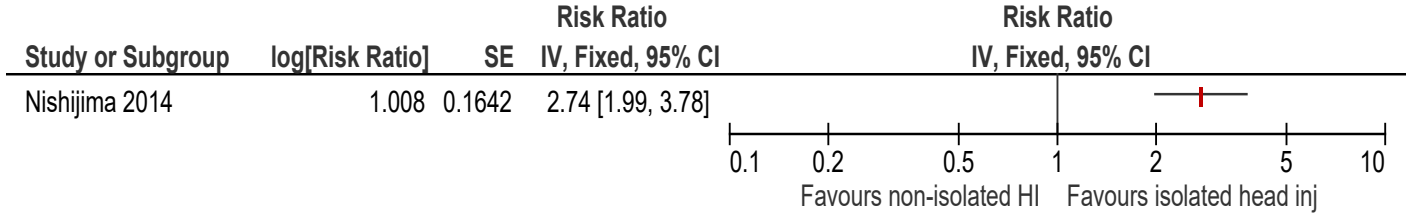
Figure 106: Increasing severity of extracranial injury (measured on ISS, per 1-unit increase) for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission



MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)

2

Figure 107: Non-isolated head injury vs. isolated head injury for predicting need for ICU admission (acute critical care intervention) within 48 h of ED arrival



MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury

1

Appendix F – GRADE tables

F.1 Adults/children – Clinical decision rules – sensitivity/specificity results

Note that full GRADE tables for diagnostic accuracy results are provided in section 1.1.6 and there are no appendix tables for this type of data.

F.2 Adults/children – Clinical decision rules – odds ratio results

Table 48: Clinical evidence profile: Adults – Hull Salford Cambridge Decision Rule

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Score >0 vs. score 0 on decision rule developed in the paper for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) - (≥15 years with blunt mild TBI, GCS ≥13 and intracranial haemorrhage on CT). **Decision rule included multiple variables, with following required for discharge: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination – not meeting at least one of these criteria meant admission was indicated with score >0.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	OR: 16.98 (4.16 to 69.30)	VERY LOW
Score >0 vs. score 0 on decision rule (validation in an existing cohort) for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration indicated by new deficit or drop in GCS of more than 1 point) - (≥16 years with GCS ≥13 attending ED, with either skull fracture, intracranial haemorrhage or cerebral contusion on first CT scan – excluded those with GCS unknown in ED and where diffuse axonal injury was sole injury on CT) – CENTER TBI population								

Decision rule included multiple variables, with following required for discharge: initial GCS 15, single simple skull fracture or haemorrhage <5 mm, up to two extracranial bony or organ injuries not requiring hospital admission, not anticoagulated/taking antiplatelets, no cerebellar/brain stem injuries, and normal neurological examination – not meeting at least one of these criteria meant admission was indicated with score >0								
1	Cohort study	very serious[1,4]	no serious inconsistency	serious[3]	no serious imprecision	none	OR: 23.33 (1.42 to 382.05)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[4] Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding domains

Table 49: Clinical evidence profile: Adults – BIG criteria

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
BIG score >1 vs. BIG 1 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) within 30 days post-ED admission - (≥15 years with blunt mild TBI, GCS ≥13 and intracranial haemorrhage on CT). **Decision rule included multiple variables, with following required for discharge: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated – not meeting at least one of these criteria meant admission was indicated with score >1**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	OR: 10.68 (2.59 to 43.99)	VERY LOW
BIG score >1 vs. BIG 1 for predicting need for hospital admission (composite of seizure as inpatient or at 2 week follow-up, death attributed to TBI within 30 days of first attendance, intubation recorded within 30 days of presentation, admission to ICU for any reason apart from close monitoring, neurosurgical intervention and recorded neurological deterioration								

indicated by new deficit or drop in GCS of more than 1 point) within 30 days post-ED admission - (≥16 years with GCS ≥13 attending ED, with either skull fracture, intracranial haemorrhage or cerebral contusion on first CT scan – excluded those with GCS unknown in ED and where diffuse axonal injury was sole injury on CT) – CENTER TBI population **Decision rule included multiple variables, with following required for discharge: no anticoagulation or antiplatelets, GCS 13-15, normal first neurological examination, injury severity on CT was subdural ≤4 mm, extradural ≤4 mm, 1 intracerebral haemorrhage ≤4 mm, trace subarachnoid haemorrhage, no skull fractures and no intraventricular haemorrhage, and not intoxicated – not meeting at least one of these criteria meant admission was indicated with score >1**								
1	Cohort study	very serious[1,4]	no serious inconsistency	serious[3]	no serious imprecision	none	OR: 2.69 (1.44 to 5.00)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[4] Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding domains

Table 50: Clinical evidence profile: Adults – Nishijima 2014 decision rule

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
≥1 four variables (GCS <15, non-isolated head injury, ≥65 years and presence of swelling or shift on initial cranial CT) vs. none for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **Decision rule included following four variables, with those with at least one of the criteria being considered to be positive as per the decision rule: admission GCS <15, non-isolated head injury, age 65 years or older and the presence of swelling or shift on initial cranial CT**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	OR: 37.49 (9.15 to 153.49)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study participation and outcome measurement domains

[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome time-point was at 48 h which is shorter than that specified as ideal in the protocol

Table 51: Clinical evidence profile: Adults – Pruitt 2017 decision rule – at least one high-risk predictor

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission with ninety percent of those with follow-up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	OR: • 41.84 (5.72 to 305.86) for derivation set • 12.13 (3.70 to 39.75) for validation set	VERY LOW
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death) with ninety percent of those with follow-up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use**								

1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[4]	serious[5] for validation set and none for derivation set	none	OR: • 10.49 (1.40 to 78.80) for derivation set • 2.82 (0.64 to 12.51) for validation set	VERY LOW
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting worsening repeat CT scan (defined as an increase in lesion size ≥ 2 mm, new midline shift, or the presence of a new area of haemorrhage) with ninety percent of those with follow-up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use**							
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	OR: • 20.70 (1.24 to 344.61) for derivation set • 7.58 (1.00 to 57.24) for validation set	VERY LOW
≥1 six variables (>1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use) vs. none for predicting neurosurgical procedure (intracranial pressure monitoring or operations) during admission with ninety percent of those with follow-up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **Decision rule included following six variables, with those with at least one of the criteria being considered to be positive as per the decision rule: >1 SDH lesion per patient, SDH thickness > 5 mm, presence of any midline shift, GCS < 14, warfarin use or clopidogrel use**							
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[4]	no serious imprecision	none	OR: • 41.81 (2.55 to 686.72) for derivation set • 23.59 (3.20 to 173.60) for validation set	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, outcome measurement and study confounding domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.

[4] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days.
[5] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)

Table 52: Clinical evidence profile: Children – Greenberg 2017 decision rule – CHIIDA score >0 or >2

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Score >0 on CHIIDA rule for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) with follow-up 7-90 days post-ED visit (varies between patients) - (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders) **CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	OR: 16.95 (6.76 to 42.50)	VERY LOW
Score >2 on CHIIDA rule for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) with follow-up 7-90 days post-ED visit (varies between patients) - (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders) **CHIIDA decision rule: developed based on multivariate risk model to predict need for ICU admission. Each variable in the model was assigned a point value ranging from 2 to 7, and each patient's score could range from 0 to 24. Variables were assigned the following number of points: depressed skull fracture (7 points); midline shift (7 points); epidural haematoma (5 points); GCS 13 (5 points) and GCS 14 (2 points).**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	OR: OR: 14.96 (7.54 to 29.67)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

F.3 Adults – Injury severity scales

Table 53: Clinical evidence profile: Head AIS score (unclear how analysed)

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Increasing head AIS score (increments analysed unclear) for predicting neurosurgical intervention at unclear time-point/possibly within same admission - (≥15 years with blunt mild TBI, GCS ≥13 and intracranial haemorrhage on CT) **MV analysis included: hospital length of stay, ICU length of stay, days of mechanical ventilation, head-AIS score, Injury Severity Score, skull fracture, abnormal initial neurological examination, subdural haemorrhage, subarachnoid haemorrhage.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 12.87 (6.47 to 25.58)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome time-point was unclear and possibly an initial management decision rather than also including any delayed interventions

1 **Table 54: Clinical evidence profile: Injury Severity Scale (ISS)**

Quality assessment							Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (including publication bias where possible)	Effect (95% CI)	
Increasing ISS score (increments analysed unclear) for predicting head CT progression on repeat CT within 24 h of initial CT - (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) **MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 1.07 (1.02 to 1.12)	VERY LOW
Increasing ISS score (increments analysed unclear) for predicting good outcome (GOS >4) at unclear time-point, possibly within same admission - (median age 48-49 years, patients with mild TBI defined as intracranial haemorrhage of 1 cm or less and GCS of at least 13 at time of arrival – excluded those with additional intracranial injuries, patients transferred to another acute care facility and those leaving against medical advice) **MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).**								
1	Cohort study	very serious[1,4]	no serious inconsistency	serious[5]	no serious imprecision	none	Adjusted OR: 0.87 (0.81 to 0.94)	VERY LOW
The following ISS categories were compared with ISS 0-6 category for predicting neurosurgical intervention at unclear time-point, possibly within the same admission: • **ISS 7-11** • **ISS 12-18** • **ISS 19-27** • **ISS >27** **(age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded)** **MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).**								

1	Cohort study	very serious[1,6]	no serious inconsistency	very serious[7]	no serious imprecision	none	Adjusted OR for individual groups vs. ISS 0-6 group: • OR 2.35 (1.35 to 4.09) for ISS 7-11 • OR 3.37 (1.94 to 5.86) for ISS 12-18 • OR 18.90 (10.82 to 33.00) for ISS 19-27 • OR 7.01 (3.67 to 13.40) for ISS >27	VERY LOW (applicable for all groups)

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[4] Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
[5] Downgraded by 1 increment for indirectness as GOS may not be a good representation of clinical deterioration and the time-point it is reported at is unclear, possibly within the same admission which is much shorter than 30 days specified in the protocol
[6] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[7] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

F.43 Adults/children – Specific features/measurements of lesions

Table 55: Clinical evidence profile: Adults/children – Subdural haemorrhage/haematoma measurements

Quality assessment	Effect	Quality

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (including publication bias where possible)	Effect (95% CI)	
Adults – Subdural haemorrhage ≤6 mm vs. >6 mm for predicting discharge within 24 h - (≥16 years with blunt head trauma, isolated cranial trauma – excluded those with GCS <13 or trauma to other organ systems requiring service other than neurosurgery) **MV analysis: full list of variables included not given but included at least the following three variables that were significantly associated with the outcome: GCS, isolated traumatic subarachnoid haemorrhage and subdural haematoma thickness ≤6 mm**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 3.10 (2.14 to 4.50)	VERY LOW
Adults – Subdural haemorrhage >10 mm vs. ≤10 mm for predicting progression on repeat CT within 6 h - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 4.80 (1.90 to 12.13)	VERY LOW
Adults – Subdural haemorrhage >10 mm vs. ≤10 mm for predicting for predicting neurosurgical intervention at unclear time-point, possibly within same admission - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[6]	no serious imprecision	none	Adjusted OR: 3.40 (2.10 to 5.50)	VERY LOW
Adults – Subdural haemorrhage width ≥4 mm vs. <4 mm for predicting neurosurgical intervention at median time from admission to surgery 16.1 h - (aged ≥16 years, diagnosed complicated mild TBI with either altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24 h or focal neurological deficit, and a complication including intracranial haemorrhage or skull fracture on initial CT – excluded penetrating injury, cerebral tumour and cerebral aneurysm) **MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.**								

1	Cohort study	very serious[1,7]	no serious inconsistency	very serious[8]	no serious imprecision	none	Adjusted OR: 3.76 (1.29 to 10.93)	VERY LOW
Adults – Max subdural haemorrhage thickness >5 mm vs. ≤5 mm for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission with ninety percent of those with follow-up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel**								
1	Cohort study	very serious[1,9]	no serious inconsistency	very serious[10]	no serious imprecision	none	Adjusted OR: 5.10 (2.42 to 10.75)	VERY LOW
Adults – Increasing initial volume of subdural haematoma lesion (ml) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery at ~1 week post-injury - (aged ≥15 years, acute trauma-related subdural haematoma diagnosed on CT, mild head injury with GCS 13-15, no focal neurological deficits, no significant mass effect, no significant midline shift, relatively small volume of subdural haematoma and medically managed at time of admission – excluded those where surgery performed within 24 h, neurological deterioration within 48 h, vascular abnormality, haemorrhage localised only to falx or tentorium cerebelli, bilateral acute subdural haematoma, other significant organ injury and those refusing surgical treatment) **MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present**								
1	Cohort study	very serious[1,11]	no serious inconsistency	very serious[12]	serious[13]	none	Adjusted OR: 2.52 (0.15 to 41.10)	VERY LOW
Adults – Increasing initial volume of subdural haematoma lesion (ml) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery at ~1 week post-injury - (aged ≥15 years, acute trauma-related subdural haematoma diagnosed on CT, mild head injury with GCS 13-15, no focal neurological deficits, no significant mass effect, no significant midline shift, relatively small volume of subdural haematoma and medically managed at time of admission – excluded those where surgery performed within 24 h, neurological deterioration within 48 h, vascular abnormality, haemorrhage localised only to falx or tentorium cerebelli, bilateral acute subdural haematoma, other significant organ injury and those refusing surgical treatment) **MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present**								
1	Cohort study	very serious[1,11]	no serious inconsistency	very serious[12]	no serious imprecision	none	Adjusted OR: 1.43 (1.09 to 1.89)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for outcome measurement, study confounding and statistical analysis/reporting domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome is indirect relevant to review protocol as there could be other

factors contributing to length of stay other than clinical deterioration
[4] Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[6] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol
[7] Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
[8] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol (might represent initial decision to perform surgery in some cases rather than delayed events due to clinical deterioration)
[9] Risk of bias was identified for study attrition, outcome measurement and study confounding domains
[10] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.
[11] Risk of bias was identified for study participation, prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
[12] Downgraded by 2 increments for indirectness as although there is some suggestion from the flow chart that only those with smaller injuries were included, this is not consistently clear within the paper; in addition, there is possible risk factor indirectness as measurements from up to three CT scans were included rather than only including those on the first CT scan and outcome is limited to a time period of 1 week, which is shorter than the 30 days in the protocol
[13] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)

Table 56: Clinical evidence profile: Adults – Epidural haemorrhage measurements

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Epidural haemorrhage >10 mm vs. ≤10 mm for predicting progression on repeat CT within 6 h - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 7.90 (2.40 to 26.01)	VERY LOW

Epidural haemorrhage >10 mm vs. ≤10 mm for predicting for predicting neurosurgical intervention at unclear time-point, possibly within same admission - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[4]	no serious imprecision	none	Adjusted OR: 3.50 (1.40 to 8.75)	VERY LOW
Increasing epidural haemorrhage volume as a continuous variable (per 1 cubic centimetre increase) for predicting delayed neurosurgical intervention (indicating failed non-operative management) within same admission (median hospital stay 8 days whole cohort) - (aged 15-75 years, acute TBI and traumatic intracranial haemorrhage on CT, admitted within 24 h of TBI, initial non-operative management – excluded penetrating injuries, moderate-severe TBI with GCS <13, negative CT for intracranial haemorrhage, immediate neurosurgical intervention and chronic/pre-existing intracranial haemorrhages only on initial CT) **MV analysis: has performed adjustment but does not provide details of those included in the final model**								
1	Cohort study	very serious[1,5]	no serious inconsistency	very serious[4]	no serious imprecision	none	Adjusted OR: 1.19 (1.04 to 1.36)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[4] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol
[5] Risk of bias was identified for study participation, prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains

Table 57: Clinical evidence profile: Adults/children – Specific features on CT

Quality assessment	Effect	Quality

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (including publication bias where possible)	Effect (95% CI)	
Adults – Degree of midline shift (mm) as a continuous variable (increments unclear) for predicting haematoma enlargement leading to surgery at ~1 week post-injury - (aged ≥15 years, acute trauma-related subdural haematoma diagnosed on CT, mild head injury with GCS 13-15, no focal neurological deficits, no significant mass effect, no significant midline shift, relatively small volume of subdural haematoma and medically managed at time of admission – excluded those where surgery performed within 24 h, neurological deterioration within 48 h, vascular abnormality, haemorrhage localised only to falx or tentorium cerebelli, bilateral acute subdural haematoma, other significant organ injury and those refusing surgical treatment) **MV analysis: full list of variables not provided but included the following significant ones at least: maximum thickness of haematoma in mm (continuous, increments unclear); volume of haematoma in ml (continuous, increments unclear); midline shift degree in mm (continuous, increments unclear); cerebral contusion present; and subarachnoid haemorrhage present**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 1.09 (1.02 to 1.17)	VERY LOW
Adults – Midline shift vs. no midline shift for predicting neurosurgical intervention at median time from admission to surgery 16.1 h - (aged ≥16 years, diagnosed complicated mild TBI with either altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24 h or focal neurological deficit, and a complication including intracranial haemorrhage or skull fracture on initial CT – excluded penetrating injury, cerebral tumour and cerebral aneurysm) **MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 7.51 (3.32 to 16.99)	VERY LOW
Adults – Midline shift vs. no midline shift for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission with ninety percent of those with follow-up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel**								
1	Cohort study	very serious[1,6]	no serious inconsistency	very serious[7]	no serious imprecision	none	Adjusted OR: 4.73 (2.42 to 9.24)	VERY LOW
Adults – Presence vs. absence of swelling or shift on admission CT for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than**								

15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.								
1	Cohort study	very serious[1,8]	no serious inconsistency	very serious[9]	no serious imprecision	none	Adjusted RR: 4.11 (3.08 to 5.48)	VERY LOW
Adults – The following CT injury severity categories were compared with simple skull fracture category for predicting need for neurosurgical specialist admission at 30 days post-ED admission: • **Complex skull fracture** • **1-2 bleeds <5 mm (total)** • **No or minimal mass effect** • **Significant midline shift** • **High/mixed density lesion** • **Cerebellar/brain stem injury** **(≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals)** **MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)**								
1	Cohort study	very serious[1,10]	no serious inconsistency	serious[11]	serious[12] (first three groups) or none (last three groups)	none	Adjusted OR for individual groups vs. simple skull fracture group: • OR 0.90 (0.17 to 4.90) for complex skull fracture group • OR 0.80 (0.16 to 4.10) for 1-2 bleeds <5 mm (total) group • OR 2.30 (0.55 to 9.70) for no/minimal mass effect group • OR 7.40 (1.62 to 33.90) for significant midline shift group • OR 37.10 (8.14 to 168.99) for high/mixed density lesion group • OR 8.50 (1.29 to 56.20) for cerebellar/brainstem injury group	VERY LOW
Adults – The following CT injury severity categories were compared with simple skull fracture category for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI at 30 days post-ED admission:								

• **Complex skull fracture** • **1-2 bleeds <5 mm (total)** • **No or minimal mass effect** • **Significant midline shift** • **High/mixed density lesion** • **Cerebellar/brain stem injury** **(≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals)** **MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)**								
1	Cohort study	very serious[1,10]	no serious inconsistency	serious[11]	serious[12] (first three groups) or none (last three groups)	none	Adjusted OR for individual groups vs. simple skull fracture group: • OR 1.40 (0.46 to 4.30) for complex skull fracture group • OR 1.10 (0.39 to 3.10) for 1-2 bleeds <5 mm (total) group • OR 2.30 (0.90 to 5.88) for no/minimal mass effect group • OR 6.80 (2.50 to 18.49) for significant midline shift group • OR 21.60 (7.69 to 60.70) for high/mixed density lesion group • OR 7.00 (1.91 to 25.70) for cerebellar/brainstem injury group	VERY LOW
Adults – Mass effect vs. no mass effect on CT for predicting head CT progression on repeat CT within 24 h of initial CT - (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) **MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT**								
1	Cohort study	very serious[1,13]	no serious inconsistency	very serious[14]	no serious imprecision	none	Adjusted OR: 2.02 (1.08 to 3.78)	VERY LOW
Adults – Mass effect vs. no mass effect on CT for predicting craniotomy being performed at unclear time-point, possibly within same admission - (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external)								

MV analysis: full list not provided but those that were significant and were included were initial mass effect, new/worse epidural haemorrhage on repeat CT, new/worse mass effect on repeat CT and new/worse herniation on repeat CT								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[15]	no serious imprecision	none	Adjusted OR: 5.24 (1.96 to 14.01)	VERY LOW
Children – Any midline shift vs. no midline shift for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) with follow-up 7-90 days post-ED visit (varies between patients) - (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders) **MV analysis: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15**								
1	Cohort study	very serious[1,16]	no serious inconsistency	very serious[17]	no serious imprecision	none	OR: 6.50 (3.70 to 11.42)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study participation, prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
[3] Downgraded by 2 increments for indirectness as although there is some suggestion from the flow chart that only those with smaller injuries were included, this is not consistently clear within the paper; in addition, there is possible risk factor indirectness as measurements from up to three CT scans were included rather than only including those on the first CT scan and outcome is limited to a time period of 1 week, which is shorter than the 30 days in the protocol
[4] Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol (might represent initial decision to perform surgery in some cases rather than delayed events due to clinical deterioration)
[6] Risk of bias was identified for study attrition, outcome measurement and study confounding domains
[7] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.
[8] Risk of bias was identified for study participation and outcome measurement domains
[9] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol
[10] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[11] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[12] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
[13] Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
[14] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[15] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of craniotomy, the time-point is unclear and possibly only captures events during same hospital admission rather than within 30 days
[16] Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding

[17] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

F.5 Adults/children – GCS

Table 58: Clinical evidence profile: Adults – GCS 15 vs. GCS 13-14

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
GCS 15 vs. GCS 13-14 for predicting discharge within 24 h - (≥16 years with blunt head trauma, isolated cranial trauma – excluded those with GCS <13 or trauma to other organ systems requiring service other than neurosurgery) **MV analysis: full list of variables included not given but included at least the following three variables that were significantly associated with the outcome: GCS, isolated traumatic subarachnoid haemorrhage and subdural haematoma thickness ≤6 mm**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 2.90 (1.90 to 4.43)	VERY LOW
GCS 15 vs. GCS 13-14 for predicting worsening of brain lesion on repeat head CT within average 13 h following initial CT - (mean age 51 years, patients admitted with mild head injury following blunt trauma with GCS 13-15 and loss of consciousness, short-term amnesia, headache, emesis or dizziness, all with head CT shortly after ED arrival and neurosurgical consultation requested) **MV analysis: only those that were significant were reported and a full list of variables included not given: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 0.32 (0.12 to 0.82)	VERY LOW

GCS 15 vs. GCS 13-14 for predicting favourable outcome (alive, admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention) at unclear time-point, possibly within same admission - (aged ≥18 years, admitted with blunt head trauma to trauma centre and ICU, mild TBI with GCS 13-15 at arrival in ED and intracranial haemorrhage confirmed on CT scan – excluded those dying within 24 h of admission, transferred from another facility, requiring emergency surgical intervention within 24 h, those not admitted to the ICU, left against advice, penetrating injuries, pregnancy and being in police custody) **MV analysis: GCS of 15 at admission to ICU, isolated subarachnoid haemorrhage, age <55 years, ED blood pressure, Marshall score, head AIS, and ISS <25**								
1	Cohort study	very serious[1,6]	no serious inconsistency	very serious[7]	no serious imprecision	none	Adjusted OR: 5.50 (1.61 to 18.80)	VERY LOW
GCS 15 vs. GCS 13-14 for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.**								
1	Cohort study	very serious[1,8]	no serious inconsistency	very serious[9]	no serious imprecision	none	Adjusted RR: 0.34 (0.24 to 0.47)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for outcome measurement, study confounding and statistical analysis/reporting domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome is indirect relevant to review protocol as there could be other factors contributing to length of stay other than clinical deterioration
[4] Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains as identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with a positive CT (14.0% had no finding on initial CT) and it is also not specific to those with small intracranial injuries; for outcome, lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[6] Risk of bias was identified for study attrition, outcome measurement, study confounding and statistical analysis/reporting domains
[7] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the composite outcome was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol
[8] Risk of bias was identified for study participation and outcome measurement domains
[9] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

1 **Table 59: Clinical evidence profile: Adults/children – GCS 14 vs. GCS 15**

Quality assessment							Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (including publication bias where possible)	Effect (95% CI)	
Adults – GCS 14 vs. GCS 15 for predicting need for neurosurgical specialist admission at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 2.30 (1.60 to 3.31)	VERY LOW
Adults – GCS 14 vs. GCS 15 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 1.60 (1.22 to 2.10)	VERY LOW
Adults – GCS 14 vs. GCS 15 for predicting head CT progression on repeat CT within 24 h of initial CT - (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) **MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 3.11 (1.77 to 5.48)	VERY LOW

Adults – GCS 14 vs. GCS 15 for predicting neurosurgical intervention at unclear time-point, possibly within same admission - (age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded) **MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[6]	serious[7]	none	Adjusted OR: 1.12 (0.97 to 1.29)	VERY LOW
Children – GCS 14 vs. GCS 15 for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) with follow-up 7-90 days post-ED visit (varies between patients) - (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders) **MV analysis: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15**								
1	Cohort study	very serious[1,8]	no serious inconsistency	very serious[9]	serious[7]	none	OR: 1.60 (0.82 to 3.12)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[4] Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[6] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol
[7] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
[8] Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding
[9] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

Table 60: Clinical evidence profile: Adults/children – GCS 13 vs. GCS 15

Quality assessment							Effect	Quality

Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (including publication bias where possible)	Effect (95% CI)	
Adults – GCS 13 vs. GCS 15 for predicting need for neurosurgical specialist admission at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 3.70 (2.32 to 5.90)	VERY LOW
Adults – GCS 13 vs. GCS 15 for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 2.30 (1.60 to 3.31)	VERY LOW
Adults – GCS 13 vs. GCS 15 for predicting head CT progression on repeat CT within 24 h of initial CT - (≥18 years arriving with GCS 13-15, head AIS at least 1, repeat CT within 24 h and no associated injuries – AIS score 0 for chest, abdomen, extremity and external) **MV analysis: full list not provided but those that were significant and were included were GCS, ISS and mass effect on CT**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 4.00 (2.02 to 7.93)	VERY LOW
Children – GCS 13 vs. GCS 15 for predicting composite outcome – neurosurgical intervention (e.g. intracranial pressure monitor placement and haematoma evacuation), intubation for >24 h for head trauma or death) with follow-up 7-90 days post-ED visit (varies between patients) - (aged <18 years, mild TBI, non-penetrating head trauma, and ED CT scan showing intracranial injury [intracranial haemorrhage, cerebral oedema, skull diastasis, midline shift, pneumocephalus, depressed skull fracture (depressed by at least the width of the skull), traumatic infarction, diffuse axonal injury, herniation, shear injury or sigmoid sinus thrombosis] – excluded those with trivial history or presentation, penetrating TBI, pre-existing comorbid neurological disease and bleeding disorders)								

MV analysis: depressed skull fracture, midline shift presence, epidural haematoma present, GCS score 13 or GCS 14 vs. GCS 15								
1	Cohort study	very serious[1,6]	no serious inconsistency	very serious[7]	no serious imprecision	none	OR: 3.40 (1.50 to 7.71)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[4] Risk of bias was identified for prognostic factor measurement, study confounding and statistical analysis/reporting domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[6] Risk of bias was identified for study attrition, prognostic factor measurement, outcome measurement and study confounding
[7] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and follow-up varies between 7 days and 90 days (meaning some had follow-up much shorter/longer than ideal 30 days in protocol)

Table 61: Clinical evidence profile: Adults – GCS 13 vs. GCS 14-15

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
GCS 13 vs. GCS 14-15 for predicting composite outcome of CT progression, change in neurologic status, need for surgery or death/comfort measures only at unclear time-point, possibly within same admission (mean length of stay was 3.6 and 8.3 days in those with and without outcome) - (≥16 years, CT-confirmed mild traumatic intracranial haemorrhage with GCS 13-15 presenting to ED – excluded those with penetrating head trauma) **MV analysis: final list unclear but following were considered for inclusion: age, hospital length of stay, sex, past medical history (such as anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 4.50 (2.47 to 8.20)	VERY LOW
Adults – GCS 13 vs. GCS 14-15 for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission with ninety percent of those with follow-up including clinical								

visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 4.09 (1.18 to 14.22)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome was measured up to discharge which is a much shorter period than the 30 days in the protocol and also includes components that may not present as clinical deterioration (e.g. progression on CT only)
[4] Risk of bias was identified for study attrition, outcome measurement and study confounding domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.

Table 62: Clinical evidence profile: Adults – GCS as a continuous measure/unclear increments

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
GCS motor scores on admission (unclear increments, possibly per 1-unit increase between 13 and 15?) for predicting good outcome (GOS >4) at unclear time-point, possibly within same admission - (median age 48-49 years, patients with mild TBI defined as intracranial haemorrhage of 1 cm or less and GCS of at least 13 at time of arrival – excluded those with additional intracranial injuries, patients transferred to another acute care facility and those leaving against medical advice) **MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 13.96 (2.23 to 87.30)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains

[3] Downgraded by 1 increment for indirectness as GOS may not be a good representation of clinical deterioration and the time-point it is reported at is unclear, possibly within the same admission which is much shorter than 30 days specified in the protocol

F.63 Adults – Anticoagulation/antiplatelet treatment

Table 63: Clinical evidence profile: Anticoagulation/antiplatelet use vs. no use

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Anticoagulant/antiplatelet use vs. no use for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)**							
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 1.40 (1.03 to 1.90)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries

Table 64: Clinical evidence profile: Antiplatelet therapy vs. no antiplatelet therapy

Quality assessment	Effect	Quality

Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Antiplatelet therapy vs. no antiplatelet therapy for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.**							
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted RR: 1.54 (1.03 to 2.30)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study participation and outcome measurement domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

Table 65: Clinical evidence profile: Anticoagulation disorder vs. no anticoagulation disorder

Quality assessment							**Effect**	**Quality**
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Anticoagulation disorder (any condition increasing risk of bleeding e.g. vitamin K deficiency, haemophilia, thrombocytopenia, chronic anticoagulation therapy) vs. no anticoagulation disorder for predicting neurosurgical intervention at unclear time-point, possibly within same admission - (age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded)								

MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	serious[4]	none	Adjusted OR: 0.85 (0.67 to 1.09)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol
[4] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)

Table 66: Clinical evidence profile: Warfarin use vs. no warfarin use

Adults – Warfarin use vs. no warfarin use for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission with ninety percent of those with follow-up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	serious[4]	none	Adjusted OR: 2.21 (0.97 to 5.01)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, outcome measurement and study confounding domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.
[4] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)

Table 67: Clinical evidence profile: Clopidogrel use vs. no clopidogrel use

Adults – Clopidogrel use vs. no clopidogrel use for predicting composite outcome of neurologic decline (decreasing mental status, regardless of cause, worsening neurologic examination, or death), worsening repeat CT scan or neurosurgical procedure (intracranial pressure monitoring or operations) during admission with ninety percent of those with follow-

up including clinical visits occurring greater than 30 days after initial presentation - (isolated subdural haemorrhage which included individuals with multiple SDHs but excluded patients with other types of haemorrhagic lesions, GCS 13-15, and age ≥16 years – excluded those with penetrating mechanism of injury, GCS <13, those with lesions other than SDH, and aged <16 years) **MV analysis: >1 SDH in a single patient, presence of any midline shift, maximum SDH thickness >5 mm, GCS 13 (vs. 14-15), use of warfarin and use of clopidogrel**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 2.70 (1.00 to 7.31)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, outcome measurement and study confounding domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the follow-up duration was unclear, though they reported that of those with clinical follow-up, 90% had follow-up >30 days. There was also indirectness for this outcome as it included 'worsening on CT' which is a radiological outcome rather than specifically clinical deterioration.

F.7 Adults – Age

Table 68: Clinical evidence profile: Age as a continuous variable (increments unclear)

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Increasing age as a continuous variable (increments unclear) for predicting good outcome (GOS >4) at unclear time-point, possibly within the same admission - (median age 48-49 years, patients with mild TBI defined as intracranial haemorrhage of 1 cm or less and GCS of at least 13 at time of arrival – excluded those with additional intracranial injuries, patients transferred to another acute care facility and those leaving against medical advice)								

MV analysis: trauma surgeon only vs. neurosurgical consultation, age as a continuous variable (increments unclear), GCS motor at admission as a continuous variable between 13 and 15 (increments unclear) and ISS as a continuous variable (increments unclear).								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 0.94 (0.91 to 0.97)	VERY LOW
Increasing age as a continuous variable (increments unclear) for predicting neurosurgical intervention at unclear time-point, possibly within the same admission - (age ≥18 years, diagnosed intracranial injury, admitted to hospital and with GCS 14-15 in ED – skull fractures, penetrating injury and AIS score >1 in other body region excluded) **MV analysis: age, anticoagulation disorder, ED GCS, ED systolic blood pressure, ED pulse, ED respiratory rate, ISS category (various vs. score of 0-6) and type of head injury (isolated subdural haemorrhage, isolated subarachnoid haemorrhage, isolated epidural haemorrhage or multiple injury types vs. contusion).**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 1.00 (1.00 to 1.00)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
[3] Downgraded by 1 increment for indirectness as GOS may not be a good representation of clinical deterioration and the time-point it is reported at is unclear, possibly within the same admission which is much shorter than 30 days specified in the protocol
[4] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

Table 69: Clinical evidence profile: Age as a continuous variable (per 1-unit increase)

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Increasing age as a continuous variable (per 1-unit increase) for predicting need for neurosurgical specialist admission at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals)								

MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 1.00 (1.00 to 1.00)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries

Table 70: Clinical evidence profile: Age – specific thresholds used as risk factors

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Age ≥65 vs. <65 years for predicting progression on repeat CT within 6 h - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	serious[4]	none	Adjusted OR: 1.40 (0.73 to 2.70)	VERY LOW
Age >65 vs. ≤65 years for predicting worsening of brain lesion on repeat head CT at average 13 h following initial CT - (mean age 51 years, patients admitted with mild head injury following blunt trauma with GCS 13-15 and loss of consciousness, short-term amnesia, headache, emesis or dizziness, all with head CT shortly after ED arrival and neurosurgical consultation requested) **MV analysis: only those that were significant were reported and a full list of variables included not given: time from injury to CT <90 min; age >65 years; GCS score <15; and multiple lesions on initial head CT**								

1	Cohort study	very serious[1,5]	no serious inconsistency	very serious[6]	no serious imprecision	none	Adjusted OR: 3.33 (1.29 to 8.60)	VERY LOW
Age ≥65 vs. <65 years for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.**								
1	Cohort study	very serious[1,7]	no serious inconsistency	very serious[8]	no serious imprecision	none	Adjusted RR: 1.46 (1.05 to 2.03)	VERY LOW
Age ≥60 vs. <60 years for predicting composite outcome of CT progression, change in neurologic status, need for surgery or death/comfort measures only at unclear time-point, possibly within same admission (mean length of stay was 3.6 and 8.3 days in those with and without outcome) - (≥16 years, CT-confirmed mild traumatic intracranial haemorrhage with GCS 13-15 presenting to ED – excluded those with penetrating head trauma) **MV analysis: final list unclear but following were considered for inclusion: age, hospital length of stay, sex, past medical history (such as anticoagulant/antiplatelet use, alcohol or drug use), mechanism of injury, GCS, type of lesion**								
1	Cohort study	very serious[1,5]	no serious inconsistency	very serious[9]	no serious imprecision	none	Adjusted OR: 1.60 (1.10 to 2.33)	VERY LOW
Age <55 vs. ≥55 years for predicting favourable outcome (alive, admission to ICU ≤24 h, no in-hospital complications and no neurosurgical intervention) at unclear time-point, possibly within same admission - (aged ≥18 years, admitted with blunt head trauma to trauma centre and ICU, mild TBI with GCS 13-15 at arrival in ED and intracranial haemorrhage confirmed on CT scan – excluded those dying within 24 h of admission, transferred from another facility, requiring emergency surgical intervention within 24 h, those not admitted to the ICU, left against advice, penetrating injuries, pregnancy and being in police custody) **MV analysis: GCS of 15 at admission to ICU, isolated subarachnoid haemorrhage, age <55 years, ED blood pressure, Marshall score, head AIS, and ISS <25**								
1	Cohort study	very serious[1,10]	no serious inconsistency	very serious[11]	no serious imprecision	none	Adjusted OR: 3.50 (1.09 to 11.20)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[4] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
[5] Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting domains

[6] Downgraded by 2 increments for indirectness as the population was not specific to those with a positive CT (14.0% had no finding on initial CT) and it is also not specific to those with small intracranial injuries; for outcome, lesion progression may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[7] Risk of bias was identified for study participation and outcome measurement domains
[8] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol
[9] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome was measured up to discharge which is a much shorter period than the 30 days in the protocol and also includes components that may not present as clinical deterioration (e.g. progression on CT only)
[10] Risk of bias was identified for study attrition, outcome measurement, study confounding and statistical analysis/reporting domains
[11] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the composite outcome was reported at an unclear time-point, possibly within the same admission which was much shorter than 30 days specified in the protocol

F.82 Adults – Blood measurements

Table 71: Clinical evidence profile: Blood measurements

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Platelet ≤100,000 mm-3 vs. >100,000 mm-3 for predicting progression on repeat CT within 6 h - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	serious[4]	none	Adjusted OR: 1.30 (0.47 to 3.60)	VERY LOW

Platelet ≤100,000 mm-3 vs. >100,000 mm-3 for predicting neurosurgical intervention at unclear time-point, possibly within same admission - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[5]	serious[4]	none	Adjusted OR: 1.60 (0.53 to 4.80)	VERY LOW
Lactate ≤2.5 vs. >2.5 for predicting progression on repeat CT within 6 h - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	serious[4]	none	Adjusted OR: 2.10 (0.89 to 4.95)	VERY LOW
Lactate ≤2.5 vs. >2.5 for predicting neurosurgical intervention at unclear time-point, possibly within same admission - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[5]	serious[4]	none	Adjusted OR: 1.90 (0.62 to 5.82)	VERY LOW
Base deficit >4 vs. ≤4 for predicting progression on repeat CT within 6 h - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery) **MV analysis: loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.**								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[3]	no serious imprecision	none	Adjusted OR: 2.80 (1.60 to 4.90)	VERY LOW
Base deficit >4 vs. ≤4 for predicting neurosurgical intervention at unclear time-point, possibly within same admission - (aged ≥18 years, isolated traumatic brain injury with scores <3 on AIS for other body regions and score of at least 3 for head, GCS 13-15 on presentation, intracranial injury including skull fracture or intracranial haemorrhage on initial head CT, and routine repeat head CT – excluded those on antiplatelets/anticoagulants, transferred from other institutions and those having emergency neurosurgery)								

MV analysis: age ≥65 years; loss of consciousness; displaced skull fracture; subdural haemorrhage >10 mm; epidural haemorrhage >10 mm; platelet ≤100,000; lactate ≤2.5; and base deficit >4.								
1	Cohort study	very serious[1,2]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 21.00 (1.60 to 275.64)	VERY LOW
Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L) for predicting need for neurosurgical specialist admission at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)**								
1	Cohort study	very serious[1,6]	no serious inconsistency	serious[7]	serious[4]	none	Adjusted OR: 0.99 (0.98 to 1.00)	VERY LOW
Increasing haemoglobin as a continuous variable (per 1-unit increase, g/L) for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)**								
1	Cohort study	very serious[1,6]	no serious inconsistency	serious[7]	serious[4]	none	Adjusted OR: 0.99 (0.98 to 1.00)	VERY LOW

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for prognostic factor measurement, outcome measurement and study confounding domains
[3] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of CT lesion worsening may not always lead to clinical deterioration (indirect relative to examples of clinical deterioration in protocol such as death, readmission or seizures)
[4] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol
[6] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[7] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries

F.92 Adults – Abnormal neurological examination

Table 72: Clinical evidence profile: abnormal neurological symptoms/examination findings

Quality assessment							Effect	Quality
Number of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations (including publication bias where possible)	Effect (95% CI)	
Abnormal vs. normal neurological examination for predicting need for neurosurgical specialist admission at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 1.90 (1.20 to 3.00)	VERY LOW
Abnormal vs. normal neurological examination for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals)								

MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 1.70 (1.20 to 2.41)	VERY LOW
Unilateral weakness vs. no unilateral weakness on neurological assessment for predicting neurosurgical intervention at median time from admission to surgery 16.1 h - (aged ≥16 years, diagnosed complicated mild TBI with either altered consciousness, loss of consciousness ≤30 min, post-traumatic amnesia <24 h or focal neurological deficit, and a complication including intracranial haemorrhage or skull fracture on initial CT – excluded penetrating injury, cerebral tumour and cerebral aneurysm) **MV analysis: full list of variables not provided but included the following significant ones at least: unilateral weakness on neurological assessment, subarachnoid haemorrhage, subdural haemorrhage ≥4 mm width and midline shift.**								
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted OR: 3.76 (1.29 to 10.93)	VERY LOW

Unilateral weakness vs. no unilateral weakness on neurological assessment for predicting neurosurgical intervention

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[4] Risk of bias was identified for prognostic factor measurement, outcome measurement, study confounding and statistical analysis/reporting
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of neurosurgical intervention was reported at an unclear time-point, possibly within the same admission which may be much shorter than 30 days specified in the protocol (might represent initial decision to perform surgery in some cases rather than delayed events due to clinical deterioration)

F.10 Adults – Frailty/comorbidities

1 **Table 73: Clinical evidence profile: Frailty/comorbidities**

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
The following categories on Rockwood Frailty Score were individually compared to a group of people <50 years (frailty score not assessed/applicable) for predicting need for neurosurgical specialist admission at 30 days post-ED admission: • **Frailty score 1-3** • **Frailty score 4-6** • **Frailty score 7-9** **(≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals)** **MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	serious[4] (second comparison only) or no serious imprecision (first and third comparisons)	none	Adjusted OR: • Frailty score 1-3, 1.90 (1.16 to 3.10) • Frailty score 4-6, 0.70 (0.27 to 1.80) • Frailty score 7-9, 0.09 (0.01 to 0.70)	VERY LOW (for all groups)

Hypoxia vs. no hypoxia prior to admission for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.**								
1	Cohort study	very serious[1,5]	no serious inconsistency	very serious[6]	no serious imprecision	none	Adjusted RR: 1.52 (1.03 to 2.24)	VERY LOW
Presence vs. absence of any high-risk comorbidity (atrial fibrillation or flutter, bleeding disorder, congestive heart failure, coronary artery disease, end-stage liver disease, pulmonary disease requiring oxygen at home or end-stage renal disease requiring dialysis) for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.**								
1	Cohort study	very serious[1,5]	no serious inconsistency	very serious[6]	no serious imprecision	none	Adjusted RR: 1.58 (1.07 to 2.33)	VERY LOW

Unilateral weakness vs. no unilateral weakness on neurological assessment for predicting neurosurgical intervention

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[4] Downgraded by 1 increment as serious imprecision was present as the confidence intervals crossed the null line (1.0)
[5] Risk of bias was identified for study participation and outcome measurement domains
[6] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

F.11 Adults – Extracranial injury

Table 74: Clinical evidence profile: Extracranial injury/non-isolated head injury

Quality assessment							Effect	Quality
Number of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations (including publication bias where possible)**	**Effect (95% CI)**	
Increasing severity of extracranial injury (measured on ISS, per 1-unit increase) for predicting need for neurosurgical specialist admission at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals) **MV analysis: age (years per 1-unit increase), GCS (vs. score of 15), abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture), skull fracture (complex present vs. not), subdural bleed (present vs. not), extracranial injury (ISS per 1-unit increase) and Rockwood Frailty Scale score (three categories versus people <50 years)**								
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 1.06 (1.03 to 1.09)	VERY LOW
Increasing severity of extracranial injury (measured on ISS, per 1-unit increase) for predicting deterioration (composite of death due to TBI, neurosurgery, seizure, >1 drop in GCS, ICU admission for TBI, intubation or hospital readmission for TBI) at 30 days post-ED admission - (≥16 years old; presenting with GCS 13-15 attending ED following acute TBI; and injuries reported on CT brain scan (skull fractures, extradural haemorrhage, subdural haemorrhage with an acute component, intracerebral haemorrhage, contusions, subarachnoid haemorrhage and intraventricular haemorrhage – considered traumatic in aetiology when mechanism of injury or injuries indicating trauma were recorded – excluded non-traumatic injuries, pre-existing CT abnormalities and patients transferred from other hospitals)								

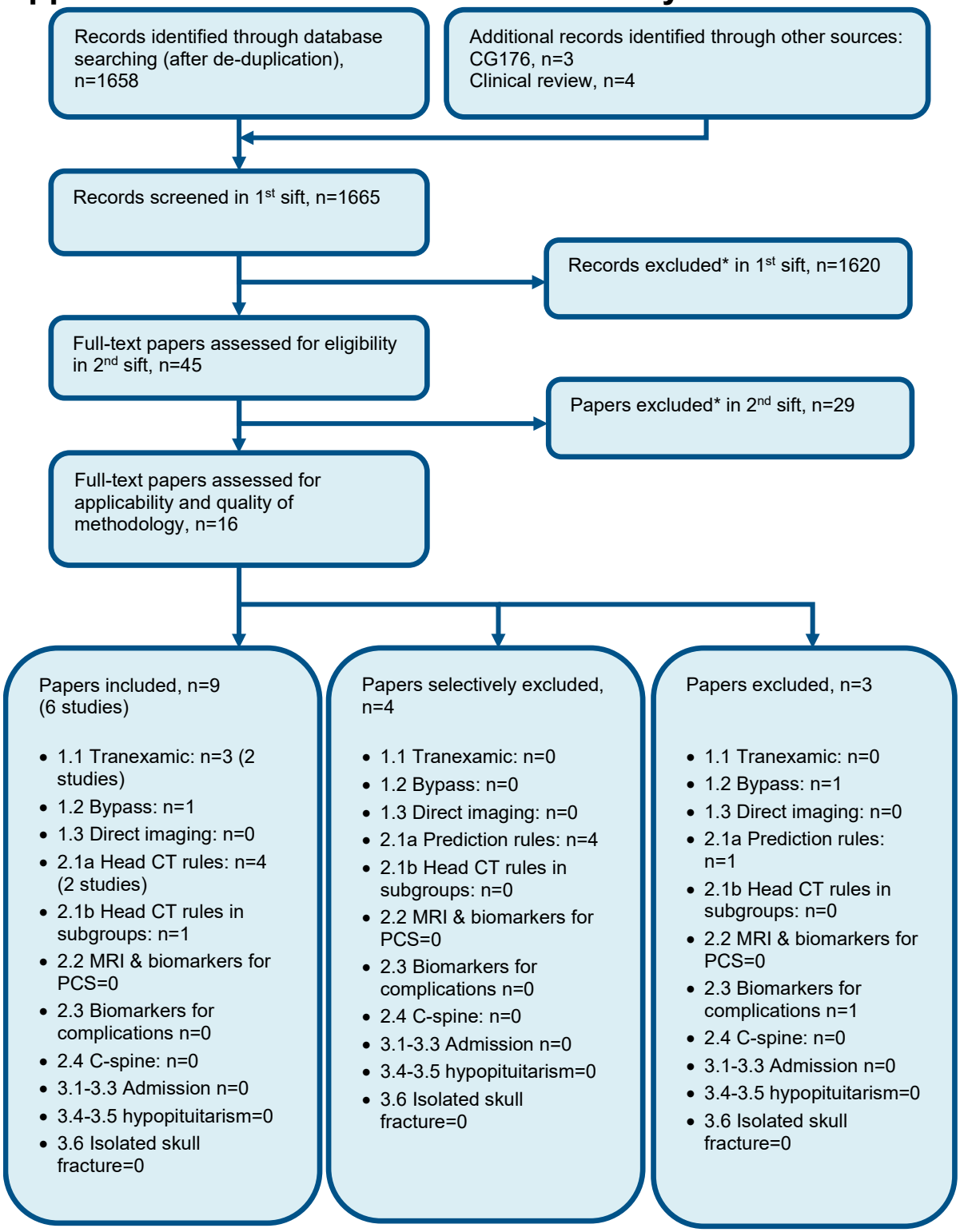
Unilateral weakness vs. no unilateral weakness on neurological assessment for predicting

MV analysis: GCS (vs. score of 15), preinjury anticoagulation or antiplatelets, abnormal neurological examination, haemoglobin (g/L per 1-unit increase), injury severity on CT (categories described above under prognostic factors, versus simple skull fracture) and extracranial injury (ISS per 1-unit increase)									neurosurgical intervention
1	Cohort study	very serious[1,2]	no serious inconsistency	serious[3]	no serious imprecision	none	Adjusted OR: 1.03 (1.01 to 1.05)	VERY LOW	
Non-isolated head injury vs. isolated head injury for predicting need for ICU admission (acute critical care intervention within 48 h of ED arrival) - (aged ≥18 years, mild traumatic intracranial haemorrhage on initial CT, initial GCS 13-15 – excluded those with pre-existing DNR orders and those using preinjury anticoagulation drugs) **MV analysis: Age ≥65 years, non-fall from standing, mechanism of injury (fall from height, motor vehicle collision, pedestrian/bicyclist struck, direct blow to the head, other or unknown mechanism of injury), pre-injury antiplatelet use (aspirin or clopidogrel), the presence of any pre-defined high risk co-morbidity (atrial fibrillation or atrial flutter, bleeding disorder, congestive heart failure, coronary artery disease, end stage liver disease, pulmonary disease requiring home oxygen, and end stage renal disease requiring dialysis) GCS score less than 15 at the time of admission, hypotension (systolic blood pressure less than 90 mmHg at any point in the ED), hypoxia (pulse oximetry reading less than 95% at any point in the ED), presence of intracranial swelling (cisterns are compressed or absent) or midline shift on initial cranial CT, presence of a depressed skull fracture, and non-isolated head injury.**									
1	Cohort study	very serious[1,4]	no serious inconsistency	very serious[5]	no serious imprecision	none	Adjusted RR: 2.74 (1.99 to 3.78)	VERY LOW	

[1] Downgraded by 1 increment if the majority of the evidence was at moderate risk of bias, and downgraded by 2 increments if the majority of evidence was at high risk of bias
[2] Risk of bias was identified for study attrition, prognostic factor measurement and outcome measurement domains
[3] Downgraded by 1 increment for indirectness as the population was not specific to those with small intracranial injuries
[4] Risk of bias was identified for study participation and outcome measurement domains
[5] Downgraded by 2 increments for indirectness as the population was not specific to those with small intracranial injuries, and the outcome of need for ICU admission was reported at 48 h, which is much shorter than 30 days specified in the protocol

1

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 – Health economic model

Modelling was not undertaken for this question.

1 Appendix J – Excluded studies

2 Clinical studies

3 Table 75: Studies excluded from the clinical review

Study	Code [Reason]
AbdelFattah, K. R., Eastman, A. L., Aldy, K. N. et al. (2012) A prospective evaluation of the use of routine repeat cranial CT scans in patients with intracranial hemorrhage and GCS score of 13 to 15. The Journal of Trauma and Acute Care Surgery 73(3): 685-8	- Prognostic data for risk factors relevant to review protocol not reported
af Geijerstam, J. L. and Britton, M. (2003) Mild head injury - mortality and complication rate: meta-analysis of findings in a systematic literature review. Acta Neurochirurgica 145(10): 843-50; discussion 850	- Systematic review used as source of primary studies
Ahmad, T.; Imran, S.; Sarfraz, K. (2015) Risk factors of progressive epidural hematoma in patients with head trauma. Rawal Medical Journal 40(3): 303-306	- Not limited to GCS 13-15
Albers, C. E., von Allmen, M., Evangelopoulos, D. S. et al. (2013) What is the incidence of intracranial bleeding in patients with mild traumatic brain injury? A retrospective study in 3088 Canadian CT head rule patients. BioMed Research International 2013: 453978	- Only a very small proportion were CT-positive and results not provided separately for this subgroup
Albertine, P., Borofsky, S., Brown, D. et al. (2016) Small subdural hemorrhages: is routine intensive care unit admission necessary?. American Journal of Emergency Medicine 34(3): 521-4	- Not limited to GCS 13-15
Allison, R. Z., Nakagawa, K., Hayashi, M. et al. (2017) Derivation of a Predictive Score for Hemorrhagic Progression of Cerebral Contusions in Moderate and Severe Traumatic Brain Injury. Neurocritical Care 26(1): 80-86	- Population limited to moderate or severe TBI (GCS <13)
Ament, J. D., Greenan, K. N., Tertulien, P. et al. (2017) Medical necessity of routine admission of children with mild traumatic brain injury to the intensive care unit. Journal of Neurosurgery. Pediatrics. 19(6): 668-674	- Insufficient reporting of data for individual risk factors
Atalay, T., Ak, H., Gulsen, I. et al. (2019) Risk factors associated with mortality and survival of acute subdural hematoma: A retrospective	- All already treated surgically to be included

Study	Code [Reason]
study. Journal of Research in Medical Sciences 24: 27	
Aziz, H., Rhee, P., Pandit, V. et al. (2013) Mild and moderate pediatric traumatic brain injury: replace routine repeat head computed tomography with neurologic examination. The Journal of Trauma and Acute Care Surgery 75(4): 550-4	- Prognostic data for risk factors relevant to review protocol not reported
Baraniskin, A., Steffens, C., Harders, A. et al. (2014) Impact of pre-hospital antithrombotic medication on the outcome of chronic and acute subdural hematoma. Journal of Neurological Surgery 75(1): 31-6	- Population limited to moderate or severe TBI (GCS <13)
Bardes, J. M., Turner, J., Bonasso, P. et al. (2016) Delineation of Criteria for Admission to Step Down in the Mild Traumatic Brain Injury Patient. American Surgeon 82(1): 36-40	- No multivariate analysis
Bata, S. C. and Yung, M. (2014) Role of routine repeat head imaging in paediatric traumatic brain injury. ANZ Journal of Surgery 84(6): 438-41	- Not limited to GCS 13-15
Bee, T. K., Magnotti, L. J., Croce, M. A. et al. (2009) Necessity of repeat head CT and ICU monitoring in patients with minimal brain injury. Journal of Trauma-Injury Infection & Critical Care 66(4): 1015-8	- Data not reported in an extractable format or a format that can be analysed
Behrouz, R., Misra, V., Godoy, D. A. et al. (2017) Clinical Course and Outcomes of Small Supratentorial Intracerebral Hematomas. Journal of Stroke and Cerebrovascular Diseases 26(6): 1216-1221	- Population - spontaneous haemorrhages not following trauma
Borczuk, P., Penn, J., Peak, D. et al. (2013) Patients with traumatic subarachnoid hemorrhage are at low risk for deterioration or neurosurgical intervention. The Journal of Trauma and Acute Care Surgery 74(6): 1504-9	- No multivariate analysis
Bossers, S. M., Pol, K. M., Oude Ophuis, E. P. A. et al. (2018) Discrepancy between the initial assessment of injury severity and post hoc determination of injury severity in patients with apparently mild traumatic brain injury: a retrospective multicenter cohort analysis. European Journal of Trauma & Emergency Surgery 44(6): 889-896	- Outcome not relevant to review protocol

Study	Code [Reason]
Boulouis, G., Hak, J. F., Kerleroux, B. et al. (2021) Hemorrhage Expansion After Pediatric Intracerebral Hemorrhage. Stroke 52(2): 588-594	- Population - limits only to those receiving repeat CT which may bias population towards a group that have all already experienced clinical deterioration
Brown, A. W., Pretz, C. R., Bell, K. R. et al. (2019) Predictive utility of an adapted Marshall head CT classification scheme after traumatic brain injury. Brain Injury 33(5): 610-617	- Data not reported in an extractable format or a format that can be analysed - Insufficient reporting of data for individual risk factors
Brown, C. V., Weng, J., Oh, D. et al. (2004) Does routine serial computed tomography of the head influence management of traumatic brain injury? A prospective evaluation. Journal of Trauma-Injury Infection & Critical Care 57(5): 939-43	- Not limited to GCS 13-15 - Prognostic data for risk factors relevant to review protocol not reported
Buchele, G., Rapp, K., Bauer, J. M. et al. (2020) Risk of traumatic intracranial haemorrhage is increased in older people exposed to oral anticoagulation with phenprocoumon. Aging Clinical and Experimental Research 32(3): 441-447	- Outcome not relevant to review protocol
Calvi, M. R., Beretta, L., Dell'Acqua, A. et al. (2011) Early prognosis after severe traumatic brain injury with minor or absent computed tomography scan lesions. Journal of Trauma-Injury Infection & Critical Care 70(2): 447-51	- Population limited to moderate or severe TBI (GCS <13)
Carlson, A. P., Ramirez, P., Kennedy, G. et al. (2010) Low rate of delayed deterioration requiring surgical treatment in patients transferred to a tertiary care center for mild traumatic brain injury. Neurosurgical Focus 29(5): e3	- Prognostic data for risk factors relevant to review protocol not reported
Chan, C. H. (2010) Clinical predictors of minor head injury patients presenting with Glasgow coma scale score of 14 or 15 and requiring neurosurgical intervention. Hong Kong Journal of Emergency Medicine 17(3): 256-261	- Study design not relevant to this review protocol
Chen, M., Li, Z., Yan, Z. et al. (2022) Predicting neurological deterioration after moderate traumatic brain injury: development and validation of a prediction model based on data collected on admission. Journal of Neurotrauma 39:371-378.	- Not limited to GCS 13-15

Study	Code [Reason]
Chien, S. C., Tu, P. H., Liu, Z. H. et al. (2021) Neurological deteriorations in mild brain injuries: the strategy of evaluation and management. European journal of trauma and emergency surgery : official publication of the European Trauma Society. 24	- No multivariate analysis
Chieregato, A., Fainardi, E., Morselli-Labate, A. M. et al. (2005) Factors associated with neurological outcome and lesion progression in traumatic subarachnoid hemorrhage patients. Neurosurgery 56(4): 671-80; discussion 671	- Not limited to GCS 13-15
Chojak, R., Kozba-Gosztyla, M., Pawlowski, M. et al. (2021) Deterioration After Mild Traumatic Brain Injury: A Single-Center Experience With Cost Analysis. Frontiers in neurology [electronic resource]. 12: 588429	- No multivariate analysis
Choudhry, O. J., Prestigiacomo, C. J., Gala, N. et al. (2013) Delayed neurological deterioration after mild head injury: cause, temporal course, and outcomes. Neurosurgery 73(5): 753-60; discussion 760	- Limits population to those experiencing deterioration rather than looking at predictors for deterioration
Dacey, R. G., Jr., Alves, W. M., Rimel, R. W. et al. (1986) Neurosurgical complications after apparently minor head injury. Assessment of risk in a series of 610 patients. Journal of Neurosurgery 65(2): 203-10	- Only a very small proportion were CT-positive and results not provided separately for this subgroup
Dalle Ore, C. L., Rennert, R. C., Schupper, A. J. et al. (2018) The identification of a subgroup of children with traumatic subarachnoid hemorrhage at low risk of neuroworsening. Journal of Neurosurgery. Pediatrics. 22(5): 559-566	- Data not reported in an extractable format or a format that can be analysed
Della Pepa, G. M., Covino, M., Menna, G. et al. (2021) Are oral anticoagulants a risk factor for mild traumatic brain injury progression? A single-center experience focused on of direct oral anticoagulants and vitamin K antagonists. Acta Neurochirurgica 30: 30	- Population - limits only to those receiving repeat CT which may bias population towards a group that have all already experienced clinical deterioration
Dowlatshahi, D., Smith, E. E., Flaherty, M. L. et al. (2011) Small intracerebral haemorrhages are associated with less haematoma expansion and better outcomes. International Journal of Stroke 6(3): 201-206	- Population - excluded injuries as a result of head trauma

Study	Code [Reason]
Dua, V., Ahuja, N., Bhagat, H. et al. (2016) Outcome in patients with head injury: Do extra-cranial injuries worsen prognosis?. Anaesthesia, Pain and Intensive Care 20(4): 411-416	- Not limited to GCS 13-15 - Data not reported in an extractable format or a format that can be analysed
Espersen, J. O. and Petersen, O. F. (1982) Computerized tomography (CT) in patients with head injuries. Assessment of outcome based upon initial clinical findings and initial CT scans. Acta Neurochirurgica 65(12): 81-91	- Population not limited to GCS 13-15 and not all with confirmed injury on CT
Fabbri, A., Servadei, F., Marchesini, G. et al. (2013) Antiplatelet therapy and the outcome of subjects with intracranial injury: the Italian SIMEU study. Critical Care (London, England) 17(2): r53	- Not limited to GCS 13-15
Fabbri, A., Servadei, F., Marchesini, G. et al. (2008) Observational approach to subjects with mild-to-moderate head injury and initial non-neurosurgical lesions. Journal of Neurology, Neurosurgery & Psychiatry 79(10): 1180-5	- Prognostic data for risk factors relevant to review protocol not reported
Feuerman T, Wackym PA, Gade GF et al. (1988) Value of skull radiography, head computed tomographic scanning, and admission for observation in cases of minor head injury. Neurosurgery 22(3): 449-453	- No multivariate analysis
Fiorelli, E. M., Bozzano, V., Bonzi, M. et al. (2020) Incremental Risk of Intracranial Hemorrhage After Mild Traumatic Brain Injury in Patients on Antiplatelet Therapy: Systematic Review and Meta-Analysis. Journal of Emergency Medicine 59(6): 843-855	- Population is not those with confirmed abnormality on initial CT
Franschman, G., Boer, C., Andriessen, T. M. et al. (2012) Multicenter evaluation of the course of coagulopathy in patients with isolated traumatic brain injury: relation to CT characteristics and outcome. Journal of Neurotrauma 29(1): 128-36	- Population limited to moderate or severe TBI (GCS <13)
Geoffrey Christopher Darby (2015) Mild Traumatic Brain Injury: The Feasibility of Reducing Repetitive Head CT Scans in Stable Patients.	- Population - limits only to those receiving repeat CT which may bias population towards a group that have all already experienced clinical deterioration
Godano, U., Serracchioli, A., Servadei, F. et al. (1992) Intracranial lesions of surgical interest in	- Prognostic data for risk factors relevant to review protocol not reported

Study	Code [Reason]
minor head injuries in paediatric patients. Childs Nervous System 8(3): 136-8	
Greenberg, J. K., Stoev, I. T., Park, T. S. et al. (2014) Management of children with mild traumatic brain injury and intracranial hemorrhage. The Journal of Trauma and Acute Care Surgery 76(4): 1089-95	- No multivariate analysis
Greuters, S., van den Berg, A., Franschman, G. et al. (2011) Acute and delayed mild coagulopathy are related to outcome in patients with isolated traumatic brain injury. Critical Care (London, England) 15(1): r2	- Population limited to moderate or severe TBI (GCS <13)
Gul, H. F., Simsek, A. T., Dolanbay, T. et al. (2021) Evaluation of blood glucose and inflammation markers in pediatric head injuries. Eastern Journal of Medicine 26(1): 67-74	- Data not reported in an extractable format or a format that can be analysed
Hamilton, M.; Mrazik, M.; Johnson, D. W. (2010) Incidence of delayed intracranial hemorrhage in children after uncomplicated minor head injuries. Pediatrics 126(1): e33-9	- Population is not those with confirmed abnormality on initial CT
Hollingworth, W., Vavilala, M. S., Jarvik, J. G. et al. (2007) The use of repeated head computed tomography in pediatric blunt head trauma: factors predicting new and worsening brain injury. Pediatric Critical Care Medicine 8(4): 348-56; CEU quiz 357	- Not limited to GCS 13-15 - Prognostic data for risk factors relevant to review protocol not reported
Hylek, E. M. and Singer, D. E. (1994) Risk factors for intracranial hemorrhage in outpatients taking warfarin. Annals of Internal Medicine 120(11): 897-902	- Population - excluded injuries as a result of head trauma - Study design not relevant to this review protocol
Iaccarino, C., Schiavi, P., Picetti, E. et al. (2014) Patients with brain contusions: predictors of outcome and relationship between radiological and clinical evolution. Journal of Neurosurgery 120(4): 908-18	- Data not reported in an extractable format or a format that can be analysed
Karanci, Y. and Oktay, C. (2021) Repeat CT after blunt head trauma and Glasgow Coma Scale score 13-15 without neurological deterioration is very low yield for intervention. European journal of trauma and emergency surgery : official publication of the European Trauma Society. 23	- No multivariate analysis

Study	Code [Reason]
Marincowitz, C., Lecky, F. E., Townend, W. et al. (2018) The Risk of Deterioration in GCS13-15 Patients with Traumatic Brain Injury Identified by Computed Tomography Imaging: A Systematic Review and Meta-Analysis. Journal of Neurotrauma 35(5): 703-718	- Systematic review used as source of primary studies
Marincowitz, C., Paton, L., Lecky, F. et al. (2021) 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 08: 08	- Prognostic data for risk factors relevant to review protocol not reported
Miller EC; Holmes JF; Derlet RW (1997) Utilizing clinical factors to reduce head CT scan ordering for minor head trauma patients. The Journal of emergency medicine 15(4): 453-457	- Population is not those with confirmed abnormality on initial CT
Mizu, D., Matsuoka, Y., Huh, J. Y. et al. (2021) Head CT findings and deterioration risk in children with head injuries and Glasgow Coma Scales of 15. American Journal of Emergency Medicine 50: 399-403	- Prognostic data for risk factors relevant to review protocol not reported
Mota, R.B., Formoso, V.R.Y., Gomes, S.M. et al. (2022) The Paediatric Resuscitation Room: Demographic analysis and predictors for admittance in Intensive Care Units. Critical Care and Shock 25(2): 85-96	- Population not relevant to this review protocol
Nagesh, M., Patel, K. R., Mishra, A. et al. (2019) Role of repeat CT in mild to moderate head injury: an institutional study. Neurosurgical Focus 47(5): e2	- Not limited to GCS 13-15
Nagy, K. K., Joseph, K. T., Krosner, S. M. et al. (1999) The utility of head computed tomography after minimal head injury. Journal of Trauma-Injury Infection & Critical Care 46(2): 268-70	- Population is not those with confirmed abnormality on initial CT
Nahmias, J., Doben, A., DeBusk, G. et al. (2018) Mild Traumatic Brain Injuries Can Be Safely Managed without Neurosurgical Consultation: The End of a Neurosurgical "Nonsult". American Surgeon 84(5): 652-657	- Prognostic data for risk factors relevant to review protocol not reported
Narayan, R. K., Maas, A. I., Servadei, F. et al. (2008) Progression of traumatic intracerebral hemorrhage: a prospective observational study. Journal of Neurotrauma 25(6): 629-39	- Not limited to GCS 13-15

Study	Code [Reason]
Quigley, M. R., Chew, B. G., Swartz, C. E. et al. (2013) The clinical significance of isolated traumatic subarachnoid hemorrhage. The Journal of Trauma and Acute Care Surgery 74(2): 581-4	- Data not reported in an extractable format or a format that can be analysed
Rhame, K., Le, D., Ventura, A. et al. (2021) Management of the mild traumatic brain injured patient using a multidisciplinary observation unit protocol. American Journal of Emergency Medicine 46: 176-182	- Full text paper not available
Ros, S. P. and Ros, M. A. (1989) Should patients with normal cranial CT scans following minor head injury be hospitalized for observation?. Pediatric Emergency Care 5(4): 216-8	- Population not relevant to this review protocol
Sharifuddin, A., Adnan, J., Ghani, A. R. et al. (2012) The role of repeat head computed tomography in the management of mild traumatic brain injury patients with a positive initial head CT. Medical Journal of Malaysia 67(3): 305-8	- Data not reported in an extractable format or a format that can be analysed
Shin, S. S., Marsh, E. B., Ali, H. et al. (2020) Comparison of Traumatic Intracranial Hemorrhage Expansion and Outcomes Among Patients on Direct Oral Anticoagulants Versus Vitamin k Antagonists. Neurocritical Care 32(2): 407-418	- Specific to anticoagulation population rather than general population
Sifri, Z. C., Homnick, A. T., Vaynman, A. et al. (2006) A prospective evaluation of the value of repeat cranial computed tomography in patients with minimal head injury and an intracranial bleed. Journal of Trauma-Injury Infection & Critical Care 61(4): 862-7	- No multivariate analysis
Simma, B.; Lutschg, J.; Callahan, J. M. (2013) Mild head injury in pediatrics: algorithms for management in the ED and in young athletes. American Journal of Emergency Medicine 31(7): 1133-8	- Review article but not a systematic review
Soleimani, T., Mosher, B., Ochoa-Frongia, L. et al. (2021) Delayed Intracranial Hemorrhage After Blunt Head Injury With Direct Oral Anticoagulants. Journal of Surgical Research 257: 394-398	- Population is not those with confirmed abnormality on initial CT

Study	Code [Reason]
Son, S., Yoo, C. J., Lee, S. G. et al. (2013) Natural course of initially non-operated cases of acute subdural hematoma : the risk factors of hematoma progression. Journal of Korean Neurosurgical Society 54(3): 211-9	- Data not reported in an extractable format or a format that can be analysed - Not limited to GCS 13-15
Soysal, E., Horvat, C. M., Simon, D. W. et al. (2021) Clinical Deterioration and Neurocritical Care Utilization in Pediatric Patients With Glasgow Coma Scale Score of 9-13 After Traumatic Brain Injury: Associations With Patient and Injury Characteristics. Pediatric Critical Care Medicine 22(11): 960-968	- Population limited to moderate or severe TBI (GCS <13)
Stein, S. C., Young, G. S., Talucci, R. C. et al. (1992) Delayed brain injury after head trauma: significance of coagulopathy. Neurosurgery 30(2): 160-5	- Population limited to moderate or severe TBI (GCS <13)
Suehiro, E., Koizumi, H., Fujiyama, Y. et al. (2014) Predictors of deterioration indicating a requirement for surgery in mild to moderate traumatic brain injury. Clinical Neurology & Neurosurgery 127: 97-100	- Data not reported in an extractable format or a format that can be analysed
Sumritpradit P; Setthalikhit T; Chumnanvej S (2016) Assessment and Predicting Factors of Repeated Brain Computed Tomography in Traumatic Brain Injury Patients for Risk-Stratified Care Management: A 5-Year Retrospective Study. Neurology research international 2016: 2737028	- No multivariate analysis
Teeratakulpisarn, P., Angkasith, P., Wannakul, T. et al. (2021) What are the strongest indicators of intracerebral hemorrhage in mild traumatic brain injury?. Trauma Surgery & Acute Care Open 6(1): e000717	- Outcome not relevant to review protocol
Tender, G. C. and Awasthi, D. (2003) Risk stratification in mild head injury patients: the head injury predictive index. Journal of the Louisiana State Medical Society 155(6): 338-42	- Population is not those with confirmed abnormality on initial CT
Turcato, G., Zaboli, A., Zannoni, M. et al. (2021) Risk factors associated with intracranial bleeding and neurosurgery in patients with mild traumatic brain injury who are receiving direct oral anticoagulants. American Journal of Emergency Medicine 43: 180-185	- Outcome not relevant to review protocol

Study	Code [Reason]
Valovich McLeod, T. C. (2005) The Prediction of Intracranial Injury After Minor Head Trauma in the Pediatric Population. Journal of Athletic Training 40(2): 123-125	- Systematic review used as source of primary studies
Vestlund, S., Tryggmo, S., Vedin, T. et al. (2021) Comparison of the predictive value of two international guidelines for safe discharge of patients with mild traumatic brain injuries and associated intracranial pathology. European Journal of Trauma & Emergency Surgery 03: 03	- Prognostic data for risk factors relevant to review protocol not reported
Wang, J. Z., Witiw, C. D., Scantlebury, N. et al. (2019) Clinical significance of posttraumatic intracranial hemorrhage in clinically mild brain injury: a retrospective cohort study. CMAJ open 7(3): E511-E515	- Prognostic data for risk factors relevant to review protocol not reported
Washington, C. W. and Grubb, R. L., Jr. (2012) Are routine repeat imaging and intensive care unit admission necessary in mild traumatic brain injury?. Journal of Neurosurgery 116(3): 549-57	- Data not reported in an extractable format or a format that can be analysed

Health Economic studies

Published health economic studies that met the inclusion criteria (relevant population, comparators, economic study design, published 2006 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.

Appendix K – Research recommendations – full details

K.1 Research recommendation

What are the indications for admission using clinical decision rules in people with a Glasgow Coma Scale score of 13 to 15 (a mild head injury) and a confirmed abnormality on a CT scan?

K.1.1 Why this is important

Some patients who experience a head injury have small injuries identified on CT scanning which does not require immediate neurosurgery. Whilst these injuries may worsen and require intervention in some cases, most will remain unchanged. There is currently a lack of evidence to enable clinicians to accurately identify which injuries are at highest risk of deterioration, resulting in some patients being admitted to hospital unnecessarily, whilst some may be discharged and subsequently deteriorate. Research to aid identification of those patients at highest risk of worsening injury, and those more likely to remain stable, would enable clinicians to select patients who require admission and observation, and those who may be safely discharged home.

K.1.2 Rationale for research recommendation

Importance to 'patients' or the population	There is currently a lack of evidence to support clinicians in deciding which people with small intracranial injuries may be safely discharged, and which patients require admission due to a higher risk of injury progression. Some people may therefore be discharged and experience subsequent deterioration (and delayed treatment), whilst others are unnecessarily admitted and exposed to the risks associated with hospital admission. Generation of evidence which identifies those at higher, and lower, risk of deterioration requiring intervention would support safe admission and discharge decisions among clinicians.
Relevance to NICE guidance	High quality research in this area, which accurately identifies which people are at higher risk of requiring intervention, and those in whom this is unlikely, would enable NICE to recommend which people with small intracranial injuries require admission to hospital, and which may be safely discharged.
Relevance to the NHS	Being able to accurately identify people with small intracranial injuries who are more likely to require intervention for worsening injury would enable more targeted utilisation of healthcare resource. Those at low risk may be safely discharged, reducing demand on hospital inpatient beds (and reducing exposure to hospital based risks to individuals), whilst those at higher risk would be admitted to specialised units, and observed for signs of deterioration facilitating early intervention.
National priorities	This is not relevant to a national priority area.
Current evidence base	Seventeen observational studies (one prospective and sixteen retrospective studies)

	were included in the review. All evidence included in the review was graded very low quality based on GRADE. This was most often because of risk of bias associated with studies (all but one were retrospective and had associated limitations such as blinding in terms of outcome assessment and concerns about prognostic factor measurement. In addition, despite multivariate analysis being performed there were concerns that remained about the variables included for all but three studies relative to those mentioned as important in the protocol) and indirectness. Some clinical decision rules showed promise, but due to limitations couldn't be employed in this update.
Equality considerations	Should apply to all ages, from babies through to older people, all ethnicities etc – no issues specific to those with disabilities.

K.1.31 Modified PICO table

Population	Inclusion: Infants, children and adult with all intracranial injuries Positive CT scan and GCS 13-15 • Adults (aged ≥16 years) • Children (aged ≥1 to <16 years) • Infants (aged <1 year) Exclusion: Adults, and children (including infants under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury.
Risk factor	Clinical decision rules Example: Hull Salford Cambridge Decision Rule (HSC DR), Brain Injury Guideline (BIG) criteria Key confounders: • Severity of injury (based on GCS) • Anti-coagulant • Anti-platelet therapy
Outcome	Diagnostic accuracy to be reported by test sensitivity/specificity
Study design	Prospective validation study Systematic reviews and meta-analyses of the above
Timeframe	Medium term – before the next update of the guideline
Additional information	None

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