National Institute for Health and Care Excellence

Draft

Head Injury: assessment and early management (update)

[D] Evidence reviews for clinical decision rules selecting people with head injury for imaging

NICE guideline <number>

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

September 2022

Draft for Consultation

These evidence reviews were developed by the Guideline Development Team NGC

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1 Clinical decision rules selecting people with head injury for imaging

1.1 Review questions

- What is the diagnostic accuracy of clinical decision rule/s for selecting adults, young people, children and babies with head injury for CT or MRI head scan?

- What is the clinical and cost effectiveness of clinical decision rules for selecting adults, young people, children and babies with head injury for CT or MRI head scan?

1.1.1 Introduction

Head injuries are very common, but the majority will have no consequences and need no specific treatment. However, some patients have on-going symptoms (known as postconcussion syndrome) and a minority will require urgent intervention (such as neurosurgery). It is essential that injuries requiring urgent intervention are detected and acted on quickly to prevent further injury to the brain. As most people do not need any intervention it is neither feasible nor sensible to perform a CT head scan on everyone who has a head injury. A number of clinical decision rules have therefore been developed that help clinicians to identify patients at risk who require a CT head scan. This approach is especially important in children due to the technical difficulties of a CT head scan and the risks from ionising radiation.

The Committee wished to evaluate evidence regarding clinical decision rules in order to provide recommendations that would maximise the chances of detecting clinically important traumatic brain injury and intervening rapidly, while minimising the number of unnecessary CT head scans that are performed.

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	Infants, children and adult with suspected or confirmed head injury Exclusion: Adults, young people and children (including babies under 1 year) with superficial injuries to the eye or face without suspected or confirmed head or brain injury.
Target condition	Traumatic brain injury with need for imaging In diagnostic accuracy review, assessed by obtaining diagnostic accuracy statistics of the index tests for the following: • Need for neurosurgical intervention • Any acute intracranial abnormality In diagnostic test and treat review, assessed by comparing clinical outcomes between groups where different clinical decision rules have been used, as detailed below under ‘statistical measures or outcomes’.
Index tests or comparators	For adults: validated clinical decision rules including NEXUS, NOC, CHR, Canadian CT-rules, New Orleans criteria or CHALICE

	For children: all clinical decision rules, including new ones that have not been validated. New/additional rules may include post-traumatic amnesia, updated Canadian CT rules, updated CHALICE, CATCH, ECARN, CHIP rule and Scandinavian rule. Separate decision rules exist for children and adults.
Reference standards	For diagnostic accuracy: • CT or MR imaging • Negative follow-up at 1 month for adults, 2 weeks for children For diagnostic test and treat: • Any validated clinical decision rule compared to each other. Only common reference standards will be pooled
Statistical measures or outcomes	All outcomes are considered equally important for decision making and therefore have all been rated as critical: Diagnostic accuracy outcomes (sensitivity and specificity as primary outcomes) of clinical decision tool/triage tool for: • need for neurosurgical intervention • any acute intracranial abnormality Diagnostic test and treat outcomes: • All-cause Mortality – at ≤30 days • Quality of life - 3 months or more • Objectively applied score of disability e.g. Glasgow Outcome Score (GOS) or extended GOS - at 3 months or more • Length of stay in acute care (until discharged home or to rehabilitation) • Serious adverse event at – ≤30 days
Study design	For diagnostic accuracy: • Diagnostic cohort studies (prospective and retrospective) • Systematic reviews and meta-analyses of the above • Case-control studies will be excluded. For diagnostic test and treat: • Randomised controlled trials (RCTs) • Systematic reviews of RCTs. If no RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders, starting with prospective cohort studies. Key confounders: • Age • GCS or pupillary response at presentation • Severity of injury (intra/extracranial)

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.

In terms of quality assessment as part of this update, the studies included as part of the Health Technology Assessment (HTA)[74] did not have a risk of bias summary rating and instead within the HTA report there was a grid indicating which features of the assessment each study met or did not meet based on the QUADAS tool. Instead of re-doing quality assessment for each of these studies, the grid presented in the HTA report was used to assess whether some concerns or high risk of bias for each study was present. This may be a limitation as newly included studies and those not part of the HTA but included previously have been assessed using QUADAS-2.

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

1.1.4 Diagnostic evidence

1.1.4.1 Included studies

Diagnostic accuracy

Thirty-three studies in adults and forty-two studies in children and infants were included in the review for diagnostic accuracy of clinical decision rules. This included thirteen and fourteen studies for adults and children/infants, respectively, included previously as part of a HTA report[74] reviewing minor head injury, two and three studies for adults[11, 78] and children/infants[25, 28, 71], respectively, that were included previously and were published after the cut-off date of the HTA report and a further twelve[1, 15, 18, 27, 46, 47, 49, 52-54, 57, 61, 75, 76, 92, 94, 96, 97] and twenty-five studies[3, 5, 7, 9, 10, 12, 14, 23, 26, 30, 31, 34, 44, 45, 48, 51, 55, 58, 59, 63, 72, 80, 81, 93, 98], respectively, that were identified as part of the current review update; these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence summary below in Tables 4-51 and references in References . The assessment of the evidence quality was conducted with emphasis on test sensitivity and specificity as this was identified by the committee as the primary measure in guiding decision-making. Clinical decision thresholds of sensitivity/specificity =0.9 and 0.60 above which a test would be recommended and 0.7 and 0.4 below which a test is of no clinical use were set by the committee. The lower thresholds were primarily used in the assessment of imprecision and less so for assessing clinical usefulness, as it was noted that for specificity in many cases existing rules would not meet 0.40 but have a very good sensitivity.

Note that the number of references and papers referred to in tables may not match the total number of studies included in the review as in some cases there were multiple papers covering a single study, and where the same dataset has been analysed for the same clinical decision rule this has been counted as a single study to avoid double-counting. Also, the number of studies cited in the HTA report does not match those given above which were included as part of this review, as some studies in the HTA were not able to be included as part of this review.

It was agreed as part of the protocol that validated clinical decision rules only would be included for adults and therefore studies deriving new adult clinical decision rules were excluded, which is the reason that some in the HTA were excluded from this review. For children and infants, the protocol allowed inclusion of derivation studies and was not limited to validated rules. One study in the HTA was however excluded from this review in the previous version as the committee agreed it did not meet the inclusion criteria of the review as the population was children admitted to hospital rather than seen in the emergency department.

New evidence was identified for the following clinical decision rules in adults:

- Canadian CT Head Rule (CCHR) – high and medium risk
- CCHR – high and medium risk adapted to cohort

- CCHR – high risk only
- CCHR – moderate risk only (not previously covered)
- CCHR – high and medium risk with cut-point ≥2 (not previously covered)
- New Orleans Criteria (NOC)
- NOC adapted to cohort
- NOC with cut-point ≥2 (not previously covered)
- NICE 2014 guideline recommendations (not previously covered)
- National Emergency X-Radiography Utilization Study (NEXUS) II
- CT in Head Injury Patients (CHIP) simple

New evidence was identified for the following clinical decision rules in children/infants:

- NEXUS II
- Children's Head injury ALgorithm for prediction of Clinically Important Events (CHALICE)
- Pediatric Emergency Care Applied Research Network (PECARN) ≥2 or PECARN in general (not split into age groups)
- PECARN high risk only, not split into age groups (not previously covered)
- PECARN <2 years
- Canadian Assessment of Tomography for Childhood Head injury (CATCH) – original 7-item rule
- CATCH – refined 8-item version (not previously covered)
- CATCH – any high risk predictor only (not previously covered)
- Pittsburgh Infant Brain Injury Score (Berger et al. 2016) – score ≥2 (not previously covered)
- A simplified clinical decision rule (not previously covered)

The majority of the evidence identified was in those with mild head injury (defined as GCS 13-15 in many studies, with others limiting further to those with GCS 14-15). There were however some studies that included any severity of head injury, but no studies that appeared to focus solely on those with moderate or severe head injury only. In the previous update of this review, the committee noted that this may be explained as there is consensus in the field for this population and evidence that points to the fact that all patients with moderate or severe head injury should have a CT head scan.

The included HTA report[74] stated that the index test was the application of a clinical decision rule. The target conditions were stated as the need for neurological intervention (defined as any intracranial injury seen on CT or MR imaging head scan that required neurosurgery) and any intracranial injury (defined as any intracranial abnormality detected on CT or MR imaging head scan due to trauma). Inclusion criteria for reference standards were CT head scan, CT head scan or follow-up (for those with no CT head scan), or MR imaging. A summary of the included HTA report is given in appendices D.2 and D.4, which contains tables reproduced from the report, detailing individual papers and clinical decision rules for adults, children and infants.

Across studies, the reference standard used differed. Some studies had performed a CT in every participant, while others performed a CT only according to rules within the institution, meaning a proportion had CT while others did not. In most studies where not all participants had a CT it was clear that some form of follow-up was used instead, however, the length and method of this follow-up varied between studies, with some not following up for the length specified as ideal in the protocol and methods of follow-up limited to medical record review in some rather than formal in-person or telephone follow-ups. Where the duration of follow-up did not meet that specified in the review protocol, this was considered as part of the risk of

bias assessment for each study and downgrading applied appropriately. Outcome definition also differed across studies, particularly for intracranial injury. Some studies only reported those considered to be clinically significant, with definitions of this similar but not always identical across studies, while others reported a broader range of injuries, for example including any brain injury visible on CT scan. Differences in reference standards and outcome definitions across studies were considered carefully when deciding whether pooling of studies was possible for each specific clinical decision rule.

Studies in children were separated into two groups of children and, infants and young children. The term infants and young children is used in this review instead of infants alone, as infants is defined in the guideline as those <1 year of age, but studies included in the infant category from the HTA was not limited to those <1 year of age. Studies where the population was children and there is a maximum age criterion indicating that younger children have been included rather than all children were included under the infants and young children category.

Foks 2018[27] and Babl 2017/2019[5, 7]

These two studies present multiple different analyses in different populations. This includes rules used specifically in the population they were developed in and also the whole population or a comparative population, where all rules were applied, ignoring any inclusion or exclusion criteria specific to each rule. The latter type of analysis may be less relevant in terms of interpreting results given that the rules are being used ins some people that they were not developed for use in. As Foks 2018 provides results for an adapted rule in the whole population for CCHR and NOC rules for intracranial injury outcomes, this analysis was presented as well as the analysis where the rule was used only in the specific population it was developed in, and the un-adapted version of the rule used in the whole population not used. However, results for neurosurgery outcome were only presented using the un-adapted rules in the whole population and this was therefore presented given no other results for this outcome where available.

The Babl 2019 paper reports data for the NEXUS II decision rule, which is not reported in the 2017 paper. Results are available across the two papers for all four decision rules in terms of outcomes as defined in each specific rule and in the rule-specific population (those meeting inclusion criteria and no criteria excluding them from the rule). In addition, the 2017 paper also provides results in a comparative population for three of the four rules (all apart from NEXUS II), which ignores inclusion and exclusion criteria for specific rules and uses all rules in the same group of people, and uses identical outcome definitions, to allow easier comparison. Although this analysis allows easier comparison, the use of the decision rules in some people that the rules were not designed for (i.e. in people that were excluded when the rule was developed) means the results may be less reliable than the results when used in the intended population for each rule, which is why both results in the rule-specific populations and comparative population are both presented where reported.

See also the study selection flow chart in Appendix C, sensitivity and specificity forest plots and receiver operating characteristics (ROC) curves (for analyses where meta-analysis was possible) in Appendix E, and study evidence tables in Appendix D.

Diagnostic test and treat

The literature was also searched for diagnostic test and treat studies comparing clinical outcomes of participants where two different clinical decision rules had been used. Even though the review protocol was not limited to randomised controlled trials and allowed non-randomised studies to be included, no studies were identified that could be included in this review as no studies compared outcomes for two different clinical decision rules.

1.1.4.2 Excluded studies

See the excluded studies list in Appendix I.

1.1.5 Summary of studies included in the diagnostic evidence

Table 2: Summary of studies included in the evidence review – adults

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Arab 2015[1] Saudi Arabia N=368 Retrospective	Adults (≥14 years) with minor head injury (GCS 13-15), presenting within 24 h Mean (SD) age: 30.5 (17.3 years), range 14-106 years 78% male GCS: • 6.7% GCS 13/14 93.3% GCS 15	Canadian CT Head Rule – high and medium risk	CT (all had CT)	Unclear	**Abnormality on CT scan:** defined as soft tissue swelling, extradural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haemorrhage, intraventricular haemorrhage, cortical contusions, brain oedema, diffuse axonal injury, brain herniation/midline shift, skull fracture and facial bone fracture	NA	New study added as part of current update
Arienta 1997[2] Italy N=10,000 Retrospective	Patients with head injury at ED, including those ≥6 years Median age 31 years, range 6-95 years 45.6% female GCS unclear, do not appear to have limited by severity of head injury	Arienta et. al 1997 rule	CT (7.7%) or follow-up telephone call	Follow-up duration for those without CT at enrolment unclear	**Intracranial lesion:** definition not provided but injuries identified and counted included extradural haematoma, cortical contusion, subarachnoid haemorrhage, pneumocephalus, depressed fracture with contusion, intracerebral haematoma and subdural haematoma	NA	Study previously included

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Bouida 2013[11] Tunisia N=1582 Prospective	Patients at least 10 years old with mild head injury (GCS 13-15), presenting within 24 h Mean (range) age: 32 (14-97) years 76.6% male GCS: • 21.0% GCS 13/14 79.0% GCS 15	Canadian CT Head Rule – high and medium risk New Orleans Criteria	CT (70.9%) or structured telephone interview follow-up	Events within 30 days counted for neurosurgery outcome	**Intracranial lesion:** defined as any acute intracranial finding revealed on CT that was attributable to acute injury	**Need for neurosurgical intervention:** Defined as either death or need for any of the following procedures within 30 days of the traumatic event: craniotomy, monitoring of intracranial pressure, or the need for intubation for the treatment of head injury	Study included previously
Chobdari 2018[15] Iran N=264 Unclear if prospective or retrospective	Patients referred for CT due to minor head trauma Age: • 31.7% 30-45 years • 18.7% 14-29 years 79.9% male GCS unclear, but only minor head injury included	Canadian CT Head Rule – high and medium risk with cut-point of ≥2 New Orleans Criteria – cut-point of ≥2	CT (all had CT)	Unclear	**Abnormality on CT scan:** no definition provided	NA	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Davey 2018[18] USA N=240 Prospective	Adults (at least 18 years) with minor and minimal head injury where CT had been ordered Mean age not reported, had to be at least 18 years 38.6% male 100% GCS 15 (<15 was exclusion criterion)	Canadian CT Head Rule – medium and high risk	CT (all had CT)	Unclear	**Positive non-contrast head CT:** defined as positive for intracranial haemorrhage	NA	New study added as part of current update
Fabbri 2005[24] (also Stein 2009[87] paper reporting same study) Italy N=7955 Retrospective	Adults/adolescents (≥10 years) with mild head injury (GCS 14-15) attending the ED Median (IQR) age: 44 (27-71) years %male/female unclear GCS at least 2 h after injury: • GCS 14 in 6.6% GCS 15 in 93.4%	Canadian CT Head Rule • High and medium risk • High risk (neurosurgery outcome only) NCWFNS high and medium risk (Neurotraumatology Committee of the World Federation of Neurosurgical Societies)	CT (52.5%) or unclear	Unclear, 7-day time-point used for intracranial injury and neurosurgery outcomes in Fabbri 2005 paper Stein 2009 – unclear, 6-month time-point mentioned to	**Fabbri 2005 – any post traumatic lesion at CT within 7 days:** defined as any post-traumatic lesion at CT within 7 days from trauma: depressed skull fracture, intracerebral haematoma/brain contusions, subarachnoid haemorrhage, subdural haematoma, epidural haematoma, intraventricular haemorrhage **Stein 2009 – any lesion:** defined as surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other	**Fabbri 2005 – surgical lesion:** defined as haematoma evacuation or skull fracture elevation within first 7 days of injury **Stein 2009 – surgical intracranial lesion:** defined as intracranial haematoma large enough to require surgical evacuation	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
		NICE lenient (2003/2007 guideline versions) New Orleans Criteria Nexus II Scandinavian criteria (note these are not all reported in the same paper)		assess if any delayed surgery occurred	intracranial abnormality diagnosed on CT)		
Foks 2018[27] The Netherlands N=4557 Prospective	Adults (≥16 years) presenting with minor head injury (GCS 13-15) within 24 h of injury Mean (range) age: 53.1 (16.0-101.0) years 58.3% male GCS: • 3.1% GCS 13 • 11.0% GCS 14	CHIP (CT in Head Injury Patients) New Orleans Criteria Canadian CT Head Rule high and medium risk NICE guideline recommendations (2014)	CT or imputation – 82.1% in whole population had CT and data imputed for those without CT	Unclear - up to 30-day review of medical records mentioned for neurosurgery outcome	**Intracranial traumatic finding on CT:** defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture **And**	**Neurosurgical intervention:** definition not provided	New study added as part of current update For New Orleans Criteria and Canadian CT Head Rule, provides results in various ways: • Original rule in intended population

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
	85.9% GCS 15				**Potential neurosurgical lesion on CT:** defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation		• Original rule used without adaptation to inclusion/exclusion criteria of specific rules in whole population • Adapted version of the rule used in the whole population
Haydel 2000[38] USA N=520 and N=909 in phase 1 and 2, respectively	Patients with minor head injury, at least 3 years old and presenting within 24 h of injury Mean (range) age: • Phase 1, 36 (3-97) years • Phase 2, 36 (3-94) years 65% male in both phase 1 and phase 2 groups	New Orleans Criteria	CT (all had CT)	Those with positive CT followed until discharge to assess neurosurgical intervention	**Any acute traumatic intracranial injury on CT:** defined as a subdural, epidural or parenchymal haematoma, subarachnoid haemorrhage, cerebral contusion or depressed skull fracture	NA	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Prospective	GCS unclear, but only minor head injury included						
Holmes 1997[40] USA N=264 Prospective	Patients presenting to ED with head trauma and a GCS of 14, presenting within 4 h of injury and undergoing CT Mean (SD) age: 39.1 (17.1) years for those with normal CT and 39.8 (19.2) years for those with abnormal CT scan 68.6% males GCS 14 – all had GCS 14	Miller et. al criteria	CT (all had CT)	Those with abnormal CT followed to discharge, those with normal CT not studied further	**Abnormal CT scan:** defined as any CT scan showing an acute traumatic lesion (skull fractures or intracranial lesions: cerebral oedema, contusion, parenchymal haemorrhage, epidural haematoma, subdural haematoma, subarachnoid haemorrhage or intraventricular haemorrhage)	**Neurosurgery:** no definition provided	Study included previously
Ibanez 2004[43] Spain N=1101	Patients >14 years presenting to the ED with mild head injury (GCS 14 or 15) Mean (SD) age: 46.7 (23.9) years, range 15-99 years 52.0% male GCS: • 4.6% GCS 14 95.4% GCS 15	Canadian CT Head Rule – high and medium risk New Orleans Criteria NCWFNS high and medium risk (Neurotraumatology Committee of the World Federation of Neurosurgical Societies)	CT (all had CT)	Unclear	**Relevant positive CT scan:** defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions	NA	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
		Scandinavian criteria Arienta et al. 1997 rule SIGN 2000 CT urgently EFNS CT recommended and mandatory					
Jones 2020[46] USA N=679 Prospective	Adults (≥16 years) with mild traumatic brain injury (GCS 13-15) and having CT scan as part of clinical care Age: • 89.0% <65 years • 11.0% ≥65 years GCS: • <15, 7.2% 15, 92.8%	Canadian CT Head Rule – high and medium risk New Orleans Criteria	CT (all had CT)	Unclear	**Traumatic intracranial injury on head CT:** defined as the presence of any of the following: subdural haematomas, epidural haematomas, subarachnoid haemorrhage, cerebral oedema, skull fracture and cerebral contusions	NA	New study added as part of current update
Kavalci 2014[47]	Adults (at least 18 years) with acute minor head injury (GCS 13-15)	Canadian CT Head Rule –	CT (all had CT)	Unclear	**Traumatic lesions on head CT scan:** defined as subarachnoid	NA	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Turkey N=175 Prospective	presenting within 24 h of injury Mean (SD) age: 49.1 (20.7) years 60.6% male GCS: • 13, 4.0% • 14, 5.1% 15, 90.9%	high and medium risk New Orleans Criteria			haemorrhage, epidural haemorrhage, subdural haematoma, intraparenchymal hematoma, compression fracture, cerebral oedema and contusion		
Korley 2013[49] USA N=169 Prospective	Adults (at least 18 years) with mild traumatic brain injury (GCS 14-15) presenting within 24 h of injury Median (IQR) age: • With CT, 41 (27-62) years • Without CT, 38 (27-51) years 49.1% male GCS: • 14, 5.9% 15, 94.1%	Canadian CT Head Rule – high and medium risk New Orleans Criteria	CT (76.9%) or structured telephone follow-up at 14-60 days post-enrolment	Up to 14-60 days for those not receiving CT at enrolment	**Acute traumatic finding on CT:** defined as subdural, epidural or parenchymal hematoma; subarachnoid haemorrhage; cerebral contusion; or depressed skull fracture	NA	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Lamba 2021[52] India N=101 Prospective	Adults (>16 years) with minor traumatic brain injury (GCS 13-15) presenting to the ED within 30 min of the injury Age: 42.6% between age of 21 and 30 years 69.3% males GCS proportions not reported (13-15 to be included)	Canadian CT Head Rule – high and medium risk	CT (all had CT)	Neurosurgical unit transfer advised if CT positive and neuro-observation in ED for 12 h if CT normal	**Intracranial lesion:** definition not provided, but all cases were either haemorrhages or contusions	NA	New study added as part of current update
Li 2022[53] USA N=463 Retrospective	Adults (18 or over) transported to ED with suspected TBI, with a blood draw as part of standard care. Age (SD): 50.8 (22.7) 61.8% males GCS (median Q1, Q3): 15 (14, 15)	Canadian CT rule; New Orleans Criteria; NEXUS II; ACEP Clinical Policy.	CT (all had CT)	Unclear	Traumatic brain injury – closed head injuries including skull fracture (6.7%), pneumocephalus (2.2%), intracranial hemorrhage (24.6%), mass effect (5.2%), and brain parenchymal injuries (7.8%).	NA	New study added as part of current update
Lo 2016[54] Hong Kong, China	Patients with minor head injury (GCS 13-15 or GCS 15 only depending on decision rule) presenting within 24 h of injury (>16 years specifically for	Canadian CT Head Rule New Orleans Criteria	CT (all had CT)	Unclear, other than 7-day period used to confirm	**Clinically important brain injury on CT:** defined as all types of brain injuries with positive CT findings except the following: solitary contusion of less than 5	**Need for neurosurgical intervention:** defined as death within 7 days of head injury or	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=383 or N=431 for Canadian CT head Rule and New Orleans Criteria populations, respectively Retrospective	Canadian CT Head Rule and ≥1 year for New Orleans Criteria) Age: • 30.0 and 25.8% >65 years • 71.0 and 62.6% between 17 and 65 years • 0 and 11.6% between 1 and 16 years % male/female not reported GCS: • 13-15 for Canadian CT Head Rule All GCS 15 for New Orleans criteria			neurosurgery outcome	mm in diameter; localised subarachnoid blood less than 1 mm thick; smear subdural haematoma less than 4 mm thick; or closed depressed skull fracture not through the inner table	need for any of following within 7 days: burr hole, craniotomy, craniectomy, and elevation of skull fracture or intracranial pressure monitoring	
Madden 1995[56] USA N=540 in phase 1 and N=273 in phase 2	Patients presenting to ED with acute head trauma and who had CT ordered Age: • 13-30 years, 46% and 55% in phase 1 and 2	Madden et. al 1995 rule	CT (all had CT)	Unclear	**Clinically significant CT scan:** defined as pathology related to trauma affecting the bony calvaria or cerebrum (including non-depressed skull fractures, excluding scalp haematomas, those with no bony skull or intracerebral pathology	NA	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Prospective	• 31-59 years, 34% and 55% in phase 1 and 2 67.8% and 70.7% male in phase 1 and 2 GCS – proportion of those with GCS recorded: 14 or 15, 79.3% (of 396) in phase 1 and unclear in phase 2						
Mata-Mbemba 2016[57] Japan N=142 Prospective	Adults (≥17 years) with mild traumatic brain injury presenting within 24 h of injury and CT being performed Mean (SD) age: 50 (21.7) years, range 17-88 years 67.6% male GCS: • 13, 21.1% • 14, 31.7% 15, 47.2%	Canadian CT Head Rule – high and medium risk New Orleans criteria	CT (all had CT)	Unclear	**Clinically important CT finding:** defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table	NA	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Miller 1997[60] USA N=2143 Prospective	Patients presenting to the ED within 2 h of injury with GCS 15 following head injury Mean age unclear, no restriction on age to be included % male/female unclear GCS 15 – inclusion criterion	Miller et. al criteria	CT (all had CT)	Unclear, hospital records of those with positive CT followed until discharge	**Abnormal CT scan:** defined as acute traumatic intracranial lesion (contusion, parenchymal haematoma, epidural haematoma, subdural haematoma, subarachnoid haemorrhage) or a skull fracture	**Surgical intervention:** defined as craniotomy to repair an acute traumatic injury or placement of a monitoring bolt	Study included previously
Mower 2005[62] USA N=13,728 Prospective	Patients presenting with acute blunt trauma that underwent head CT (those with delayed presentation excluded) Median (IQR) age: 37 (23-52) years 66% males GCS unclear, appear to have included any injury severity	NEXUS II	CT (all had CT)	Unclear	**Significant intracranial injury:** defined as any injury that may require neurosurgical intervention, (craniotomy, intracranial pressure monitoring, mechanical ventilation), lead to rapid clinical deterioration or result in significant long-term neurological impairment	NA	Study included previously
Mower 2017[61] USA	Patients with acute blunt head trauma undergoing head CT imaging, presenting within 24 h of injury	Nexus II – n=11,770 Canadian CT Head Rule –	CT (all had CT)	Unclear, other than 7-day time-point mentione	**Clinically significant head injury on CT:** included all injuries evident on CT head imaging apart from the following in neurologically	**Need for neurosurgical intervention:** defined as death due to head	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=11,770 Prospective	Median (IQR) age: 50.0 (29.0-71.6) years, range 0.01-103.7 years 61.3% male GCS unclear, appear to have included any injury severity	high-risk only or moderate risk only – n=7759		d for neurosurgical intervention	intact individuals: solitary small contusions, localized subarachnoid haemorrhage less than 1 mm thick, thin subdural hematomas less than 4 mm thick, isolated pneumocephaly and closed depressed skull fractures that did not violate the inner table	injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring, within 7 days of head injury	
Ono 2007[67] Japan N=1064 in cohort 1 and N=168 in cohort 2 Unclear if prospective or retrospective	Patients with head injury presenting with 6 h of trauma at emergency hospital, with GCS ≥14 and undergoing CT Mean (SD) age: 46 (23) years (range 10 to 104 years) in cohort 1 and unclear in cohort 2 58.4% male in cohort 1 and unclear in cohort 2 GCS: • 14, 14.3% in cohort 1 and unclear in cohort 2 15, 95.7% in cohort 1 and unclear in cohort 2	Ono et al. 2007 rule	CT (all had CT)	Unclear	**Intracranial lesion:** definition not given, but injuries that occurred and were counted included subdural and epidural haematoma, subarachnoid haemorrhage, contusion, pneumocephalus	NA	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Papa 2012[75] USA N=431 Prospective	Adults (at least 18 years) with mild traumatic brain injury suspected (GCS 13-15) Mean (SD) age: 38.3 (18.0) years in GCS 15 only and 38.4 (18.0) in GCS 13-15 population 64% male and 36% female GCS: • 13, 5.10% • 14, 22.04% 15, 72.95%	Canadian CT Head Rule – high and medium risk New Orleans Criteria	CT (99.3% had CT) or unclear	Unclear how those without CT had outcome confirmed, 7-day time-point for neurosurgery outcome	**Clinically important brain injury:** defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table **And** **Any traumatic intracranial lesion on CT:** any brain injury on CT, no further details given	**Need for neurosurgical intervention:** defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury (shown on CT)	New study added as part of current update Note that the study presents results in those with GCS 15 only for New Orleans Criteria in line with the inclusion criteria or the decision rule. Results for Canadian CT Head Rule were also provided in this subpopulation but not presented as the analysis with most participants was favoured.
Pek 2015[76] Singapore	Adults (at least 16 years) with minimal or mild head injury (GCS 13-15)	Canadian CT Head Rule • High risk	CT or follow-up (29.4% had CT)	Follow-up duration for those without CT at	**Clinically important brain injury:** defined as any acute brain finding on CT that would require hospital admission or neurosurgical	**Need for neurological intervention:** defined as death due to head	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=1127 Retrospective	Mean age not reported, had to be at least 16 years % male/female not reported Proportion with each GCS score unclear, 13-15 to be included	High and medium risk		enrolment unclear	follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table	injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring, within 7 days of head injury	
Ro 2011[78] Korea N=7131 Prospective	Patients presenting with sustained acute blunt head trauma Mean age was 39.9-46.1 years depending on the clinical decision rule % male was 68.5-69.8 depending on the clinical decision rule GCS unclear, appears to have included any GCS severity	Canadian CT Head Rule – high and medium risk New Orleans Criteria Nexus II	CT and/or follow-up by telephone at 6 months	Follow-up by telephone at 6 months in all participants, 7-day time-point for neurosurgery outcome	**Clinically important brain injury:** defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull	**Need for neurosurgical intervention:** defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
					fracture not through the inner table		
Rosengren 2004[79] Australia N=240 Retrospective	Patients presenting to ED with blunt head trauma and a GCS 15 and undergoing CT Average (range) age: 38 (14-95) years 70% males GCS 15 – inclusion criterion	Canadian CT Head Rule – high and medium risk	CT (all had CT)	Unclear	**Clinically significant intracranial injury:** defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table	**Neurological intervention:** no definition provided	Study included previously
Smits 2005[83] (also Smits 2007[84] reporting same study)	Adults (>16 years) presenting after blunt head injury within 24 h of injury and a GCS of 13-15 <u>For 3181 included in most analyses:</u> Mean (range) age: 41.4 (16.0-102.3) years	Canadian CT Head Rule – high and medium risk • Original rule in intended population	CT (all had CT)	Unclear, 30-day time-point mentioned for neurosurgery outcome	**Smits 2005 – any neurocranial traumatic finding on CT:** defined as any skull or skull base fracture and any intracranial traumatic lesion **Smits 2007 – any intracranial traumatic findings on CT:** defined as	**Neurosurgical intervention:** defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
The Netherlands N=2028 for Canadian CT Head Rule and New Orleans Criteria N=3181 for all decision rules apart from Canadian CT head rule and New Orleans Criteria used in intended population (n=2028 or n=1307 depending on outcome)	70.5% male GCS: • 13, 4.7% • 14, 17.9% • 15, 77.4%	• Adapted rule in whole population New Orleans Criteria • Original rule in intended population • Adapted rule in whole population CHIP (CT in Head Injury Patients) NCWFNS high and medium risk (Neurotraumatology Committee of the World Federation of Neurosurgical Societies)			all neurocranial traumatic findings except for isolated linear skull fractures	depressed skull fracture or ventricular drainage) performed within 30 days of the event	

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
		EFNS criteria NICE lenient and strict criteria (2003 and 2007 guideline versions) SIGN criteria Scandinavian criteria (note these are not all reported in the same paper)					
Stiell 2001[90] Canada N=3121 Prospective	Adults (at least 16 years) with blunt head trauma and minor head injury presenting to ED with GCS 13-15 within 24 h of injury Mean (SD) age: 38.7 (18.0) years 69% male GCS: • 13, 4.0% • 14, 17.0%	Canadian CT Head Rule: • high and medium risk • high risk	CT (67.0%) or follow-up by telephone interview	14 day telephone interview for those not having CT at enrol, 7-day time-point for neurosurgery outcome	**Clinically important brain injury on CT:** defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm	**Need for neurological intervention:** defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure	Study included previously

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
	15, 80.0%				thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table	monitoring, or intubation for head injury (shown on CT)	
Stiell 2005[89] Canada N=2707 Prospective	Adults (at least 16 years) with blunt head trauma and minor head injury presenting to ED with GCS 13-15 within 24 h of injury Mean (SD) age: 38.4 (18.0) years 69.6% male GCS: • 13, 4.0% • 14, 20.4% 15, 75.7%	Canadian CT Head Rule: • high and medium risk • high risk New Orleans Criteria	CT (80.2%) or follow-up by telephone interview	14 day telephone interview for those not having CT at enrolment, 7-day time-point for neurosurgery outcome	**Clinically important brain injury on CT:** all brain injuries were considered clinically important unless the patient was neurologically intact and had 1 of the following lesions on CT: solitary contusion of less than 5 mm in diameter, localised subarachnoid blood less than 1 mm thick, smear subdural hematoma less than 4 mm thick, or closed depressed skull fracture not through the inner table	**Need for neurological intervention:** defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury (shown on CT)	Study included previously
Tan 2018[92] Singapore N=349	Adults (at least 16 years) with minor head injury (GCS 13-15) presenting within 24 h Median (IQR) age: 48 (30-68) years	Canadian CT Head Rule – high and medium risk	CT (71.0%) or follow-up	14-day follow-up of those not having CT at enrolment	**Clinically significant CT finding:** defined as epidural haematoma, subdural haematoma of thickness ≥ 4 mm, subarachnoid haemorrhage of thickness > 1 mm, intracerebral haematoma,	NA	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Retrospective	62.5% male GCS: • 13, 5.4% • 14, 11.2% 15, 83.4%				intraventricular haemorrhage, diffuse cerebral oedema, cerebral contusion of diameter ≥ 5 mm, pneumocephalus and depressed skull fracture		
Vaniyapong 2020[94] Thailand N=1164 Retrospective	Adults (at least 16 years) with mild traumatic brain injury (GCS 13-15) presenting within 24 h Median (IQR) age: 34 (22-56) years 63.4% male GCS: • 13, 1.46% • 14, 9.02% 15, 89.52%	Canadian CT Head Rule – high and medium risk	CT (41.9%) and/or follow-up	Clinical follow-up at 7 days by attendance or telephone	**Traumatic intracranial finding on CT scan:** defined as any types of intracranial haemorrhage (for example, subdural haemorrhage, epidural haematoma, subarachnoid haemorrhage and intracerebral haematoma) and depressed skull fracture	**Neurosurgical intervention:** defined as interventions within 7 days of injury, including craniotomy or craniectomy, elevation of skull fracture, external ventricular drainage, Burr holes and intracranial pressure monitoring	New study added as part of current update
Yang 2017[96] China N=625 Retrospective	Adults (>18 years) with mild traumatic brain injury (GCS 13-15) undergoing CT within 24 h of injury Mean (SD) age: 47.0 (19.7) years 54.2% male	Canadian CT Head Rule – high and medium risk New Orleans Criteria	CT (all had CT)	Unclear	**Positive finding on CT:** definition not provided but those identified included cranial fracture, epidural haematoma, subdural haematoma, intracerebral haematoma, subarachnoid haemorrhage and cerebral contusions	NA	New study added as part of current update

Study	Population	Index test(s)	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
	GCS: • 13, 2.72% • 14, 2.40% 15, 94.88%						
Yarlagadda 2019[97] USA N=332 Retrospective	Adults that had an inpatient fall with any type of degree of injury, unclear if all had suspected head injury Mean (SD) age: 67.9 (17.4) years 52.0% males GCS unclear, includes any severity of injury	New Orleans Criteria	CT (57.0%) or unclear	Unclear how outcome confirmed in those without CT at enrolment	**Positive head CT finding:** defined as any acute intracranial process, no further details given	NA	New study added as part of current update Population appears to be different to other studies as is specifically those who have fallen as inpatients Also, majority were on anticoagulation/antithrombotic treatment

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2 **Table 3: Summary of studies included in the evidence review – children and infants**

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Atabaki 2008[4] USA and Canada	Patients <21 years with closed head trauma undergoing CT (GCS 13-15) Mean age, 8.9 years:	Atabaki 2008 rule	CT (all had CT)	Unclear, medical record review but unclear at	**Intracranial injury:** defined as subdural, epidural, subarachnoid, intraparenchymal and intraventricular haemorrhages as well as	**Neurosurgery:** defined as neurosurgery, including craniotomy, craniectomy,	Study included previously

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=1000 Prospective	• <2 years, 18.8% • ≥2 years, 81.2% 64.1% male GCS: • 13, 3.1% • 14, 11.7% 15, 85.2%			what time-point	contusion and cerebral oedema	evacuation or intracranial pressure monitoring	
Atabaki 2016[3] USA N=8627 Prospective	Children <18 years within blunt head trauma (GCS 14-15) presenting within 24 h of injury Mean (SD) age: 6.8 (5.4) years 62.6% male GCS 14-15 to be included	PECARN >2 years (N=6311) PECARN <2 years (N=2185)	CT (33.6% for whole population, unclear for those > and <2 years) and/or clinical follow-up	Between 1 week and 3 months after ED visit	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT	NA	New study added as part of current update
Babl 2017[5] and Babl 2019[7] Australia and New Zealand N=20,137 (N=20,109	Children (<18 years) with head injury of any severity presenting to ED Mean (SD) age: 5.7 (4.7) years 36.3% female GCS:	PECARN >2 years (N=11,152) PECARN <2 years (N=4011) CATCH (N=4957)	CT or systematic follow-up Proportion with CT unclear from 2017 paper but said to be	Up to six follow-up attempts made up to 90 days post-injury	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT	**Neurosurgery:** definition not provided, but the following procedures were reported to have occurred and were included under neurosurgery: intracranial pressure	New study added as part of current update Babl 2019 reports NEXUS II results not reported in Babl 2017 paper

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
in 2019 paper) Prospective (APHIRST)	• 3-8, 0.6% • 9-12, 0.5% • 13, 0.7% • 14, 2.9% • 15, 95.4% Taken from 2017 paper – identical in 2019 paper for age and sex but GCS not reported	• Any predictor • Any high-risk predictor CHALICE (N=20,029) NEXUS II (N=20,109) (note results also given in comparative population where all could be compared, which consisted of n=18,913 participants, or N=5046 and N=13,867 for PECARN < and > 2 years)	9.76% in 2019 paper (slightly lower patient number of N=20,109)		**And/or** **Traumatic brain injury on CT:** defined as intracranial haemorrhage or contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus skull fracture depressed at least the width of the table of the skull **And/or** **Clinically significant intracranial injury:** defined as death as a result of head injury, need for neurosurgical intervention or marked abnormality on CT scan **And/or** **Clinically important intracranial injury:** defined as presence of ≥1 CT	monitoring, craniotomy, haematoma evacuation, elevation of depressed skull fracture, dura repair, tissue debridement and lobectomy	

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
					findings (substantial epidural or subdural haematoma; substantial cerebral contusion; extensive subarachnoid haemorrhage; signs of herniation; basal cistern compression or midline shift; haemorrhage in the posterior fossa; intraventricular haemorrhage; bilateral haemorrhage of any type; depressed or diastatic skull fracture; pneumocephalus; diffuse cerebral oedema; diffuse axonal injury) Note that one/more of these outcomes are reported for each decision rule and differ depending on the decision rule used		
Berger 2016[9] USA N=1040 (N=862 analysed)	Infants (at least 30 days and <1 year) appearing to have symptoms associated with increased risk of abusive head trauma Mean (SD) age: 4.7 (3.1) months 52% male	Pittsburgh Infant Brain Injury Score (PIBIS) derived in study – score of ≥2 (other scores mentioned but most data provided for cut-off of 2, with	Neuroimaging (CT or MRI – 69.4%) at enrolment or during follow-up, as well as medical record follow-up	Medical record review for 6 months after enrolment up or up to 1 year of age (whicheve	**Abnormal neuroimaging at enrolment or during follow-up**: no definition provided	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Prospective	GCS unclear, only includes 'well-appearing' infants but with symptoms associated with an increased risk of abusive head trauma	limited data provided for others)		r occurred later)			
Bertsimas 2019[10] USA N=42,412 (split into development and validation cohorts) Retrospective	Children (<18 years) with head trauma (GCS 14-15) presenting to ED within 24 h of injury Mean (SD) age: 7.1 (5.5) years 37.7% female GCS: • 14, 3.2% 15, 96.8%	PECARN < 2 years (N=8502 and N=2216 development and validation) PECARN ≥2 years (N=25, 283 and N=6411 development and validation)	CT and/or follow-up 35.3% in total had CT, though this is for development and validation cohorts combined and across decision rules. Proportion unclear specific cohorts and decision rules.	For those discharged with no CT, telephone survey between 7-90 days after ED visit and medical/morgue records checked if not contactable	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT	NA	New study added as part of current update Also reports results for a machine learning OCT developed in the paper but this was not included as it was a machine learning approach rather than a specific clinical decision rule
Bozan 2019[12]	Children (<18 years) with minor blunt head trauma (GCS 14-15)	PECARN (not separated into < and >2 years)	CT (all had CT)	Unclear	**Intracranial pathology on CT:** defined as linear fracture, skull base fracture, epidural haematoma,	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Turkey N=256 Prospective	Median (IQR) age: 3 (1.0-7.8) years 59.8% male GCS: • 14, 12.1% 15, 87.9%	CATCH			compression fracture, parenchymal haemorrhage, contusion, and subdural haematoma		
Buchanich 2007[13] USA N=97 Retrospective	Children aged <3 years with mild head injury with initial GCS 14-15 in ED having CT within 24 h of injury Mean (SD) age: 15.2 (11.4) months 84% male GCS unclear but had to be 14-15 to be included	Buchanich et al. 2007 rule	CT (all had CT)	Follow-up questionnaire/telephone interview, time-point unclear	**Intracranial injury:** defined as intracranial haematoma, intracranial haemorrhage, cerebral contusion and/or cerebral oedema	NA	Study included previously
Cho 2022[14] South Korea (N=448 analysed)	Children (<19 years) presenting with head trauma within 24 hours of the injury to 2 paediatric EDs. *Age, mean (IQR) months: 2.7 (0-4)*	PECARN (Paediatric Emergency Care Applied Research Network)	CT scan (14.7%) or followed up after discharge	Follow-up phone call by nurse between 7 days and 90 days after discharge	Clinically important traumatic brain injury: (defined as death from traumatic brain injury, neurosurgical intervention for TBI, intubation of more than 24 h for TBI and hospital admission of 2 nights or more for traumatic brain injury in association	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
	58% male *Patients had to have GCS 14 or above to be included.* GCS 14: 2 (0.4)				with evidence of TBI on CT).		
Da Dalt 2006[16] Italy N=3806 (N=3798 analysed) Prospective	Children (<16 years) with blunt head trauma of any severity, presenting to ED within 24 h of injury Age: • <2 years, 36.7% • 2-4 years, 27.4% • 5-9 years, 22.6% • ≥10 years, 12.3% 60.8% male GCS: • 14 or normal for age, 98.7% • 11-13, 0.5% • <11, 0.3% Rapid drop by two points, 0.5%	Da Dalt et al. group A+B vs. C+D	CT (2.0%) or follow-up	Follow-up telephone interview 10 days after discharge and hospital records checked for readmissions for 1 month post-study conclusion	**Intracranial injury:** defined as intracranial injury identified on CT at initial presentation or during any hospital admission or readmission, no further details provided	NA	Study included previously
Dietrich 1993[20] USA	Those at children's hospital undergoing CT scan for head trauma, of any severity	Dietrich et al. 1993 rule – separately for >2 years	CT (all had CT)	Unclear	**Intracranial pathology:** defined as epidural or subdural haematoma, cerebral contusions or lacerations, intraventricular	NA	Study included previously

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=322 (N=185 analysed) Prospective	Mean (range) age: 7.1 years (10 days to 21 years), 20% <2 years 62% male GCS unclear, most appeared to be GCS 15 (note this is for n=322 not number analysed)	(N=166) and < 2 years (N=19)			haemorrhage pneumocephaly or cerebral oedema, with or without skull fracture		
Dunning 2006[21, 22] UK N=22,772 (n=22,579 analysed) Prospective	Children (<16 years) presenting with head injury of any severity at ED Mean age: 5.7 years (largest proportion between 2 and 11 years, 57.4%) 64.8% male GCS: • <13, 0.9% • 13, 0.3% • 14, 1.0% 15, 96.6%	CHALICE RCS guidelines	CT scan (3.3%) or follow-up	Unclear	**Clinically significant intracranial injury:** defined as death as a result of head injury, requirement for neurosurgical intervention or marked abnormalities on the CT scan	**Neurosurgery:** definition not provided	Study included previously
Easter 2014[23]	Children (<18 years) with minor head injury (GCS 13-15) presenting within 24 h of injury	PECARN (not reported separately for <2 and >2	CT (19% for whole population, unclear	For those without CT, medical	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need	**Traumatic brain injury requiring neurosurgery:**	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
USA N=1009 Prospective	Median (IQR) age: 6.1 (2.6-13.7) years 64.0% male GCS: • 13, 0.4% • 14, 4.0% 15, 95.0%	years) – N=1049 or N=981 depending on outcome CATCH (N=1002) CHALICE (N=858)	for proportion analysed for each specific decision rule) or follow-up	records used if had been evaluated as a follow-up at ED or outpatient practice or telephone interview arranged, time-point unclear	for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT **And** **Any traumatic brain injury on CT:** definition not provided	need for neurosurgery included craniotomy, elevation of skull fracture, monitoring of intracranial pressure, or intubation for elevated intracranial pressure	
Fabbri 2011[25] Italy N=2391 Prospective	Children (≤10 years) with head injury of any severity presenting within 24 h of injury Median (IQR) age: 3 (1-5) years 64.8% male GCS: • 13, 2.5% • 14, 7.3% 15, 90.2%	NEXUS Fabbri et al. 2011 rule	CT (11.9%) and follow-up	7-day time-point used for intracranial injury outcome, structured telephone interview for all at 6-month follow-up	**Intracranial lesion:** defined as post-traumatic lesion on CT scan within 7 days after injury. Posttraumatic lesions requiring admission to hospital and follow-up included: intracerebral hematoma or brain contusion, traumatic subarachnoid haemorrhage, subdural haemorrhage, epidural hematoma, intraventricular haemorrhage and a depressed skull fracture.		Study included previously
Ferrara 2016[26]	Children (≤14 years)	PECARN <2 years (N=14)	CT (71.0%) or unclear	Unclear if/how those	**Positive CT scan:** definition not provided	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Italy N=38 Retrospective	With traumatic brain injury of any severity Age: • <2 years, 36.8% • ≥2 years, 63.2% 67% and 43% in <2- and ≥2-year subgroups GCS unclear, any severity head injury included	PECARN ≥2 years (N=24)		without CT were followed up to			There is uncertainty in the results and could not be added to the Forest plot as raw data could not be calculated from accuracy data – the numbers did not match those analysed, meaning possible errors or due to small size
Fuller 2011[28] UK N=22,772 (N=15,132 analysed) Prospective	Children (5-16 years for PECARN rule and <2 years from CHALICE cohort) presenting to ED with head injury Mean age: 5.7 years 65% male GCS unclear, likely any severity included	PECARN >2 years (N=10415) PECARN <2 years (N=4717)	Unclear	Unclear	**Clinically important head injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT	NA	Study included previously
Gambacorta 2022[30] Italy N=3832	Children <18 years of age presenting to the ED within 24 hours of head trauma (GCS 14 or over) Mean (SD) age: 5.3 (4.8) years	PECARN >2 years (N= 2613) PECARN<2 years (N=1219)	CT (not all had CT scan)	Unclear	Clinically important traumatic brain injury: defined as death from traumatic brain injury; neurosurgical intervention for TBI; intubation of more than 24 hours for TBI;	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Retrospective	65.13% male				hospital admission of 2 nights or more for the TBI in associate with TBI on CT		
Gizli 2020[31] Turkey N=530 Retrospective	Children (<18 years) with blunt head trauma (GCS 13-15) Mean (SD) age: 5.89 (4.89) years 62.6% male GCS unclear, 13-15 to be included	PECARN (not reported separately for <2 and >2 years) – N=158 CATCH (N=170) CHALICE (N=69)	CT (all had CT)	Unclear	**Abnormal CT findings:** definition not provided but cases identified included epidural bleeding, subdural bleeding, and all types of skull fractures	NA	New study added as part of current update
Greenes 1999[32] USA N=608 Prospective	Children <2 years presenting to ED with complaint or diagnosis of head injury Mean (SD) age: 11.2 (6.8) months 57% males GCS unclear, appear to have included any severity	Greenes and Schutzman 1999 rule	CT (31.0%) or follow-up	Follow-up telephone calls at 2 weeks following ED visit and medical record review	**Intracranial injury:** defined as acute intracranial haematoma, cerebral contusion and/or diffuse brain swelling evident on head CT	NA	Study included previously
Greenes 2001[33] USA	Children <2 years presenting to ED with complaint or diagnosis of head injury	Greenes and Schutzman 2001 scoring system	CT (all had CT)	Follow-up telephone calls at 2 weeks following	**Intracranial injury:** defined as cerebral contusion, cerebral oedema or intracranial haematoma noted on CT	NA	Study included previously Same study as 1999 paper but focuses

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=422 (subsample of 608 patients included in 1999 paper)	Mean (SD) age: 11.6 (6.8) months, range 3 days to 23 months % male/female unclear GCS unclear, appear to have included any severity			ED visit and medical record review			on asymptomatic subpopulation
Gupta 2018[34] USA N=1018 Prospective	Children (<18 years) with acute blunt head trauma presenting within 24 h of injury and undergoing head CT Median (IQR) age: 11.9 (4.5-15.5) years, range 0.01-17.9 years 75% female GCS unclear, possibly included any severity	NEXUS II	CT (all had CT)	Unclear	**Clinically significant head injury on CT:** defined as all injuries evident on CT head imaging apart from the following in neurologically intact individuals: solitary small contusions, localized subarachnoid haemorrhage less than 1 mm thick, thin subdural hematomas less than 4 mm thick, isolated pneumocephaly, and closed depressed skull fractures that did not violate the inner table d 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	**Need for neurosurgical intervention:** defined as death due to head injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring within 7 days of head injury	New study added as part of current update
Guzel 2009[35]	Children (≤16 years) with minor head injury (GCS 13-15)	Guzel et al. 2009 rule	CT (all had CT)	Unclear	**Positive CT scan:** definition not reported	NA	Study included previously

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Turkey N=916 (N=337 analysed – those that had CT) Retrospective	Mean (SD) age: 6.00 (3.42) and 4.90 (3.71) years for CT positive and negative groups 66.2% GCS: • 13, 5.3% • 14, 4.5% 15, 91.2%						
Haydel 2003[39] USA N=175 Prospective	Children (5-17 years) with major mechanisms of injury resulting in minor head injury (normal GCS or modified coma scale in infants and normal brief neurologic examination) Mean age: 12.8 years %male/female unclear GCS unclear, normal GCS or modified coma scale required	New Orleans Criteria	CT (all had CT)	Unclear	**Intracranial injury on head CT:** defined as any acute traumatic intracranial lesion, including subdural epidural or parenchymal haematoma, subarachnoid haemorrhage, cerebral contusion or depressed skull fracture	**Need for neurosurgical or medical intervention in those with injury on CT:** need for neurosurgical or medical intervention in those with injury on CT, no further information	Study included previously
Ide 2017[45] Japan	Children (<18 years) with reported history of blunt head trauma presenting to ED within 24 h and initial GCS 14-15	PECARN <2 years (N=792)	CT (14.1% and 12.2% in >2 and <2	Return visits within 4 weeks after initial	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=2208 Retrospective	Mean (SD) age: • 13 (7-18) months in <2 years • 54 (36-88) months in >2 years 56.2% and 67.5% male in <2 and >2 year groups GCS: • 14, 4.8% and 2.7% in <2 year and >2 year groups • 15, 95.2% and 97.3% in <2 year and >2 year groups	PECARN >2 years (N=1416)	year groups) or follow-up	evaluation examined to identify missed injuries, no formal follow-up visit	>24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT		
Ide 2020[44] Japan N=6585 Prospective	Children (<16 years) with minor head trauma (GCS 14-15) presenting within 24 h of injury • Median (IQR) age: 13 (7-18) months for <2 year group • 56 (37-90) months for ≥2 year group	PECARN <2 years (N=2237) PECARN ≥2 years (N=4348)	CT (7.8% or 5.5% for ≥2 year and <2 year groups) or follow-up	Collected outcome data through health records at least 2 weeks after first examination	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
	% male/female not reported GCS: • 14, 1.1 and 1.0% for <2 and ≥2 year groups 15, 98.9 and 99.0% for <2 and ≥2 year groups						
Kim 2020[48] Korea N=433 (N=224 analysed – those that had CT) Retrospective	Children <2 years with minor head trauma (GCS 14-15) presenting to ED within 24 h of injury Mean (SD) age: 11.6 (5.5) months 63.9% male GCS unclear, GCS 14-15 to be included	PECARN <2 years	CT (all had CT)	Unclear	**Practically important traumatic brain injury:** defined as a clinically essential traumatic brain injury including all cranial abnormalities (e.g. skull fracture) detected by computed tomography	NA	New study added as part of current update
Kupperman 2009[50] USA N=42,412 (split into derivation and validation	Children (<18 years) with head trauma and GCS 14-15, presenting within 24 h of injury Mean (SD) age: 7.1 (5.5) years % male/female unclear	PECARN <2 years (N=2216) and N=8502 in development and validation cohorts) PECARN ≥2 years (N=6411 and N=25,283 in	CT or follow-up Proportion with CT varied depending on development or	Those discharged without CT had telephone survey 7-90 days post ED visit and medical/m	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association	**Neurosurgery:** definition not provided	Study included previously

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
populations) Prospective	GCS: 14, 3.0% 15, 97.0%	development and validation cohorts)	validation cohort and <2 and ≥2 year groups (31.0-37.3%)	orgue records checked for those uncontactable	with traumatic brain injury on CT		
Kwon 2021[51] South Korea N=271 Retrospective	Children (0-5 years old) with blunt head trauma and GCS 14 or over admitted to the ED within 24 hours of injury. Mean age (range): < 2 years group: 12 (1-23 months); 2-5 years group: 48 (24-71 months)	PECARN, < 2 years (N=78); PECARN, 2-5 years (N=173)	CT (all had CT)	Unclear	**Clinically important traumatic brain injury:** defined as minor blunt head trauma	**Neurosurgery:** NA	New study added as part of current update
Lorton 2016[55] France N=1499 Prospective	Children (<16 years) with minor head trauma (GCS 14-15) presenting to ED within 24 h of injury Median (IQR) age: 3.0 (1.7-6.0) years 64% male GCS: • 14, 1.5%	PECARN <2 years (N=421) PECARN ≥2 years (N=1078)	CT (5.1% for whole population, unclear for specific >2 year group) or follow-up	Contacted by telephone between 30 and 90 days post hospital visit	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
	15, 98.5%						
Meral Atis 2022[58] Turkey N=1004 Prospective	Children (<18 years of age, presenting to the Emergency Neurosurgery Outpatient Clinic (GCS score of 13 or higher) 65.4% male GCS: • 13, 0.2% • 14, 0.3% • 15, 99.5%	PECARN (N=1004); CATCH and CHALICE (N=966)	CT (all had CT)	Unclear	**Presence of a pathology in** head CT scans (head CT positivity)	NA	New study added as part of current update
Mihindu 2014[59] USA N=493 Retrospective	Children (<18 years with mild traumatic brain injury (GCS 14-15) and undergoing head CT Age, not reported % male/female not reported GCS unclear, 14-15 to be included	PECARN (not reported separately for <2 and >2 year groups)	CT (all had CT)	Unclear	**Clinically important traumatic brain injury:** clinical events used by PECARN were used to define clinically important traumatic brain injury (death attributable to TBI, neurosurgical intervention, and intubation for more than 24 hours, but not hospital stay for greater than two nights secondary to traumatic brain injury	NA	New study added as part of current update
Nakhjavan-Shahraki 2017[63] Iran	Children (<18 years) with mild traumatic brain injury (GCS 14-15) presenting to ED within 24 h of injury Mean (SD): 7.9 (5.3) years	PECARN <2 years (N=114) PECARN ≥2 years (N=480)	CT (55.4% in whole population, unclear for	Follow-up for 2 weeks by phone	**Clinically important traumatic brain injury:** defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=594 Prospective	79.3% male GCS unclear, 14-15 to be included		specific ≥2 year and <2 year groups) and/or follow-up		injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT		
Oman 2006[66] and Sun 2007[91] USA N= 1666 whole population, N=309 and N=208 <3 and <2 year subpopulations Prospective	Children (<18 years) presenting with blunt head trauma and undergoing CT Median (IQR) age: 11.3 (4.4-15.9) years 64% male GCS unclear, possibly includes any severity	NEXUS II (Oman 2006) Pilot PECARN (Sun 2007) Note that number in whole population analysed identical for both rules, but for <3 year subgroup used in Oman paper (N=309) and <2 year subgroup used in Sun paper (N=208)	CT (all had CT)	Unclear	**Clinically important/significant intracranial injury:** defined as any injury that may require neurosurgical intervention, lead to rapid clinical deterioration, or result in significant long-term neurological impairment	NA	Study included previously Oman 2006 provides results for NEXUS II and Sun 2007 provides results for Pilot PECARN
Osmond 2006[70] Canada	Children (≤16 years) presenting with minor head injury (GCS 13-15) Mean age: 9.2 years	CATCH	CT or unclear (proportion with CT unclear)	Follow-up at 14 days by telephone	**Brain injury:** defined as high and medium risk (any acute intracranial finding revealed on CT that was attributable to acute injury,	**Neurological intervention:** defined as craniotomy, elevation of skull	Study included previously

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=3781 Prospective	64.6% male GCS: • 13, 2.5% • 14, 7.2% 15, 90.3%				including closed depressed skull fracture and pneumocephalus, but excluding non-depressed skull fractures and basilar skull fractures) (assumed identical to Osmond 2010 as unclear from abstract)	fracture, intubation, intracranial pressure monitor and/or anticonvulsants within 7 days	
Osmond 2010[71] Canada N=3866 Prospective	Children (≤16 years) presenting with minor head injury (GCS 13-15) presenting within 24 h of injury Median (IQR) age: 10 (5-14) years, range 0-16 years 64.8% male GCS: • 13, 2.5% • 14, 7.3% • 15, 90.2%	CATCH	CT (52.8%) or follow-up	Follow-up at 14 days for those discharged without CT	**Brain injury:** defined as high and medium risk (any acute intracranial finding revealed on CT that was attributable to acute injury, including closed depressed skull fracture and pneumocephalus, but excluding non-depressed skull fractures and basilar skull fractures)	**Neurological intervention:** defined as high risk (death within 7 days secondary to head injury or need for craniotomy, elevation of skull fracture, monitoring of intracranial pressure or insertion of an endotracheal tube for treatment of head injury)	Study included previously
Osmond 2012[69] Canada	Children (≤16 years) presenting with minor head injury (GCS 13-15) Mean age: 9.8 years	CATCH	CT (34.9%) or follow-up	Follow-up at 14 days for those discharge	**Brain injury:** defined as high and medium risk (any acute intracranial finding revealed on CT that was attributable to acute injury,	**Neurological intervention:** defined as high risk (death within 7 days	Study included previously

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
N=4060 (N=4048 analysed) Prospective	64.5% male GCS: • 13, 2.2% • 14, 6.5% • 15, 91.3%			d without CT	including closed depressed skull fracture and pneumocephalus, but excluding non-depressed skull fractures and basilar skull fractures)	secondary to head injury or need for craniotomy, elevation of skull fracture, monitoring of intracranial pressure or insertion of an endotracheal tube for treatment of head injury)	
Osmond 2018[72] Canada N=4494 (n=4060 analysed) Prospective	Children (≤16 years) presenting with acute minor head injury (GCS 13-15) within 24 h of injury Mean age: 9.7 years, range 1 month to 16 years (11.4% <2 years) 64.5% male GCS: • 13, 2.2% • 14, 6.5% • 15, 91.3%	CATCH – original 7-item CATCH – refined 8-item	CT (34.0%) or follow-up	Follow-up at 14 days for those discharged without CT	**Brain injury:** defined as high and medium risk (any acute intracranial finding revealed on CT that was attributable to acute injury, including closed depressed skull fracture and pneumocephalus, but excluding non-depressed skull fractures and basilar skull fractures)	**Neurological intervention:** defined as high risk (death within 7 days secondary to head injury or need for craniotomy, elevation of skull fracture, monitoring of intracranial pressure or insertion of an endotracheal tube for treatment of head injury)	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Palchak 2003[73] N=2043 USA Prospective	Children (<18 years) presenting with blunt head trauma of any severity Mean (range) age: 8.3 years (10 days to 17.9 years) 65% male Median GCS: 15	Pilot PECARN <2 years (N=194) Pilot PECARN whole population (N=2043)	CT (all had CT <2 years and 62.2% had CT ≥2 years)	Unclear	**Traumatic brain injury on CT scan or requiring acute intervention:** defined as traumatic brain injury identified on CT scan or requiring acute intervention or intervention by one or more of: neurosurgical procedure, ongoing antiepileptic pharmacotherapy beyond 7 days, the presence of a neurological deficit that persisted until discharge from the hospital, or two or more nights of hospitalisation because of treatment of the head injury	**Need for neurosurgical intervention:** definition not provided	Study included previously
Quayle 1997[77] USA N=322 Prospective	Children (<18 years) presenting to ED with mild-severe non-trivial head injury Mean age: 4 years 10 months 59% males GCS unclear, any severity included if non-trivial	Quayle 1997 rule	CT (all had CT)	Followed up at 3-7 days post discharge	**Intracranial injury:** definition not provided	NA	Study included previously
Schonfeld 2014[80]	Children (<18 years in USA and <15 years in Italy) with minor blunt head trauma	PECARN <2 years (N=956 for clinically	Neuroimaging (CT or MRI,	Follow-up for 2 weeks by	**Clinically important traumatic brain injury:** defined as death from	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
USA and Italy N=2439 Prospective/retrospective	(initial GCS 14-15) presenting to ED within 24 h of injury Age: • <2 years, 39% • ≥2 years, 61% 59% male GCS not reported, 14-15 to be included	important injury and N=121 for positive CT finding) PECARN ≥2 years (N=1472 for clinically important injury and N=251 for positive CT finding)	majority CT) or follow-up 15.0% had CT and 0.1% MRI in whole population, proportion not clear for specific <2 year and ≥2 year groups	phone/medical records	traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT **And** **Positive CT finding:** defined as any of the following: intracranial haemorrhage or contusion, traumatic infarction, sigmoid sinus thrombosis, diffuse axonal injury, pneumocephalus, midline shift or signs of brain herniation, diastasis of the skull, and/or skull fracture		
Sert 2020[81] Turkey N=2490 Retrospective	Children (<18 years) with minor blunt head trauma (GCS 14-15) admitted to the ED and undergoing CT Mean (SD) age: 6.6 (4.5) years 69.9% female GCS:	CATCH PECARN (not presented separately for <2 and ≥2 year groups)	CT (all had CT)	Unclear	**New traumatic intracranial injury on CT:** defined as linear or non-linear skull fracture, any intracranial haemorrhage (epidural, subdural, subarachnoid, intracerebral), pneumocephalus, contusion or cerebral oedema	**Neurosurgical intervention or death:** defined as death due to head trauma or neurosurgical procedure, including invasive intracranial pressure measurement	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
	• 14, 10% • 15, 90%					by any method, burr hole procedure, craniotomy, haematoma removal, surgical repair of displaced skull fracture and dura repair	
Thiam 2015[93] Singapore N=1179 Prospective	Children (<16 years) presenting to ED following head injury within 72 h of injury Mean age: 4.4 years 74.6% male GCS: • 13, 0.1% • 14, 1.4% • 15, 98.2%	CATCH CHALICE PECARN (not reported separately for <2 and ≥2 year groups) • High and medium risk • High risk only	CT (1.02%) or follow-up	Follow-up duration of 72 h for those discharged	**Positive CT findings:** defined as epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haematoma, cerebral oedema, depressed fracture and contusion	NA	New study added as part of current update
Yogo 2021[98] Japan N=645	Median age (IQR): 5 (2-9) 68% male GCS: • <15, 11%	PECARN; CATCH and CHALICE (reported separately for <2 and ≥2 year groups)	CT (all had CT)	Unclear	**Clinically important traumatic brain injury**	NA	New study added as part of current update

Study	Population	Index test	Reference standard	Follow-up	Definition for intracranial injury	Definition for neurosurgery	Comments
Retrospective							

See Appendix D for full evidence tables.

1.1.6 Summary of the diagnostic evidence

The assessment of the evidence quality was conducted with emphasis on test sensitivity and specificity as this was identified by the committee as the primary measure in guiding decision-making. Clinical decision thresholds of sensitivity/specificity =0.9 and 0.60 above which a test would be recommended and 0.7 and 0.4 below which a test is of no clinical use were set. The lower thresholds were primarily used in the assessment of imprecision and less so for assessing clinical usefulness, as it was noted that for specificity in many cases existing rules would not meet 0.40 but have a very good sensitivity. Of sensitivity and specificity, it was agreed that sensitivity is the most important measure as the consequences of these decision rules missing people with injuries on CT (meaning they are not sent for CT) may be severe.

Based on the variation in reference standards and outcome definitions across studies, results for each decision rule were split into two different types of reference standard and three broad outcome definitions. This was because it was agreed in the protocol that studies would only be pooled or grouped together if reference standards were the same and because it was identified that outcome definitions for intracranial injury varied greatly across studies and may affect subsequent results for sensitivity and specificity.

The two reference standard groups were studies where all of those included had a CT and studies where only a proportion (often only a small proportion) had a CT at enrolment based on indications according to the clinician or as set at the institutions the studies were performed in. Separating into these two groups was thought to be appropriate as it was noted that in studies where all of them had a CT initially there may have been a stronger suspicion of head injury that would be picked up on CT, possibly introducing bias based on a more selective population, whereas those only performing CT on a proportion of the cohort likely included a broader spectrum of participants presenting to the emergency department where a decision about CT imaging is required. Although for the latter group the type and duration of follow-up varied, these were still grouped together as the general approach of only performing CT at enrolment in a proportion was common among studies.

The outcome groupings that results were separated into were as follows: any intracranial injury, clinically important/more serious injuries and neurosurgery. Definitions within each of these three groups were not identical across studies, but these three groupings were thought to be most appropriate in order not to group anything that was too different together but also not split results into individual studies for many of the outcomes as this would be more difficult to interpret. All definitions for a particular analysis are provided as footnotes in the following tables.

Meta-analysis has been performed where possible (at least three studies for the same decision rule, with similar reference standard and outcome, and where the model converged), but for most this was not possible either because of less than three studies available or because the model would not converge. For those where meta-analysis could not be performed based on the model not converging, median values have been given where appropriate as well as the results for each individual study.

In addition to results for each specific decision rule, two studies (Foks 2018[27] for adults and Babl 2017/2019[5, 7] for children/infants) report results for the most commonly used decision rules. Forest plots of results for all of these tests from the same study are presented in E.1.7 and E.1.19, respectively, for comparative purposes as they are the only studies comparing this many rules in a single study.

Adults – NICE 2014 guideline

Table 4: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NICE 2014 guideline

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Foks 2018[27] – original rule in the whole population	1	4557	CT or imputation – 82.1% had CT and data imputed for those without CT	Unclear - up to 30-day review of medical records mentioned for neurosurgery outcome	Intracranial traumatic finding on CT[a]	0.72 (0.68 to 0.77)	0.61 (0.59 to 0.62)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Serious[d]	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Foks 2018[27] – original rule in	1	4557	CT or imputation – 82.1% had CT	Unclear - up to 30-day review	Potential neurosurgical lesion on CT[e]	0.85 (0.75 to 0.92)	0.59 (0.57 to 0.60)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
the whole population			and data imputed for those without CT	of medical records mentioned for neurosurgery outcome				Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having CT												
Foks 2018[27] – original rule in the whole population	1	4557	CT or imputation – 82.1% had CT and data imputed for those without CT	Up to 30-day review of medical records mentioned for neurosurgery outcome	Neurosurgical intervention[f]	0.89 (0.65 to 0.99)	0.58 (0.57 to 0.60)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture*

[b] *Defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation*

[c] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[d] *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*

[e] *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*

[f] *Definition not provided*

Adults – CCHR high and medium risk

Table 5: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – CCHR high and medium risk

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT – meta-analysis performed												
CCHR high and medium risk	9	5779	CT (all had CT)	Unclear for 8 studies, other mentioned neuro-observation in ED for 12 h if CT normal and neurosurgical transfer if positive	Varies across studies, definitions given in footnotes[a-h]	0.90 (0.77 to 0.97)	0.42 (0.32 to 0.53)	Sensitivity				
								Serious[i]	None	None	Serious[j]	LOW
								Specificity				
								Serious[i]	None	None	Serious[k]	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – meta-analysis performed												
CCHR high and	5	12,553	CT (41.9%-82.1%)	Follow-up was 7 days (n=1	Varies across studies,	0.94 (0.80 to 0.99)	0.42 (0.23 to 0.63)	Sensitivity				
								Very serious[i]	None	None	Serious[j]	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
medium risk			Those that did not have CT either had structured telephone follow-up (n=2 studies), imputation (n=1 study) or it was unclear (n=2 studies)	study), 14-60 days (n=1 study), 15 days (n=1 study) or unclear (n=2 studies)	definitions given in footnotes[l-p]			Specificity				
								Very serious[i]	None	Serious[q]	Very Serious[k]	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT – meta-analysis performed												
CCHR high and medium risk	4	1196	CT (all had CT)	Unclear for all	Varies across studies, definition for one given in footnote[r] and remaining three studies given in footnote[s]	0.88 (0.69 to 0.97)	0.35 (0.18 to 0.57)	Sensitivity				
								Serious[i]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Serious[i]	None	None	Serious[k]	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – meta-analysis performed												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
CCHR high and medium risk	6	9683	CT (29.4%-82.1%), unclear proportion in one study Those that did not have CT either had follow-up (telephone follow-up in 3 studies and unclear in 2 studies) or imputation (n=1 study)	14 days (n=3 studies), 6 months (n=1 study) or unclear (n=2 studies)	Varies across studies, definitions given in footnotes[t-w], with three studies sharing the same definition[u]	0.93 (0.73 to 0.99)	0.48 (0.34 to 0.62)	Sensitivity				
								Very serious[i]	None	Serious[q]	Serious[j]	VERY LOW
								Specificity				
								Very serious[i]	None	Serious[q]	Very serious[k]	VERY LOW
Neurosurgery (definitions vary) with all having CT – no meta-analysis as model would not converge												
CCHR high and medium risk	4	3082	CT (all had CT)	See individual studies below	See individual studies below	Median value across studies: 1.00 (0.59 to 1.00) Point estimates range from 0.80 to 1.00 across studies	Corresponding specificity: 0.37 (0.35 to 0.39) Point estimates range from 0.36 to 0.67 across studies	See individual GRADE ratings for each study below				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Lo 2016[54]	1	383	CT (all had CT)	7-day period used to confirm neurosurgery outcome	Need for neurosurgical intervention[x]	0.80 (0.44 to 0.97)	0.36 (0.31 to 0.41)	Sensitivity				
								Serious[i]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Serious[i]	None	None	Serious[k]	LOW
Papa 2012[75]	1	431	CT (99.3% had CT) or unclear	Unclear how those without CT had outcome confirmed, 7-day time-point for neurosurgery outcome	Need for neurosurgical intervention[y]	1.00 (0.48 to 1.00)	0.67 (0.62 to 0.71)	Sensitivity				
								Serious[i]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Serious[i]	None	None	None	MODERATE
Rosengren 2004[79]	1	240	CT (all had CT)	Unclear	Neurological intervention[z]	1.00 (0.03 to 1.00)	0.48 (0.41 to 0.54)	Sensitivity				
								Very serious[i]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Very serious[i]	None	None	None	LOW
Smits 2005[83]	1	2028	CT (all had CT)	30-day time-point mentioned	Neurosurgical	1.00 (0.59 to 1.00)	0.37 (0.35 to 0.39)	Sensitivity				
								Very serious[i]	None	None	Very serious[j]	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				for neurosurgery outcome	intervention[aa]			Specificity				
								Very serious[i]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having – meta-analysis performed												
CCHR high and medium risk	4	14,372	CT (41.9%-82.1%), unclear proportion in one study Those that did not have CT either had follow-up by telephone (n=2 studies), follow-up by telephone/attendance (n=1 study) or imputation (n=1 study)	7 days (n=1 study), 30 days (n=1 study) or 6 months (n=2 studies)	Varies across studies, definitions given in footnotes[ab-ae]	0.97 (0.88 to 1.00)	0.36 (0.19 to 0.59)	Sensitivity				
								Very serious[i]	None	None	Serious[j]	VERY LOW
								Specificity				
								Very serious[i]	None	Serious[q]	Serious[k]	VERY LOW

[a] *Defined as soft tissue swelling, extradural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haemorrhage, intraventricular haemorrhage, cortical contusions, brain oedema, diffuse axonal injury, brain herniation/midline shift, skull fracture and facial bone fracture*

[b] *Defined as positive for intracranial haemorrhage*

[c] *Defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusion*

[d] *Defined as the presence of any of the following: subdural haematomas, epidural haematomas, subarachnoid haemorrhage, cerebral oedema, skull fracture and cerebral contusions*

[e] *Defined as subarachnoid haemorrhage, epidural haemorrhage, subdural haematoma, intraparenchymal hematoma, compression fracture, cerebral oedema and contusion*

[f] *Definition not provided, but all cases were either haemorrhages or contusions*

[g] *Defined as any skull or skull base fracture and any intracranial traumatic lesion*

[h] *Definition not provided but those identified included cranial fracture, epidural haematoma, subdural haematoma, intracerebral haematoma, subarachnoid haemorrhage and cerebral contusions*

[i] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[j] *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.*

[k] *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.*

[l] *Defined as* any acute intracranial finding revealed on CT that was attributable to acute injury

[m] *Defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture*

[n] *Defined as subdural, epidural or parenchymal hematoma; subarachnoid haemorrhage; cerebral contusion; or depressed skull fracture*

[o] *Defined as any lesion: surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other intracranial abnormality diagnosed on CT)*

[p] *Defined as any types of intracranial haemorrhage (for example, subdural haemorrhage, epidural haematoma, subarachnoid haemorrhage and intracerebral haematoma) and depressed skull fracture*

[q] *Downgraded by one increment as apparent heterogeneity based on point estimates and lack of overlap of confidence intervals across studies*

[r] *Defined as all types of brain injuries with positive CT findings except the following: solitary contusion of less than 5 mm in diameter; localised subarachnoid blood less than 1 mm thick; smear subdural haematoma less than 4 mm thick; or closed depressed skull fracture not through the inner table*

[s] *Defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table*

[t] *Defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation*

[u] *Defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table*

[v] *All brain injuries were considered clinically important unless the patient was neurologically intact and had 1 of the following lesions on CT: solitary contusion of less than 5 mm in diameter, localised subarachnoid blood less than 1 mm thick, smear subdural hematoma less than 4 mm thick, or closed depressed skull fracture not through the inner table*

[w] *Defined as epidural haematoma, subdural haematoma of thickness ≥ 4 mm, subarachnoid haemorrhage of thickness > 1 mm, intracerebral haematoma, intraventricular haemorrhage, diffuse cerebral oedema, cerebral contusion of diameter ≥ 5 mm, pneumocephalus and depressed skull fracture*

[x] *Defined as death within 7 days of head injury or need for any of following within 7 days: burr hole, craniotomy, craniectomy, and elevation of skull fracture or intracranial pressure monitoring*

[y] *Defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury (shown on CT)*

[z] *Definition not provided*

[aa] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

[ab] *Definition not provided*

[ac] *Defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury*

[ad] *Defined as intracranial haematoma large enough to require surgical evacuation*

[ae] *Defined as interventions within 7 days of injury, including craniotomy or craniectomy, elevation of skull fracture, external ventricular drainage, Burr holes and intracranial pressure monitoring*

Adults – CCHR high and medium risk adapted to cohort

Table 6: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – CCHR high and medium risk adapted to cohort

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Smits 2005[83]	1	3181	CT (all had CT)	Unclear, 30-day time-point mentioned for neurosurgery outcome	Any neurocranial traumatic finding on CT[a]	0.85 (0.80 to 0.89)	0.40 (0.38 to 0.41)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Foks 2018[27] – adapted version of the	1	4557	CT or imputation – 82.1% had CT and data	Unclear - up to 30-day review of	Intracranial traumatic finding on CT[d]	0.82 (0.78 to 0.85)	0.42 (0.40 to 0.43)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
rule used in the whole population, accounting for inclusion/exclusion criteria of the rule			imputed for those without CT	medical records mentioned for neurosurgery outcome				Very serious [b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Foks 2018[27] – adapted version of the	1	4557	CT or imputation – 82.1% had CT and data	Unclear - up to 30-day review of	Potential neurosurgical lesion on CT[e]	0.88 (0.78 to 0.94)	0.40 (0.39 to 0.42)	Sensitivity				
								Very serious [b]	None	None	Serious [f]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
rule used in the whole population, accounting for inclusion/exclusion criteria of the rule			imputed for those without CT	medical records mentioned for neurosurgery outcome				Very serious [b]	None	None	Serious [c]	VERY LOW
Neurosurgery (definitions vary) with all having CT												
Smits 2005[83]	1	3181	CT (all had CT)	30-day time-point mentioned for neurosurgery outcome	Neurosurgical intervention[g]	1.00 (0.80 to 1.00)	0.37 (0.36 to 0.39)	Sensitivity				
								Very serious [b]	None	None	Serious [f]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW

[a] *Defined as any skull or skull base fracture and any intracranial traumatic lesion*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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] *Defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture*

[e] *Defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation*

[f] *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.*

[g] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

Adults – CCHR high risk

Table 7: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – CCHR high risk

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Any lesion on CT[a]	0.97 (0.95 to 0.98)	0.51 (0.50 to 0.52)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Rosengren 2004[79]	1	240	CT (all had CT)	Unclear	Clinically significant intracranial injury[c]	0.50 (0.19 to 0.81)	0.77 (0.71 to 0.83)	Sensitivity				
								Very serious[b]	None	None	Serious[d]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT – no meta-analysis as only two studies												
Mower 2017[61]	1	7759	CT (all had CT)	7-day time-point mentioned for neurosurgical intervention	Need for neurosurgical intervention[e]	0.97 (0.92 to 0.99)	0.59 (0.58 to 0.60)	Sensitivity				
								None	None	None	None	HIGH
								Specificity				
								None	None	None	None	HIGH
Rosengren 2004[79]	1	240	CT (all had CT)	Unclear	Neurological intervention[f]	1.00 (0.03 to 1.00)	0.77 (0.71 to 0.82)	Sensitivity				
								Very serious[b]	None	None	Very serious[d]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having CT – meta-analysis performed												
	5	16,492				0.96 (0.74 to 1.00)	0.64 (0.47 to 0.78)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
CCHR high risk			CT (29.4%-80.2%) Those that did not have CT either had follow-up by telephone (n=3 studies), follow-up with method unclear (n=1 study) or unclear how outcome was confirmed (n=1 study)	7 days (n=2 studies), 30 days (n=1 study), 6 months (n=1 study) or unclear (n=1 study)	Varies across studies, definitions given in footnotes[g-j], with two studies having the same definition[j]			Very serious[b]	None	Serious[k]	Serious[d]	VERY LOW
								Specificity				
								Very serious[b]	None	Serious[k]	Serious[l]	VERY LOW

[a] *Defined as any lesion: surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other intracranial abnormality diagnosed on CT)*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[c] *Defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table*

[d] *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.*

[e] *Defined as death due to head injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring, within 7 days of head injury*

[f] *Definition not provided*

[g] *Defined as either death or need for any of the following procedures within 30 days of the traumatic event: craniotomy, monitoring of intracranial pressure, or the need for intubation for the treatment of head injury*

[h] *Defined as death due to head injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring, within 7 days of head injury*

[i] *Defined as intracranial haematoma large enough to require surgical evacuation*

[j] *Defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury (shown on CT)*

[k] *Downgraded by one increment as apparent heterogeneity based on point estimates and lack of overlap of confidence intervals across studies*

[l] *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*

Adults – CCHR moderate risk

Table 8: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – CCHR moderate risk

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												
Mower 2017[61]	1	7759	CT (all had CT)	Unclear	Clinically significant head injury on CT[a]	0.98 (0.96 to 0.99)	0.12 (0.12 to 0.13)	Sensitivity				
								None	None	None	None	HIGH
								Specificity				
								None	None	None	None	HIGH

[a] *included all injuries evident on CT head imaging apart from the following in neurologically intact individuals: solitary small contusions, localized subarachnoid haemorrhage less than 1 mm thick, thin subdural hematomas less than 4 mm thick, isolated pneumocephaly and closed depressed skull fractures that did not violate the inner table*

Adults – CCHR high and medium risk with cut-point ≥2

Table 9: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – CCHR high and medium risk with cut-point ≥2

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
	1	264		Unclear		0.76 (0.68 to 0.83)	0.74 (0.65 to 0.81)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Chobdari 2018[15]			CT (all had CT)		Abnormality on CT scan[a]			Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Definition not provided*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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 – NOC

Table 10: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NOC

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT – meta-analysis performed												
NOC	8	5831	CT (all had CT)	Unclear in 7 studies, remaining study followed until discharge	Varies across studies, definitions given in footnotes[a-g]	0.96 (0.90 to 0.99)	0.20 (0.11 to 0.34)	Sensitivity				
								Serious[h]	None	Serious[i]	Serious[j]	VERY LOW
								Specificity				
								Serious[h]	None	Serious[i]	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – no meta-analysis as model would not converge												
NOC	4	10,853	See individual studies below	See individual studies below	See individual studies below	Median value across studies: 0.99 (0.98 to 1.00) Point estimates range from 0.86 to 1.00 across studies	Corresponding specificity: 0.33 (0.32 to 0.34) Point estimates range from 0.03 to 0.33 across studies	See individual GRADE ratings for each study below				
Bouida 2013[11]	1	1582	CT (70.9%) or structured	If no return to ED within 15 days	Intracranial lesion[k]	0.86 (0.80 to 0.90)	0.28 (0.26 to 0.31)	Sensitivity				
								Serious[h]	None	None	None	MODERATE
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			telephone interview follow-up	with specific criteria, considered negative for outcome				Serious[h]	None	None	None	MODERATE
Foks 2018[27] – original rule in the subpopulation it was designed for use in	1	1147	CT or imputation – 82.1% in whole population had CT and data imputed for those without CT (proportion for this subgroup unclear)	Unclear - up to 30-day review of medical records mentioned for neurosurgery outcome	Intracranial traumatic finding on CT[l]	0.99 (0.95 to 1.00)	0.03 (0.02 to 0.05)	Sensitivity				
								Very serious[h]	None	None	None	LOW
								Specificity				
								Very serious[h]	None	None	None	LOW
Korley 2013[49]	1	169	CT (76.9%) or structured telephone	Up to 14-60 days for those not receiving	Acute traumatic finding on CT[m]	1.00 (0.48 to 1.00)	0.03 (0.01 to 0.07)	Sensitivity				
								Very serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			follow-up at 14-60 days post-enrolment	CT at enrolment				Very serious[h]	None	None	None	LOW
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Any lesion on CT[n]	0.99 (0.98 to 1.00)	0.33 (0.32 to 0.34)	Sensitivity				
								Very serious[h]	None	None	None	LOW
								Specificity				
								Very serious[h]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – Yarladgadda 2019 presented separately based on population difference (inpatients with falls, with most being on anticoagulation)												
Yarlagadda 2019[97]	1	332	CT (57.0%) or unclear	Unclear how outcome confirmed in those without CT at enrolment	Positive head CT finding[o]	0.86 (0.42 to 1.00)	0.25 (0.20 to 0.30)	Sensitivity				
								Very serious[h]	Serious[p]	None	Very serious[j]	VERY LOW
								Specificity				
								Very serious[h]	Serious[p]	None	None	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT – no meta-analysis as model would not converge												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
NOC	4	1052	CT (all had CT)	See individual studies below	See individual studies below	Median value across studies: Between 0.93 (0.66 to 1.00) and 1.00 (0.72 to 1.00) Point estimates range from 0.92 to 1.00 across studies	Corresponding specificity: Between 0.10 (0.07 to 0.14) and 0.17 (0.08 to 0.30) Point estimates range from 0.04 to 0.17 across studies	See individual GRADE ratings for each study below				
Lo 2016[54]	1	431	CT (all had CT)	Unclear, other than 7-day period used to confirm neurosurgery outcome	Clinically important brain injury on CT[q]	0.92 (0.84 to 0.97)	0.17 (0.13 to 0.21)	Sensitivity				
								Serious[h]	None	None	Serious[j]	LOW
								Specificity				
								Serious[h]	None	None	None	MODERATE
Mata-Mbemba 2016[57]	1	67	CT (all had CT)	Unclear	Clinically important CT finding[r]	0.93 (0.66 to 1.00)	0.17 (0.08 to 0.30)	Sensitivity				
								None	None	None	Very serious[j]	LOW
								Specificity				
								None	None	None	None	HIGH
Papa 2012[75]	1	314	CT (all had CT)	Unclear	Clinically importa	1.00 (0.72 to 1.00)	0.10 (0.07 to 0.14)	Sensitivity				
								Serious[h]	None	None	Serious[j]	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
					nt brain injury[r]			Serious[h]	None	None	None	MODERATE
Rosengren 2004[79]	1	240	CT (all had CT)	Unclear	Clinically significant intracranial injury[r]	1.00 (0.69 to 1.00)	0.04 (0.02 to 0.07)	Sensitivity				
								Very serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Very serious[h]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – meta-analysis performed												
NOC	3	3626	CT (75.6%-82.1%)	14 days (n=1 study), 6 months (n=1	Varies across studies, definitions given	0.97 (0.82 to 1.00)	0.10 (0.02 to 0.44)	Sensitivity				
								Very serious[h]	None	None	Serious[j]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			Those that did not have CT either had follow-up by telephone (n=2 studies) or imputation (n=1 study)	study) or unclear (n=1 study)	in footnotes[s-u]			Very serious[h]	None	None	Serious[v]	VERY LOW
Neurosurgery (definitions vary) with all having CT – no meta-analysis as model would not converge												
NOC	4	2292	CT (all had CT)	See individual studies below	See individual studies below	Median value across studies: 1.00 (0.16 to 1.00) Point estimates from all four studies were 1.00	Corresponding specificity: 0.05 (0.04 to 0.07) Point estimates range from 0.04 to 0.15 across studies	See individual GRADE ratings for each study below				
Lo 2016[54]	1	431	CT (all had CT)	7-day period used to confirm neurosurgery outcome	Need for neurosurgical intervention[w]	1.00 (0.72 to 1.00)	0.15 (0.12 to 0.19)	Sensitivity				
								Serious[h]	None	None	Serious[j]	LOW
								Specificity				
								Serious[h]	None	None	None	MODERATE

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Papa 2012[75]	1	314	CT (all had CT)	7-day time-point for neurosurgery outcome	Need for neurosurgical intervention[x]	1.00 (0.29 to 1.00)	0.10 (0.07 to 0.13)	Sensitivity				
								Serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Serious[h]	None	None	None	MODERATE
Rosengren 2004[79]	1	240	CT (all had CT)	Unclear	Neurological intervention[y]	1.00 (0.03 to 1.00)	0.04 (0.02 to 0.07)	Sensitivity				
								Very serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Very serious[h]	None	None	None	LOW
Smits 2005[83]	1	1307	CT (all had CT)	30-day time-point mentioned for neurosurgery outcome	Neurosurgical intervention[z]	1.00 (0.16 to 1.00)	0.05 (0.04 to 0.07)	Sensitivity				
								Very serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Very serious[h]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having CT – no meta-analysis as model would not converge												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
NOC	5	17,458	See individual studies below	See individual studies below	See individual studies below	Median value across studies: 1.00 (0.81 to 1.00) Point estimates range from 0.82 to 1.00 across studies	Corresponding specificity: 0.04 (0.04 to 0.05) Point estimates range from 0.04 to 0.31 across studies	See individual GRADE ratings for each study below				
Bouida 2013[11]	1	1582	CT (70.9%) or structured telephone interview follow-up	Events within 30 days counted for neurosurgery outcome	Need for neurosurgical intervention[aa]	0.82 (0.65 to 0.93)	0.26 (0.23 to 0.28)	Sensitivity				
								Serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Serious[h]	None	None	None	MODERATE
Foks 2018[27] – original rule in the whole population, apparently without adaptation to the cohort	1	4557	CT or imputation – 82.1% had CT and data imputed for those without CT	Up to 30-day review of medical records mentioned for neurosurgery outcome	Neurosurgical intervention[ab]	1.00 (0.81 to 1.00)	0.04 (0.04 to 0.05)	Sensitivity				
								Very serious[h]	None	None	Serious[j]	VERY LOW
								Specificity				
								Very serious[h]	None	None	None	LOW
	1	657				1.00 (0.54 to 1.00)	0.20 (0.17 to 0.24)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Ro 2011[78]			CT and/or follow-up by telephone at 6 months	Follow-up by telephone at 6 months in all participants, 7-day time-point for neurosurgery outcome	Need for neurosurgical intervention[ac]			Serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				
								Serious[h]	None	None	None	MODERATE
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Surgical intracranial lesion[ad]	0.99 (0.95 to 1.00)	0.31 (0.30 to 0.32)	Sensitivity				
								Very serious[h]	None	None	None	LOW
								Specificity				
								Very serious[h]	None	None	None	LOW
Stiell 2005[89]	1	2707	CT (80.2%) or follow-up by	14 day telephone interview for those not	Need for neurological intervention[ae]	1.00 (0.63 to 1.00)	0.12 (0.11 to 0.14)	Sensitivity				
								Very serious[h]	None	None	Very serious[j]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			telephone interview	having CT at enrolment – 7-day time-point for neurosurgery outcome				Very serious [h]	None	None	None	LOW

[a] *Defined as a subdural, epidural or parenchymal haematoma, subarachnoid haemorrhage, cerebral contusion or depressed skull fracture*

[b] *Defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions*

[c] *Defined as the presence of any of the following: subdural haematomas, epidural haematomas, subarachnoid haemorrhage, cerebral oedema, skull fracture and cerebral contusions*

[d] *Defined as subarachnoid haemorrhage, epidural haemorrhage, subdural haematoma, intraparenchymal hematoma, compression fracture, cerebral oedema and contusion*

[e] *any brain injury on CT, no further details given*

[f] *Defined as any skull or skull base fracture and any intracranial traumatic lesion*

[g] *Definition not provided but those identified included cranial fracture, epidural haematoma, subdural haematoma, intracerebral haematoma, subarachnoid haemorrhage and cerebral contusions*

[h] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

i Downgraded by one increment as apparent heterogeneity based on point estimates and lack of overlap of confidence intervals across studies

[j] *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*

[k] *Defined as any acute intracranial finding revealed on CT that was attributable to acute injury*

[l] *Defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture*

[m] *Defined as subdural, epidural or parenchymal hematoma; subarachnoid haemorrhage; cerebral contusion; or depressed skull fracture*

[n] *Defined as any lesion: surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other intracranial abnormality diagnosed on CT)*

[o] *Defined as any acute intracranial process, no further details given*

[p] *Population is more specific as it only includes inpatients with falls and it is unclear whether there was a suspicion of head injury for all patients*

[q] *Defined as all types of brain injuries with positive CT findings except the following: solitary contusion of less than 5 mm in diameter; localised subarachnoid blood less than 1 mm thick; smear subdural haematoma less than 4 mm thick; or closed depressed skull fracture not through the inner table*

[r] *Defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table*

[s] *Defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation*

[t] *Defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table*

[u] *All brain injuries were considered clinically important unless the patient was neurologically intact and had 1 of the following lesions on CT: solitary contusion of less than 5 mm in diameter, localised subarachnoid blood less than 1 mm thick, smear subdural hematoma less than 4 mm thick, or closed depressed skull fracture not through the inner table*

[v] *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*

[w] *Defined as death within 7 days of head injury or need for any of following within 7 days: burr hole, craniotomy, craniectomy, and elevation of skull fracture or intracranial pressure monitoring*

[x] *Defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury (shown on CT)*

[y] *Definition not provided*

[z] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

[aa] *Defined as either death or need for any of the following procedures within 30 days of the traumatic event: craniotomy, monitoring of intracranial pressure, or the need for intubation for the treatment of head injury*

[ab] *Definition not provided*

[ac] *Defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury*

[ad] *Defined as intracranial haematoma large enough to require surgical evacuation*

[ae] *Defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury (shown on CT)*

Adults – NOC adapted to cohort

Table 11: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NOC adapted to cohort

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Smits 2005[83]	1	3181	CT (all had CT)	Unclear, 30-day time-point mentioned for neurosurgery outcome	Any neurocranial traumatic finding on CT[a]	0.99 (0.98 to 1.00)	0.03 (0.03 to 0.04)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Foks 2018[27] – adapted version of the rule used in the whole population, accounting for inclusion/exclusion criteria of the rule	1	4557	CT or imputation – 82.1% had CT and data imputed for those without CT	Unclear - up to 30-day review of medical records mentioned for neurosurgery outcome	Intracranial traumatic finding on CT[c]	0.99 (0.97 to 1.00)	0.04 (0.03 to 0.05)	Sensitivity				
								Very serious [b]	None	None	None	LOW
								Specificity				
								Very serious [b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												
Mata-Mbemba 2016[57]	1	142	CT (all had CT)	Unclear	Clinically important CT finding[d]	0.98 (0.89 to 1.00)	0.10 (0.05 to 0.18)	Sensitivity				
								None	None	None	Serious[e]	MODERATE
								Specificity				
								None	None	None	None	HIGH
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
	1	4557				1.00 (0.95 to 1.00)	0.04 (0.03 to 0.04)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Foks 2018[27] – adapted version of the rule used in the whole population, accounting for inclusion/exclusion criteria of the rule			CT or imputation – 82.1% had CT and data imputed for those without CT	Unclear - up to 30-day review of medical records mentioned for neurosurgery outcome	Potential neurosurgical lesion on CT[f]			Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Smits 2005[83]	1	3181	CT (all had CT)	30-day time-point mentioned for neurosurgery outcome	Neurosurgical intervention[g]	1.00 (0.80 to 1.00)	0.03 (0.02 to 0.04)	Sensitivity				
								Very serious[b]	None	None	Serious[e]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as any skull or skull base fracture and any intracranial traumatic lesion*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[c] *Defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture*

[d] *Defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table*

[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*

[f] *Defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation*

[g] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

Adults – NOC with cut-point ≥2

Table 12: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NOC with cut-point ≥2

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Chobdari 2018[15]	1	264	CT (all had CT)	Unclear	Abnormality on CT scan[a]	0.31 (0.23 to 0.39)	0.69 (0.60 to 0.77)	Sensitivity				
								Very serious[b]	None	None	None	LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
								Specificity				
								Very serious [b]	None	None	None	LOW

[a] *Definition not provided*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

Adults – NEXUS II

Table 13: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NEXUS II

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury with all having CT												
Li 2022[53]	1	463	CT (all had CT)	Unclear	Traumatic brain injury[j]	0.98 (0.94 to 1.00)	0.24 (0.19 to 0.29)	Sensitivity				
								Serious [b]	None	None	None	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
								Serious[b]	None	None	None	LOW
Intracranial injury – any injury with only a proportion having CT												
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Any lesion on CT[a]	0.97 (0.95 to 0.98)	0.47 (0.46 to 0.48)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT – no meta-analysis as only two studies												
Mower 2005[62]	1	13728	CT (all had CT)	Unclear	Significant intracranial injury[c]	0.98 (0.97 to 0.99)	0.14 (0.13 to 0.14)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Mower 2017[61]	1	11770	CT (all had CT)	Unclear, other than 7-day	Clinically significa	0.99 (0.98 to 1.00)	0.16 (0.25 to 0.26)	Sensitivity				
								None	None	None	None	HIGH
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				time-point used to measure neurosurgery outcome	nt head injury on CT[d]			None	None	None	None	HIGH
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Ro 2011[78]	1	2951	CT and/or follow-up by telephone at 6 months	Follow-up by telephone at 6 months in all participants	Clinically important brain injury[e]	0.89 (0.86 to 0.91)	0.46 (0.44 to 0.49)	Sensitivity				
								Serious[b]	None	None	Serious[f]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Neurosurgery (definitions vary) with all having CT												
Mower 2017[61]	1	11770	CT (all had CT)	7-day time-point used to measure neurosurgery outcome	Need for neurosurgical intervention[g]	1.00 (0.99 to 1.00)	0.25 (0.24 to 0.26)	Sensitivity				
								None	None	None	None	HIGH
								Specificity				
								None	None	None	None	HIGH
Neurosurgery (definitions vary) with only a proportion having CT												
Ro 2011[78]	1	2951	CT and/or follow-up by telephone	Follow-up by telephone at 6	Need for neurosurgical	0.95 (0.90 to 0.98)	0.41 (0.40 to 0.43)	Sensitivity				
								Serious[b]	None	None	None	MODERATE
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			at 6 months	months in all participants, 7-day time-point for neurosurgery outcome	intervention[h]			Serious[b]	None	None	None	MODERATE
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Surgical intracranial lesion[i]	1.00 (0.97 to 1.00)	0.44 (0.43 to 0.45)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as any lesion: surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other intracranial abnormality diagnosed on CT)*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[c] *Defined as any injury that may require neurosurgical intervention, (craniotomy, intracranial pressure monitoring, mechanical ventilation), lead to rapid clinical deterioration or result in significant long-term neurological impairment*

[d] *Included all injuries evident on CT head imaging apart from the following in neurologically intact individuals: solitary small contusions, localized subarachnoid haemorrhage less than 1 mm thick, thin subdural hematomas less than 4 mm thick, isolated pneumocephaly and closed depressed skull fractures that did not violate the inner table*

[e] *Defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up – all brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table*

[f] *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*

[g] *Defined as death due to head injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring, within 7 days of head injury*

[h] *Defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury*

[i] *Defined as intracranial haematoma large enough to require surgical evacuation*

Adults – CHIP simple decision rule

Table 14: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – CHIP simple decision rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Smits 2007A[84]	1	3181	CT (all had CT	Unclear, 30-day time-point mentioned for neurosurgery outcome	Any intracranial traumatic findings on CT[a]	0.96 (0.93 to 0.98)	0.25 (0.23 to 0.27)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Foks 2018[27] – original rule in the whole population	1	4557	CT or imputation – 82.1% had CT and data imputed for those without CT	Unclear - up to 30-day review of medical records mentioned for neurosurgery outcome	Intracranial traumatic finding on CT[c]	0.94 (0.91 to 0.96)	0.22 (0.20 to 0.23)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Foks 2018[27] – original rule in the whole population	1	4557	CT or imputation – 82.1% had CT and data imputed for those without CT	Unclear - up to 30-day review of medical records mentioned for neurosurgery outcome	Potential neurosurgical lesion on CT[d]	0.97 (0.91 to 1.00)	0.20 (0.19 to 0.22)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Smits 2007B[84]	1	3181	CT (all had CT	30 day time-point used for neurosurg	Neurosurgical intervention[e]	1.00 (0.80 to 1.00)	0.23 (0.22 to 0.25)	Sensitivity				
								Very serious[b]	None	None	Serious[f]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				ery outcome				Very serious [b]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having CT												
Foks 2018[27] – original rule in the whole population	1	4557	CT or imputation – 82.1% had CT and data imputed for those without CT	Up to 30-day review of medical records mentioned for neurosurgery outcome	Neurosurgical intervention[g]	0.94 (0.73 to 1.00)	0.20 (0.19 to 0.21)	Sensitivity				
								Very serious [b]	None	None	Serious[f]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW

[a] *Defined as any intracranial traumatic findings on CT that included all neurocranial traumatic findings except for isolated linear skull fractures*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[c] *Defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture*

[d] *Defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation*

[e] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

[f] *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*

[g] *Definition not provided*

Adults – NCWFNS high and medium risk (no new evidence)

Table 15: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NCWFNS high and medium risk

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Ibanez 2004[43]	1	1102	CT (all had CT)	Unclear	Relevant positive CT scan[a]	0.98 (0.92 to 1.00)	0.14 (0.12 to 0.16)	Sensitivity				
								Serious[b]	None	None	None	MODERATE
								Specificity				
								Serious[b]	None	None	None	MODERATE
Smits 2007A[84]	1	3181	CT (all had CT	Unclear, 30-day time-point mentioned for neurosurgery outcome	Any intracranial traumatic findings on CT[c]	0.98 (0.96 to 0.99)	0.03 (0.02 to 0.04)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Fabbri 2005[24]	1	7955	CT (52.5%) or unclear	Unclear, 7-day time-point used for intracranial injury outcome	Any post-traumatic lesion at CT within 7 days[d]	0.98 (0.96 to 0.99)	0.46 (0.45 to 0.47)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Smits 2007A[84]	1	3181	CT (all had CT	30 day time-point used for neurosurgery outcome	Neurosurgical intervention[e]	0.94 (0.71 to 1.00)	0.03 (0.02 to 0.03)	Sensitivity				
								Very serious[b]	None	None	Serious[f]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having CT												
Fabbri 2005[24]	1	7955	CT (52.5%) or unclear	Unclear, 7-day time-point used for neurosurgery outcome	Surgical lesion[g]	0.99 (0.95 to 1.00)	0.44 (0.42 to 0.45)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[c] *Any intracranial traumatic findings on CT that included all neurocranial traumatic findings except for isolated linear skull fractures*

[d] *Defined as any post-traumatic lesion at CT within 7 days from trauma: depressed skull fracture, intracerebral haematoma/brain contusions, subarachnoid haemorrhage, subdural haematoma, epidural haematoma, intraventricular haemorrhage*

[e] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

[f] *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.*

[g] *Defined as haematoma evacuation or skull fracture elevation within first 7 days of injury*

Adults – NICE lenient (2003 and 2007 guideline versions) (no new evidence)

Table 16: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NICE lenient (2003 and 2007 guideline versions)

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Smits 2007A[84]	1	3181	CT (all had CT	Unclear, 30-day time-point mentione	Any intracranial traumati	0.82 (0.77 to 0.86)	0.46 (0.44 to 0.48)	Sensitivity				
								Very serious [b]	None	None	None	LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				d for neurosurgery outcome	c findings on CT[a]			Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – no meta-analysis as only two studies												
Fabbri 2005[24]	1	7955	CT (52.5%) or unclear	Unclear, 7-day time-point used for intracranial injury outcome	Any post-traumatic lesion at CT within 7 days[c]	0.94 (0.91 to 0.95)	0.70 (0.69 to 0.71)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Any lesion on CT[d]	0.99 (0.98 to 1.00)	0.31 (0.30 to 0.32)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Smits 2007B[84]	1	3181	CT (all had CT	30 day time-point used for neurosurg	Neurosurgical intervention[e]	0.94 (0.71 to 1.00)	0.44 (0.42 to 0.45)	Sensitivity				
								Very serious[b]	None	None	Serious[f]	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				ery outcome				Specificity				
								Very serious [b]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having CT – no meta-analysis as only two studies												
Fabbri 2005[24]	1	7955	CT (52.5%) or unclear	Unclear, 7-day time-point used for neurosurgery outcome	Surgical lesion[g]	0.94 (0.88 to 0.98)	0.67 (0.65 to 0.68)	Sensitivity				
								Very serious [b]	None	None	Serious [f]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Surgical intracranial lesion[h]	0.98 (0.93 to 1.00)	0.29 (0.28 to 0.30)	Sensitivity				
								Very serious [b]	None	None	None	LOW
								Specificity				
								Very serious [b]	None	None	None	LOW

[a] *Any intracranial traumatic findings on CT that included all neurocranial traumatic findings except for isolated linear skull fractures*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted*

without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.

[c] *Defined as any post-traumatic lesion at CT within 7 days from trauma: depressed skull fracture, intracerebral haematoma/brain contusions, subarachnoid haemorrhage, subdural haematoma, epidural haematoma, intraventricular haemorrhage*

[d] *Defined as any lesion: surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other intracranial abnormality diagnosed on CT)*

[e] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

[f] *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.*

[g] *Defined as haematoma evacuation or skull fracture elevation within first 7 days of injury*

[h] *Defined as intracranial haematoma large enough to require surgical evacuation*

Adults – NICE strict (2003 or 2007 guideline version pre-2014) (no new evidence)

Table 17: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – NICE strict (2003 or 2007 guideline version pre-2014)

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Neurosurgery (definitions vary) with all having CT												
Smits 2007B[84]	1	3181	CT (all had CT	30 day time-point used for neurosurg	Neurosurgical intervention[a]	0.88 (0.64 to 0.99)	0.63 (0.61 to 0.65)	Sensitivity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				ery outcome				Very serious [b]	None	None	None	LOW

[a] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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 – Scandinavian lenient criteria (no new evidence)

Table 18: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – Scandinavian lenient criteria

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT – no meta-analysis as only two studies												
Ibanez 2004[43]	1	1101	CT (all had CT)	Unclear	Relevant positive	0.84 (0.75 to 0.91)	0.60 (0.57 to 0.63)	Sensitivity				
								Serious [b]	None	None	Serious [c]	LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
					CT scan[a]			Specificity				
								Serious[b]	None	None	Serious[d]	LOW
Smits 2007A[84]	1	3181	CT (all had CT	Unclear, 30-day time-point mentioned for neurosurgery outcome	Any intracranial traumatic findings on CT[e]	0.93 (0.90 to 0.96)	0.21 (0.20 to 0.23)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Any lesion on CT[f]	0.96 (0.94 to 0.98)	0.53 (0.52 to 0.54)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Smits 2007B[84]	1	3181	CT (all had CT	30 day time-point used for neurosurg	Neurosurgical intervention[g]	0.94 (0.71 to 1.00)	0.20 (0.19 to 0.21)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				ery outcome				Specificity				
								Very serious [b]	None	None	None	LOW
Neurosurgery (definitions vary) with only a proportion having CT												
Stein 2009[87]	1	7955	CT (52.5%) or unclear	Unclear, 6-month time-point mentioned to assess if any delayed surgery occurred	Surgical intracranial lesion[h]	0.99 (0.95 to 1.00)	0.50 (0.49 to 0.51)	Sensitivity				
								Very serious [b]	None	None	None	LOW
								Specificity				
								Very serious [b]	None	None	None	LOW

[a] *Defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

[e] *Defined as any intracranial traumatic findings on CT that included all neurocranial traumatic findings except for isolated linear skull fractures*

[f] *Defined as any lesion: surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other intracranial abnormality diagnosed on CT)*

[g] *Defined as any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed skull fracture or ventricular drainage) performed within 30 days of the event*

[h] *Defined as intracranial haematoma large enough to require surgical evacuation*

Adults – Arienta et al. 1997 rule (no new evidence)

Table 19: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – Arienta et al. 1997 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Ibanez 2004[43]	1	1101	CT (all had CT)	Unclear	Relevant positive CT scan[a]	0.88 (0.79 to 0.94)	0.54 (0.51 to 0.57)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Arienta 1997[2]	1	9917	CT (7.7%) or follow-up telephone call	Follow-up duration for those without CT at enrolment unclear	Intracranial lesion[d]	1.00 (0.96 to 1.00)	0.91 (0.91 to 0.92)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Definition not provided but injuries identified and counted included extradural haematoma, cortical contusion, subarachnoid haemorrhage, pneumocephalus, depressed fracture with contusion, intracerebral haematoma and subdural haematoma*

Adults – Madden et al. 1995 rule (no new evidence)

Table 20: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – Madden et al. 1995 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												
Madden 1995[56] – phase I cohort	1	537	CT (all had CT)	Unclear	Clinically significant CT scan[a]	0.97 (0.91 to 0.99)	0.21 (0.17 to 0.25)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Madden 1995[56] – phase II cohort	1	273	CT (all had CT)	Unclear	Clinically significant CT scan[a]	0.95 (0.85 to 0.99)	0.21 (0.15 to 0.26)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
								Very serious [b]	None	None	None	LOW

[a] *Defined as pathology related to trauma affecting the bony calvaria or cerebrum (including non-depressed skull fractures, excluding scalp haematomas, those with no bony skull or intracerebral pathology)*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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 – Ono et al. 2007 rule (no new evidence)

Table 21: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – Ono et al. 2007 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
	1	1064		Unclear		1.00 (0.93 to 1.00)	0.30 (0.28 to 0.33)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Ono 2007[67] – original cohort			CT (all had CT)		Intracranial lesion[a]			Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Ono 2007[67] – second cohort	1	168	CT (90.5%) or unclear	Unclear how those without CT had outcome confirmed	Intracranial lesion[a]	1.00 (0.75 to 1.00)	0.35 (0.27 to 0.43)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Serious[d]	VERY LOW

[a] *Definition not given, but injuries that occurred and were counted included subdural and epidural haematoma, subarachnoid haemorrhage, contusion, pneumocephalus*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

Adults – SIGN 2000 CT urgently (no new evidence)

Table 22: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – SIGN 2000 CT urgently

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT – no meta-analysis as only two studies												
Ibanez 2004[43]	1	1102	CT (all had CT)	Unclear	Relevant positive CT scan[a]	0.65 (0.54 to 0.75)	0.74 (0.72 to 0.77)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Smits 2007A[84]	1	3181	CT (all had CT	Unclear, 30-day time-point mentioned for neurosurgery outcome	Any intracranial traumatic findings on CT[d]	0.99 (0.97 to 1.00)	0.02 (0.02 to 0.03)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Defined as any intracranial traumatic findings on CT that included all neurocranial traumatic findings except for isolated linear skull fractures*

Adults – EFNS CT recommended and mandatory (no new evidence)

Table 23: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – EFNS CT recommended and mandatory

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT – no meta-analysis as only two studies												
Ibanez 2004[43]	1	1101	CT (all had CT)	Unclear	Relevant positive CT scan[a]	0.96 (0.90 to 0.99)	0.28 (0.25 to 0.31)	Sensitivity				
								Serious[b]	None	None	None	MODERATE
								Specificity				
								Serious[b]	None	None	None	MODERATE
Smits 2007A[84]	1	3181	CT (all had CT	Unclear, 30-day time-point mentioned for neurosurgery outcome	Any intracranial traumatic findings on CT[d]	1.00 (0.99 to 1.00)	0.00 (0.00 to 0.00)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as an acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted*

without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.

[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*

[d] *Defined as any intracranial traumatic findings on CT that included all neurocranial traumatic findings except for isolated linear skull fractures*

Adults – Miller et al. criteria (no new evidence)

Table 24: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in adults – Miller et al. criteria

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT – no meta-analysis as only two studies												
Holmes 1997[40]	1	264	CT (all had CT)	Those with abnormal CT followed to discharge, those with normal CT not studied further	Abnormal CT scan[a]	0.51 (0.34 to 0.69)	0.69 (0.62 to 0.75)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Miller 1997[60]	1	2143	CT (all had CT)	Unclear, hospital records of those with positive	Abnormal CT scan[c]	0.65 (0.57 to 0.73)	0.53 (0.60 to 0.65)	Sensitivity				
								Very serious[b]	None	None	Serious[d]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				CT followed until discharge				Very serious [b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Holmes 1997[40]	1	264	CT (all had CT)	Those with abnormal CT followed to discharge, those with normal CT not studied further	Neurosurgery[e]	0.50 (0.07 to 0.93)	0.66 (0.60 to 0.72)	Sensitivity				
								Very serious [b]	None	None	Very serious [d]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW
Miller 1997[60]	1	2143	CT (all had CT)	Unclear, hospital records of those with positive CT followed until discharge	Surgical intervention[f]	1.00 (0.48 to 1.00)	0.61 (0.59 to 0.63)	Sensitivity				
								Very serious [b]	None	None	Very serious [d]	VERY LOW
								Specificity				
								Very serious [b]	None	None	Serious [g]	VERY LOW

[a] *Defined as any CT scan showing an acute traumatic lesion (skull fractures or intracranial lesions: cerebral oedema, contusion, parenchymal haemorrhage, epidural haematoma, subdural haematoma, subarachnoid haemorrhage or intraventricular haemorrhage)*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[c] *Defined as acute traumatic intracranial lesion (contusion, parenchymal haematoma, epidural haematoma, subdural haematoma, subarachnoid haemorrhage) or a skull fracture*

[d] *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*

[e] *No definition provided*

[f] *Defined as craniotomy to repair an acute traumatic injury or placement of a monitoring bolt*

[g] *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*

Adults – summary matrix table

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

Note that this summary table only includes clinical decision rules for which new evidence was identified as part of this update as the evidence for those with no new evidence in this update was considered insufficient to recommend them in the previous guideline version and there is no new evidence on which to base changes to that decision.

Table 25: Summary matrix tables for adults

	Outcome/reference standard

	Any injury – all with CT		Any injury – proportion with CT		Clinically important injury – all with CT		Clinically important injury – proportion with CT		Neurosurgery – all with CT		Neurosurgery – proportion with CT	
NICE 2014 guideline	-	-	Sens 0.72 N=4557	Spec 0.61 N=4557	-	-	Sens 0.85 N=4557	**Spec 0.59 N=4557**	-	-	Sens 0.89 N=4557	**Spec 0.58 N=4557**
CCHR – medium and high risk	Sens 0.90 N=5831	Spec 0.42 N=5831	Sens 0.94 N=12,553	Spec 0.42 N=12,553	Sens 0.88 N=1196	Spec 0.35 N=1196	Sens 0.93 N=9683	Spec 0.48 N=9683	Sens 1.00 N=3082	**Spec 0.37 N=3082**	Sens 0.97 N=14,372	Spec 0.36 N=14,372
CCHR adapted to cohort	**Sens 0.85 N=3181**	Spec 0.40 N=3181	**Sens 0.82 N=4557**	**Spec 0.42 N=4557**	-	-	Sens 0.88 N=4557	Spec 0.40 N=4557	Sens 1.00 N=3181	**Spec 0.37 N=3181**	-	-
CCHR – high risk only	-	-	**Sens 0.97 N=7955**	**Spec 0.51 N=7955**	Sens 0.50 N=240	**Spec 0.77 N=240**	-	-	**Sens 0.97**/1.00 **N=7759**/N=240	Spec 0.59/0.77 N=7759/N=240	Sens 0.96 N=16,492	Spec 0.64 N=16,492

CCHR – moderate risk only	-	-	-	-	**Sens 0.98 N=7759**	**Spec 0.12 N=7759**	-	-	-	-	-	-
CCHR cut-point ≥2	Sens 0.76 N=264	**Spec 0.74 N=264**	-	-	-	-	-	-	-	-	-	-
New Orleans Criteria	Sens 0.96 N=5831	**Spec 0.20 N=5831**	**Sens 0.99 N=10,853 (exc. Yarlagadda – 0.86, N=332)**	**Spec 0.33 N=10,853 (Yarlagadda – 0.25, N=332)**	Sens 0.93/1.00 N=1052	**Spec 0.10/0.17 N=1052**	Sens 0.97 N=3626	Spec 0.10 N=3626	Sens 1.00 N=2292	**Spec 0.05 N=2292**	Sens 1.00 N=17,458	**Spec 0.04 N=17,458**
NOC – adapted to cohort	**Sens 0.99 N=3181**	**Spec 0.03 N=3181**	**Sens 0.99 N=4557**	**Spec 0.04 N=4557**	Sens 0.98 N=142	**Spec 0.10 N=142**	**Sens 1.00 N=4557**	**Spec 0.04 N=4557**	Sens 1.00 N=3181	**Spec 0.03 N=3181**	-	-

NOC–cut-point ≥2	**Sens 0.31 N=264**	**Spec 0.69 N=264**	-	-	-	-	-	-	-	-	-	-
NEXUS II	-	-	**Sens 0.97 N=7955**	**Spec 0.47 N=7955**	**Sens 0.98/0.99 N=13,728/N=11,770**	**Spec 0.14/0.16 N=13,728/N=11,770**	Sens 0.89 N=2951	**Spec 0.46 N=2951**	**Sens 1.00 N=11,770**	**Spec 0.25 N=11,770**	**Sens 0.95/1.00 N=2951/N=7955**	**Spec 0.41/0.44 N=2951/N=7955**
CHIP simple decision rule	**Sens 0.96 N=3181**	**Spec 0.25 N=3181**	**Sens 0.94 N=4557**	**Spec 0.22 N=4557**	-	-	**Sens 0.97 N=4557**	**Spec 0.20 N=4557**	Sens 1.00 N=3181	**Spec 0.23 N=3181**	Sens 0.94 N=4557	**Spec 0.20 N=4557**

1 Sens, sensitivity; Spec, specificity.

2

Children – CHALICE

Table 26: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – CHALICE

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT – not meta-analysed as only 2 studies												
Gizli 2020[31]	1	69	CT (all had CT)	Unclear	Abnormal CT findings[a]	0.89 (0.52 to 1.00)	0.20 (0.11 to 0.32)	Sensitivity				
								Serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Meral Atis 2022[58]	1	1004	CT (all had CT)	Unclear	Presence of a pathology in head CT	0.07 (0.01 to 0.24)	0.91 (0.89 to 0.93)	Sensitivity				
								Serious[b]	None	None	None	MODERATE
								Specificity				
								Serious[b]	None	None	None	MODERATE
Intracranial injury – any injury (definitions vary) with only a proportion having CT – no meta-analysis as only two studies (Yogo 2021 did not have enough extractable data)												
Easter 2014[23]	1	858	CT (19% for whole population, unclear for	For those without CT, medical records	Any traumatic brain injury on CT[d]	0.64 (0.47 to 0.79)	0.85 (0.83 to 0.88)	Sensitivity				
								Very serious[b]	Serious[e]	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			proportion analysed for CHALICE) or follow-up	used if had been evaluated as a follow-up at ED or outpatient practice or telephone interview arranged, time-point unclear				Very serious[b]	Serious[e]	None	None	VERY LOW
Thiam 2015[93]	1	1179	CT (1.02%) or follow-up	Follow-up duration of 72 h for those discharged	Positive CT findings[f]	0.83 (0.36 to 1.00)	0.76 (0.74 to 0.79)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having a CT												
Yogo 2021[98]	1	306	CT (all had CT)	Unclear	Clinically important	0.64 (0.49 to 0.77)	0.60 (0.58 to 0.62)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
					traumatic brain injury			Serious[b]	None	None	Serious[o]	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative population where multiple rules could be applied	1	18913	CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Traumatic brain injury on CT[g]	0.90 (0.86 to 0.94)	0.79 (0.78 to 0.79)	Sensitivity				
								Very serious[b]	Serious[h]	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	Serious[h]	None	None	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – meta-analysis												
CHALICE	3	43,466	CT (3.3% to ~19%), unclear proportion	Up to 6 follow-up attempts up to 90 days	Varies across studies, definitions given	0.94 (0.73 to 0.99)	0.84 (0.61 to 0.94)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			in one study For those without CT, follow-up performed in all three studies	post-injury (n=1 study), medical records/telephone interview at unclear timepoint (n=1 study) or unclear (n=1 study)	in footnotes[i-k]			Very serious[b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative population where multiple rules could be applied	1	18913	CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Clinically important traumatic brain injury[k]	0.93 (0.87 to 0.96)	0.79 (0.78 to 0.79)	Sensitivity				
								Very serious[b]	Serious[h]	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	Serious[h]	None	None	VERY LOW
Neurosurgery (definitions vary) with only a proportion having CT												
	3	42,543				0.95 (0.71 to 0.99)	0.83 (0.60 to 0.94)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
CHALICE			CT (3.3% to ~19%), unclear proportion in one study For those without CT, follow-up performed in all three studies	Up to 6 follow-up attempts up to 90 days post-injury (n=1 study), medical records/telephone interview at unclear timepoint (n=1 study) or unclear (n=1 study)	Varies across studies, definitions given in footnotes[l-n]			Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Definition not provided but cases identified included epidural bleeding, subdural bleeding, and all types of skull fractures*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Definition not provided*

[e] *If people had not been evaluated by follow-up, a proxy outcome assessment tool that was adapted from a validated follow-up tool used for minor head injury was used*

[f] *Defined as epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haematoma, cerebral oedema, depressed fracture and contusion*

[g] *Defined as intracranial haemorrhage or contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus skull fracture depressed at least the width of the table of the skull*

[h] *Downgraded by 1 increment as the rule is being used in the whole population, ignoring any inclusion/exclusion criteria specific to the rule (included for purposes of comparing between rules in the same study as slightly different outcome definitions used in rule-specific populations)*

[i] *Defined as death as a result of head injury, need for neurosurgical intervention or marked abnormality on CT scan*

[j] *Defined as death as a result of head injury, requirement for neurosurgical intervention or marked abnormalities on the CT scan*

[k] *Defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT*

[l] *Definition not provided, but the following procedures were reported to have occurred and were included under neurosurgery: intracranial pressure monitoring, craniotomy, haematoma evacuation, elevation of depressed skull fracture, dura repair, tissue debridement and lobectomy*

[m] *Definition not provided*

[n] *Need for neurosurgery included craniotomy, elevation of skull fracture, monitoring of intracranial pressure, or intubation for elevated intracranial pressure*

o 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

Children – PECARN ≥2 years

Table 27: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – PECARN ≥2 years

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT – no meta-analysis as only two studies and could not obtain raw data for Ferrara 2016												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Ferrara 2016[26]	1	24	CT (71.0%) or unclear	Unclear if/how those without CT were followed up to confirm outcome	Positive CT scan[a]	Note: sensitivity and specificity values could not be used to calculate raw data as raw data calculated did not match sample size, meaning there are possible errors in data or a result of the small sample size						
						0.999 (0.158 to 1.000)	0.478 (0.163 to 0.677)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Very serious[d]	VERY LOW
Schonfeld 2014[80]	1	251	Neuroimaging (CT or MRI, majority	Follow-up for 2 weeks by phone/me	Positive CT finding[e]	1.00 (0.88 to 1.00)	0.08 (0.05 to 0.12)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			CT) or follow-up 15.0% had CT and 0.1% MRI in whole population, proportion not clear for specific ≥2 year group and this specific outcome	dical records				Very serious [b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative populati	1	13867	CT (proportion unclear) or systemati	Up to six follow-up attempts made up to 90	Traumatic brain injury on CT[f]	0.99 (0.97 to 1.00)	0.52 (0.51 to 0.53)	Sensitivity Very serious [b]	Serious [g]	None	None	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
on where multiple rules could be applied			c follow-up	days post-injury				Very serious [b]	Serious [g]	None	None	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having a CT												
Kwon 2021[51]	1	173	CT (all had CT)	Unclear	Clinically significant traumatic brain injury	0.75 (0.35 to 0.97)	0.33 (0.26 to 0.40)	Sensitivity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – meta-analysis performed												
PECARN ≥2 years	11	38,594	CT (7.8%-37.3%), proportion unclear in	2 weeks (n=3 studies), 4 weeks (n=1	Clinically important traumati	0.98 (0.95 to 0.98)	0.65 (0.56 to 0.73)	Sensitivity				
								Very serious [b]	None	None	None	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			n=6 studies For those without CT, follow-up was clearly performed in 9 studies, through methods such as telephone and/or medical record review. It was unclear how outcome was confirmed in the remaining study.	study), 1 week – 3 months (n=1 study), 7-90 days (3 studies), 30-90 days (1 study), up to 6 months (n=1 study), or unclear (n=1 study)	c brain injury[h]			Very serious [b]	None	Serious[i]	None	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – Bertimsas 2019 data presented separately as was a re-analysis of the same dataset used in Kupperman 2009 – no meta-analysis as only two studies/cohorts												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Bertsimas 2019[10] – development cohort	1	25283	CT and/or follow-up 35.3% in total had CT, though this is for development and validation cohorts combined and across decision rules. Proportion unclear for this specific cohort and decision rule.	For those discharged with no CT, telephone survey between 7-90 days after ED visit and medical/morgue records checked if not contactable	Clinically important traumatic brain injury[h]	0.97 (0.93 to 0.99)	0.58 (0.57 to 0.58)	Sensitivity				
								Serious[b]	None	None	None	MODERATE
								Specificity				
								Serious[b]	None	None	None	MODERATE
Bertsimas 2019[10] –	1	6411	CT and/or follow-up	For those discharged with no CT,	Clinically important	0.97 (0.89 to 1.00)	0.58 (0.56 to 0.59)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
validation cohort			35.3% in total had CT, though this is for development and validation cohorts combined and across decision rules. Proportion unclear for this specific cohort and decision rule.	telephone survey between 7-90 days after ED visit and medical/morgue records checked if not contactable	traumatic brain injury[h]			Serious[b]	None	None	None	MODERATE
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative populati	1	13867	CT (proportion unclear) or systemati	Up to six follow-up attempts made up to 90	Clinically important traumati	0.99 (0.95 to 1.00)	0.52 (0.51 to 0.53)	Sensitivity				
								Very serious[b]	Serious[g]	None	None	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
on where multiple rules could be applied			c follow-up	days post-injury	c brain injury[h]			Very serious [b]	Serious[g]	None	None	VERY LOW
Neurosurgery (definitions vary) with only a proportion having CT – no meta-analysis as only two studies												
Babl 2017[5] – comparative population where multiple rules could be applied	1	13867	CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Neurosurgery[i]	1.00 (0.81 to 1.00)	0.52 (0.51 to 0.52)	Sensitivity				
								Very serious [b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW
Kupperman 2009[50] cohort 2	1	6411	CT (34.7%) or follow-up	Those discharged without CT had telephone	Neurosurgery[i]	1.00 (0.72 to 1.00)	0.59 (0.58 to 0.61)	Sensitivity				
								Very serious [b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				survey 7-90 days post ED visit and medical/morgue records checked for those uncontactable				Very serious [b]	None	None	Serious [d]	VERY LOW

[a] *Definition not provided*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

[e] *Defined as any of the following: intracranial haemorrhage or contusion, traumatic infarction, sigmoid sinus thrombosis, diffuse axonal injury, pneumocephalus, midline shift or signs of brain herniation, diastasis of the skull, and/or skull fracture*

[f] *Defined as intracranial haemorrhage or contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus skull fracture depressed at least the width of the table of the skull*

[g] *Downgraded by 1 increment as the rule is being used in the whole population, ignoring any inclusion/exclusion criteria specific to the rule (included for purposes of comparing between rules in the same study as slightly different outcome definitions used in rule-specific populations)*

[h] *Defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT*

[i] *Downgraded by one increment as apparent heterogeneity based on point estimates and lack of overlap of confidence intervals across studies*

[j] *Definition not provided*

Children – PECARN not split into age groups

Table 28: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – PECARN not split into age groups

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT - meta-analysis performed												
PECARN not split into age groups (Bozan 2019[12] Sert 2020[81] Meral Atis 2022)	3	2824	CT (all had CT)	Unclear	Pathology on CT	0.91 (0.71 to 0.98)	0.54 (0.26 to 0.54)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	Serious[g]	MODERATE
Intracranial injury – any injury (definitions vary) with only a proportion having CT – no meta-analysis as only two studies												
Easter 2014[23]	1	1049	CT (19% for whole population, unclear	For those without CT, medical	Any traumatic brain	0.98 (0.90 to 1.00)	0.60 (0.57 to 0.63)	Sensitivity				
								Very serious[b]	Serious[f]	None	None	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			for proportion analysed for PECARN) or follow-up	records used if had been evaluated as a follow-up at ED or outpatient practice or telephone interview arranged, time-point unclear	injury on CT[e]			Specificity				
								Very serious [b]	Serious [f]	None	Serious [g]	VERY LOW
Thiam 2015[93]	1	1179	CT (1.01%) and/or follow-up	Follow-up of 72 h post-discharge by telephone	Positive CT finding[h]	1.00 (0.54 to 1.00)	0.62 (0.59 to 0.64)	Sensitivity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
								Specificity				
								Very serious [b]	None	None	Serious [g]	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT (no meta-analysis as only 2 studies)												
Mihindu 2014[59]	1	493	CT (all had CT)	Unclear	Clinically important	1.00 (0.92 to 1.00)	0.40 (0.35 to 0.45)	Sensitivity				
								Serious [b]	None	None	None	MODERATE
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
					traumatic brain injury[i]			Serious[b]	None	None	Serious[g]	LOW
Yogo 2021[98]	1	306	CT (all had CT)	Unclear	Clinically important traumatic brain injury	0.89 (0.77 to 0.96)	0.40 (0.38 to 0.40)	Sensitivity				
								Serious[b]	None	None	Serious[c]	MODERATE
								Specificity				
								Serious[b]	None	None	None	MODERATE
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Easter 2014[23]	1	981	CT (19% for whole population, unclear for proportion analysed for PECARN) or follow-up	For those without CT, medical records used if had been evaluated as a follow-up at ED or outpatient practice or telephone interview arranged, time-point unclear	Clinically important traumatic brain injury[j]	1.00 (0.84 to 1.00)	0.62 (0.59 to 0.65)	Sensitivity				
								Very serious[b]	Serious[f]	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	Serious[f]	None	Serious[g]	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Neurosurgery (definitions vary) with all having CT												
Sert 2020[81]	1	2490	CT (all had CT)	Unclear	Neurosurgical intervention or death[k]	1.00 (0.84 to 1.00)	0.61 (0.59 to 0.63)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	Serious[g]	LOW
Neurosurgery (definitions vary) with only a proportion having CT												
Easter 2014[23]	1	981	CT (19% for whole population, unclear for proportion analysed for PECARN) or follow-up	For those without CT, medical records used if had been evaluated as a follow-up at ED or outpatient practice or telephone interview arranged, time-point unclear	Traumatic brain injury requiring neurosurgery[l]	1.00 (0.40 to 1.00)	0.61 (0.58 to 0.64)	Sensitivity				
								Very serious[b]	Serious[f]	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	Serious[f]	None	Serious[g]	VERY LOW

[a] *Defined as linear fracture, skull base fracture, epidural haematoma, compression fracture, parenchymal haemorrhage, contusion, and subdural haematoma*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Defined as linear or non-linear skull fracture, any intracranial haemorrhage (epidural, subdural, subarachnoid, intracerebral), pneumocephalus, contusion or cerebral oedema*

[e] *Definition not provided*

[f] *If people had not been evaluated by follow-up, a proxy outcome assessment tool that was adapted from a validated follow-up tool used for minor head injury was used*

[g] *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*

[h] *Defined as epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haematoma, cerebral oedema, depressed fracture and contusion*

[i] *Clinical events used by PECARN were used to define clinically important traumatic brain injury (death attributable to TBI, neurosurgical intervention, and intubation for more than 24 hours, but not hospital stay for greater than two nights secondary to traumatic brain injury*

[j] *Defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT*

[k] *Defined as death due to head trauma or neurosurgical procedure, including invasive intracranial pressure measurement by any method, burr hole procedure, craniotomy, haematoma removal, surgical repair of displaced skull fracture and dura repair*

[l] *Need for neurosurgery included craniotomy, elevation of skull fracture, monitoring of intracranial pressure, or intubation for elevated intracranial pressure*

Children – PECARN high risk, not split into age groups

Table 29: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – PECARN high risk only, not split into age groups

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Thiam 2015[93]	1	1179	CT (1.01%) and/or follow-up	Follow-up of 72 h post-discharge by telephone	Positive CT finding[a]	1.00 (0.54 to 1.00)	0.97 (0.95 to 0.98)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haematoma, cerebral oedema, depressed fracture and contusion*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

Children – CATCH original 7-item rule

Table 30: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – CATCH (original 7-item rule)

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definition varies) with all having CT – no meta-analysis as model would not converge, both sensitivity and specificity appear to differ across the four studies so median/range not reported												
Bozan 2019[12]	1	256	CT (all had CT)	Unclear	Intracranial pathology on CT[a]	0.47 (0.24 to 0.71)	0.84 (0.79 to 0.88)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Gizli 2020[31]	1	170	CT (all had CT)	Unclear	Abnormal CT findings[d]	0.59 (0.36 to 0.79)	0.50 (0.42 to 0.58)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Meral Atis 2022	1	966	CT (all had CT)	Unclear	Presence of a pathology in head CT	0.89 (0.72 to 0.98)	0.47 (0.44 to 0.51)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Sert 2020[81]	1	2490	CT (all had CT)	Unclear	New traumatic	0.92 (0.86 to 0.95)	0.66 (0.64 to 0.68)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
					intracranial injury on CT[e]			Specificity				
								Serious[b]	None	None	None	MODERATE
Intracranial injury – clinically important/serious injuries (definitions vary) – all having a CT												
Yogo 2021[98]	1	306	CT (all had CT)	Unclear	Clinically important traumatic brain injury	0.85 (0.72 to 0.93)	0.61 (0.59 to 0.62)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	Serious[k]	LOW
Intracranial injury – any injury (definition varies) with only a proportion having CT – meta-analysis performed												
CATCH original 7-item rule	7	22,893	CT (1.01%-52.8%), proportion unclear in	Up to 72 h post-discharge (n=1 study), 14	Varies across studies, definitions given	0.97 (0.92 to 0.99)	0.59 (0.44 to 0.71)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			n=3 studies For those that did not have CT, all used follow-up, which varied in method and duration	days (n=4 studies). up to 6 follow-up attempts up to 90 days post-injury (n=1 study) or unclear time-point (n=1 study)	in footnotes[f-i], with four studies having the same definition[h]			Very serious[b]	None	Serious[j]	Serious[k]	VERY LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative population where multiple rules could be	1	18913	CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Traumatic brain injury on CT[f]	0.88 (0.83 to 0.91)	0.71 (0.70 to 0.71)	Sensitivity				
								Very serious[b]	Serious[l]	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	Serious[l]	None	None	LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
	1	1002				0.90 (0.70 to 0.99)	0.44 (0.41 to 0.47)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Easter 2014[23]			CT (19% for whole population, unclear for proportion analysed for CATCH) or follow-up	For those without CT, medical records used if had been evaluated as a follow-up at ED or outpatient practice or telephone interview arranged, time-point unclear	Clinically important traumatic brain injury[m]			Very serious[b]	Serious[n]	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	Serious[n]	None	None	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative populati	1	18913	CT (proportion unclear) or systemati	Up to six follow-up attempts made up to 90	Clinically important traumati	0.92 (0.87 to 0.96)	0.70 (0.70 to 0.71)	Sensitivity				
								Very serious[b]	Serious[l]	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
on where multiple rules could be			c follow-up	days post-injury	c brain injury[m]			Very serious[b]	Serious[l]	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Sert 2020[81]	1	2490	CT (all had CT)	Unclear	Neurosurgical intervention or death[o]	1.00 (0.84 to 1.00)	0.62 (0.60 to 0.64)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Neurosurgery (definitions vary) with only a proportion having CT – meta-analysis performed												
CATCH original 7-item rule	6	35,669	CT (34.0%-52.8%), proportion unclear in	14 days (n=4 studies), up to 6 follow-up	Varies across studies, definitions given	0.95 (0.86 to 0.99)	0.68 (0.49 to 0.82)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			n=3 studies For those that did not have CT, all used follow-up, which varied in method and duration	attempts up to 90 days post-injury (n=1 study) or unclear time-point (n=1 study)	in footnotes[p-s], with three studies having the same definitions[s]			Very serious[b]	None	Serious[j]	Serious[k]	VERY LOW

[a] *Defined as linear fracture, skull base fracture, epidural haematoma, compression fracture, parenchymal haemorrhage, contusion, and subdural haematoma*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Definition not provided but cases identified included epidural bleeding, subdural bleeding, and all types of skull fractures*

[e] *Defined as linear or non-linear skull fracture, any intracranial haemorrhage (epidural, subdural, subarachnoid, intracerebral), pneumocephalus, contusion or cerebral oedema*

[f] *Defined as intracranial haemorrhage or contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus skull fracture depressed at least the width of the table of the skull*

[g] *Definition not provided*

[h] *Defined as high and medium risk (any acute intracranial finding revealed on CT that was attributable to acute injury, including closed depressed skull fracture and pneumocephalus, but excluding non-depressed skull fractures and basilar skull fractures)*

[i] *Defined as epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haematoma, cerebral oedema, depressed fracture and contusion*

[j] *Downgraded by one increment as apparent heterogeneity based on point estimates and lack of overlap of confidence intervals across studies*

[k] *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*

[l] *Downgraded by 1 increment as the rule is being used in the whole population, ignoring any inclusion/exclusion criteria specific to the rule (included for purposes of comparing between rules in the same study as slightly different outcome definitions used in rule-specific populations)*

[m] *Defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT*

[n] *If people had not been evaluated by follow-up, a proxy outcome assessment tool that was adapted from a validated follow-up tool used for minor head injury was used*

[o] *Defined as death due to head trauma or neurosurgical procedure, including invasive intracranial pressure measurement by any method, burr hole procedure, craniotomy, haematoma removal, surgical repair of displaced skull fracture and dura repair*

[p] *Definition not provided, but the following procedures were reported to have occurred and were included under neurosurgery: intracranial pressure monitoring, craniotomy, haematoma evacuation, elevation of depressed skull fracture, dura repair, tissue debridement and lobectomy*

[q] *Need for neurosurgery included craniotomy, elevation of skull fracture, monitoring of intracranial pressure, or intubation for elevated intracranial pressure*

[r] *Defined as craniotomy, elevation of skull fracture, intubation, intracranial pressure monitor and/or anticonvulsants within 7 days*

[s] *Defined as high risk (death within 7 days secondary to head injury or need for craniotomy, elevation of skull fracture, monitoring of intracranial pressure or insertion of an endotracheal tube for treatment of head injury)*

Children – CATCH original 7-item rule – any of four high risk factors

Table 31: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – CATCH rule (any one of four high-risk predictors)

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Neurosurgery (definitions vary) with only a proportion having CT												
Babl 2017[5] – rule-specific population for CATCH	1	4957	CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Need for neurological intervention for traumatic brain injury[a]	0.95 (0.76 to 1.00)	0.84 (0.83 to 0.85)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as intracranial pressure monitoring, elevation of depressed skull fracture, ventriculostomy, haematoma evacuation, lobectomy, tissue debridement, dura repair, other*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

Children – CATCH revised 8-item version < 2 years of age

Table 32: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – CATCH 8-item rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – clinically important/more serious injuries (definitions vary) – all with CT												
Kwon 2021[51]	1	78	CT (all had CT scans)	Unclear	Clinically important traumatic brain injury	1.00 (0.59 to 1.00)	0.20 (0.11 to 0.31)	Sensitivity				
								Very serious [b]	None	None	Very serious [b]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW

[a] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[b] *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*

Children – CATCH revised 8-item version ≥2 years of age

Table 33: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – CATCH 8-item rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Kwon 2021[51]	1	173	CT (all had CT scans)	Unclear	Clinically important traumatic brain injury	1.00 (0.63 to 1.00)	0.13 (0.08 to 0.19)	Sensitivity				
								Very serious [a]	None	None	Very serious [b]	LOW
								Specificity				
								Very serious [a]	None	None	None	LOW

[a] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[b] *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*

Children – CATCH revised 8-item version (no age specification)

Table 34: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – CATCH (refined 8-item version Osmond et al. 2018)

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Osmond 2018[72]	1	4060	CT (34.0%) or follow-up	Follow-up at 14 days for those discharged without CT	Brain injury[a]	0.99 (0.97 to 1.00)	0.48 (0.46 to 0.49)	Sensitivity				
								Serious[b]	None	None	None	MODERATE
								Specificity				
								Serious[b]	None	None	None	MODERATE
Neurosurgery (definitions vary) with only a proportion having CT												
Osmond 2018[72]	1	4060	CT (34.0%) or follow-up	Follow-up at 14 days for those discharged without CT	Neurosurgical intervention[c]	1.00 (0.85 to 1.00)	0.46 (0.44 to 0.47)	Sensitivity				
								Serious[b]	None	None	Serious[d]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE

[a] *Defined as high and medium risk (any acute intracranial finding revealed on CT that was attributable to acute injury, including closed depressed skull fracture and pneumocephalus, but excluding non-depressed skull fractures and basilar skull fractures)*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[c] *Defined as high risk (death within 7 days secondary to head injury or need for craniotomy, elevation of skull fracture, monitoring of intracranial pressure or insertion of an endotracheal tube for treatment of head injury)*

[d] *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*

Children – NEXUS II

Table 35: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – NEXUS II

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												
Gupta 2018[34]	1	1018	CT (all had CT)	Unclear	Clinically significant head injury evident on CT[a]	1.00 (0.87 to 1.00)	0.33 (0.30 to 0.36)	Sensitivity				
								None	None	None	Serious[b]	MODERATE
								Specificity				
								None	None	None	None	HIGH
Oman 2006[66]	1	1666	CT (all had CT)	Unclear	Clinically important/significant intracranial injury[c]	0.99 (0.95 to 1.00)	0.15 (0.13 to 0.17)	Sensitivity				
								Serious[d]	None	None	None	MODERATE
								Specificity				
								Serious[d]	None	None	None	MODERATE
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Babl 2019[7]	1	20109	CT (9.8%) or systematic follow-up	Up to six follow-up attempts made up to 90	Clinically important intracra	0.99 (0.97 to 1.00)	0.47 (0.47 to 0.48)	Sensitivity				
								Very serious[d]	None	None	None	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				days post-injury	nial injury[e]			Very serious[d]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Gupta 2018[34]	1	1018	CT (all had CT)	7-day time-point used for neurosurgical outcome	Need for neurosurgical intervention[f]	0.98 (0.89 to 1.00)	0.34 (0.31 to 0.37)	Sensitivity				
								None	None	None	Serious[b]	MODERATE
								Specificity				
								None	None	None	None	HIGH

[a] *Defined as all injuries evident on CT head imaging apart from the following in neurologically intact individuals: solitary small contusions, localized subarachnoid haemorrhage less than 1 mm thick, thin subdural hematomas less than 4 mm thick, isolated pneumocephaly, and closed depressed skull fractures that did not violate the inner table*

[b] *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*

[c] *Defined as any injury that may require neurosurgical intervention, lead to rapid clinical deterioration, or result in significant long-term neurological impairment*

[d] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[e] *Defined as presence of ≥1 CT findings (substantial epidural or subdural haematoma; substantial cerebral contusion; extensive subarachnoid haemorrhage; signs of herniation; basal cistern compression or midline shift; haemorrhage in the posterior fossa; intraventricular haemorrhage; bilateral haemorrhage of any type; depressed or diastatic skull fracture; pneumocephalus; diffuse cerebral oedema; diffuse axonal injury)*

[f] *Defined as death due to head injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring within 7 days of head injury*

Children – Pilot PECARN (no new evidence)

Table 36: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – Pilot PECARN

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												
Sun 2007[91]	1	1666	CT (all had CT)	Unclear	Clinically important/significant intracranial injury[a]	0.91 (0.84 to 0.95)	0.43 (0.40 to 0.45)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Palchak 2003[73]	1	2043	CT (62.2%) or intervention being performed	Unclear	Traumatic brain injury on CT scan or requiring acute intervention[d]	1.00 (0.97 to 1.00)	0.43 (0.40 to 0.45)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery												

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Palchak 2003[73]	1	2043	CT (62.2%) or intervention being performed	Unclear	Need for neurosurgical intervention[e]	1.00 (0.88 to 1.00)	0.64 (0.62 to 0.66)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as any injury that may require neurosurgical intervention, lead to rapid clinical deterioration, or result in significant long-term neurological impairment*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Defined as traumatic brain injury identified on CT scan or requiring acute intervention or intervention by one or more of: neurosurgical procedure, ongoing antiepileptic pharmacotherapy beyond 7 days, the presence of a neurological deficit that persisted until discharge from the hospital, or two or more nights of hospitalisation because of treatment of the head injury*

[e] *Definition not provided*

Children – Atabaki 2008 rule (no new evidence)

Table 37: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – Atabaki 2008 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Atabaki 2008[3]	1	1000	CT (all had CT)	Unclear, medical record review but unclear at what time-point	Intracranial injury[a]	0.95 (0.87 to 0.99)	0.49 (0.46 to 0.52)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Neurosurgery (definitions vary) with all having CT												
Atabaki 2008[3]	1	1000	CT (all had CT)	Unclear, medical record review but unclear at what time-point	Neurosurgery[d]	1.00 (0.54 to 1.00)	0.46 (0.43 to 0.49)	Sensitivity				
								Serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE

[a] *Defined as subdural, epidural, subarachnoid, intraparenchymal and intraventricular haemorrhages as well as contusion and cerebral oedema*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Defined as neurosurgery, including craniotomy, craniectomy, evacuation or intracranial pressure monitoring*

Children – Da Dalt et al. group A+B vs. C+D (no new evidence)

Table 38: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – Da Dalt et al. group A+B vs. C+D

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Da Dalt 2006[16]	1	3798	CT (2.0%) or follow-up	Follow-up telephone interview 10 days after discharge and hospital records checked for readmissions for 1 month post-study conclusion	Intracranial injury[a]	1.00 (0.85 to 1.00)	0.87 (0.86 to 0.88)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as intracranial injury identified on CT at initial presentation or during any hospital admission or readmission, no further details provided*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this*

being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.

[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

Children – Dietrich et al. 1993 rule ≥2 years (no new evidence)

Table 39: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – Dietrich et al. 1993 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Dietrich 1997[20]	1	166	CT (all had CT)	Unclear	Intracranial pathology [a]	1.00 (0.79 to 1.00)	0.00 (0.00 to 0.02)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE

[a] Defined as epidural or subdural haematoma, cerebral contusions or lacerations, intraventricular haemorrhage pneumocephaly or cerebral oedema, with or without skull fracture

[b] 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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.

[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

Children – Guzel et al. 2009 rule (no new evidence)

Table 40: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – Guzel et al. 2009 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Guzel 2009[35]	1	337	CT (all had CT)	Unclear	Positive CT scan[a]	0.69 (0.56 to 0.79)	0.43 (0.37 to 0.49)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Serious[d]	VERY LOW

[a] *Definition not reported*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

Children – NOC (no new evidence)

Table 41: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – NOC

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Haydel 2003[39]	1	175	CT (all had CT)	Unclear	Intracranial injury on head CT[a]	1.00 (0.77 to 1.00)	0.25 (0.19 to 0.33)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Neurosurgery (definitions vary) with all having CT												
Haydel 2003[39]	1	175	CT (all had CT)	Unclear, those with abnormal CT scans admitted and followed until discharge	Need for neurosurgical or medical intervention in those with injury on CT[d]	1.00 (0.54 to 1.00)	0.24 (0.18 to 0.31)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as any acute traumatic intracranial lesion, including subdural epidural or parenchymal haematoma, subarachnoid haemorrhage, cerebral contusion or depressed skull fracture*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Need for neurosurgical or medical intervention in those with injury on CT, no further information*

Children – Quayle 1997 rule (no new evidence)

Table 42: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – Quayle 1997 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Quayle 1997[77]	1	321	CT (all had CT)	Followed up at 3-7 days post discharge	Intracranial injury[a]	0.44 (0.25 to 0.65)	0.85 (0.81 to 0.89)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Definition not reported*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

Children – RCS guidelines (no new evidence)

Table 43: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in children – RCS guidelines

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Dunning 2006[21]	1	22772	CT scan (3.3%) or follow-up	Unclear	Clinically significant ntracranial injury[a]	0.86 (0.82 to 0.90)	0.95 (0.94 to 0.95)	Sensitivity				
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as death as a result of head injury, requirement for neurosurgical intervention or marked abnormalities on the CT scan*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

1 **Infants and young children – PECARN <2 years**

2 **Table 44: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – PECARN <2 years rule**

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Ferrara 2016[26]	1	14	CT (71.0%) or unclear	Unclear if/how those without CT were followed up to confirm outcome	Positive CT scan[a]	Note: sensitivity and specificity values could not be used to calculate raw data as raw data calculated did not match sample size, meaning there are possible errors in data or a result of the small sample size						
						0.999 (0.158 to 1.000)	0.625 (0.245 to 0.915)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Very serious[d]	VERY LOW
Schonfeld 2014[80]	1	121	Neuroimaging (CT or MRI, majority	Follow-up for 2 weeks by phone/me	Positive CT finding[e]	0.95 (0.82 to 0.99)	0.18 (0.10 to 0.28)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
			CT) or follow-up 15.0% had CT and 0.1% MRI in whole population, proportion not clear for specific >2 year group	dical records				Very serious [b]	None	None	None	LOW
Intracranial injury – any injury (definitions vary) with only a proportion having CT – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative populati	1	5046	CT (proportion unclear) or systemati	Up to six follow-up attempts made up to 90	Traumatic brain injury on CT[f]	1.00 (0.95 to 1.00)	0.59 (0.58 to 0.61)	Sensitivity				
								Very serious [b]	Serious [g]	None	None	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
on where multiple rules could be applied			c follow-up	days post-injury				Very serious[b]	Serious[g]	None	Serious[d]	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT – no meta-analysis as only 2 studies with extractable data (Gambacorta 2022 did not have the data to create a 2x2 table)												
Kim 2020[48]	1	224	CT (all had CT)	Unclear	Practically important traumatic brain injury[h]	0.94 (0.81 to 0.99)	0.41 (0.34 to 0.49)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	Serious[d]	LOW
Kwon 2021[51]	1	78	CT (all had CT)	Unclear	Clinically important traumatic brain injury	0.85 (0.42 to 0.99)	0.18 (0.1 to 0.29)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Gambacorta[30]	1	1219	CT (8%) or follow-up	Not reported	Clinically important	0.89 (0.89 to 0.99)	0.49 (0.34 to 0.64)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
					traumatic brain injury			Specificity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – no meta-analysis as model would not converge												
PECARN <2 years	10	26,151	See individual studies below	See Individual studies below		Median value across studies: 0.99 (0.93 to 1.00) Point estimates range from 0.86 to 1.00 across studies	Corresponding specificity: 0.54 (0.53 to 0.55) Point estimates range from 0.41 to 0.74 across studies	See individual GRADE ratings for each study below				
Atabaki 2016[3]	1	2185	CT (33.6% for whole population, unclear for those <2 years) and/or clinical follow-up	Between 1 week and 3 months after ED visit	Clinically important traumatic brain injury[i]	0.33 (0.86 to 1.00)	0.54 (0.51 to 0.56)	Sensitivity				
								None	None	None	Serious [c]	MODERATE
								Specificity				
								None	None	None	None	HIGH
	1	4011				1.00 (0.91 to 1.00)	0.54 (0.52 to 0.55)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Babl 2017[5] – rule-specific population for PECARN <2 years			CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Clinically important traumatic brain injury[i]			Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Cho 2022[14]	1	448	CT (14.7% had CT) or follow-up	Follow-up 7-90 days post-injury	Clinically important traumatic brain injury	1.0 (0.20 to 1.0)	0.81 (0.75 to 0.86)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	VERY LOW
Fuller 2011[29]	1	4717	Unclear	Unclear	Clinically important head injury[i]	1.00 (0.80 to 1.00)	0.63 (0.61 to 0.64)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
								Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Ide 2017[45]	1	792	CT (12.2%) or follow-up	Return visits within 4 weeks after initial evaluation examined to identify missed injuries, no formal follow-up visit	Clinically important traumatic brain injury[i]	0.86 (0.57 to 0.98)	0.74 (0.70 to 0.77)	Serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Serious[b]	None	None	None	LOW
Ide 2020[44]	1	2237	CT (5.5%) or follow-up	Collected outcome data through health records at least 2 weeks after first examination	Clinically important traumatic brain injury[i]	0.87 (0.60 to 0.98)	0.71 (0.69 to 0.73)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
	1	8502				0.99 (0.93 to 1.00)	0.54 (0.53 to 0.55)	Sensitivity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Kupperman 2009[50] – cohort 1			CT (31.0%) or follow-up	Those discharged without CT had telephone survey 7-90 days post ED visit and medical/morgue records checked for those uncontactable	Clinically important traumatic brain injury[i]			Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW
Kupperman 2009[50] – cohort 2	1	2216	CT (31.3%) or follow-up	Those discharged without CT had telephone	Clinically important traumati	1.00 (0.86 to 1.00)	0.54 (0.52 to 0.56)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
				survey 7-90 days post ED visit and medical/morgue records checked for those uncontactable	c brain injury[l]			Very serious [b]	None	None	None	LOW
Lorton 2016[55]	1	421	CT (5.1% for whole population, unclear for specific <2 year group) or follow-up	Contacted by telephone between 30 and 90 days post hospital visit	Clinically important traumatic brain injury[i]	1.00 (0.29 to 1.00)	0.64 (0.59 to 0.68)	Sensitivity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
								Specificity				
								Very serious [b]	None	None	Serious [d]	VERY LOW
Nakhjavan-Shahraki 2017[63]	1	114	CT (55.4% in whole population, unclear for specific <2 year group) and/or follow-up	Follow-up for 2 weeks by phone	Clinically important traumatic brain injury[i]	0.92 (0.64 to 1.00)	0.41 (0.31 to 0.51)	Sensitivity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
								Specificity				
								Very serious [b]	None	None	Serious [d]	VERY LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Schonfeld 2014[80]	1	956	Neuroimaging (CT or MRI, majority CT) or follow-up 15.0% had CT and 0.1% MRI in whole population, proportion not clear for specific >2 year group	Follow-up for 2 weeks by phone/medical records	Clinically important traumatic brain injury[i]	1.00 (0.54 to 1.00)	0.57 (0.54 to 0.61)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Serious[d]	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – Bertimsas 2019 data presented separately as was a re-analysis of the same dataset used in Kupperman 2009 – no meta-analysis as only two studies/cohorts												
Bertsimas 2019[10] – develop	1	8502	CT and/or follow-up	For those discharged with no CT,	Clinically important	0.99 (0.93 to 1.00)	0.54 (0.53 to 0.55)	Sensitivity				
								Serious[b]	None	None	None	MODERATE
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
ment cohort				telephone survey between 7-90 days after ED visit and medical/morgue records checked if not contactable	traumatic brain injury[i]			Serious[b]	None	None	None	MODERATE
Bertsimas 2019[10] –	1	2216	CT and/or follow-up	For those discharged with no CT,	Clinically important	0.33 (0.86 to 1.00)	0.53 (0.51 to 0.55)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
validation cohort				telephone survey between 7-90 days after ED visit and medical/morgue records checked if not contactable	traumatic brain injury[i]			Serious[b]	None	None	None	MODERATE
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT – Babl 2017 comparative population presented separately for purposes of comparing results across rules												
Babl 2017[5] – comparative population where multiple rules could be applied	1	5046	CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Clinically important traumatic brain injury[i]	0.33	(0.92 to 1.00)	0.59 (0.58 to 0.60)	Sensitivity			
								Very serious[b]	None	None	None	LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Neurosurgery (definitions vary) with only a proportion having CT – no meta-analysis as only two studies												
Babl 2017[5] – comparative population where multiple rules could be applied	1	5046	CT (proportion unclear) or systematic follow-up	Up to six follow-up attempts made up to 90 days post-injury	Neurosurgery[j]	1.00 (0.54 to 1.00)	0.59 (0.57 to 0.60)	Sensitivity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW
Kupperman 2009[50] cohort 2	1	2216	CT (31.3%) or follow-up	Those discharged without CT had telephone survey 7-90 days post ED visit and medical/morgue records checked for those uncontactable	Neurosurgery[k]	1.00 (0.48 to 1.00)	0.53 (0.51 to 0.55)	Sensitivity				
								Very serious [b]	None	None	Very serious [c]	VERY LOW
								Specificity				
								Very serious [b]	None	None	None	LOW

[a] *Definition not provided*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

[e] *Defined as any of the following: intracranial haemorrhage or contusion, traumatic infarction, sigmoid sinus thrombosis, diffuse axonal injury, pneumocephalus, midline shift or signs of brain herniation, diastasis of the skull, and/or skull fracture*

[f] *Defined as intracranial haemorrhage or contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus skull fracture depressed at least the width of the table of the skull*

[g] *Downgraded by 1 increment as the rule is being used in the whole population, ignoring any inclusion/exclusion criteria specific to the rule (included for purposes of comparing between rules in the same study as slightly different outcome definitions used in rule-specific populations)*

[h] *Defined as a clinically essential traumatic brain injury including all cranial abnormalities (e.g. skull fracture) detected by computed tomography*

[l] *Defined as death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT*

[j] *Definition not provided, but the following procedures were reported to have occurred and were included under neurosurgery: intracranial pressure monitoring, craniotomy, haematoma evacuation, elevation of depressed skull fracture, dura repair, tissue debridement and lobectomy*

[k] *Definition not provided*

Infants and young children – Pittsburgh Infant Brain Injury Score, score ≥2 (Berger et al. 2016)

Table 45: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – Pittsburgh Infant Brain Injury Score, score ≥2 (Berger et al. 2016)

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Berger 2016[9]	1	861	Neuroimaging (CT or MRI – 69.4%) at enrolment or during follow-up, as well as medical record follow-up	Medical record review for 6 months after enrolment up or up to 1 year of age (whichever occurred later)	Abnormal neuroimaging at enrolment or during follow-up[a]	0.93 (0.89 to 0.96)	0.53 (0.49 to 0.57)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Definition not provided*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

Infants and young children – Pilot PECARN (no new evidence)

Table 46: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – Pilot PECARN

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												
Sun 2007[91]	1	208	CT (all had CT)	Unclear	Clinically important/significant intracranial injury[a]	1.00 (0.59 to 1.00)	0.11 (0.07 to 0.16)	Sensitivity				
								Serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE
Intracranial injury – clinically important/more serious injuries (definitions vary) with only a proportion having CT												
Palchak 2003[73]	1	194	CT (100%) or173equiring173onn being performed	Unclear	Traumatic brain injury on CT scan or173equiringgacute intervention[d]	1.00 (0.78 to 1.00)	0.34 (0.27 to 0.41)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Serious[e]	VERY LOW

[a] *Defined as any injury that may require neurosurgical intervention, lead to rapid clinical deterioration, or result in significant long-term neurological impairment*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *Defined as traumatic brain injury identified on CT scan or requiring acute intervention or intervention by one or more of: neurosurgical procedure, ongoing antiepileptic pharmacotherapy beyond 7 days, the presence of a neurological deficit that persisted until discharge from the hospital, or two or more nights of hospitalisation because of treatment of the head injury*

[e] *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*

Infants and young children – Buchanich et al. 2007 rule (no new evidence)

Table 47: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – Buchanich et al. 2007 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Buchanich 2007[13]	1	97	CT (all had CT)	Follow-up questionnaire/telephone interview, time-point unclear	Intracranial injury[a]	1.00 (0.85 to 1.00)	0.40 (0.29 to 0.52)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Serious[d]	VERY LOW

[a] *Defined as intracranial haematoma, intracranial haemorrhage, cerebral contusion and/or cerebral oedema*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

Infants and young children – Dietrich et al. 1993 rule (no new evidence)

Table 48: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – Dietrich et al. 1993 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Dietrich 1993[20]	1	19	CT (all had CT)	Unclear	Intracranial pathology [a]	1.00 (0.03 to 1.00)	0.17 (0.04 to 0.41)	Sensitivity				
								Serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Serious[b]	None	None	Serious[d]	LOW

[a] *Defined as epidural or subdural haematoma, cerebral contusions or lacerations, intraventricular haemorrhage pneumocephaly or cerebral oedema, with or without skull fracture*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

Infants and young children – Greenes and Schutzman 1999 rule (no new evidence)

Table 49: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – Greenes and Schutzman 1999 rule

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Greenes 1999[32]	1	608	CT (31.0%) or follow-up	Follow-up telephone calls at 2 weeks following ED visit and medical record review	Intracranial injury[a]	0.53 (0.34 to 0.72)	0.72 (0.68 to 0.76)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE

[a] *Defined as acute intracranial haematoma, cerebral contusion and/or diffuse brain swelling evident on head CT*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

Infants and young children – Greenes and Schutzman 2001 scoring system (no new evidence)

Table 50: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – Greenes and Schutzman 2001 scoring system

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with all having CT												
Greenes 2001[33]	1	172	CT (all had CT)	Follow-up telephone calls at 2 weeks following ED visit and medical record review	Intracranial injury[a]	1.00 (0.75 to 1.00)	0.40 (0.32 to 0.48)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	Serious[d]	LOW

[a] *Defined as cerebral contusion, cerebral oedema or intracranial haematoma noted on CT*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

Infants and young children – NEXUS II (no new evidence)

Table 51: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – NEXUS II

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Fabbri 2011[25]	1	2391	CT (11.9%) and follow-up	7-day time-point used for intracranial injury outcome, structured telephone interview for all at 6-month follow-up	Intracranial lesion[a]	0.89 (0.65 to 0.99)	0.59 (0.57 to 0.61)	Sensitivity				
								Very serious[b]	None	None	Very serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	Serious[d]	VERY LOW
Intracranial injury – clinically important/more serious injuries (definitions vary) with all having CT												
Oman 2006[66]	1	309	CT (all had CT)	Unclear	Clinically important/significant intracranial injury[e]	1.00 (0.86 to 1.00)	0.05 (0.03 to 0.09)	Sensitivity				
								Serious[b]	None	None	Serious[c]	LOW
								Specificity				
								Serious[b]	None	None	None	MODERATE

[a] Defined as post-traumatic lesion on CT scan within 7 days after injury. Posttraumatic lesions requiring admission to hospital and follow-up included: intracerebral hematoma or brain contusion, traumatic subarachnoid haemorrhage, subdural haemorrhage, epidural hematoma, intraventricular haemorrhage and a depressed skull fracture.

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

[d] *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*

[e] *Defined as any injury that may require neurosurgical intervention, lead to rapid clinical deterioration, or result in significant long-term neurological impairment*

Infants and young children – Fabbri et al. 2011 (no new evidence)

Table 52: Clinical evidence summary: diagnostic test accuracy of clinical decision rules in infants – Fabbri et al. 2011

Index Test/study	Number of studies	n	Ref. standard	Follow-up	Outcome definition	Sensitivity (95% CI)	Specificity (95% CI)	Risk of bias	Indirectness	Inconsistency	Imprecision	GRADE
Intracranial injury – any injury (definitions vary) with only a proportion having CT												
Fabbri 2011[25]	1	2391	CT (11.9%) and follow-up	7-day time-point used for intracranial injury outcome, structured telephone interview for all at 6-month follow-up	Intracranial lesion[a]	1.00 (0.81 to 1.00)	0.76 (0.74 to 0.78)	Sensitivity				
								Very serious[b]	None	None	Serious[c]	VERY LOW
								Specificity				
								Very serious[b]	None	None	None	LOW

[a] *Defined as post-traumatic lesion on CT scan within 7 days after injury. Posttraumatic lesions requiring admission to hospital and follow-up included: intracerebral hematoma or brain contusion, traumatic subarachnoid haemorrhage, subdural haemorrhage, epidural hematoma, intraventricular haemorrhage and a depressed skull fracture.*

[b] *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. Some of the most common reasons that studies were downgraded for risk of bias across clinical decision rules and studies were: a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard. See individual evidence tables for each study for details for each specific study.*

[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*

Children/infants – matrix summary table

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

Note that this summary table only includes clinical decision rules for which new evidence was identified as part of this update as the evidence for those with no new evidence in this update was considered insufficient to recommend them in the previous guideline version and there is no new evidence on which to base changes to that decision.

Table 53: Summary matrix tables for children/infants

	Outcome/reference standard											
	Any injury – all with CT		**Any injury – proportion with CT**		**Clinically important injury – all with CT**		**Clinically important injury – proportion with CT**		**Neurosurgery – all with CT**		**Neurosurgery – proportion with CT**	
NICE 2014 guideline	No studies assessing the accuracy of the NICE guideline recommendations for children											
CHALICE	Sens 0.89/0.07 N=69/1004	**Spec** **0.20/0.91** **N=69/1004**	Sens 0.64/0.83 N=858/ N=1179	**Spec** **0.85/0.76** **N=858/ N=1179**	**Sens** 0.64 N=306	**Spec** 0.60 N=306	Sens 0.94 N=43,466	**Spec** **0.84** **N=43,466**	-	-	Sens 0.95 N=42,453	**Spec** **0.83** **N=42,453**

PECARN ≥2 years	-	-	Sens 0.999/1.00 N=24/N=251	Spec 0.478/**0.08** N=24/**N=251**	**Sens** 0.75 N=173	**Spec** **0.33** **N=173**	**Sens** **0.98/0.97** **N=68,594/ N=31,694**	Spec 0.65/**0.58** N=68,594/ **N=31,694**	-	-	**Sens** **1.00/1.00** **N=13,867 /N=6411**	Spec **0.52**/0.59 **N=13,867** /N=6411
PECARN <2 years	-	-	Sens 0.999/0.95 N=14/N=121	Spec 0.625/**0.18** N=14/**N=121**	Sens 0.94/0.85/0.89 N=224/N=78/N=1219	Spec 0.41/0.18/0.49 N=224/N=78/N=1219	**Sens** **0.99**/1.00 **N=26,151/** N=2216	**Spec** **0.54/0.53** **N=26,151/ N=2216**	-	-	Sens 1.00/1.00 N=5046/ N=2216	**Spec** **0.59/0.53** **N=5046/ N=2216**
PECARN not split into age groups	Sens 0.91 N=2824	**Spec** 0.54 N=2824	**Sens** **0.98/**1.00 **N=1049/** N=1179	Spec 0.60/0.62 N=1049/ N=1179	**Sens** 1.00/0.89 N=799	Spec **0.40/0.40** **N=799**	Sens 1.00 N=981	Spec 0.62 N=981	Sens 1.00 N=2490	Spec 0.61 N=2490	Sens 1.00 N=981	Spec 0.61 N=981
PECARN high risk only (not split into age)	-	-	Sens 1.00 N=1179	**Spec** **0.97** **N=1179**	-	-	-	-	-	-	-	-
CATCH 7-	Sens	**Spec**	**Sens** **0.97**	Spec 0.59	-	-	Sens 0.90	**Spec** **0.44**	Sens	**Spec**	Sens 0.95	Spec 0.68

item rule	0.47/0.59/0.92/0.89 N=256/N=170/N=2490/n=966	**0.84/0.50/0.6/0.46** **N=256/N=170/N=2490/N=966**	**N=22,893**	N=22,893			N=1002	**N=1002**	1.00 N=2490	**0.62** **N=2490**	N=35,669	N=35,669
CATCH 7-item rule high risk only	-	-	-	-	0.85 N=306	0.61 N=61	-	-	-	-	Sens 0.95 N=4957	Spec 0.84 N=4957
CATCH refined 8-item rule (no age specification)	-	-	**Sens** **0.99** **N=4060**	**Spec** **0.48** **N=4060**		-	-	-	-	-	Sens 1.00 N=4060	**Spec** **0.46** **N=4060**
CATCH refined 8-item rule (≥2 years	-	-	-	-	**1.00** **N=78**	**0.20** **N=78)**						
CATCH	-	-	-	-	**1.0** **N=173**	**0.13** **N=173**						

refined 8-item rule (< 2 years)												
NEXUS II	-	-	-	-	Sens 1.00/**0.99** N=1018/**N=1666**	**Spec** **0.33/0.15** **N=1018/N=1666**	**Sens** **0.99** **N=20,109**	**Spec** **0.47** **N=20,109**	Sens 0.98 N=1018	**Spec** **0.34** **N=1018**		
Pittsburgh Infant Brain Injury Score ≥2	-	-	Sens 0.93 N=861	**Spec** **0.53** **N=861**	-	-	-	-	-	-	-	-

1 Sens, sensitivity; Spec, specificity.

1.1.7 Economic evidence

1.1.7.1 Included studies

Two studies (in four papers) were included.[17, 41, 42, 74] Both compared prediction rules for children and one compared rules for adults[41, 42, 74]. One[41, 42, 74] was included in the guideline previously and the other[17] is new. These are summarised in the economic evidence profile tables below for adults and children (Table 54 and Table 55) and the evidence tables in Appendix G.

1.1.7.2 Excluded studies

The three economic studies and the de novo economic costing which were included in the 2003 guideline and 2007 update were selectively excluded in the 2014 update, due to the availability of more applicable evidence with fewer methodological limitations. Two other studies were excluded. All the excluded studies are listed in Appendix I, with reasons for exclusion given.

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

1.1.8 Summary of included economic evidence

Table 54: Health economic evidence profile: Prediction rules for adults

Study	Applicability	Limitations	Other comments	Total cost (mean per patient)[c]	Total QALYs (mean per patient)	Cost effectiveness	Uncertainty
Pandor 2011[41, 42, 74] (UK)	Directly applicable [a]	Potentially serious limitations [b]	Decision tree and Markov model based on systematic review of accuracy. Population: Adults with minor head injury. Lifetime horizon.	**Adults aged 40 years:** Discharge all: £3305 Abnormal arrival GCS: £2991. CT all: £2955. NCWFNS: £2911. Scandinavian: £2905. NEXUS II: £2908. NICE 2007: £2923. CCHR (high risk): £2918. NOC: £2922. CCHR (high or medium risk): £2909. **Adults aged 75 years:** Discharge all: £1716 Abnormal arrival GCS: £1543 CT all:£1567 NCWFNS: £1523 NICE 2007: £1535 NEXUS II: £1520 Scandinavian: £1517 NOC: £1534 CCHR (high risk): £1521 CCHR (high or medium risk): £1521	**Adults aged 40 years:** Discharge all: 18.6633 Abnormal arrival GCS: 18.6839 CT all: 18.6868 NCWFNS: 18.6878 Scandinavian: 18.6880 NEXUS II: 18.6880 NICE 2007: 18.6881 CCHR (high risk): 18.6882 NOC: 18.6884 CCHR (high or medium risk): 18.6888 **Adults aged 75 years:** Discharge all: 7.8277 Abnormal arrival GCS: 7.8363 CT all: 7.8368 NCWFNS:7.8376 NICE 2007: 7.8376 NEXUS II: 7.8377 Scandinavian: 7.8377 NOC: 7.8378 CCHR (high risk): 7.8378 CCHR (high or medium risk): 7.8381	**Adults aged 40 years:** The following strategies were dominated by the Scandinavian rule: Discharge all; Abnormal arrival GCS; CT all; NCWFNS. The following strategies were dominated by the CCHR rule: NICE 2007, CCHR (high risk); NOC. The NEXUS II strategy was extendedly dominated. CCHR (high or medium risk) versus Scandinavian: £3879 per QALY gained. **Adults aged 75 years:** The following strategies were dominated by the Scandinavian rule: Discharge all; Abnormal arrival GCS; CT all; NCWFNS; NICE 2007; NEXUS II; The following strategies were dominated by the CCHR rule: NOC; CCHR (high risk).	CCHR was most cost-effective strategy in all one-way sensitivity analyses. When alternativeestimates of prevalence were used, the NEXUS II rule was dominant (although the differences were very small).

Study	Applicability	Limitations	Other comments	Total cost (mean per patient)[c]	Total QALYs (mean per patient)	Cost effectiveness	Uncertainty
					Incremental (2-1): (CI NR; p = NR)	CCHR (high or medium risk) versus Scandinavian: £10,397 per QALY gained	

(a) Study set in the UK. NHS and personal social services perspective used. Outcomes and costs discounted at a rate of 3.5%.
(b) Estimating the benefit of treating neurosurgical and non-neurosurgical lesions relied upon observational data with small numbers; the model assumed that hospital admission and treatment provided no benefit for patients with a non-neurosurgical lesion that did not deteriorate or those with a normal CT scan, as no clear evidence was found of these benefits. Limitations of the primary data used in the model were especially important for the children analyses, as very little validation of clinical decision rules has been conducted in this area.
(c) For patients with and without intracranial lesion.

Table 55: Health economic evidence profile: Prediction rules for children

Study	Applica-bility	Limitations	Other comments	Total cost (mean per patient)[f]	Total QALYs (mean per patient)	Cost effectiveness	Uncertainty
Dalziel 2019[17] (Australia/New Zealand)	Partially applicable [a]	Potentially serious limitations [b]	Patient-level simulation model using the APHIRST validation cohort (Babl 2017[5] and Babl 2019[7]) Population: Children younger than 18 years with head injury and GCS 13-15 on presentation to ED. Lifetime horizon.	Usual care: £3,208 CHALICE: £3,225 PECARN: £3,230 CATCH: £3,242 [c]	Usual care: 16.97686 CHALICE: 16.97567 PECARN: 16.97604 CATCH: 16.97581	Usual care dominates CHALICE, PECARN and CATCH CATCH was dominated by PECARN PECARN cost £13,514 per QALY compared with CHALICE, although net health benefit at £20,000 per QALY was almost identical.	Usual care is dominant compared with CHALICE, PECARN and CATCH in 62%, 60% and 61% of the simulations, respectively. Sensitivity analyses on discount rates and cancer latency did not change the results. When moving intermediate risk in PECARN to low or high risk, usual care remained the most cost-effective strategy.
Pandor 2011[126,202] (UK)	Directly applicable [d]	Potentially serious limitations [e]	Decision tree and Markov model based on systematic review of accuracy. Population: Children with minor head injury. Lifetime horizon.	**Child aged 10 years:** CHALICE: £3567 PECARN: £3611 UCD: £3608 Atabaki et al: £3621 CT all: £3666 Discharge all: £4115	**Children aged 10 years:** CHALICE: 22.4156 PECARN: 22.4119 UCD: 22.4112 Atabaki et all: 22.4108 CT all: 22.4072 Discharge all: 22.3847	**Children aged 10 years:** -**When CHALICE is included as decision rule, then** CHALICE is the dominant strategy -**When CHALICE is excluded from the possible decision rules**, then the strategies “CT all”, “Discharge all” and “Atabaki et al” are all dominated by the UCD rule; the ICER for	CHALICE was most cost-effective strategy in all one-way sensitivity analyses.[g] When alternative estimates of prevalence were used, CHALICE was still most cost effective. When validation cohort data was used for children, CHALICE was

Study	Applica-bility	Limitations	Other comments	Total cost (mean per patient)[f]	Total QALYs (mean per patient)	Cost effectiveness	Uncertainty
				Child aged 1 year: CHALICE: £3648 PECARN: £3699 UCD: £3700 Atabaki et all: £3713 CT all: £3771 Discharge all: £4206	**Children aged 1 year:** CHALICE: 22.9857 PECARN: 22.9787 UCD: 22.9760 Atabaki et all: 22.9764 CT all: 22.9663 Discharge all: 22.9549	PECARN versus UCD is £3,929. **Children aged 1 year:** -**When CHALICE is included as decision rule, then** CHALICE is the dominant strategy -**When CHALICE is excluded from the possible decision rules**, then the strategies "CT all", "Discharge all" and "Atabaki et al" are all dominated by the UCD rule; the ICER for PECARN versus UCD is £14,000.	dominated by UCD and NEXUS II.

Abbreviations: APHIRST= Australasian Pediatric Head Injury Rules Study, CATCH= Canadian Assessment of Tomography for Childhood Head Injury; CHALICE= Prediction of Important Clinical Events; CT = Computed tomography; GOS = Glasgow outcome scale; ICER= incremental cost-effectiveness ratio; PECARN= Pediatric Emergency Care Applied Research Network; QALYs= quality-adjusted life years. CT = Computed tomography; GOS = Glasgow outcome scale; QALYs= quality-adjusted life years.

(a) Australian Medicare perspective. QoL score in GOS states estimated through standard gamble approach instead of validated questionnaire. Usual care was defined as defined as management by clinicians according to current, unstandardized, local practice in Australia and New Zealand and may be different than usual care in the UK.

(b) PECARN algorithm is built to allow clinical discretion but this could not be implemented in the model. It is not clear how mortality was modelled for those in the different GOS stages. Most of the immediate costs were calculated from a single centre in Melbourne

(c) 2016 Australian dollars converted to UK pounds.[68] Cost components incorporated: ED, Emergency SSU, general ward, ICU, cranial CT scan, intubation, neurosurgery, GOS-E state cost of care, cancer cost.

(d) Study set in the UK. NHS and personal social services perspective used. Outcomes and costs discounted at a rate of 3.5%.

(e) Estimating the benefit of treating neurosurgical and non-neurosurgical lesions relied upon observational data with small numbers; the model assumed that hospital admission and treatment provided no benefit for patients with a non-neurosurgical lesion that did not deteriorate or those with a normal CT scan, as no clear evidence was found of these benefits. Limitations of the primary data used in the model were especially important for the children analyses, as very little validation of clinical decision rules has been conducted in this area.

(f) For patients with and without intracranial lesion.

(g) When CHALICE was excluded from the possible decision rules for children, in consideration of the fact that it is not yet been validated, it was not possible to assess the impact of uncertainty over the findings of the cost-effectiveness analysis, as the report did not address this issue.

Table 56: Sensitivity and specificity of decision rules used in economic evaluations

Rule	Sensitivity (Nerosurgery)		Sensitivity (Non-neurosurgery)		Specificity	
	Dalziel 2019	Pandor 2011	Dalziel 2019	Pandor 2011	Dalziel 2019	Pandor 2011
Discharge all		0%		0%		100%
CT all		100%		100%		0%
Children						
Usual care	100%		99%			
CHALICE	92%	100%	93%	98%	79%	87%
PECARN	88%	100%	88%	96%	83%	59%
CATCH	96%		91%		70%	
Atabaski		100%		95%		49%
UCD		100%		99%		43%
Adults						
CCHR - high		99%		97%		49%
CCHR - high & medium		99%		99%		53%
NCWFNS		99%		95%		53%
NOC		99%		99%		67%
NEXUS II		100%		97%		53%
NICE 2007		98%		100%		69%
Scandinavian		99%		95%		53%

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.

Code	Description	Unit cost
RD01A	Magnetic Resonance Imaging Scan of One Area, without Contrast, 19 years and over	£146.75
RD01B	Magnetic Resonance Imaging Scan of One Area, without Contrast, between 6 and 18 years	£215.63
RD01C	Magnetic Resonance Imaging Scan of One Area, without Contrast, 5 years and under	£140.83
RD20A	Computerised Tomography Scan of One Area, without Contrast, 19 years and over	£88.06
RD20B	Computerised Tomography Scan of One Area, without Contrast, between 6 and 18 years	£159.25
RD20C	Computerised Tomography Scan of One Area, without Contrast, 5 years and under	£104.27
PF	Plain Film (including x-ray)	£28.62

Direct access costs from NHS Reference costs: 2019-2020 version 2

1.1.11 Evidence statements

Economic

- One cost–utility analysis comparing prediction rules for selecting adults with head injury for imaging found that:
  - the Scandinavian rule dominated (less costly and more effective): Discharge all; Abnormal arrival GCS; CT all and NCWFNS.
  - the CCHR (high or medium risk) rule dominated: NICE 2007; CCHR (high risk); and NOC and that the NEXUS II strategy was extendedly dominated.
  - CCHR (high or medium risk) was found to be cost effective compared to the Scandinavian rule (ICER: £3879 per QALY gained).
  - This analysis was assessed as directly applicable with potentially serious limitations.
- One cost–utility analysis comparing prediction rules for selecting children with head injury for imaging found that
  - usual care dominated (less costly and more effective): CHALICE; PECARN; and CATCH prediction rules.
  - PECARN dominated CATCH and that PECARN was cost effective compared to CHALICE (ICER: £13,514 per QALY gained).
  - This analysis was assessed as partially applicable with potentially serious limitations.
- Another cost–utility analysis comparing prediction rules for selecting children with head injury for imaging found that
  - CHALICE dominated (less costly and more effective): PECARN; UCD; Atabaki et al; CT all; and Discharge all.
  - When CHALICE was excluded as a comparator, UCD dominated: CT all; Discharge all; and Atabaki et al.
  - PECARN was cost effective compared to UCD (ICERs: £3,929 and £14,000 per QALY gained for children aged 10 and 1 years respectively).
  - This analysis was assessed as directly applicable with potentially serious limitations.

1.1.12 The committee's discussion and interpretation of the evidence

1.1.12.1. The outcomes that matter most

Diagnostic accuracy

Diagnostic accuracy for any acute intracranial abnormality and need for neurosurgical intervention were the outcomes prioritised for the diagnostic accuracy component of this review. Sensitivity and specificity were the measures agreed for use in assessing diagnostic accuracy. Sensitivity was considered the most important measure by the guideline committee for this review question because a clinical decision rule should select all patients with suspected intracranial injury for head imaging. The consequences of missing a patient with intracranial injury would have serious implications, including death.

Diagnostic test and treat

For the diagnostic test and treat component of the review, all outcomes were considered equally important for decision-making and were primary outcomes, including all-cause mortality at ≤30 days, quality of life at ≥3 months, objectively reported scores of disability (such as the Glasgow Outcome Score) at ≥3 months, length of stay in acute care (until discharge or to rehabilitation) and serious adverse events at ≤30 days.

No studies meeting the review protocol criteria were identified, as there were no studies comparing clinical outcomes between two different clinical decision rules.

1.1.12.2 The quality of the evidence

Thirty-three studies in adults and forty-two studies in children and infants were included in the review for diagnostic accuracy of clinical decision rules. No evidence was identified for the diagnostic test and treat component of the review.

It was noted that the majority of the evidence was in those with mild head injury (defined as GCS 13-15 in many studies, but with some limiting further to those with GCS 14-15). Some studies did include any severity of head injury but there were no studies appearing to focus on those with moderate or severe head injury only. However, the committee explained that the lack of diagnostic accuracy studies for clinical decision rules in these populations may be because there is consensus that all patients with moderate and severe head injury should have head imaging.

Reference standards used across studies differed, with some performing a CT in every patient and others only performing CT in a proportion of those included according to hospital specific rules. For most studies where not all had a CT as part of the reference standard, some form of follow-up was used instead. The length and method of follow-up varied with some not following up for the length specified as ideal in the protocol and methods of follow-up limited to medical record review rather than formal in-person or telephone follow-up. Where the duration of follow-up did not match that in the protocol this was downgraded as appropriate.

Outcome definition in studies also different across studies, particularly for intracranial injury, with some reporting any confirmed intracranial injury on imaging, some reporting only those injuries that were clinically significant and others reporting both. Both of these definitions were accepted for inclusion in the review but the two were kept separate and not pooled together given the difference in the seriousness of the two definitions.

Given the differences between studies described above, the pooling of results was limited. However, for some clinical decision rule-reference standard-outcome combinations pooling of at least three studies was possible. In some cases, more than three studies were identified but results were not eventually pooled as the model would not converge. For groupings

where pooling could not be performed, results were presented separately for each study and a median/range across the studies provided where possible.

Most of the included evidence was graded low to very low based on the assessment of risk of bias using the QUADAS-2 checklist, indirectness in relation to the protocols (applicability in the QUADAS-2 checklist) and a measure of imprecision for sensitivity and specificity. Inconsistency was also assessed for those where pooling was possible.

- Some of the most common reasons that studies were downgraded for risk of bias included a consecutive sample not being enrolled or this being unclear, it being unclear if the index test and/or reference standard were interpreted without knowledge of the other, the interval between index test and reference standard being unclear and not all patients within a study having the same reference standard
- Indirectness was not present in most cases but a number of studies were downgraded for one of the following reasons:
    - They were very specific populations that may not be representative of the general population this review would apply to; this included one study focused on only those with inpatient falls and most were on anticoagulation, differing from the other studies included in the review
    - One study used a proxy outcome assessment tool for those that had not been evaluated by follow-up
    - Some analyses in a number of studies used unadapted decision rules in populations that they were not originally intended to be used in, which consisted of using the original rule in the whole population and ignoring inclusion/exclusion criteria specific to the rule.
- For groupings where meta-analysis of results was possible, some were downgraded for inconsistency based on the variation in point estimates across studies and the degree of overlap of confidence intervals across studies
- Imprecision was assessed separately for sensitivity and specificity. Thresholds of ≥90% and ≥60% for sensitivity and specificity, respectively, were used as values above which a test would be recommended and values of 0.7 and 0.4 below which a test is of no clinical use were set for sensitivity and specificity, respectively. The lower values were used primarily for assessing imprecision and less so for interpreting which decision rule should be favoured as it was noted that for specificity in many cases existing rules would not meet 0.40 but have a very good sensitivity.

The limitations associated with the evidence were taken into account when considering any possible changes to existing recommendations. It was noted that there was only one study each for children and adults that compared most of the commonly used decision rules in the same study population. Individual limitations of evidence for particular rules that affected decision-making are discussed under benefits and harms below.

1.1.12.3 Benefits and harms

Clinical decision rules for head imaging in adults

It was noted that the existing recommendations for clinical decision rules for head imaging in adults were largely based on the Canadian CT Head Rule (CCHR), which involves identifying high and medium risk factors, with some modifications aiming to improve the sensitivity of this rule further. Updated evidence for this decision rule demonstrated the good sensitivity of this rule when used as intended, with values >90% for all but one outcome-reference standard combination identified across the studies. Specificity values were however poor, with all being <60%. However, it was noted that specificity values of decision rules are often

low as they prioritise very high sensitivity. Adapted versions of this rule which involved adding exclusion criteria as additional risk factors did not result in the same sensitivity values with most of these analyses having values <90%. Using the rule slightly differently by using only high risk criteria as indicators for imaging retained good sensitivity and led to an improvement in specificity, while using any moderate risk criterion as an indicator for imaging retained the good sensitivity but led to even poorer specificity. One study suggesting use of a cut-off score of ≥2 as an indicator for imaging had a good specificity but relatively poor sensitivity.

Evidence identified for other decision rules, including New Orleans Criteria (NOC), NEXUS II and the CHIP simple decision rule, demonstrated sensitivity values similar to that of CCHR, with most analyses reporting values >90%. However, specificity values for NOC and the CHIP simple rule were noticeably lower across all analyses compared to CCHR high and medium risk rule (<30% for all CHIP analyses and <20% or even <10% for most NOC analyses). The NEXUS II decision rule had specificity values similar to those of CCHR (between 35% and 48% for CCHR and between 14% and 47% for NEXUS II); however, NEXUS II was only reported by four studies compared to the CCHR rule which was more widely reported with up to 8 studies pooled in meta-analyses depending on the reference standard and outcome reported. In addition, there was less certainty about the specificity of the NEXUS II rule given a number of the analyses reported values <30%, while for CCHR all analyses reported values above 35%.

Only one study had assessed the performance of the existing NICE Head Injury guideline recommendations for head imaging based on the 2014 guideline. The study reported sensitivity values that were poorer than the CCHR (72% for any injury, 85% for clinically important injury and 89% for neurosurgery) but with specificity values that were better compared to other decision rules (61% for any injury, 59% for clinically important injury and 58% for neurosurgery). Although the sensitivity results of this study suggested poorer results for the NICE 2014 guideline, the results for the CCHR rule in this study were considerably lower than other studies reporting the CCHR rule, with values <90%. Given that the NICE 2014 guideline was largely based on the CCHR rule with some amendments to improve sensitivity the committee agreed it was unclear why sensitivity of the NICE recommendations would be poorer than other rules and unclear why the CCHR rule also did not perform as well in this study as in other studies, suggesting there may be some differences between this study and other studies reporting CCHR which may have affected the results. In addition, the committee agreed that in their clinical experience the sensitivity of the NICE recommendations was not as low as suggested in this single study.

The committee agreed that in terms of current practice, the recommendations in the NICE guideline are in widespread use and there have been studies showing good adherence to them. In their opinion the recommendations are sensible and are widely accepted.

Based on a discussion of all the factors mentioned above, it was agreed that there was insufficient evidence to change clinical decision rule recommendations for head imaging in adults. As the NICE recommendations were largely based on the CCHR rule, this decision was further supported by cost-effectiveness evidence which demonstrated the CCHR rule to be the most cost-effective of multiple decision rules assessed.

Clinical decision rules for head imaging in children/infants

It was noted that the existing recommendations for clinical decision rules for head imaging in children/infants were largely based on the CHALICE rule, with some modifications based on current practice and experience allowing the option for an observation period with imaging if their condition deteriorated in some children rather than immediate imaging.

Updated evidence identified for this decision rule demonstrated the good sensitivity of this rule when considering clinically important injuries or neurosurgery outcomes, with values >90% overall. The sensitivity value for CHALICE in detecting any head injuries, regardless of

clinical importance, was not as good, with values <90%. In two studies sensitivity was >80% for this outcome but for another it was much lower at 64%. It should be noted that the number of participants analysed for clinically important injuries and neurosurgery outcomes was >40,000, while it was much lower for any severity of injury (N=69 to N=1179). Specificity values for the CHALICE rule were good overall, with most analyses reporting values >70%, including for clinically important injuries and neurosurgery outcomes and again >40,000 participants analysed for clinically important injuries and neurosurgery outcomes. There were two studies where all had a CT as the reference standard, one small study of n=69 participants where specificity was poor for any severity of injury, with a value of 20%; another larger (n=966) but contradictory study showed very low sensitivity (7%) but high specificity 91%. Overall, there was evidence from >40,000 participants analysed that the CHALICE rule has a good sensitivity (>90%) as well as a good specificity (>80%) in terms of clinically important injuries and neurosurgery outcomes, with sensitivity for any head injury lower and a similar or lower specificity (based on 69-1179 participants).

In the previous update of this guideline, the committee stated that an improvement in specificity relative to the NICE recommendations would be required in order to warrant switching to another decision rule for children. No evidence assessing the performance of the NICE recommendations for performing head imaging in children was identified as part of this review and the performance of these recommendations could therefore not be assessed directly in this update. The performance of other rules, such as PECARN and CATCH, were therefore compared with the CHALICE rule to decide whether any changes to recommendations should be made given CHALICE is the rule that the NICE recommendations were based on.

Evidence for the PECARN decision rule, which is split into ≥2 years and <2 years, demonstrated high sensitivity values (>90%) for clinically important injuries and neurosurgery outcomes, as was the case for CHALICE, but also for any severity of injury which was not demonstrated for CHALICE. However, as for CHALICE the data for any severity of injury was based on a much smaller number of participants compared to analysis of >60,000 participants available for clinically important injuries and neurosurgery outcomes. For clinically important injuries and neurosurgery outcomes, sensitivity values for the PECARN groupings did appear to be slightly better compared to CHALICE, but the specificity values for PECARN were considerably lower than CHALICE as they were either just over the 60% threshold for specificity or below it, while values for CHALICE were >80% for both outcomes. Using a variation of the PECARN rule by only considering those with high risk criteria for imaging demonstrated a good sensitivity (100%) and specificity (97%); however, this was not a version that was used often across studies and was only reported by a single study. The slight increase in the sensitivity of PECARN over CHALICE in terms of clinically important injuries and neurosurgery was not thought to outweigh the larger differences in specificity between the two rules, with CHALICE having a much higher specificity and sensitivity still >90%.

For the CATCH decision rule, data for the original 7-item rule provided sensitivity values that were similar to or slightly better than the CHALICE rule for clinically important injuries and neurosurgery outcomes, with >30,000 participants analysed for neurosurgery but <5000 in total for clinically important injuries. A higher number of participants (>20,000) were analysed for any severity of injury for this rule compared to CHALICE and PECARN, and results suggested good sensitivity values >90% for this rule, though this was much lower in some individual studies. Overall, specificity values for CATCH-7 were similar to those of PECARN, with all analyses reporting values either just higher than 60% or below 60%. Using a variation of the CATCH-7 rule by only considering those with high risk criteria for imaging demonstrated a good sensitivity (95%) and specificity (84%); however, this was not a version that was used often across studies and was only reported by a single study.

Additionally, one study assessed the performance of a modified version of the CATCH rule, including an additional eighth item. This rule demonstrated high sensitivity values for any

severity of injury and neurosurgery; however, specificity values were lower than the original CATCH-7 rule and other decision rules assessed at <50%. Additionally, given it was only reported in one study the number of participants these values are based on is lower than for other decision rules.

For the NEXUS II decision rule in children, results demonstrated high sensitivity values for any severity of injury, clinically important injuries and neurosurgery outcomes, with >20,000 participants analysed for clinically important injuries and much lower numbers for the other outcomes. However, specificity was much lower for this rule across all three outcomes compared to other decision rules, particularly CHALICE, as values were <50% in all cases.

There was one study assessing the performance of a newly developed rule, the Pittsburgh Infant Brain Inventory Score, specifically in infants between 30 days and 1 year. Data in the study was incompletely reported for many of the thresholds but data was available to calculate sensitivity and specificity using a cut-off score of ≥2. The results indicated good sensitivity of 93% for any severity of injury, but the specificity value was <60% at 53%. The number of patients included and analysed was relatively small with n=891 compared to other decision rules. The lack of external validation for this decision rule also limited the evidence for this rule.

The committee agreed that in terms of current practice, the recommendations in the NICE guideline are in widespread use and used with little variation. In their opinion the recommendations are currently well-accepted and used with good effect. Overall, although PECARN and CATCH-7 may have slightly better sensitivity values compared to CHALICE, specificity values for CHALICE are much better than other rules assessed and sensitivity values for CHALICE are still >90% for clinically important injuries and neurosurgery outcomes. The committee noted that the PECARN rule and NICE guideline are not very different in terms of the content of the rules and also noted that the PECARN guidance is more vague with no timings given, which is seen as less useful compared to the NICE guideline. In addition, it was noted that PECARN and CATCH rules do not apply to all of those with head injury and are more specific populations compared to the NICE guideline recommendations largely based on CHALICE. Therefore, should other rules be used there may be a potential increase in scan rates. Furthermore, because current practice is so widespread a change to a different rule would involve an increased cost from retraining staff across the UK.

Based on a discussion of all the factors mentioned above, it was agreed that there was insufficient evidence to change clinical decision rule recommendations for head imaging in children. As the NICE recommendations were largely based on the CHALICE rule, this decision was further supported by cost-effectiveness evidence from an NHS setting, which demonstrated the CHALICE rule to be most cost-effective of multiple decision rules assessed, which included PECARN but not CATCH or NEXUS II. However, cost-effectiveness evidence from an Australian study suggested PECARN was slightly more effective and borderline cost-effective compared to CHALICE.

1.1.12.4 Cost effectiveness and resource use

Two cost-utility analyses were included that evaluated different prediction tools

- An NHS health technology assessment looking at risk tools for both adults and children based on a systematic review
- An Australian study comparing risk tools for children based on an external validation study

Both studies sought to capture the impact of radiation on cancer incidence in addition to the impact on the treatment of head injury.

For adults, the Canadian CT head rule was the most effective and cost-effective rule in the base case analysis

For children:

- In the NHS study, the CHALICE rule was more cost effective
- In the Australian study, PECARN was slightly more effective and borderline cost-effective compared to CHALICE. Curiously, locally determined usual care dominated the decision rules, despite having a lower CT rate.
- Sensitivity and specificity were both noticeably lower in the Australian study (for both CHALICE and PECARN)

The result of an economic evaluation in this area is likely to be highly dependent on the estimated sensitivity and specificity of each rule. The NHS study also found the optimal adult rule to be sensitive to the pre-test prevalence of intracranial bleeding.

The differences in mean cost and mean QALYs between strategies appeared very small but the population is very large (about 1 million adults and children each year have a minor head injury in England) and therefore an increase in cost of only £1 per person would be a significant cost impact for the NHS.

The committee decided that the new clinical and cost-effectiveness did not provide strong evidence for changing the previous recommendations:

- For adults, the Canadian CT head rule (but with less urgent CT) for people whose only risk factor was their old age).
- The CHALICE rule for children.

1.1.12.5 Other factors the committee took into account

The committee noted that nystagmus would be regarded as focal neurology, and if detected in the emergency department, would be an indication for CT scanning.

The committee highlighted the importance of safeguarding with respect to the possibility of non-accidental injury and made a cross reference to the relevant NICE guidance (See NICE's guidelines on child maltreatment, on child neglect and abuse, on domestic violence and abuse, and on safeguarding adults in care homes for clinical features that may be associated with maltreatment).

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Appendices

Appendix A – Review protocols

Review protocol for clinical decision rules for selecting people with head injury for imaging

ID	Field	Content
0.	PROSPERO registration number	CRD42021283530
1.	Review title	2.1 a (i) What is the diagnostic accuracy of clinical decision rule/s for selecting adults, children and infants with head injury for CT or MRI head scan? - 2.1a (ii) What is the clinical and cost effectiveness of clinical decision rules for selecting adults, children and infants with head injury for CT or MRI head scan?
2.	Review question	2.1 a (i) What is the diagnostic accuracy of clinical decision rule/s for selecting adults, children and infantswith head injury for CT or MRI head scan? - 2.1a (ii) What is the clinical and cost effectiveness of clinical decision rules for selecting adults, children and infants with head injury for CT or MRI head scan?
3.	Objective	To determine which patients should receive imaging of the head.
4.	Searches	The following databases (from inception) will be searched: • Cochrane Central Register of Controlled Trials (CENTRAL)

		• Cochrane Database of Systematic Reviews (CDSR) • Embase • MEDLINE • Epistemonikos Searches will be restricted by: • English language studies • Human studies • Letters and comments excluded Other searches: • Inclusion lists of systematic reviews The searches may be re-run 6 weeks before the final committee meeting and further studies retrieved for inclusion if relevant. The full search strategies will be published in the final review. Medline search strategy to be quality assured using the PRESS evidence-based checklist (see methods chapter for full details).
5.	Condition or domain being studied	Head Injury

6.	Population	i) Inclusion: Infants, children and adult with suspected or confirmed head injury ii) Strata: • 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.
7.	Tests/clinical decision rules	Validated clinical decision rules for adults: Validated clinical decision rules including NEXUS, NOC, CHR, Canadian CT-rules, New Orleans criteria or CHALICE All clinical decision rules for children New/additional decision rules: post traumatic amnesia (also an outcome), updated Canadian CT rules, updated CHALICE, CATCH, PECARN, CHIP rule, Scandinavian rule . Noted that separate decision rules exist for infants,children and adults. Mixed population studies will be included and downgrade for indirectness. Cut-off of 60% will be used for all age groups
8.	Reference standard	For diagnostic accuracy: • CT or MR imaging

		• Negative follow-up at 1 month for adults, 2 weeks for children For diagnostic test and treat: • Any validated clinical decision rule compared to each other. Only common reference standard will be pooled.
9.	Types of study to be included	Diagnostic accuracy: Diagnostic cohort studies (prospective and retrospective) Systematic reviews and meta-analyses of the above Case-control studies will be excluded. Diagnostic Test and treat: Randomised controlled trials (RCTs), systematic reviews of RCTs. If no RCT evidence is available, non-randomised studies will be considered if they adjust for key confounders, starting with prospective cohort studies. Key confounders: • Age • GCS or pupillary response at presentation • Severity of injury (intra/extracranial)
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. Diagnostic accuracy: Studies that do not report sensitivity and specificity, or insufficient data to derive these values.

11.	Context	The key clinical issue is to have a decision rule which is as sensitive and specific as possible in order to minimise the number of false negatives which can have catastrophic consequences.
12.	Primary outcomes (critical outcomes)	All outcomes are considered equally important for decision making and therefore have all been rated as critical: Diagnostic accuracy outcomes • Diagnostic accuracy of clinical decision tool/triage tool for need for neurosurgical intervention • Diagnostic accuracy of clinical decision tool/triage tool for any acute intracranial abnormality Clinical test & treat outcomes • All-cause Mortality – at ≤30 days • Quality of life - 3 months or more • Objectively applied score of disability e.g. Glasgow Outcome Score (GOS) or extended GOS - at 3 months or more • Length of stay in acute care (until discharged home or to rehabilitation) • Serious adverse event at – ≤30 days
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	For diagnostic reviews • Diagnostic test accuracy studies: QUADAS-2 Assessment will be independently quality assured by a second reviewer. Disagreements between the reviewers will be resolved by discussion, with involvement of a third party where necessary. For test and treat: Risk of bias will be assessed using the appropriate checklist as described in Developing NICE guidelines: the manual. For Intervention reviews Systematic reviews: Risk of Bias in Systematic Reviews (ROBIS) Randomised Controlled Trial: Cochrane RoB (2.0) Non randomised study, including cohort studies: Cochrane ROBINS-I
15.	Strategy for data synthesis	For diagnostic accuracy evidence:

		• Aggregate data on diagnostic accuracy of investigations will be collected and synthesized in a quantitative data analysis. • Endnote will be used for bibliography, citations, sifting and reference management. • WinBUGS will be used for meta-analysis of diagnostic accuracy studies if included studies are sufficiently homogeneous. • If meta-analysis is not possible, data will be presented as individual values in adapted GRADE profile tables and plots of un-pooled sensitivity and specificity from RevMan software.Where available, outcome data from new studies will be meta-analysed with corresponding data included in CG 176. For clinical effectiveness evidence: • Pairwise meta-analyses will be performed using Cochrane Review Manager (RevMan5). Fixed-effects (Mantel-Haenszel) techniques will be used to calculate risk ratios for the binary outcomes where possible. Continuous outcomes will be analysed using an inverse variance method for pooling weighted mean differences. • Heterogeneity between the studies in effect measures will be assessed using the I^2 statistic and visually inspected. An I^2 value greater than 50% will be considered indicative of substantial heterogeneity. Sensitivity analyses will be conducted based on pre-specified subgroups using stratified meta-analysis to explore the heterogeneity in effect estimates. If this does not explain the heterogeneity, the results will be presented pooled using random-effects. • GRADEpro will be used to assess the quality of evidence for each outcome, taking into account individual study quality and the meta-analysis results. The 4 main quality elements (risk of bias, indirectness, inconsistency and imprecision) will be appraised for each outcome. Publication bias is tested for when there are more than 5 studies for an outcome. • The risk of bias across all available evidence was evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/

		Where meta-analysis is not possible, data will be presented and quality assessed individually per outcome. Where available, outcome data from new studies will be meta-analysed with corresponding data included in CG 176.	
16.	Analysis of sub-groups	Subgroups that will be investigated if heterogeneity is present: Older adults • older/frail adults who have suffered a fall Older adults as > 64 years but frailty can start as young as 50. Refer to definitions used in studies,	
17.	Type and method of review	☒	Intervention
		☒	Diagnostic
		☐	Prognostic
		☐	Qualitative
		☐	Epidemiologic
		☐	Service Delivery
		☐	Other (please specify)
18.	Language	English	
19.	Country	England	

<table>
<tr><td>20.</td><td>Anticipated or actual start date</td><td colspan="3">[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.]</td></tr>
<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]</td></tr>
</table>

		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 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.	
31.	Keywords	Clinical decision rules,head injury	
32.	Details of existing review of same topic by same authors	N/A	
33.	Current review status	☒	Ongoing
		☐	Completed but not published
		☐	Completed and published

		☐	Completed, published and being updated
		☐	Discontinued
34.	Additional information	[Provide any other information the review team feel is relevant to the registration of the review.]	
35.	Details of final publication	www.nice.org.uk	

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2 **Health economic review protocol**

3 **Table 57: Health economic review protocol**

Review question	All questions – health economic evidence
Objectives	To identify health economic studies relevant to any of the review questions.
Search criteria	• Populations, interventions and comparators must be as specified in the clinical review protocol above. • Studies must be of a relevant health economic study design (cost–utility analysis, cost-effectiveness analysis, cost–benefit analysis, cost–consequences analysis, comparative cost analysis). • Studies must not be a letter, editorial or commentary, or a review of health economic evaluations. (Recent reviews will be ordered although not reviewed. The bibliographies will be checked for relevant studies, which will then be ordered.) • Unpublished reports will not be considered unless submitted as part of a call for evidence. • Studies must be in English.
Search strategy	A health economic study search will be undertaken using population-specific terms and a health economic study filter – see appendix B below. The search covered all years
Review strategy	Studies not meeting any of the search criteria above will be excluded. Studies published before 2006, abstract-only studies and studies from non-OECD countries or the USA will also be excluded. Studies published in 2006 or later that were included in the previous guidelines will be reassessed for inclusion and may be included or selectively excluded based on their relevance to the questions covered in this update and whether more applicable evidence is also identified.

Each remaining study will be assessed for applicability and methodological limitations using the NICE economic evaluation checklist which can be found in appendix H of Developing NICE guidelines: the manual (2014).[64]

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.[64]

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 58: Database parameters, filters and limits applied

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

Medline (Ovid) search terms

1.	craniocerebral trauma/ or exp brain injuries/ or coma, post-head injury/ or exp head injuries, closed/ or head injuries, penetrating/ or exp intracranial hemorrhage, traumatic/ or exp skull fractures/
2.	((skull or cranial) adj3 fracture*).ti,ab.
3.	((head or brain or craniocerebral or cranial or cerebral or skull) adj4 (injur* or trauma*)).ti,ab.
4.	(trauma* and ((subdural or intracranial) adj2 (h?ematoma* or h?emorrhage* or bleed*))).ti,ab.
5.	or/1-4

6.	letter/
7.	editorial/
8.	news/
9.	exp historical article/
10.	Anecdotes as Topic/
11.	comment/
12.	case report/
13.	(letter or comment*).ti.
14.	or/6-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animals/ not humans/
18.	exp Animals, Laboratory/
19.	exp Animal Experimentation/
20.	exp Models, Animal/
21.	exp Rodentia/
22.	(rat or rats or mouse or mice or rodent*).ti.
23.	or/16-22
24.	5 not 23
25.	limit 24 to English language
26.	(NEXUS or NOC or CHIP or New Orleans criteria or CHALICE or PECARN).ti,ab.
27.	((Canadian or Scandinavian) adj2 (assess* or rule*)).ti,ab.
28.	or/26-27
29.	25 and 28
30.	tomography/ or exp tomography, emission-computed/ or exp tomography, x-ray/
31.	(compute* adj2 tomograph*).ti,ab.
32.	magnetic resonance imaging/
33.	MRI.ti,ab.
34.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph*)).ti,ab.
35.	(CT or CAT or PET or SPECT).ti,ab.
36.	or/30-35
37.	predict.ti.
38.	(validat* or rule*).ti,ab.
39.	(predict* and (outcome* or risk* or model*)).ti,ab.
40.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
41.	decision*.ti,ab. and Logistic models/
42.	(decision* and (model* or clinical*)).ti,ab.
43.	(prognostic and (history or variable$ or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
44.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
45.	ROC curve/
46.	or/37-45
47.	triage/

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

14 Embase (Ovid) search terms

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

14.	or/8-13
15.	randomized controlled trial/ or random*.ti,ab.
16.	14 not 15
17.	animal/ not human/
18.	nonhuman/
19.	exp Animal Experiment/
20.	exp Experimental Animal/
21.	animal model/
22.	exp Rodent/
23.	(rat or rats or mouse or mice or rodent*).ti.
24.	or/16-23
25.	7 not 24
26.	limit 25 to English language
27.	(NEXUS or NOC or CHIP or New Orleans criteria or CHALICE or PECARN).ti,ab.
28.	((Canadian or Scandinavian) adj2 (assess* or rule*)).ti,ab.
29.	or/27-28
30.	26 and 29
31.	tomography/
32.	brain tomography/
33.	exp computer assisted tomography/
34.	exp emission tomography/
35.	exp x-ray tomography/
36.	(compute* adj2 tomograph*).ti,ab.
37.	nuclear magnetic resonance imaging/
38.	MRI.ti,ab.
39.	((MR or magnetic resonance or NMR) adj2 (imag* or tomograph*)).ti,ab.
40.	(CT or CAT or PET or SPECT).ti,ab.
41.	or/31-40
42.	predict.ti.
43.	(validat* or rule*).ti,ab.
44.	(predict* and (outcome* or risk* or model*)).ti,ab.
45.	((history or variable* or criteria or scor* or characteristic* or finding* or factor*) and (predict* or model* or decision* or identif* or prognos*)).ti,ab.
46.	decision*.ti,ab. and Statistical model/
47.	(decision* and (model* or clinical*)).ti,ab.
48.	(prognostic and (history or variable* or criteria or scor* or characteristic* or finding* or factor* or model*)).ti,ab.
49.	(stratification or discrimination or discriminate or c statistic or "area under the curve" or AUC or calibration or indices or algorithm or multivariable).ti,ab.
50.	Receiver operating characteristic/
51.	or/42-50
52.	emergency health service/
53.	(triage* or overtriage* or triaging).ti,ab.
54.	(predict* adj4 (tool* or index* or indices or score* or scoring or scale* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.

55.	(risk* adj4 (tool* or index* or indices or score* or scoring or scale* or model* or system* or algorithm* or stratif* or criteria or calculat*)).ti,ab.
56.	(prognos* adj4 (tool* or index* or indices or scale* or system* or algorithm* or stratif* or calculat*)).ti,ab.
57.	((clinical or decision*) adj4 (tool or strateg*)).ti,ab.
58.	exp decision support system/
59.	or/52-58
60.	exp "sensitivity and specificity"/
61.	(sensitivity or specificity).ti,ab.
62.	((pre test or pretest or post test) adj probability).ti,ab.
63.	(predictive value* or PPV or NPV).ti,ab.
64.	likelihood ratio*.ti,ab.
65.	((area under adj4 curve) or AUC).ti,ab.
66.	(receive* operat* characteristic* or receive* operat* curve* or ROC curve*).ti,ab.
67.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness)).ti,ab.
68.	diagnostic accuracy/
69.	diagnostic test accuracy study/
70.	gold standard.ab.
71.	exp diagnostic error/
72.	(false positiv* or false negativ*).ti,ab.
73.	differential diagnosis/
74.	(diagnos* adj3 (performance* or accurac* or utilit* or value* or efficien* or effectiveness or precision or validat* or validity or differential or error*)).ti,ab.
75.	or/60-74
76.	51 or 59 or 75
77.	26 and 41 and 76
78.	30 or 77

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

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

#16.	MeSH descriptor: [Magnetic Resonance Imaging] this term only
#17.	MRI:ti,ab
#18.	((MR or magnetic resonance or NMR) NEAR/2 (imag* or tomograph*)):ti,ab
#19.	(CT or CAT or PET or SPECT):ti,ab
#20.	#12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19
#21.	#11 AND #20

Epistemonikos search terms

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

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 59: 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	

Database	Dates searched	Search filters and limits applied
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

26 **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)

27 **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)

28 **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

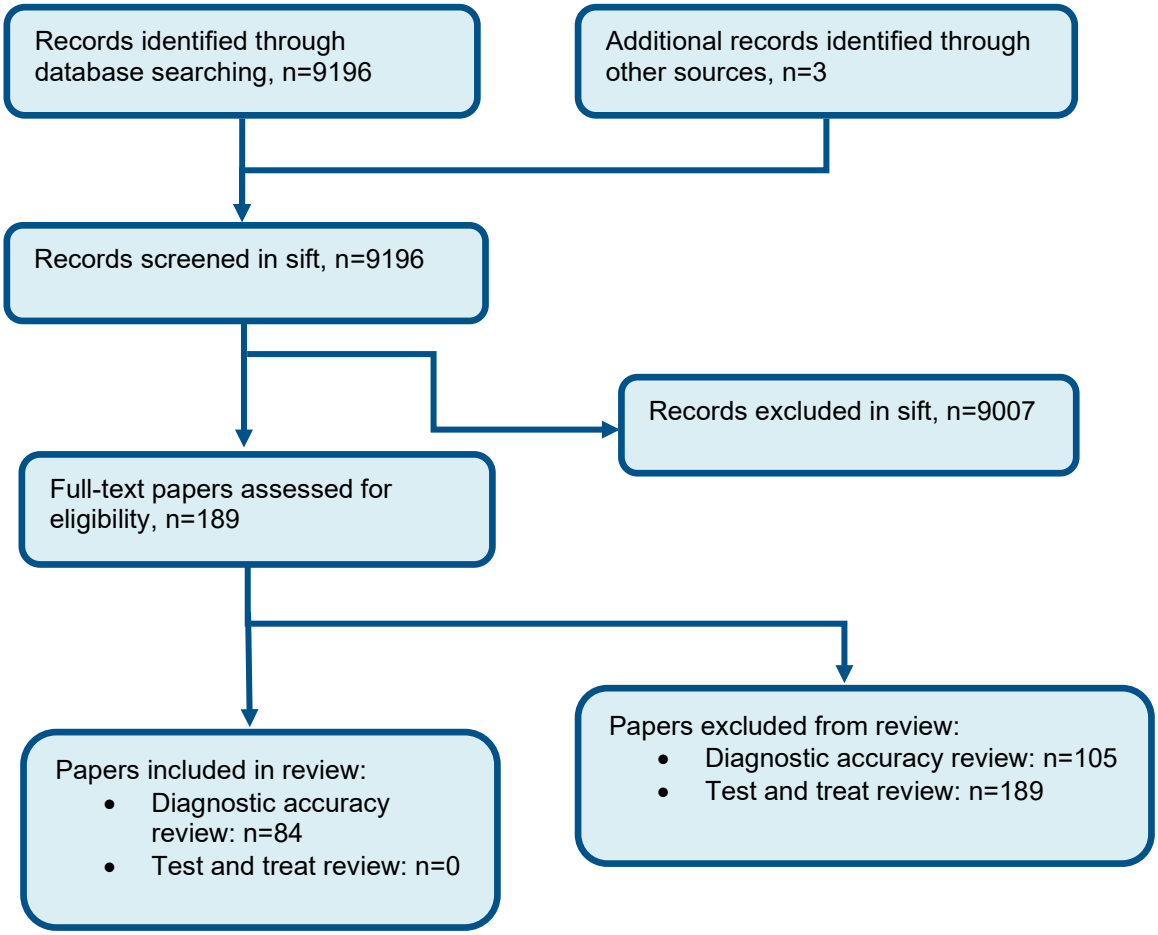
29 **INAHTA search terms**

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])

30

Appendix C –Diagnostic evidence study selection

Figure 1: Flow chart of clinical study selection for the review of clinical decision rules for selecting people with head injury for imaging



Appendix D –Diagnostic evidence

D.1 Adults – studies extracted as part of current update

Reference	Arab 2015[1]
Study type	Retrospective review of registry, cross-sectional
Study methodology	Data source: retrospective review of ED registry of head trauma from single tertiary care hospital in Saudi Arabia between June 2010 and July 2011. Selected from ED registry of head trauma by systematic randomisation by selecting every other patient using medical record numbers from the registry.
Number of patients	n = 368
Patient characteristics	Age, mean (SD): 30.5 (17.3) years, range 14-106 years Gender (male): 287 (78%) GCS 13/14: 24 (6.7%) GCS 15: 332 (93.3%) Ethnicity: not reported Setting: tertiary care hospital Country: Saudi Arabia Inclusion criteria: minor head injury, including patients with a GCS score of 13–15 on presentation with witnessed loss of consciousness, amnesia, or disorientation in the ED registry of head trauma Exclusion criteria: GCS score less than 13, aged less than 14 years (as ≥14 years is considered the age of adulthood in the institution), acute neurological deficit, penetrating skull injury, trauma of more than 24 hours, pregnancy, known history of seizures, bleeding disorder, or returned for reassessment

Reference	**Arab 2015[1]**
	Adults (threshold of 14 years used in this study) with minor head injury (Glasgow Coma Scale 13-15) presenting within 24 h of injury
Target condition(s)	Traumatic brain injury – minor head injury
Index test(s) and reference standard	Index test: Canadian CT head rule Reference standard CT (all had CT) Follow-up: Data from patient charts included, age, gender, mechanism of injury, neurological symptoms, high and medium risk factors, associated injuries and head CT findings. Information on subsequent neurosurgical intervention and neurological deterioration were recorded.
Results	Outcomes: Abnormality on CT scan. Type and prevalence of abnormalities recorded by two radiologists with at least 5 years' experience in reading trauma head CT, who were blinded to the clinical findings when reading the head CT scans. Cases with discrepancies in interpretation were further reviewed by a neuroradiologist for a final opinion. The types of abnormalities included soft tissue swelling, extradural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haemorrhage, intraventricular haemorrhage, cortical contusions, brain oedema, diffuse axonal injury, brain herniation/midline shift, skull fracture and facial bone fracture. Need for surgical intervention mentioned in the paper but no data to calculate diagnostic accuracy for this outcome. Abnormality on CT scan TP: 12 FP: 128 TN: 221 FN: 6

Reference	**Arab 2015[1]**
	Sensitivity % 95% CI: 66.67 (40.99-86.66) Specificity% 95% CI: 63.31 (57.93-68.46) PPV % 95% CI: 8.82 (4.64-14.91) NPV % 95% CI: 97.27 (94.16-98.99)
Source of funding	Received no specific grant from any public, commercial or not-for-profit sector.
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Possible inappropriate exclusions, and unclear if index test applied without knowledge of reference standard and if index test and reference standard applied at similar time due to retrospective nature of study. Indirectness (QUADAS 2 – applicability): none
Comments	-

4

Reference	**Chobdari 2018[15]**
Study type	Observational analysis study, unclear if prospective or retrospective
Study methodology	Data source: patients referred to Hospital CT scan department due to minor head trauma included following CT scan results
Number of patients	n = 264
Patient characteristics	**Appears to only give patient characteristics for the 139 that were positive on CT** Age: *30-45 years: 31.7%* 14-29 years: 18.7% GCS not reported Gender: 79.9% male and 20.1% female

Reference	**Chobdari 2018[15]**
	Ethnicity: not reported Setting: hospital CT scan department Country: Iran Inclusion criteria: patients referred to Hospital's CT scan department due to minor head trauma undergoing a CT Exclusion criteria: none reported Adults with minor head injury
Target condition(s)	Traumatic brain injury – minor head trauma
Index test(s) and reference standard	Index test: • Canadian CT Head Rule • New Orleans Criteria Reference standard CT (all had CT) No mention of any follow-up.
Results	Outcomes: Abnormality (positive) on CT scan. No other details provided in terms of types of abnormalities included and process for assessing and confirming (e.g. whether more than one researcher confirmed). 139 were CT-positive and 125 CT-negative. Abnormality on CT scan – Canadian CT Head Rule (positive if ≥2) TP: 106 FP: 33 TN: 92

Reference	Chobdari 2018[15]
	FN: 33 Sensitivity % 95% CI: 76.2 (CIs not reported) Specificity% 95% CI: 73.7 (CIS not reported) PPV calculated using excel sheet: 76.2 NPV calculated using excel sheet: 73.7 <u>Abnormality on CT scan – New Orleans Criteria (positive if ≥2)</u> TP: 43 FP: 39 TN: 86 FN: 96 Sensitivity % 95% CI: 31.0 (CIs not reported) Specificity% 95% CI: 69.0 (CIS not reported) PPV % calculated using excel sheet: 52.0 NPV % calculated using excel sheet: 47.0
Source of funding	Funded by Mashhad University of Medical Sciences
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Limited description of patient enrolment including whether the sample was consecutive or random, unclear whether index test was interpreted and applied without knowledge of the reference standard and unclear time interval between reference standard and index test Indirectness (QUADAS 2 – applicability): none
Comments	-

5

Reference	**Davey 2018[18]**
Study type	Prospective study
Study methodology	Data source: identified patients screened by research assistant for inclusion, identified by monitoring tracking board in electronic medical record. Conducted between 9th May 2014 and 9th May 2016. Conducted at two large, urban, academic EDs including one level I trauma centre and one level II trauma centre. Patients enrolled between after CT had been ordered but before scan had been reviewed or results provided by Department of Radiology.
Number of patients	n = 390 (240 analysed)
Patient characteristics	Age: not reported (>18 years to be included) Gender: 38.6% male and 61.4% female GCS 15 (<15 was an exclusion criterion) 27.1% receiving at least one anticoagulant or antiplatelet Ethnicity: not reported Setting: two large, urban, academic EDs including one level I trauma centre and one level II trauma centre Country: USA Inclusion criteria: presenting with minor or minimal head injury with head CT ordered by clinician; aged at least 18 years Exclusion criteria: English not listed as primary spoken language; clinical intoxication; previous recent (<30 day) intracranial injury (triage history and notes or non-contrast CT scan in electronic medical record); GCS <15; neurological deficits; loss of consciousness; witnessed disorientation; or any patient considered a 'trauma code' by the institutional guidelines. Adults (at least 18 years) with minor and minimal head injury
Target condition(s)	Traumatic brain injury – minimal or minor head injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule Reference standard

Reference	**Davey 2018[18]**
	Non-contrast head CT No mention of any follow-up.
Results	Outcomes: Positive non-contrast head CT scan. Defined as any CT read by attending radiologists as positive for intracranial haemorrhage. Canadian CT Head Rule retrospectively applied to patients to determine whether they would have required the CT based on this rule. <u>Positive CT scan (intracranial haemorrhage) – Canadian CT Head Rule (score of 2 or 3, moderate or high risk)</u> TP: 5 FP: 167 TN: 68 FN: 0 Sensitivity % 95% CI: 100.0 (48.0-100.0) Specificity% 95% CI: 29.0 (23.0-35.0) PPV % calculated using excel sheet: 3.0% NPV % calculated using excel sheet: 100%
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear whether index test was applied without knowledge of the results of the index test, time interval between index test and reference standard unclear and substantial attrition between enrolment and analysis. Indirectness (QUADAS 2 – applicability): none
Comments	-

6

Reference	**Foks 2018[27]**
Study type	Prospective cohort study
Study methodology	Data source: conducted between March 2015 and December 2016 as part of a multicentre study in the Netherlands, including three university ED departments (level 1 trauma centres) and six non-university EDs (trauma level 1 for two, level 2 for two and level 3 for two). All located in an urban location. During patient inclusion, neurologists and emergency physicians followed local guideline for CT scanning in those with minor head injury. Most centres used same national guideline based on CHIP rule with two following a slightly adapted guideline. Consecutively included.
Number of patients	n = 4557 (data from six centres where CT performed or data for those with no CT could be imputed based on clinical characteristics, excludes others with CT from another three centres – includes 82.1% with a CT and 17.9% without a CT where data imputed) **– primary analysis** n= 4702 (data from all of those with CT performed across all nine centres) – **secondary analysis (only limited results provided)**
Patient characteristics	**Primary analysis – n=4557 with CT or data for those with no CT imputed from six centres (excluded others with CT from other three centres)** Age, mean (range): 53.1 (16.0-101.0) years Gender: 58.3% male and 41.7% female GCS: *13, 3.1%* *14, 11.0%* *15, 85.9%* Use of anticoagulation: *None, 88.8%* *Coumarin, 9.2%* *Direct oral anticoagulants, 1.2%* Use of thrombocyte aggregation inhibitors: 13.5% Ethnicity: not reported **Secondary analysis – n=4702 with CT data across all nine centres (no data that can be analysed within this analysis as limited data provided)**

Reference	Foks 2018[27]
	Age, mean (range): 55.9 (16.0-101.0) years Gender: 57.6% male and 42.4% female GCS: *13, 4.4%* *14, 14.8%* *15, 80.8%* Use of anticoagulation: *None, 86.2%* *Coumarin, 11.4%* *Direct oral anticoagulants, 1.3%* Use of thrombocyte aggregation inhibitors: not reported Ethnicity: not reported Setting: nine EDs across the Netherlands, including university and non-university Country: The Netherlands Inclusion criteria: aged ≥16 years; presentation within 24 h after blunt trauma to the head; and GCS 13-15 at presentation at ED. Patients with and without loss of consciousness or post-traumatic amnesia were included. Exclusion criteria: GCS <13; <16 years; transferred from other hospitals; or with any contraindication for CT. Adults (aged at least 16 years) with minor head injury
Target condition(s)	Traumatic brain injury – minor head injury
Index test(s) and reference standard	Index test: CT in Head Injury Patients (CHIP) New Orleans Criteria (NOC) Canadian CT Head Rule (CCHR)

Reference	**Foks 2018[27]**
	NICE guideline recommendations for head injury (1.4.7, 1.4.8 and 1.4.12 in version before new update) Reference standard CT (not all had CT) – two separate analyses done, one from six centres where all had CT or those without CT had data imputed, and a second where only data from those with CT across the nine centres were included Clinical data collected before diagnostic tests as much as possible. Head CT scans performed according to routine trauma protocol at each hospital. Interpreted by neuroradiologists aware of patient history and clinical findings but were not aware of actual score of CT decision rules. Follow-up: electronic health records reviewed 30 days after the injury to assess follow-up information about a neurosurgical intervention.
Results	Outcomes: Intracranial traumatic finding on CT – defined as a subdural haematoma, epidural haematoma, subarachnoid haemorrhage, cerebral lesions (haemorrhagic contusion, non-haemorrhagic contusion, diffuse axonal injury), intraventricular haemorrhage and skull fracture. Potential neurosurgical lesion – defined as an intracranial traumatic finding on CT that could lead to a neurosurgical intervention or death. Examples include an epidural haematoma, large acute subdural haematoma (mass), large contusion(s) (mass), depressed skull fracture, and any lesion with a midline shift or herniation. Neurosurgical interventions.
	Primary analysis population – six centres with CT or no CT with data imputed, n=4557 **Note that up to three different analyses are provided for NOC and CCHR, depending on the outcome, as the whole population of the study included some that the rules were not originally designed for use in** – applied in the whole population (n=4557), an adapted version of the rules applied in the whole population (n=4557, with inclusion/exclusion

Reference	Foks 2018[27]		
	criteria included as additional factors in the scoring) and applied only in the subpopulation the rules were originally designed for use in (n=1147 for NOC and n=1683 for CCHR.		
	Intracranial traumatic finding on CT	**Potential neurosurgical lesion on CT**	**Neurosurgical intervention**
	CHIP TP: 383 FP: 3253 TN: 897 FN: 24 Sensitivity % 95% CI: 94.1 (91.5-96.3) Specificity% 95% CI: 21.6 (20.4-22.9) PPV% calculated using excel sheet: 11.0 NPV% calculated using excel sheet: 97.0	CHIP TP: 72 FP: 3564 TN: 919 FN: 2 Sensitivity % 95% CI: 97.3 (93.1-100.0) Specificity% 95% CI: 20.5 (19.4-21.7) PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0	CHIP TP: 17 FP: 3619 TN: 920 FN: 1 Sensitivity % 95% CI: 94.4 (81.8-100.0) Specificity% 95% CI: 20.3 (19.2-21.4) PPV% calculated using excel sheet: 0.0 NPV% calculated using excel sheet: 100.0
	NOC – applied to whole population (n=4557) TP: 402 FP: 3966 TN: 184 FN: 5	NOC – applied to whole population (n=4557) TP: 74 FP: 4294 TN: 189 FN: 0	NOC – applied to whole population (n=4557) TP: 18 FP:4350 TN: 189 FN: 0

Reference	Foks 2018[27]		
	Sensitivity % 95% CI: 98.8 (97.6-99.8) Specificity% 95% CI: 4.4 (3.8-5.1) PPV% calculated using excel sheet: 9.0 NPV% calculated using excel sheet: 97.0 <u>NOC – adjusted version applied to whole population (n=4557)</u> TP: 402 FP: 3984 TN: 166 FN: 5 Sensitivity % 95% CI: 98.8 (97.6-99.8) Specificity% 95% CI: 4.0 (3.4-4.5) PPV% calculated using excel sheet: 9.0 NPV% calculated using excel sheet: 97.0 <u>NOC – in subset of those rule originally designed for (n=1147)</u> TP: 137	Sensitivity % 95% CI: 100.0 (100.0-100.0) Specificity% 95% CI: 4.2 (3.6-4.8) PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0 <u>NOC – adjusted version applied to whole population (n=4557)</u> TP: 74 FP: 4312 TN: 171 FN: 0 Sensitivity % 95% CI: 100.0 (100.0-100.0) Specificity% 95% CI: 3.8 (3.2-4.3) PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0 <u>NOC – in subset of those rule originally designed for (n=1147)</u> TP: 20	Sensitivity % 95% CI: 100.0 (100.0-100.0) Specificity% 95% CI: 4.2 (3.6-4.7) PPV% calculated using excel sheet: 0.0 NPV% calculated using excel sheet: 100.0 <u>CCHR – applied to whole population (n=4557)</u> TP: 16 FP: 2625 TN: 1914 FN: 2 Sensitivity % 95% CI: 88.9 (71.4-100.0) Specificity% 95% CI: 42.2 (40.7-43.8) PPV% calculated using excel sheet: 1.0 NPV% calculated using excel sheet: 100.0 <u>NICE</u> TP: 16 FP: 1903

Reference	Foks 2018[27]		
	FP: 973 TN: 35 FN: 2 Sensitivity % 95% CI: 98.6 (96.4-100.0) Specificity% 95% CI: 3.5 (2.4-4.5) PPV% calculated using excel sheet: 12.0 NPV% calculated using excel sheet: 95.0 <u>CCHR – applied to whole population (n=4557)</u> TP: 327 FP:2314 TN: 1836 FN: 80 Sensitivity % 95% CI: 80.3 (76.1-84.2) Specificity% 95% CI: 44.2 (42.7-45.9) PPV% calculated using excel sheet: 12.0 NPV% calculated using excel sheet: 96.0	FP: 1090 TN: 37 FN: 0 Sensitivity % 95% CI: 100.0 (100.0-100.0) Specificity% 95% CI: 3.3 (2.3-4.2) PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0 <u>CCHR – applied to whole population (n=4557)</u> TP: 65 FP: 2576 TN: 1907 FN: 9 Sensitivity % 95% CI: 87.8 (79.7-94.9) Specificity% 95% CI: 42.5 (41.0-44.1) PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0	TN: 2636 FN: 2 Sensitivity % 95% CI: 88.9 (71.4-100.0) Specificity% 95% CI: 58.1 (56.6-59.6) PPV% calculated using excel sheet: 1.0 NPV% calculated using excel sheet: 100.0

Reference	Foks 2018[27]		
	<u>CCHR – adjusted version applied to whole population (n=4557)</u> TP: 333 FP: 2409 TN: 1741 FN: 74 Sensitivity % 95% CI: 81.8 (77.6-85.7) Specificity% 95% CI: 42.0 (40.4-43.6) PPV% calculated using excel sheet: 12.0 NPV% calculated using excel sheet: 96.0 <u>CCHR – in subset of those rule originally designed for (n=1683)</u> TP: 209 FP: 821 TN: 606 FN: 47 Sensitivity % 95% CI: 81.6 (76.8-86.2) Specificity% 95% CI: 42.5 (39.9-45.1)	<u>CCHR – adjusted version applied to whole population (n=4557)</u> TP: 65 FP: 2677 TN: 1806 FN: 9 Sensitivity % 95% CI: 87.8 (79.7-94.9) Specificity% 95% CI: 40.3 (38.9-41.7) PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0 <u>CCHR – in subset of those rule originally designed for (n=1683)</u> TP: 40 FP: 990 TN: 646 FN: 7 Sensitivity % 95% CI: 85.1 (74.0-94.2) Specificity% 95% CI: 39.5 (37.2-41.9) PPV% calculated using excel sheet: 4.0	

Reference	**Foks 2018[27]**		
	PPV% calculated using excel sheet: 20.0 NPV% calculated using excel sheet: 93.0 <u>NICE</u> TP: 295 FP: 1624 TN: 2526 FN: 112 Sensitivity % 95% CI: 72.5 (67.8-77.2) Specificity% 95% CI: 60.9 (59.3-62.5) PPV% calculated using excel sheet: 15.0 NPV% calculated using excel sheet: 96.0	NPV% calculated using excel sheet: 99.0 <u>NICE</u> TP: 63 FP: 1856 TN: 2627 FN: 11 Sensitivity % 95% CI: 85.1 (76.4-92.9) Specificity% 95% CI: 58.6 (57.1-60.1) PPV% calculated using excel sheet: 3.0 NPV% calculated using excel sheet: 100.0	
	Secondary analysis population – nine centres including only those with CT, n=4702		
	Very limited results reported: NOC rule had highest sensitivity (99.1%) and lowest specificity (3.1%) for any intracranial traumatic finding on CT NICE guideline had highest specificity (50.3%) and lowest sensitivity (77.5%) for any intracranial traumatic finding on CT		
Source of funding	No specific funding for the study obtained, though one author received funding as a personal grant from St Jacobus Foundation (non-profit organisation supporting research).		
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Concerns about the reference standard used, as in the primary analysis only 82.1% had a CT and for the rest data was imputed based on risk factors, and the selection of the population		

Reference	**Foks 2018[27]**
	for the primary analysis, as it only included data from participants in six centres, despite everyone in the other three centres also having CT done which could have been included. Indirectness (QUADAS 2 – applicability): none
Comments	-

7

Reference	**Jones 2020[46]**
Study type	Prospective observational multicentre study
Study methodology	Data source: secondary analysis of a prospective observational multicentre study originally designed to evaluate the diagnostic accuracy of serum S100B and common concussive symptoms and signs for predicting traumatic intracranial injury on non-contrast head CT scan. Conducted between 2008 and 2010 in six hospital EDs across New York State and Northern Pennsylvania. Trained research assistants prospectively obtained information in on patient demographics, the timing and mechanism of injury, and a variety of concussive symptoms and signs by interview with the patient in the ED, the treating emergency care provider in the ED and abstraction of the patient medical record after the ED visit using a standardized data collection tool.
Number of patients	n = 679
Patient characteristics	Age, mean (SD): *<65 years, 89.0%* *≥65 years, 11.0%* Gender: 62.0% male and 38.0% female GCS: *<15, 7.2%* *15, 92.8%* Ethnicity: *African-American, 14.7%* *Asian, 1.0%* *Caucasian, 81.3%* *Native American, 0.6%* *Native Hawaiian, 0.1%*

Reference	**Jones 2020[46]**
	Unknown/refused, 2.2% Setting: six hospital EDs across USA Country: USA Inclusion criteria: mild traumatic brain injury (defined as a blow to the head or rapid acceleration/deceleration with a presenting GCS of 13-15, loss of consciousness ≤ 30 minutes, post-traumatic amnesia ≤24 h or neuropsychological abnormality defined as transient confusion, disorientation, impaired consciousness or altered mental status); had head CT scan as part of clinical care; had venous blood sample drawn within 6 h of injury with a valid S100B measurement; and at least 16 years old. Exclusion criteria: history of brain tumour, melanoma, Alzheimer's disease, bone fracture or stroke/surgery within the previous month. Adults (≥16 years) with mild traumatic brain injury
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule New Orleans Criteria Reference standard CT (all had CT) Head CT scans were interpreted by board-certified radiologists at each participating institution.

Reference	Jones 2020[46]
Results	Outcomes: Traumatic intracranial injury on head CT – traumatic intracranial injuries (positive CT scans) were defined as the presence of any of the following: subdural haematomas, epidural haematomas, subarachnoid haemorrhage, cerebral oedema, skull fracture and cerebral contusions. <u>Traumatic intracranial injury on head CT – Canadian CT Head Rule</u> TP: 31 FP: 459 TN: 181 FN: 8 Sensitivity % 95% CI: 79.5 (63.2-89.8) Specificity% 95% CI: 28.3 (24.8-31.8) PPV% 95% CI: 6.3 (4.2-8.5) NPV% 95% CI: 95.8 (92.9-98.6) <u>Traumatic intracranial injury on head CT – New Orleans Criteria</u> TP: 36 FP: 552 TN: 88 FN: 3

Reference	**Jones 2020[46]**
	Sensitivity % 95% CI: 92.3 (83.9-100.0) Specificity% 95% CI: 13.8 (11.1-16.4) PPV% 95% CI: 6.1 (4.2-8.1) NPV% 95% CI: 96.7 (93.0-100.0)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if consecutive or random sample enrolled, unclear if index test applied without knowledge of the reference standard and unclear time interval between the index test and reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

8

Reference	**Kavalci 2014[47]**
Study type	Prospective study
Study methodology	Data source: single tertiary centre in Turkey. All assessed by emergency physician or by supervised emergency medicine residents. Data collection done prospectively using data collection sheet. CT scan of head performed after clinical assessment for those with one of risk factors in the two decision rules. CT scans interpreted by radiologist blinded to patient data.
Number of patients	n = 175
Patient characteristics	Age, mean (SD): 49.13 (20.71) years Gender: 60.57% male and 39.43% female GCS: *13, 4.0%* *14, 5.1%* *15, 90.9%*

Reference	Kavalci 2014[47]
	Ethnicity: not reported Setting: single tertiary centre in Turkey Country: Turkey Inclusion criteria: acute minor head injury (blunt trauma to head within 24 h and GCS 13-15); at least one of the risk factors stated in the Canadian CT Head Rule or New Orleans Criteria. Exclusion criteria: GCS <13 or instable vital signs; presenting >24 h after head trauma; obvious penetrating skull injury or obvious depressed fracture; presence of major trauma; bleeding disorder or use of oral anticoagulants; contraindications for CT; pregnancy; <18 years of age; and incomplete data sheet. Adults (at least 18 years) with minor head injury
Target condition(s)	Traumatic brain injury – minor head injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule New Orleans Criteria Reference standard CT (all had CT) CT scan of head performed after clinical assessment for those with one of risk factors in the two decision rules. CT scans interpreted by radiologist blinded to patient data. Follow-up: no mention of follow-up.

Reference	Kavalci 2014[47]
Results	Outcomes: Presence of traumatic lesions on head CT scan – lesions defined as positive CT results for the study were subarachnoid haemorrhage, epidural haemorrhage, subdural haematoma, intraparenchymal hematoma, compression fracture, cerebral oedema and contusion. Note that in the paper, results are provided separately for GCS 14-15 and GCS 13. However, for the purpose of this review data for the whole population of GCS 13-15 has been extracted as a single group. <u>Presence of traumatic lesions on head CT scan – Canadian CT Head Rule</u> TP: 14 FP: 88 TN: 66 FN: 7 Sensitivity % calculated using excel sheet: 67.0 Specificity% calculated using excel sheet: 43.0 PPV% calculated using excel sheet: 14.0 NPV% calculated using excel sheet: 90.0 <u>Presence of traumatic lesions on head CT scan – New Orleans Criteria</u> TP: 12 FP: 143

Reference	**Kavalci 2014[47]**
	TN: 11 FN: 2 Sensitivity % calculated using excel sheet: 71.0 Specificity% calculated using excel sheet: 7.0 PPV% calculated using excel sheet: 9.0 NPV% calculated using excel sheet: 65.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if a consecutive or random sample was included, unclear if the reference standard was interpreted without knowledge of the index test and unclear time interval between index test and reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

9

Reference	**Korley 2013[49]**
Study type	Prospective observational study
Study methodology	Data source: ED patients presenting with acute minor traumatic brain injury. Urban academic ED of tertiary care hospital, regional I trauma centre. Convenience sample of subjects at least 18 years or older presenting within 24 h of non-penetrating trauma to the head, from August 2010 to July 2011. Enrolment occurred on days when a research assistant was available (most weekdays). Eligibility verified by treating physicians. Research assistants then identified patients through ED electronic patient tracking board and spoke to treating physicians to confirm inclusion/exclusion criteria. Only approached treating physicians after diagnostic plan for each patient had been established.
Number of patients	n = 169 (76.9% had CT)
Patient characteristics	Age, median (IQR): 41 (27-62) years for those with CT scan and 38 (27-51) years for those without CT scan *>60 years, 26.2% in those with CT and 2.6% for those without CT scan* *≥65 years, 23.1% in those with CT and 2.6% for those without CT scan* Gender: 49.1% male and 50.9% female

Reference	Korley 2013[49]
	GCS: 14-15 *14, 5.9%* *15, 94.1%* Ethnicity: *African-American, 63.9%* *White, 34.3%* *Other, 1.2%* Setting: single ED of tertiary care hospital Country: USA Inclusion criteria: ≥18 years; presenting with 24 h of non-penetrating head trauma to head; and evaluated for blunt trauma to the head (with or without loss of consciousness or post-traumatic amnesia). Exclusion criteria: no clear history of trauma; unstable vital signs; obvious depressed skull fracture; GCS score <14 on presentation; multisystem trauma; acute focal neurologic deficit; and pregnant patients. Adults (at least 18 years old) with mild traumatic brain injury
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule (CCHR) New Orleans Criteria (NOC) American College of Emergency Physicians neuroimaging criteria (ACEP) Structured data entry form completed by research assistant using electronic data capture tool. Data about physical examination obtained by interview with treating physicians. Did not ask treating physicians if met criteria for head CT based on clinical decision rules being evaluated. Reference standard CT (not all had CT – 76.9% had CT)

Reference	**Korley 2013[49]**
	Patients evaluated by treating physicians according to routine practice and head CTs obtained at their clinical discretion. Two independent emergency physicians reviewed final head CT results as reported by board-certified neuroradiologists and categorised as an acute traumatic finding or no acute traumatic finding. Blinded to patient data when interpreting CTs. For those not receiving a CT scan during index ED visit, structured telephone follow-up at 14-60 days post-enrolment performed to determine if any there were any subsequent hospital visits where they were diagnosed with acute traumatic intracranial findings for the same injuries.
Results	Outcomes: Acute traumatic finding on CT – subdural, epidural or parenchymal hematoma; subarachnoid haemorrhage; cerebral contusion; or depressed skull fracture. <u>Acute traumatic finding on CT – CCHR</u> TP: 5 FP: 104 TN: 60 FN: 0 Sensitivity % 95% CI: 100 (47.8-100.0) Specificity% 95% CI: 36.8 (28.4-45.9) PPV% calculated using excel sheet: 5.0 NPV% calculated using excel sheet: 100.0 <u>Acute traumatic finding on CT – NOC</u>

Reference	Korley 2013[49]
	TP: 5 FP: 159 TN: 5 FN: 0 Sensitivity % 95% CI: 100 (47.8-100.0) Specificity% 95% CI: 3.2 (0.9-8.0) PPV% calculated using excel sheet: 3.0 NPV% calculated using excel sheet: 100.0 <u>Acute traumatic finding on CT – ACEP guideline</u> TP: 4 FP: 147 TN: 17 FN: 1 Sensitivity % 95% CI: 80.0 (28.4-99.5) Specificity% 95% CI: 10.4 (5.6-17.1) PPV% calculated using excel sheet: 3.0 NPV% calculated using excel sheet: 94.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Sample was not consecutive or random and excluded GCS 13 which was included in most other included studies, unclear time interval between index test and reference standard and not all received the same reference standard.

Reference	**Korley 2013[49]**
	Indirectness (QUADAS 2 – applicability): none
Comments	-

10

Reference	**Lamba 2021[52]**
Study type	Prospective observational study
Study methodology	Data source: performed between July 2019 and July 2020. Included cases of minor traumatic brain injury at the ED of a single hospital, a 1500-bed tertiary care teaching hospital.
Number of patients	n = 101
Patient characteristics	Age: most (42.6%) between ages of 21 and 30 years Gender: 69.3% males and 30.7% females Ethnicity: not reported Setting: ED within a tertiary care teaching hospital Country: India Inclusion criteria: non-pregnant >16 years presenting to ED with a history of head trauma; minor traumatic brain injury (GCS 13-15) at 30 min from the incident trauma. Exclusion criteria: patients that had visited another healthcare facility before arriving at the study centre; patients on anticoagulant therapy; history of alcohol intake within 2 h prior to presenting at ED; patients in whom neurosurgeon and ED physician agreed that CT scan of brain was not necessary. Adults (>16 years) with minor traumatic brain injury
Target condition(s)	Traumatic brain injury – minor traumatic brain injury
Index test(s) and reference standard	<u>Index test:</u> Canadian Head CT Rule

Reference	**Lamba 2021[52]**
	ED residents trained by senior physicians on using the rule and promoted as standard of care. Encouraged to use web-based mobile phone applications to check criteria of the rule. Presence of any of 7 findings in the Canadian Head CT Rule warranted need for a CT scan of the brain in minor traumatic brain injury. If none of criteria were met, patient underwent consultation with neurosurgeon – if they deemed a CT brain scan necessary based on clinical opinion then CT scan would go ahead. If they agreed that head CT was not necessary, then patient would be excluded from the study (this did not apply to any patients in the study). Reference standard Non-contrast brain CT Follow-up: after CT, if intracranial lesion attributable to the trauma was identified, patient was advised transfer into neurosurgical unit. If CT was normal, patients underwent neuro-observation in the ED for at least 12 h. Patients were observed for deterioration of GCS, change in pupillary response, seizure activity, persistent vomiting, delayed appearance of signs of basal skull fracture.
Results	Outcomes: Intracranial lesion on non-contrast CT head scan. Reported that for positive CT scans, in all cases there were either haemorrhages or contusions. Intracranial lesion on CT scan – Canadian CT Head Rule (at least 1 of 7 criteria) TP: 16 FP: 46 TN: 39 FN: 0 Sensitivity % calculated using excel sheet: 100.0 Specificity % calculated using excel sheet: 46.0 PPV % calculated using excel sheet: 26.0 NPV % calculated using excel sheet: 100.0

Reference	**Lamba 2021[52]**
Source of funding	Reported to be no funding
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if sample was consecutive or random, unclear if index test and reference standard were interpreted without knowledge of the other and unclear time interval between index test and reference standard Indirectness (QUADAS 2 – applicability): none
Comments	-

11

Reference	**Lo 2016[54]**
Study type	Retrospective cohort study
Study methodology	Data source: all patients attending single ED of Princess Margaret Hospital between 1st January 2008 and 31st December 2010 with minor head injury. Data including ED records, in-patient records on clinical management system, CT film and reports were reviewed.
Number of patients	n = 383 for Canadian CT Head Rule and n=431 for New Orleans Criteria
Patient characteristics	Characteristics are given for populations where Canadian CT Head Rule (n=383) and New Orleans Criteria (n=431) could be applied, respectively Age: *>65 years: 30.0% and 25.8%* *60-65 years: 6.8% and 5.1%* *40-59 years: 32.9% and 29.0%* *17-39 years: 31.3% and 28.5%* *1-16 years: 0 (as was exclusion criterion) and 11.6%* GCS 13-15 for those analysed with Canadian CT Head Rule and all GCS 15 for those analysed with New Orleans Criteria Gender: not reported Ethnicity: not reported Setting: ED of a single hospital Country: Hong Kong, China

Reference	**Lo 2016[54]**
	Inclusion criteria: blunt trauma resulting in minor head injury (GCS of at 13-15 and witnessed loss of consciousness, definite amnesia or witnessed disorientation). Exclusion criteria: presenting to ED >24 h after head injury or no documented GCS in their records (both clinical decision rules); seizure prior to ED treatment, focal neurological deficit, bleeding disorder, on anticoagulant treatment or aged ≤16 years (for Canadian CT head rule); and aged <1 year or with GCS <15 (for New Orleans Criteria).
Target condition(s)	Traumatic brain injury – mild head injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule (at least one of the criteria) New Orleans Criteria (at least one of the criteria) Reference standard CT (all had CT) Follow-up: follow-up not mentioned, other than the 7-day period post-injury to confirm need for neurosurgical intervention
Results	Outcomes: Clinically important brain injury on CT - all kinds of brain injuries with positive CT findings except the following: 1) solitary contusion of less than 5 mm in diameter; 2) localised subarachnoid blood less than 1 mm thick; 3) smear subdural haematoma less than 4 mm thick; or 4) closed depressed skull fracture not through the inner table. Need for neurosurgical intervention – death within 7 days of head injury or need for any of following within 7 days: burr hole, craniotomy, craniectomy, and elevation of skull fracture or intracranial pressure monitoring. Clinically important brain injury on CT – Canadian CT Head Rule TP: 61 FP: 187

Reference	Lo 2016[54]
	TN: 119 FN: 16 Sensitivity % 95% CI: 80.0 (70.0-88.0) Specificity% 95% CI: 39.0 (33.0-44.0) PPV% 95% CI: 25.0 (19.0-30.0) NPV% 95% CI: 88.0 (83.0-94.0) <u>Clinically important brain injury on CT – New Orleans Criteria</u> TP: 71 FP: 295 TN: 59 FN: 6 Sensitivity % 95% CI: 92.0 (86.0-98.0) Specificity% 95% CI: 17.0 (13.0-21.0) PPV% 95% CI: 19.0 (15.0-23.0) NPV% 95% CI: 91.0 (84.0-98.0) <u>Neurosurgical intervention or death – Canadian CT Head Rule</u> TP: 8 FP: 240

Reference	**Lo 2016[54]**
	TN: 133 FN: 2 Sensitivity % 95% CI: 80.0 (55.0-100.0) Specificity% 95% CI: 36.0 (31.0-41.0) PPV% 95% CI: 3.0 (1.0-5.0) NPV% 95% CI: 99.0 (96.0-100.0) <u>Neurosurgical intervention or death – New Orleans Criteria</u> TP: 11 FP: 355 TN: 65 FN: 0 Sensitivity % 95% CI: 100.0 (100.0-100.0) Specificity% 95% CI: 15.0 (12.0-19.0) PPV% 95% CI: 3.0 (1.0-5.0) NPV% 95% CI: 100.0 (100.0-100.0)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear whether consecutive or random sample enrolled, unclear whether index test was applied without knowledge of reference standard results and the time interval between reference standard and index test Indirectness (QUADAS 2 – applicability): none
Comments	-

12

Reference	**Mata-Mbemba[57]**
Study type	Prospective study
Study methodology	Data source: consecutive patients with mild traumatic brain injury admitted to a single institution, which was a major tertiary care hospital in north-eastern Japan, in 2009 and 2010
Number of patients	n = 142
Patient characteristics	Age, mean (SD): 50 (21.7) years, range 17-88 years Gender: 67.6% male and 32.4% female GCS: *13, 21.1%* *14, 31.7%* *15, 47.2%* Ethnicity: not reported Setting: Country: Japan Inclusion criteria: recent history (<24 h) of traumatic brain injury; aged ≥17 years; presented at least one of risk factors stated in Canadian CT Head Rule or New Orleans Criteria; and initial CT performed within 24 h after injury Exclusion criteria: none reported Adults (≥17 years) with mild traumatic brain injury
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule – those with any one finding positive New Orleans Criteria – those with any one finding positive (note that intended population for this rule is more restrictive, only for those with GCS15, but authors provide results for this designed population as well as the whole population of GCS 13-15, as has been done in Smits 2005 cited in the paper)

Reference	Mata-Mbemba[57]
	Reference standard CT (all had CT) Follow-up: not mentioned.
Results	Outcomes: Clinically important CT finding – screening CT used to identify important CT findings by two neuroradiologists, defined as any acute brain finding on CT that would require hospital admission or neurosurgical follow-up. Consensus used to resolve disagreements. All brain injuries noted on CT were considered clinically important unless the patient was neurologically intact and had one of the following lesions on CT: solitary contusion <5 mm in diameter; localised subarachnoid bleed <1 mm thick; smear subdural haematoma <4 mm thick, isolated pneumocephaly; or closed depressed skull fracture not through the inner table. Clinically important CT finding – Canadian CT Head Rule (n=142, whole population of GCS 13-15) TP: 44 FP: 70 TN: 23 FN: 5 Sensitivity % 95% CI: 89.8 (CIs not reported) Specificity% 95% CI: 24.7 (CIs not reported) PPV% calculated using excel sheet: 39.0 NPV% calculated using excel sheet: 82.0 Clinically important CT finding – New Orleans Criteria (n=142, whole population of GCS 13-15)

Reference	Mata-Mbemba[57]
	TP: 48 FP: 84 TN: 9 FN: 1 Sensitivity % 95% CI: 97.9 (CIs not reported) Specificity% 95% CI: 9.8 (CIs not reported) PPV% calculated using excel sheet: 36.0 NPV% calculated using excel sheet: 90.0 Clinically important CT finding – Canadian CT Head Rule (n=67, limited to those with GCS 15 – population the other decision rule is intended to be used in – not relevant for Canadian CT Head Rule so not presented in evidence sections TP: 13 FP: 41 TN: 12 FN: 1 Sensitivity % 95% CI: 92.8 (CIs not reported) Specificity% 95% CI: 22.6 (CIs not reported) PPV% calculated using excel sheet: 24.0 NPV% calculated using excel sheet: 92.0

Reference	**Mata-Mbemba[57]**
	Clinically important CT finding – New Orleans Criteria (n=67, limited to those with GCS 15 – population this decision rule is intended to be used in) TP: 13 FP: 44 TN: 9 FN: 1 Sensitivity % 95% CI: 92.8 (CIs not reported) Specificity% 95% CI: 17.0 (CIs not reported) PPV% calculated using excel sheet: 23.0 NPV% calculated using excel sheet: 90.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): none Indirectness (QUADAS 2 – applicability): none
Comments	-

13

14

Reference	**Mower 2017[61]**
Study type	Prospective observational study
Study methodology	Data source: four hospital EDs in California, USA between April 2006 and December 2015, in a population of consecutive blunt head injury patients. Population consisted of all acute blunt head trauma patients undergoing CT head imaging at the centres. Patients enrolled when treating provider ordered CT head imaging.
Number of patients	n = 11,770 (n=11,770 could be classified by NEXUS II rule and n=7,759 could be classified by Canadian rule)
Patient characteristics	**Patients characteristics are given for the total 11,770 participants that could be classified by the NEXUS II rule**

Reference	**Mower 2017[61]**
	Age, median (IQR): 50.0 (29.0-71.6) years, range 0.01-103.7 years Gender: 61.3% male and 38.5% female, 0.23% unknown Ethnicity: *Hispanic, 17.1%* *Non-Hispanic, 82.8%* *Unknown, 0.13%* Race *Asian, 5.36%* *Black, 10.5%* *Middle Eastern, 2.80%* *Native American, 0.06%* *Other, 5.51%* *White, 75.6%* *Unknown, 0.13%* Setting: four EDs within hospitals in California, USA Country: USA Inclusion criteria: acute blunt head trauma patients undergoing CT head imaging at participating centres Exclusion criteria: penetrating trauma; delayed presentation (>24 h after injury); patients undergoing imaging for reasons unrelated to trauma; and patients transferred into a participating centre with known intracranial injuries Adults (based on median age, but children also included) with acute blunt head trauma
Target condition(s)	Traumatic brain injury – acute blunt head trauma
Index test(s) and reference standard	Index test: NEXUS II Head CT Rule – classified high-risk Canadian Head CT Rule – provides some results for high-risk classification and some for moderate-risk classification Reference standard

Reference	Mower 2017[61]
	CT (all had CT) Follow-up: no mention of any follow-up past the 7-day time-point relevant to the neurosurgical intervention outcome.
Results	Outcomes: Need for neurosurgical intervention – defined as death due to head injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring, within 7 days of head injury. Clinically significant head injury on CT imaging – included all injuries evident on CT head imaging apart from the following in neurologically intact individuals: solitary small contusions, localized subarachnoid haemorrhage less than 1 mm thick, thin subdural hematomas less than 4 mm thick, isolated pneumocephaly and closed depressed skull fractures that did not violate the inner table. Formal radiographic and outcome assignments completed without knowledge of the criteria assessments (index tests) for each patient. Two separate reviewers completed outcome assessments with a third reviewer assigning outcomes where there was disagreement between the first two reviewers. <u>Need for neurosurgical intervention – NEXUS II Head CT Rule – high-risk on this rule (n=11,770, whole population that could be assessed by this rule)</u> TP: 420 FP: 8527 TN: 2823 FN: 0 Sensitivity % 95% CI: 100.0 (99.1-100.0) Specificity% 95% CI: 24.9 (24.1-25.7)

Reference	Mower 2017[61]
	PPV% calculated using excel sheet: 5.0 NPV% 95% CI: 100.0 (99.9-100.0) <u>Clinically significant head injury on CT imaging – NEXUS II Head CT Rule – high-risk on this rule (n=11,770, whole population that could be assessed by this rule)</u> TP: 759 FP: 8188 TN: 2815 FN: 8 Sensitivity % 95% CI: 99.0 (98.0-99.6) Specificity% 95% CI: 25.6 (24.8-26.4) PPV% calculated using excel sheet: 8.0 NPV% 95% CI: 99.7 (99.4-99.9) <u>Need for neurosurgical intervention – Canadian CT Head Rule – high-risk on this rule (n=7,759, specific population that could be assessed by this rule)</u> TP: 108 FP: 3150 TN: 4498 FN: 3 Sensitivity % 95% CI: 97.3 (92.3-99.4)

Reference	Mower 2017[61]
	Specificity% 95% CI: 58.8 (57.7-59.9) PPV% 95% CI: 3.3 (2.7-4.0) NPV% 95% CI: 99.9 (99.8-100.0) Clinically significant head injury on CT imaging – Canadian CT Head Rule – (n=7,759, specific population that could be assessed by this rule) *High-risk on this rule – could not be analysed given limited data provided for high-risk* TP: 252 FP: not reported TN: not reported FN: 54 Sensitivity % 95% CI: 82.4 (75.2-86.5) Specificity% 95% CI: not reported and could not be calculated PPV% 95% CI: not reported and could not be calculated NPV% 95% CI: not reported and could not be calculated *Moderate-risk on this rule* TP: 301 FP: 6536 TN: 917

Reference	Mower 2017[61]
	FN: 5 Sensitivity % 95% CI: 98.4 (96.2-99.5) Specificity% 95% CI: 12.3 (11.6-13.1) PPV% 95% CI: 4.4 (3.9-4.9) NPV% 95% CI: 98.5 (98.7-99.8) Need for neurosurgical intervention – NEXUS II CT Head Rule – high-risk on this rule (n=7,759, specific population that could be assessed by the other rule – not used in analysis given this population not relevant to NEXUS II CT Head Rule and larger population favoured) TP: 111 FP: 5158 TN: 2490 FN: 0 Sensitivity % 95% CI: 100.0 (96.7-100.0) Specificity% 95% CI: 32.6 (31.5-33.6) PPV% 95% CI: 2.1 (1.7-2.5) NPV% 95% CI: 100.0 (99.9-100.0) Clinically significant head injury on CT imaging – NEXUS II CT Head Rule – (n=7,759, specific population that could be assessed by the other rule – not used in analysis given this population not relevant to NEXUS II CT Head Rule and larger population favoured)

Reference	**Mower 2017[61]**
	TP: 299 FP: 4970 TN: 2483 FN: 7 Sensitivity % 95% CI: 97.7 (95.3-99.1) Specificity% 95% CI: 33.3 (32.3-34.4) PPV% 95% CI: 5.7 (5.1-6.3) NPV% 95% CI: 99.7 (99.4-99.9)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): none Indirectness (QUADAS 2 – applicability): none
Comments	-

15

Reference	**Papa 2012[75]**
Study type	Prospective cohort study
Study methodology	Data source: conducted at a single tertiary care Level I trauma centre in the United States. Enrolled a consecutive sample of adult patients 24 h/day, 7 days/week presenting to the ED following a blunt minor head injury (suspected mild traumatic brain injury) within 24 h of injury. Between June 2002 and August 2005. All patient assessments were made by board-certified emergency physicians or by supervised emergency medicine residents. For patients transferred from another primary care facility or hospital, assessments were performed on arrival at the study site. Every attempt was made to keep the assessment blinded. Following examination and prior to the CT, physicians completed a standard data form that listed the criteria for each of the two rules. Physicians were also asked if the rule was positive or negative for New Orleans Criteria or low, medium, or high risk for Canadian CT Head Rule.
Number of patients	n = 431 (99.3% had CT)

Reference	**Papa 2012[75]**
Patient characteristics	Age, mean (SD): 38.3 (18.0) years in GCS 15 only and 38.4 (18.0) years in GCS 13-15 Gender: 64% male and 36% female in GCS 15 only and GCS 13-15 populations GCS: *15, n=314 (72.95%)* *14, n=95 (22.04%)* *13, n=22 (5.10%* Ethnicity: not reported Setting: single tertiary care level 1 trauma centre in USA Country: USA Inclusion criteria: aged ≥18 years; and suspected mild traumatic brain injury (determined by the treating physician based on a definition of blunt trauma to the head resulting in either witnessed loss of consciousness, definite amnesia, or witnessed disorientation with an initial ED GCS score of 13 to 15). Exclusion criteria: <18 years old; minimal head injury without loss of consciousness, amnesia, or disorientation; no clear history of trauma as the primary event (e.g., primary seizure or syncope); an obvious penetrating skull injury or obvious depressed fracture; an acute focal neurologic deficit; unstable vital signs associated with major trauma; a seizure before assessment in the ED; a bleeding disorder or use of oral anticoagulants (e.g., warfarin); returned for reassessment of the same head injury; and pregnant. Adults (at least 18 years old) with mild traumatic brain injury suspected
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule (GCS 13-15 group as designed and also GCS 15 only subgroup to compare with New Orleans Criteria) New Orleans Criteria (in GCS 15 subgroup only as this was the population it was designed for use in) Reference standard

Reference	**Papa 2012[75]**
	CT (not all had CT – 99.3% had CT in GCS 13-15 group, all but three; 100% of GCS 15 only subgroup had CT) Ordering of the CT was based solely on physician judgment and was not required for inclusion in the study. Patients underwent standard CT of the head according to the judgement of the treating physician. The study protocol did not alter physician practice. CT scans interpreted by board-certified neuroradiologists who were blinded to the contents of the data collection sheet, but were aware of the patients' clinical histories. Follow-up for those without CT unclear.
Results	Outcomes: **For those with GCS 15 only (population New Orleans Criteria was developed for use in):** • any brain injury (any traumatic intracranial lesion) on CT (primary) • clinically important brain injury (secondary) • need for neurosurgical intervention (secondary) **For those with GCS 13-15 (population Canadian CT Head Rule was developed for use in):** • clinically important brain injury (primary) • need for neurosurgical intervention (primary) Need for neurosurgical intervention was defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring, or intubation for head injury (shown on CT). Clinically important brain injury was defined as any acute traumatic lesion found on CT that would normally require admission to hospital and neurologic follow-up. All brain injuries are judged clinically important unless the patient is neurologically intact and has one of these lesions on CT: solitary contusion less than 5 mm in diameter, localised subarachnoid blood less than 1 mm thick, smear subdural haematoma less than 4 mm thick, isolated pneumocephaly, or closed depressed skull fracture not through the inner table.

Reference	Papa 2012[75]
	Canadian CT Head Rule – GCS 13-15 population (n=431) – 99.3% had CT Clinically important brain injury TP: 27 FP: 290 TN: 114 FN: 0 Sensitivity % 95% CI: 100.0 (84.0-100.0) Specificity% 95% CI: 28.2 (24.0-33.0) PPV% calculated using excel sheet: 9.0 NPV% calculated using excel sheet: 100.0 Neurosurgical intervention TP: 5 FP: 142 TN: 284 FN: 0 Sensitivity % 95% CI: 100.0 (46.0-100.0) Specificity% 95% CI: 66.7 (62.0-71.0)

Reference	Papa 2012[75]
	PPV% calculated using excel sheet: 3.0 NPV% calculated using excel sheet: 100.0 **Canadian CT Head Rule – GCS 15 only population (n=314) – 100% had CT – not used in analysis given this specific population not relevant to CCHR and largest analysis favoured** Any brain injury (any traumatic intracranial lesion) on CT TP: 22 FP: 186 TN: 106 FN: 0 Sensitivity % 95% CI: 100.0 (82.0-100.0) Specificity% 95% CI: 36.3 (31.0-42.0) PPV% calculated using excel sheet: 11.0 NPV% calculated using excel sheet: 100.0 Clinically important brain injury TP: 11 FP: 197 TN: 106 FN: 0

Reference	Papa 2012[75]
	Sensitivity % 95% CI: 100.0 (68.0-100.0) Specificity% 95% CI: 35.0 (30.0-41.0) PPV% calculated using excel sheet: 5.0 NPV% calculated using excel sheet: 100.0 Neurosurgical intervention TP: 3 FP: 60 TN: 251 FN: 0 Sensitivity % 95% CI: 100.0 (31.0-100.0) Specificity% 95% CI: 80.7 (76.0-85.0) PPV% calculated using excel sheet: 5.0 NPV% calculated using excel sheet: 100.0 **New Orleans Criteria – GCS 15 only population (n=314) – 100% had CT** Any brain injury (any traumatic intracranial lesion) on CT TP: 22 FP: 262

Reference	Papa 2012[75]
	TN: 30 FN: 0 Sensitivity % 95% CI: 100.0 (82.0-100.0) Specificity% 95% CI: 10.2 (7.0-14.0) PPV% calculated using excel sheet: 8.0 NPV% calculated using excel sheet: 100.0 <u>Clinically important brain injury</u> TP: 11 FP: 273 TN: 30 FN: 0 Sensitivity % 95% CI: 100.0 (68.0-100.0) Specificity% 95% CI: 9.9 (7.0-14.0) PPV% calculated using excel sheet: 4.0 NPV% calculated using excel sheet: 100.0 <u>Neurosurgical intervention</u> TP: 3 FP: 281

Reference	**Papa 2012[75]**
	TN: 30 FN: 0 Sensitivity % 95% CI: 100.0 (31.0-100.0) Specificity% 95% CI: 9.6 (7.0-14.0) PPV% calculated using excel sheet: 1.0 NPV% calculated using excel sheet: 100.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear time interval between index test and reference standard and although the majority received CT as the reference standard, a small proportion did not undergo CT and there were no details provided about follow-up. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Pek 2015[76]**
Study type	Retrospective observational study
Study methodology	Data source: those presenting to ED of public hospital between January 2009 and April 2009 with diagnosis indicating trauma to the head were reviewed, with those with minimal and minor head injury being included in the study retrospectively. Medical records accessed for data collection. Information about high and medium risk factors as defined by Canadian CT Head Rule, abnormality present on CT if performed, the need for neurological intervention and admission or neurological follow-up collected and used for analysis.
Number of patients	n = 1127 (29.4% had CT done)
Patient characteristics	Age, mean (SD): not reported (all at least 16 years old) Gender: not reported GCS: 13-15

Reference	**Pek 2015[76]**
	Ethnicity: not reported Setting: ED of a single hospital in Singapore Country: Singapore Inclusion criteria: presenting with minor head injury (defined as witnessed loss of consciousness, definite amnesia or witnessed disorientation in a patient with GCS 13-15) or minimal head injury (no loss of consciousness, amnesia or disorientation in a patient with a GCS of 15). Exclusion criteria: <16 years; no clear history of trauma as the primary event (e.g. primary seizure of syncope); obvious penetrating skull injury or obvious depressed fracture; acute focal neurological deficit; unstable vital signs associated with major trauma; had a seizure before assessment in the ED; bleeding disorder or used oral anticoagulants; had returned for reassessment of the same head injury; or were pregnant. Adults (at least 16 years old) with minimal or mild head injury
Target condition(s)	Traumatic brain injury – minimal or mild head injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule – provides results for high-risk and medium-risk factors within this rule Reference standard CT and/or follow-up depending on outcome and individual, 29.4% had a CT scan Follow-up: duration unclear for those not having a CT.

Reference	Pek 2015[76]
Results	Outcomes: Need for neurological intervention – defined as death within 7 days, craniotomy, elevation of skull fracture, intracranial pressure monitoring or intubation for head injury. Clinically important brain injury on CT requiring admission or neurological follow-up – all brain injuries considered clinically important unless the patient was neurologically intact and had one of these lesions on CT: solitary contusion less than 5 mm in diameter; localised subarachnoid blood less than 1 mm thick; smear subdural haematoma less than 4 mm thick; isolated pneumocephaly, or closed depressed skull fracture not through the inner table. Those without CT appear to have been included in this analysis and unclear whether they were followed up for a period to confirm no CT abnormality confirmed subsequently. CTs were reported by radiologists based in the hospital. <u>Need for neurological intervention – Canadian CT Head Rule – any high-risk factor present</u> TP: 14 FP: 261 TN: 835 FN: 17 Sensitivity % 95% CI: 45.2 (27.8-67.3) Specificity% 95% CI: 76.2 (73.5-78.7) PPV% calculated using excel sheet: 5.0 NPV% calculated using excel sheet: 98.0

Reference	**Pek 2015[76]**
	Clinically important brain injury on CT – Canadian CT Head Rule – any high-risk or medium-risk factor present TP: 52 FP: 319 TN: 737 FN: 19 Sensitivity % 95% CI: 73.2 (61.2-82.7) Specificity% 95% CI: 69.8 (66.9-72.5) PPV% 95% CI: 14.0 (10.7-18.1) NPV% 95% CI: 97.5 (96.0-98.4)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if consecutive or random sample used, unclear if index test was applied without knowledge of the reference standard, same reference standard not used in all participants and unclear process of follow-up/outcome confirmation in those that did not receive a CT scan. Indirectness (QUADAS 2 – applicability): none.
Comments	-

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Reference	**Tan 2018[92]**
Study type	Retrospective study
Study methodology	Data source: consecutive patients presenting with a cute minor head injury to ED at National University Hospital of Singapore over 6-month period between 1st January 2013 to 30th June 2013. Academic medical centre with guidelines for use of Canadian CT Head Rule for patients presenting with minor head injury to aid decision-making about whether to perform head CT. Electronic medical records used to select patients using ICD codes for primary and secondary diagnoses.
Number of patients	n = 349

Reference	**Tan 2018[92]**
Patient characteristics	Age, median (IQR): 48 (30-68) years Gender: 62.5% male and 37.5% female GCS: *13, 5.4%* *14, 11.2%* *15, 83.4%* Antiplatelet therapy: *Aspirin, 7.2%* *Clopidogrel, 1.7%* *Aspirin or clopidogrel, 1.4%* Ethnicity: not reported Setting: single ED of hospital in Singapore Country: Singapore Inclusion criteria: acute minor head injury (history of blunt head trauma to head within 24 h of presentation to ED and a GCS score of 13-15) Exclusion criteria: patients below 16 years of age; obvious penetrating skull injury or depressed skull fracture; unstable vital signs associated with major trauma; presence of bleeding disorder (e.g. haemophilia) or use of oral anticoagulants; patients returning for reassessment of the same head injury; contraindications for CT (e.g. pregnancy); and patients with neurological deficits. Adults (at least 16 years old) with minor head injury
Target condition(s)	Traumatic brain injury – minor head injury
Index test(s) and reference standard	<u>Index test:</u> Canadian CT Head Rule

Reference	**Tan 2018[92]**
	Reference standard CT or follow-up – follow-up of up to 14 days used in those that did not undergo CT evaluation to determine reattendances at the ED. 14-day time-point chosen as presence of intracranial haemorrhage, if any, would have resulted in clinically significant manifestations in these patients by then.
Results	Outcomes: Clinically significant CT finding – epidural haematoma, subdural haematoma of thickness ≥ 4 mm, subarachnoid haemorrhage of thickness > 1 mm, intracerebral haematoma, intraventricular haemorrhage, diffuse cerebral oedema, cerebral contusion of diameter ≥ 5 mm, pneumocephalus and depressed skull fracture. Clinically insignificant brain injuries were focal subarachnoid haemorrhage, cerebral contusion of thickness < 5 mm, subdural haematoma of thickness < 4 mm, isolated pneumocephalus and closed depressed skull fracture not through the inner table. CT interpretations by radiologists were considered as the reference standard. Clinically significant CT finding – Canadian CT Head Rule TP: 37 FP: 172 TN: 135 FN: 5 Sensitivity % calculated using excel sheet: 88.0 Specificity% calculated using excel sheet: 44.0 PPV% calculated using excel sheet: 18.0 NPV% calculated using excel sheet: 96.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if index test interpreted without knowledge of reference standard and not all received the same reference standard (71% had CT). Indirectness (QUADAS 2 – applicability): none

Reference	**Tan 2018[92]**
Comments	-

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Reference	**Vaniyapong 2020[94]**
Study type	Retrospective review of prospective cohort study
Study methodology	Data source: secondary analysis of recently published prospective cohort data, involving two large medical centres in Chiang Mai. Patients with mild traumatic brain injury visiting the two centres from 1st December 2013 to 31st January 2016 assessed for eligibility. Eligible patients evaluated and managed according to local mild traumatic brain injury guidelines. Those were intracranial injury highly suspected sent for emergency CT scan and treated accordingly. Those with indefinite signs may be admitted to observational unit for at least 24 h from onset of injury. If any deterioration was observed, patient would be sent for emergency CT scan. Those that were stable without signs of intracranial injury may be discharged with an appointment for follow-up visit, depending on discretion of emergency physicians.
Number of patients	n = 1164 (41.9% had CT)
Patient characteristics	Age, median (IQR): 34.0 (22.0-56.0) years Gender: 63.4% male and 36.6% female GCS: *13, 1.46%* *14, 9.02%* *15, 89.52* Ethnicity: not reported Setting: two medical centres in Thailand Country: Thailand Inclusion criteria: patients with a history of blunt head injury, aged ≥16 years, and GCS 13-14 or GCS 15 with one of the following signs or symptoms: diffuse headache, vomiting, loss of consciousness, posttraumatic amnesia, posttraumatic seizure, drug or alcohol intoxication, history of previous neurological procedure, current anticoagulant user (except antiplatelet), signs of skull base fracture, palpable stepping at the skull, and significant wound at the scalp

Reference	**Vaniyapong 2020[94]**
	Exclusion criteria: uncertain history of trauma and time from onset of injuries >24 h. Adults (at least 16 years old) with mild traumatic brain injury
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule – any one of 7 findings Newly developed and validated rule (model-based score) – cut-point of ≥2 for positive CT finding and ≥7 for surgical intervention. Developed based on a multivariate model. Newly developed and validated rule (clinical-based score) cut-point of ≥2 for positive CT finding and ≥3 for surgical intervention. Developed based on a multivariate model with input of consensus from clinical experts at the institute. Reference standard CT and/or follow-up (41.9% had CT either at initial evaluation in the ED, or during admission or follow-up) As CT scan was not done to verify outcome in all patients, clinical follow up visit at 7 days from injury was arranged. Patients whose signs/symptoms were not improved, or progressed, or could not go to regular work were scheduled for CT scans. Patients who were not present to the visit were contacted by telephone for an assessment of their conditions by research staff. No loss to follow-up at 7 days.
Results	Outcomes: Traumatic intracranial finding on CT scan – any types of intracranial haemorrhage (e.g. subdural haemorrhage, epidural haematoma, subarachnoid haemorrhage and intracerebral haematoma) and depressed skull fracture. Linear skull fracture was not considered as an intracranial finding of interest. Radiologists were unblinded when interpreting and reporting official CT results.

Reference	Vaniyapong 2020[94]
	Neurosurgical intervention – within 7 days of injury, including craniotomy or craniectomy, elevation of skull fracture, external ventricular drainage, Burr holes and intracranial pressure monitoring. <u>Traumatic intracranial finding on CT scan – Canadian CT Head Rule – any one of 7 factors present</u> TP: 214 FP: 711 TN: 209 FN: 30 Sensitivity % 95% CI: 87.7 (82.9-91.5) Specificity% 95% CI: 22.7 (20.0-25.6) PPV% calculated using excel sheet: 23.0 NPV% calculated using excel sheet: 87.0 <u>Surgical intervention required – Canadian CT Head Rule – any one of 7 factors present</u> TP: 54 FP: 871 TN: 236 FN: 3 Sensitivity % 95% CI: 94.7 (85.4-98.9) Specificity% 95% CI: 21.3 (25.6-31.0) PPV% calculated using excel sheet: 6.0

Reference	Vaniyapong 2020[94]
	NPV% calculated using excel sheet: 99.0 <u>Traumatic intracranial finding on CT scan – Model-based score (newly developed and validated) – cut-point ≥2</u> TP: 242 FP: 845 TN: 75 FN: 2 Sensitivity % 95% CI: 99.2 (97.1-99.9) Specificity% 95% CI: 8.2 (6.5-10.1) PPV% calculated using excel sheet: 22.0 NPV% calculated using excel sheet: 97.0 <u>Surgical intervention required – Model-based score (newly developed and validated) – cut-point ≥7</u> TP: 57 FP: 739 TN: 368 FN: 0 Sensitivity % 95% CI: 100.0 (93.7-100.0) Specificity% 95% CI: 33.2 (30.5-36.1) PPV% calculated using excel sheet: 7.0

Reference	Vaniyapong 2020[94]
	NPV% calculated using excel sheet: 100.0 <u>Traumatic intracranial finding on CT scan – Clinical-based score (newly developed and validated) – cut-point ≥2</u> TP: 239 FP: 771 TN: 149 FN: 5 Sensitivity % 95% CI: 98.0 (95.3-99.3) Specificity% 95% CI: 16.2 (13.9-18.7) PPV% calculated using excel sheet: 24.0 NPV% calculated using excel sheet: 97.0 <u>Surgical intervention required – clinical-based score (newly developed and validated) – cut-point ≥3</u> TP: 57 FP: 794 TN: 313 FN: 0 Sensitivity % 95% CI: 100.0 (93.7-100.0) Specificity% 95% CI: 28.3 (25.6-31.0) PPV% calculated using excel sheet: 7.0

Reference	**Vaniyapong 2020[94]**
	NPV% calculated using excel sheet: 100.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if consecutive or random sample enrolled, radiologists were not blinded when interpreting CT results, not all patients received the same reference standard (only 41.9% had a CT) and the follow-up period for those without CT was 7 days rather than at least 2 weeks specified in the protocol Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Yang 2017[96]**
Study type	Retrospective study
Study methodology	Data source: single-centre study performed in First Affiliated Hospital of Zhejiang University College of Medicine.
Number of patients	n = 625
Patient characteristics	Age, mean (SD): 47.0 (19.68) years, 79.52% 18-65 years and 20.48% ≥65 years Gender: 54.24% male and 45.76% female GCS: *13, 2.72%* *14, 2.40%* *15, 94.88%* Ethnicity: not reported

Reference	**Yang 2017[96]**
	Setting: single hospital in China Country: China Inclusion criteria: history of head trauma delivered to the institute; GCS 13-15 when patient reached the hospital; aged >18 years; and underwent cranial CT within 24 h post-head trauma Exclusion criteria: none reported Adults (>18 years) with mild traumatic brain injury
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: Canadian CT Head Rule – any one of the included items present New Orleans Criteria – any one of the included items present (usually only applied to GCS15 but was applied to whole population of GCS 13-15 in this study) Reference standard CT (all had a CT) First cranial CT post-head trauma were reviewed independently by two neurosurgeons to identify positive findings. If opinions differed then a third neurosurgeon evaluated the images. Follow-up duration not mentioned.
Results	Outcomes: Positive finding on CT – those identified included cranial fracture, epidural haematoma, subdural haematoma, intracerebral haematoma, subarachnoid haemorrhage and cerebral contusions. Full list of abnormalities that would have been included for this outcome not given. Positive CT finding – Canadian CT Head Rule – any one of included items present

Reference	Yang 2017[96]
	TP: 82 FP:272 TN: 271 FN: 0 Sensitivity % 95% CI: 100.0 (CIs not reported) Specificity% calculated using excel sheet: 50.0 (reported to be 43.36 in paper but based on raw data is 50.0) PPV% calculated using excel sheet: 23.0 NPV% calculated using excel sheet: 100.0 <u>Positive CT finding – New Orleans Criteria – any one of included items present</u> TP: 82 FP: 336 TN: 207 FN: 0 Sensitivity % 95% CI: 100.0 (CIs not reported) Specificity% calculated using excel sheet: 38.0 (reported to be 33.12 in paper but based on raw data is 38.0) PPV% calculated using excel sheet: 20.0 NPV% calculated using excel sheet: 100.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if a consecutive or random sample was enrolled, unclear if the index tests were applied without knowledge of the reference standard and unclear time interval between reference standard and index test.

Reference	**Yang 2017[96]**
	Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Yarlagadda 2019[97]**
Study type	Retrospective cohort study
Study methodology	Data source: identified inpatient falls with injury over 1 year within large health system of an urban tertiary teaching hospital, three suburban community hospitals and inpatient rehabilitation facility. All inpatient services were included. Patient safety database at the institution used to identify inpatient falls with any type or degree of injury at inpatient facilities between 1st May 2015 and 30th April 2016.
Number of patients	n = 332 (57% received a head CT scan)
Patient characteristics	Age, mean (SD): 67.9 (17.4) years Gender: 52.0% males and 48% females GCS: not reported Anticoagulation/antithrombotic: 59.6% - majority were taking Ethnicity: *Caucasian, 56%* *African-American, 39%* *Other, 5%* Setting: inpatients of tertiary hospital, three community hospitals and inpatient rehabilitation facility Country: USA Inclusion criteria: those with an inpatient fall of any type or degree of injury at five inpatient facilities Exclusion criteria: those sustaining a fall as an outpatient or in the ED Adults (based on mean age ~68 years) with an inpatient fall, not specified that it is those also with head injury

Reference	**Yarlagadda 2019[97]**
Target condition(s)	Traumatic brain injury – those with inpatient falls, unclear if all were suspected of having traumatic brain injury (indirectness). Also inpatient population rather than general population that might have suspected head injury so may also be indirect in this way.
Index test(s) and reference standard	Index test: New Orleans Criteria – completed using manual chart review including physician and nursing notes. Reference standard CT (57% received a head CT scan). Follow-up: for those that did not receive head CT, method of confirming absence of positive head CT findings was unclear and no follow-up interval mentioned.
Results	Outcomes: Positive head CT finding – defined as any acute intracranial process. Head CT result reports were reviewed for any significant findings (any acute intracranial process) as recorded in text entries by the radiologists. Clinically important brain injury on CT – NOC – positive for at least one NOC component TP: 6 FP: 244 TN: 81 FN: 1 Sensitivity % 95% CI: 85.7 (43.1-99.6) Specificity % 95% CI: 23.8 (19.2-27.8) – when calculated using excel sheet is 25.0 PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 99.0
Source of funding	Not reported

Reference	**Yarlagadda 2019[97]**
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if a consecutive or random sample was enrolled, unclear if index test was applied without knowledge of the reference standard and reference standard differed between patients, with only 57% receiving a CT scan and it being unclear how outcome was confirmed in other patients Indirectness (QUADAS 2 – applicability): serious. Population is more specific as it only includes inpatients with falls and it is unclear whether there was a suspicion of head injury for all patients.
Comments	-

D.2 Adults – studies previously included in the review

Studies extracted previously as part of the guideline (not reproduced from HTA)

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Bouida 2013[11]	Prospective diagnostic cohort (validation of Canadian CT head rule and the New Orleans Criteria)	N = 1582 (1664 with 82 excluded due to incomplete data). Inclusion criteria: Consecutive patients presenting to the emergency department with mild head injury (blunt trauma to the	Age, mean (range) = 32, (14 - 97) Sex, male = 1212 (76.6%) Initial score on GCS 15 = 1249	Baseline data recorded and included clinical criteria to define New Orleans Criteria and Canadian Head rule decision rule. Participating physicians were asked to indicate at the end of their initial assessment whether the patient was rule positive or negative. After clinical assessment, a standard CT scan of the head was performed at the discretion of the treating physician. 2 senior	Intracranial lesion (Canadian CT Head Rule)	TP = 207 FP = 472 FN= 11 TN = 892 Sensitivity = 95 (92 - 98) Specificity = 64 (62 - 68) PPV = 30 (27 - 33) NPV = 99 (98 - 100	Source of funding: Research supported by a grant from the Tunisian State Department of Research. Quality assessment

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
	Setting: Multicenter study, Tunisia	head within 24h, with a GCS of 13 - 15 and at least one of: history of loss of consciousness, short-term memory deficit, amnesia for the traumatic event, posttraumatic seizure, vomiting, headache, external evidence of injury above the clavicles, confusion, and neurological deficit. Exclusion criteria: Younger than 10 years, had a GCS < 13 or instable vital signs, were pregnant, received warfarin or had a bleeding disorder, had an obvious penetrating skull injury, or had contraindications for CT..	Received CT = 1122 (70.9%)	radiologists, blinded to the patient data, independently interpreted the CT scan. Follow up information for patients who did not undergo CT scanning was collected by structured telephone interview. Patients discharged home received instructions for observation and return to the ED for clinical reassessment if they had: headache, memory and concentration problems, seizure, focal motor findings, and inability to return to usual daily activities. Need for neurosurgical intervention: death or need for any of the following within 30 days of injury: craniotomy, monitoring of intracranial pressure, need for intubation for the treatment of head injury. Brain lesions defined as any acute intracranial finding revealed on CT that was attributable to acute injury. Patients who did not undergo CT were classified as having no clinically important brain injury if at 15 days after ED discharge none of the above criteria	Neurosurgical intervention (Canadian CT Head Rule)	TP = 34 FP = 622 FN= 0 TN = 926 Sensitivity = 100 (90 - 100) Specificity = 60 (44 - 76) PPV = 5 (3 - 7) NPV = 100 (99 - 100)	from 2022 update: Risk of bias – serious – unclear time interval between index test and reference standard and not all receiving the same reference standard Indirectness - none
					Intracranial lesion (New Orleans criteria)	TP = 187 FP = 976 FN= 31 TN = 388 Sensitivity = 86 (81 - 91) Specificity = 28 (26 - 30) PPV = 16 (14 - 18) NPV = 93 (90 - 96)	
					Neurosurgical intervention (New Orleans criteria)	TP = 28 FP = 1152 FN= 6 TN = 396 Sensitivity = 82 (69 - 95) Specificity = 26 (24 - 28)	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
				requiring return to ED are present,.		PPV = 2 (1 - 3) NPV = 99 (98 - 100)	

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Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Ro 2011[78]	Prospective diagnostic cohort (comparing CCHR, NOC and NEXUS II CT rules) Setting: 5 tertiary academic emergency departments in Korea.	N = 7131 Inclusion criteria: Consecutive patients enrolled who sustained acute blunt head trauma (any physical evidence of head trauma, unless they had an obvious penetrating head injury.	Patients with minor head injury Number of patients meeting inclusion criteria for rules: CCHR: 696 Mean age (SD) = 46.1 (±18.9) Sex, male = 477 (68.5%) NOC: 657	Used a surveillance registry to capture predictive variables for intracranial injury based on CT rules. Patients stratified according to CCHR (high and medium risk criteria), NOC and NEXUS II rules. Patients enrolled were only considered for decision rule analyses if they met the inclusion/exclusion criteria of the specific decision rules. Primary data collection was by general physicians (injury team). Not all patients underwent CT, but all patients underwent a structured proxy outcome	Clinically important brain injury (any traumatic finding identified on CT scan that required hospital admission and neurosurgical follow-up.	CCHR TP = 112 FP = 32 FN= 228 TN = 324 Sensitivity = 79.2% (70.8 – 86%) Specificity = 41.3% (37.3 – 45.5%) NOC TP = 91 FP = 433 FN= 8 TN = 125 Sensitivity = 91.9% (84.7 – 96.5%)	Source of funding: Korean Centers for Disease Control and Prevention Quality assessment from 2022 update: Risk of bias – serious – unclear time interval between index test

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
			Mean age (SD) = 42.8 (±20.7) Sex, male = 451 (68.7%) NEXUS II: 2951 Mean age (SD) = 39.9 (±22.9) Sex, male = 2059 (69.8%)	measure via telephone to capture admission and operation history and other hospital and neurologic outcomes at 6 months. CT scans were interpreted by the clinical radiologist and also independently retrospectively reviewed by an emergency physician.		Specificity = 22.4% (19 – 26.1%) NEXUS II TP = 511 FP = 1271 FN= 65 TN = 1104 Sensitivity = 88.7% (85.8 – 91.2%) Specificity = 46.5% (44.5 – 48.5%)	and reference standard and not all receiving the same reference standard Indirectness - none

Summary of studies reproduced from the HTA: decision rules for adults with mild head injury, definitions of outcomes and reference standards

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
Arienta et al. 1997[2]	Arienta et al. 1997	Intracranial lesion: not defined. Injuries listed include extradural haematoma, cortical contusion, subarachnoid haemorrhage, pneumocephalus,	CT scan or follow-up telephone call. Further details NR	762/9917 (7.7%)	Neurosurgery or death	Retrospective chart review, telephone follow-up	Quality assessment from 2022 update: Risk of bias – very serious – unclear if consecutive sample enrolled

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		depressed fracture with contusion, intracerebral haematoma and subdural haematoma					and exclusion criteria unclear, unclear if index test and reference standard were interpreted without knowledge of the other, unclear time interval between index test and reference standard and not all received the same reference standard Indirectness – none
Fabbri et al. 2005[24]; Stein et al. 2009[87]	CCHH, NCWFNS, NICE NOC, Nexus II, Scandinavian	Stein et al. 2009 – any lesion: surgical (intracranial haematoma large enough to require surgical evacuation) or nonsurgical (other intracranial abnormality diagnosed on CT) Fabbri et al. 2005 – any post-traumatic lesion at CT within 7 days from trauma:	Patients were managed accord to NCWFS guidelines where low-risk patients sent home without CT, medium risk patients given CT and observed for 3–6 hours if negative then discharged, high-	4177/7955 (52.5%)	Stein et al. 2009 – surgical intracranial lesion: intracranial haematoma large enough to require surgical evacuation Fabbri et al. 2005: Haematoma evacuation, skull fracture elevation within first 7 days of injury. Injuries after this period not considered in this analysis	Assume Hospital records	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 36 of HTA paper Indirectness - none

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		depressed skull fracture, intracerebral haematoma/brain contusions, subarachnoid haemorrhage, subdural haematoma, epidural haematoma, intraventricular haemorrhage	risk patients given CT and observed 24–48 hours. All discharged with written advice of signs and symptoms with which they should return				
Haydel et al. 2000[38]	NOC	ICI – presence of acute traumatic ICI: a subdural, epidural or parenchymal haematoma, subarachnoid haemorrhage, cerebral contusion or depressed skull fracture	CT scan	520/520 (100%) 909/909 (100%)a	NA	NA	Quality assessment from 2022 update: Risk of bias – serious – unclear if reference standard interpreted without knowledge od index test and unclear time interval between index test and reference standard Indirectness - none
Holmes et al. 1997[40]	Miller et al. 1997	Abnormal CT scan: any CT scan showing an acute traumatic lesion (skull fractures or intracranial lesions:	CT scan: patients with abnormal CT scan	264/264 (100%)	Neurosurgery	Patients with abnormal CT scan followed to discharge Those with normal CT	Risk of bias based on checklist in HTA: very serious – based on

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		cerebral oedema, contusion, parenchymal haemorrhage, epidural haematoma, subdural haematoma, subarachnoid haemorrhage or intraventricular haemorrhage)	followed to discharge; those with normal CT not studied further			not studied further	limitations described in table on page 36 of HTA paper Indirectness - none
Ibanez and Arikan 2004[43]	Ibanez and Arikan 2004, Stein 1996, Tomei et al. 1996, Arienta et al. 1997, Lapierre 1998, Murshid 1998, NOC, Scandinavian, SIGN 2000, NCWFNS, CCHR, EFNS	Relevant positive CT scan: acute intracranial lesion, not including isolated cases of linear skull fractures or chronic subdural effusions	CT scan	1101/1101 (100%)	NA	NA	Risk of bias based on checklist in HTA: serious – based on limitations described in table on page 36 of HTA paper Indirectness - none
Madden et al. 1995[56]	Madden et al. 1995	Clinically significant scan: pathology related to trauma affecting the bony calvaria or cerebrum (including non-depressed skull fractures, excluding scalp haematomas,	CT scan: scans examined for bony and soft tissue injury, herniation, pneumocephalus, penetrating injury and the size and location of any	537/537 (100%) 273/273 (100%)[(a)]	NA	NA	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 36 of HTA paper

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		those with no bony skull or intracerebral pathology)	cortical contusions, lacerations or external axial haematomas				Indirectness - none
Miller et al. 1997[60]	Miller et al. 1997	Abnormal CT scan: acute traumatic intracranial lesion (contusion, parenchymal haematoma, epidural haematoma, subdural haematoma, subarachnoid haemorrhage) or a skull fracture	CT scan: within 8 hours of injury	2143/2143 (100%)	Surgical intervention: craniotomy to repair an acute traumatic injury or placement of a monitoring bolt	Hospital records of those with positive CT scan followed until discharge	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 36 of HTA paper Indirectness - none
Mower et al. 2005[62]	NEXUS II	Significant ICI: any injury that may require neurosurgical intervention, (craniotomy, intracranial pressure monitoring, mechanical ventilation), lead to rapid clinical deterioration or result in significant long-term neurological impairment	CT scan	13,728/13,728 (100%)	NA	NA	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 36 of HTA paper Indirectness - none
Ono et al. 2007[67]	Ono et al. 2007	Intracranial lesion: not defined. Injuries listed include subdural and epidural haematoma,	CT scan	1064/1064 (100%), 152/168	NA	NA	Risk of bias based on checklist in HTA:

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		subarachnoid haemorrhage, contusion, pneumocephalus		(90.5%)[a]			very serious – based on limitations described in table on page 36 of HTA paper Indirectness - none
Rosengren et al. 2004[79]	CCHR	Clinically significant ICI: CT abnormalities not significant if patient neurologically intact and had only one of the following: solitary contusion < 5 mm in diameter, localised subarachnoid blood < 1 mm thick, smear subdural haematoma < 4 mm thick, isolated pneumocephaly, closed depressed skull fracture not through the inner table (as per Stiell et al. 2001)	CT scan	240/240 (100%)	Neurological intervention: not defined	NA	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 36 of HTA paper Indirectness - none
Smits et al. 2005[83] Smits et al. 2007[84]	CCHR, NOC, CHIP, NCWFNS, EFNS, NICE, SIGN, Scandinavian, CHIP	Any neurocranial traumatic finding on CT: any skull or skull base fracture and any intracranial traumatic lesion Smits et al. 2007 (CHIP derivation)	CT scan	3181/3181 (100%) 1307/1307 (100%)[b]	Neurosurgery: a neurosurgical intervention was any neurosurgical procedure (craniotomy, intracranial pressure monitoring, elevation of depressed	Assume patient records	Risk of bias based on checklist in HTA: very serious – based on limitations described in

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		definition differs: any intracranial traumatic findings on CT that included all neurocranial traumatic findings except for isolated linear skull fractures			skull fracture or ventricular drainage) performed within 30 days of the event		table on page 36 of HTA paper Indirectness - none
Stiell et al. 2001[90]	CCHR	Clinically important brain injury on CT: all injuries unless patient neurologically intact and had one of following: solitary contusion < 5 mm, localised subarachnoid blood < 1 mm thick, smear subdural haematoma < 4 mm thick, closed depressed skull fracture not through inner table	1. CT scan ordered on basis of judgement of physician in ED or result of follow-up telephone interview 2. Proxy telephone interview performed by registered nurse (24.4%). For those whose responses did not warrant recall for a CT scan this was the only reference standard	2078/3121 (67%)	Within 7 days: death due to head injury, craniotomy, elevation of skull fracture, intracranial pressure monitoring, intubation for head injury demonstrated on CT	Performance Of neurosurgery as reported in patient records and 14-day follow up telephone interview (interview 100% sensitive for need for neurosurgery)	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 36 of HTA paper Indirectness - none
Stiell et al. 2005[89]	CCHR, NOC	As per Stiell et al. 2006	As per Stiell et al. 2001	2171/2707 (80.2%) 1378/1822 (75.6%)[(b)]	As per Stiell et al. 200126	As per Stiell et al. 2001	Risk of bias based on checklist in HTA: very serious – based on

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
							limitations described in table on page 36 of HTA paper Indirectness - none

CHIP, CT in Head Injury Patients; EFNS, European Federation of Neurological Societies; ICD, International Classification of Diseases; NA, not applicable; NCWFNS, Neurotraumatology Committee of the World Federation of Neurosurgical Societies; NEXUS II, National Emergency X-Radiography Utilization Study II; NR, not reported.
(a) Different cohort of data.
(b) Subset of cohort.

Decision rules for adults with mild head injury reproduced from the HTA

Criteria / Decision rule	CCHR – High risk	CCHR – Medium risk	NOC	NICE 2003, 2007[a] - lenient	NICE 2003, 2007[a] - strict	NCWFNS – high risk	NCWFNS – medium risk	Arienta[b] groups β and ϒ
Tested in study by	Stiell 2001, Stiell 2005, Stein 2009, Rosengren 2004	Stiell 2001, Steill 2005, Stein 2009, Rosengren 2004, Smits 2005, Ibanez 2004[c]	Haydel 2000, Ibanez 2004, Smits 2005, Stiell 2005, Stein 2009	Fabbri 2005 (NICE 2003), Smits 2007 (NICE 2003), Stein 2009 (NICE 2007)	Smits 2007	Smits 2007	Fabbri 2005, Smits 2007, Stein 2009, Ibanez 2004[c]	Arienta 1997, Ibanez 2004[c]
Eligibility criteria[d]	GCS 13-15, clinical characteristics. Some significant exclusions.		GCS 15, clinical characteristics[e-g]	Sustained head injury		Mild, minor or trivial head injury (GCS 14-15[h])		Head Injury (GCS 9-15)
Mental status								Impaired consciousness
Focal/neurological deficits				Any		Neurological deficits		Neurological deficits

Criteria Decision rule	CCHR – High risk	CCHR – Medium risk	NOC	NICE 2003, 2007[a] - lenient	NICE 2003, 2007[a] - strict	NCWFNS – high risk	NCWFNS – medium risk	Arienta[b] groups β and ϒ
Skull fracture	Suspected open, depressed or basal			Suspected open, depressed or basal[i]		Any		Otorrhagia/otorrhoea, rhinorrhoea, signs of basal skull fracture
LOC							Any	Transitory
Vomiting	≥2		Any	Recurrent			Any	Any
Age	≥65		>60 years	≥65 years if with LOC/amnesia[a, i]		>60 years[jk]		
Amnesia		Amnesia before impact of ≥30 minutes		Amnesia before impact of ≥30 minutes				Any
Coagulopathy				If with LOC/amnesia[i]		Any		Anticoagulant therapy or coagulopathy
Seizures			Any	PTS		Pre-trauma epilepsy		Any or epileptic
Visible injury			Trauma above clavicles					Penetrating or perforated wounds
Intoxication			Any			Any		Alcoholic patients
Behaviour								Uncooperative
Headache			Any				Diffuse	
Previous neurosurgery								Intracranial operations
Failure to improve	GCS <15 at 2 hours after injury			GCS <15 at 2 hours after injury[i]		Any		

Criteria / Decision rule	CCHR – High risk	CCHR – Medium risk	NOC	NICE 2003, 2007[a] - lenient	NICE 2003, 2007[a] - strict	NCWFNS – high risk	NCWFNS – medium risk	Arienta[b] groups β and ϒ
Mechanism of injury		Dangerous[l]		Dangerous, if with LOC/amnesia[i]				
Deterioration in mental status								
Other								Subgaleal swelling

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37 **Decision rules for adults with mild head injury reproduced from HTA continued**

Criteria / Decision rule	EFNS[m] – CT mandatory	EFNS – CT recommended	Madden 1995	ONO 2007	Scandinavian – CT mandatory	Scandinavian – CT recommended	SIGN 2000 – CT as emergency	SIGN 2000 – CT urgently	NEXUS II
Tested in study by	Smits 2007	Ibanez 2004[c], Smits 2007	Madden 1995	Ono 2007	Smits 2007	Smits 2007, Smits 2007, Ibanez 2004[c]	Smits 2007	Smits 2007, Ibanez 2004[c]	Stein 2009, Mower 2005
Eligibility criteria[d]	Mild TBI, GCS 13-15		Acute head trauma	MHI	Minimal, mild and moderate head injury		Patients with head injury		Blunt head trauma
Mental status	GCS 13-15	GCS 15	GCS <15[p]	JCS >0	GCS 9-13	GCS 14-15[n]	GCS ≤12[o]	GCS <15 with failure to improve within 4 hours	Altered level of alertness
Focal/neurological deficits	Present	P	Acute papillary inequality		Present		Progressive signs	New signs that are not getting worse	Neurological deficit

Criteria Decision rule	EFNS[m] – CT mandatory	EFNS – CT recommended	Madden 1995	ONO 2007	Scandinavian – CT mandatory	Scandinavian – CT recommended	SIGN 2000 – CT as emergency	SIGN 2000 – CT urgently	NEXUS II
Skull fracture	Clinical signs skull fracture (skull base or depressed)	P	Palpable depressed skull fracture, signs of basilar skull fracture		Radiographically demonstrated skull fracture or clinical signs of depressed or basal skull fracture			Radiological/clinical evidence of a fracture. whatever the level of consciousness	Evidence of significant skull fracture
LOC		<30 minutes[p]	History of LOC or LOC>5 mins	Any	>5 minutes	≤5 minutes		O	
Vomiting	Any	P		Vomiting or nausea				Nausea or vomiting	Persistent
Age	<2 years[p] or >60 years			60 years[p]					≥65 years
Amnesia	Continued PTA	PTA <60 minutes		Any				O	
Coagulopathy	Coagulation disorders	P			Therapeutic anticoagulation or haemophilia				Coagulopathy
Seizures	Any	P			PTS				
Visible injury	Trauma above clavicles	P	Facial injury, penetrating skull injury						Scalp haematoma
Intoxication	Alcohol/drugs	P							
Behaviour			Combativeness					Irritability/altered behaviour	Abnormal behaviour
Headache	Severe	P		Any				Severe or persistent	

Criteria / Decision rule	EFNS[m] – CT mandatory	EFNS – CT recommended	Madden 1995	ONO 2007	Scandinavian – CT mandatory	Scandinavian – CT recommended	SIGN 2000 – CT as emergency	SIGN 2000 – CT urgently	NEXUS II
Previous neurosurgery					Shunt-treated hydrocephalus				
Failure to improve								Failure to improve (from GCS <15) within 4 hours of clinical observation	
Mechanism of injury	High-energy accident[q]	P						0	
Deterioration in mental status			Decreasing level of consciousness				Deteriorating level of consciousness		
Other	Unclear or ambiguous accident history	P			Multiple injuries			'Other features' are not fully enumerated[o]	

EFNS, European Federation of Neurological Societies; JCS, Japanese Coma Scale; NEXUS II, National Emergency X-Radiography Utilization Study II; PTA, post-traumatic amnesia.

(a) NICE 2003 and 2007 rules: for children < 16 years, there are additional indications listed in the 2007 update. These may have been applied by Stein et al. 2009 as their cohort included adolescents. Adults over 65 years with LOC or amnesia are included in the strict and lenient criteria in 2003 version, but only included in the strict criteria in 2007 version.

(b) Rule consists of four risk groups according to clinical characteristics, covering all severity of injury. Clinical characteristics from the two risk groups that predict need for a CT scan in patients with GCS 13–15 are presented here, taking the most inclusive definition where a characteristic is covered by more than one risk group.

(c) Assume the most inclusive version of the rule used by Ibanez and Arikan.

(d) Eligibility criteria are either the inclusion criteria of the derivation cohort or the patients the rule was intended for where there is no derivation cohort.

(e) Not listed in Smits et al.

(f) Not listed in Stiell et al.

(g) Not reported in Rosengren et al.

(h) Reported in Smits et al. as GCS 13–14.

(i) Reported in Fabbri et al. as GCS 14 or GCS < 14 at any point, signs of basal skull fracture only, any vomiting and LOC/amnesia proviso not included for coagulopathy, age and mechanism of injury.
(j) Not reported in Fabbri et al.
(k) Not reported in Stein et al.
(l) Dangerous mechanism is a pedestrian struck by a motor vehicle, an occupant ejected from a motor vehicle or a fall from an elevation of ≥ 3 feet or five stairs.
(m) Rule defines four risk categories according to clinical characteristics for those with GCS 13–15. Category 0 is discharged, category 1 is recommended to have CT or radiography, and categories 2 and 3 are required to have CT scan. Clinical characteristics for the three groups that predict need for CT scan (categories 1, 2 and 3) are presented here, taking the most inclusive definition where a characteristic is covered by more than one risk category.
(n) Reported in Smits et al. as GCS 13–14.
(o) Sign emergency reported in Smits et al.70 as GCS 13–14 at 4 hours post injury. Sign CT urgently reported as including LOC, PTA, external injury to the skull, unclear history and non-trivial mechanism of injury, which are listed as indications for skull radiography in the original rule.
(p) Reported in Smits et al. with the following differences: LOC time not defined, < 2 years not listed, all risk factors identified for CT mandatory version of the rule also listed for CT recommended version of the rule.
(q) Reported in Vos et al. as vehicle accident with initial speed > 64 km/hour, major auto deformity, intrusion into passenger compartment > 30 cm, extrication time from vehicle > 20 minutes, falls from > 6 m, rollover, auto–pedestrian accidents or motorcycle crash at speed > 32 km/hour or with separation of rider and bike.

D.3 Children/infants – studies extracted as part of the current update

Reference	Atabaki 2016[3]
Study type	Planned secondary analysis of data from a prospective observational cohort study
Study methodology	Data source: Data of children with minor blunt head trauma from 25 PECARN centres. The clinical prediction rules were derived between June 2004 and March 2006
Number of patients	n = 8,627 (eligible patients enrolled in the validation group) n= 43,904 children <18 years (enrolled in the parent study) From that population, 42,412 had GCS scores of 14 or 15, and from these, the two age-dependent prediction rules were derived on 33,785 eligible children, and subsequently validated on the 8,627 eligible patients in the current study.
Patient characteristics	*Age, mean (SD): 6.8 (5.4)* *Gender (male): 5,322 (62.6%)* *GCS: 14-15* Cranial CT rate: 2,857 (33.6%)

Reference	**Atabaki 2016[3]**
	TBI on CT: 180/2,857 (6.3%) Clinically important TBI: 87 (1.0%) Neurosurgery: 16 (0.2%) *Ethnicity*: not reported *Setting*: 25 PECARN [Pediatric Emergency Care Applied Research Network (PECARN) TBI prediction Rules]EDs *Country*: USA *Inclusion criteria*: The parent study included children <18 years with blunt head trauma and Glasgow Coma Scale (GCS) scores of 14 or 15, evaluated in any one of the PECARN EDs. For this analysis to compare clinician suspicion and the prediction rules, the study used the validation population (n = 8,627) to prevent unfair comparisons using prediction rules, which may be overfit to the data from which they were derived. The study also included only patients for whom clinician suspicion of ciTBI was documented. Clinically important TBI (ciTBI) using the following criteria: death from TBI, neurosurgery, intubation for more than 24 hours for TBI, or hospital admission of 2 nights or more associated with TBI on CT. *Exclusion criteria*: Patients were excluded for the following: ED presentation >24 hours after their injuries, penetrating trauma, known brain tumors, pre-existing neurologic disorders complicating the assessment, neuroimaging at an outside hospital before transfer, or trivial mechanisms of injury (ground level falls or walking/running into stationary objects) in the absence of signs or symptoms of head injury other than scalp abrasions or lacerations.
Target condition(s)	Traumatic brain injury
Index test(s) and reference standard	Index test PECARN Reference (gold) standard: Clinical follow-up

Reference	Atabaki 2016[3]
	Rates of clinically important TBIs (ciTBI) were determined by clinical follow-up both for admitted patients and for those discharged from the ED. For admitted patients, medical record reviews were performed and for discharged patients telephone follow-up were done between 1 week and 3 months after the ED visit. If telephone follow-up was unsuccessful, follow-up surveys were mailed with the identical script as the telephone script. If that was unsuccessful, medical records, ED process improvement records, hospital trauma registries, and morgue records were reviewed to ensure that no patients discharged from the ED and missing follow-up had ciTBIs.
Results	CT scans were obtained on 33.6% of the patients, of whom 6.3% had TBI on CT scan. One percent (87/8,496) had ciTBIs and 0.2% (16/8,496) had neurosurgery performed. Of the 2,185 patients who were <2 years of age, 25 (1.1%) had ciTBIs. Of the 6,311 patients who were 2 years of age and older, 62 (1.0%) had ciTBIs. Among patients with clinician suspicion for ciTBI <1%, 2,099/7,688 (27.3%) had CT scans performed, as did 758/808 (93.8%) of those with clinician suspicion ≥1%. Reports two separate cohorts of patients, with each cohort split into two groups of different ages (children > 2 years and <2 years). Test accuracy of having at least one predictor in the PECARN TBI age-specific prediction rules for identifying children with ciTBIs for children <2 years [pre-verbal] (n = 2,185) TP: 25 FP: 1002 TN: 1,158 FN: 0 Sensitivity % 95% CI: 100% (86.3 to 100%) Specificity% 95% CI: 53.6% (51.5 to 55.7%) NPV: 100% (99.7 to 100%) PPV: 2.4 % (1.6 to 3.6%)

Reference	Atabaki 2016[3]
	Test accuracy of PECARN TBI age-specific prediction rules for identifying children with ciTBIs for children >2 years [verbal]). TP: 60 FP: 2614 TN: 3635 FN: 2 Sensitivity % 95% CI: 96.8% (88.8% to 99.6%) Specificity % 95% CI: 58.2% (56.9% to 59.4%) NPV: 99.95% (99.80% to 99.99%) PPV: (2.2%) (1.7% to 2.9%)
Source of funding	supported by a grant from the Health Resources and Services Administration/Maternal and Child Health Bureau (HRSA/MCHB), Division of Research, Education, and Training (DRTE) and the Emergency Medical Services of Children (EMSC) Program (R40MC02461). This project was also supported in part by the Health Resources and Services Administration (HRSA), Maternal and Child Health Bureau (MCHB), Emergency Medical Services for Children (EMSC) Network Development Demonstration Program under cooperative agreements U03MC00008, U03MC00001, U03MC00003, U03MC00006, U03MC00007, U03MC22684, and U03MC22685.
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: none Indirectness *(QUADAS 2 – applicability)*: none
Comments	-

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Reference	**Babl 2017[5, 6]**
Study type	Prospective multi-centre observational study (APHIRST)
Study methodology	Data source: prospective multicentre observational study that recruited children <18 years with head injury of any severity to 10 paediatric EDs in Australia and New Zealand between April 2011 and November 2014. See Babl 2019 for secondary analysis of this study that looked at NEXUS II rather than PECARN, CATCH and CHALICE covered in this paper.
Number of patients	n = 20,137 total, but number analysed varies depending on the rule as each has different inclusion/exclusion criteria
Patient characteristics	Age, mean (SD): 5.7 (4.7) years *<2 years, 26.7%* *≥2 years, 73.3%* Gender: 36.3% female and 63.7% male GCS: *3-8, 0.6%* *9-12, 0.5%* *13, 0.7%* *14, 2.9%* *15, 95.4%* Ethnicity: not reported Setting: paediatric EDs in Australia and New Zealand Country: Australia and New Zealand Inclusion criteria: children <18 years; and presenting with head injury of any severity to paediatric EDs Exclusion criteria: trivial facial injury only; patient/family refusal to participate; referral from ED triage to external provider (not seen in ED); did not wait to be seen; and neuroimaging done before transfer to study site. Children (<18 years) with head injury of any severity (also provides a secondary analysis in more specific population to allow improved comparison between the three rules being assessed)
Target condition(s)	Traumatic brain injury – head injury of any severity

Reference	**Babl 2017[5, 6]**
Index test(s) and reference standard	Index test: PECARN CATCH CHALICE Reference standard CT or systematic follow-up Enrolled by treating ED clinician who collected data report prior to any neuroimaging. Decision to obtain CT based on clinical judgement and own criteria with the study having to impact on this process. ED and hospital management data after visit recorded and telephone follow-up for people that did not have neuroimaging. Up to six follow-up attempts made up to 90 days after injury. Data of any representing to study hospitals and having a CT scan within follow-up period prior to the phone call were used to assess outcomes. Patients representing to other hospitals based on telephone follow-up had neuroimaging and neurosurgery reports requested where applicable. Research assistants not blinded to the purpose of the study. Assumption that those not undergoing CT scan were negative for the outcome based on telephone follow-up. Senior radiologist reports used to determine CT scan results.
Results	Outcomes: Note that the outcome used differed depending on the clinical decision rule. Secondary analysis to overcome differences between the decision rules in terms of inclusion and exclusion criteria and rule-specific outcomes, homogenous comparison cohort was created (mildly injured children <18 years presenting within 24 h of injury with GCS 13-15). For this secondary analysis, clinically important traumatic brain injury as measured in PECARN was selected as the primary outcome. Clinically important traumatic brain injury – death from traumatic brain injury, need for neurosurgery, intubation >24 h for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT

Reference	Babl 2017[5, 6]
	Need for neurological intervention for traumatic brain injury – intracranial pressure monitoring, elevation of depressed skull fracture, ventriculostomy, haematoma evacuation, lobectomy, tissue debridement, dura repair, other Traumatic brain injury on CT – intracranial haemorrhage or contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus skull fracture depressed at least the width of the table of the skull Clinically significant intracranial injury – death as a result of head injury, need for neurosurgical intervention or marked abnormality on CT scan Neurosurgery – definition not provided, but the following procedures were reported to have occurred and were included under neurosurgery: intracranial pressure monitoring, craniotomy, haematoma evacuation, elevation of depressed skull fracture, dura repair, tissue debridement and lobectomy **PECARN** Clinically important traumatic brain injury – all of those this decision rule could be applied to (n=4011) – **<2 years** TP: 38 FP: 1834 TN: 2139 FN: 0 Sensitivity % 95% CI: 100.0 (90.7-100.0) Specificity% 95% CI: 53.8 (52.3-55.4) PPV% 95% CI: 2.0 (1.4-2.8)

Reference	Babl 2017[5, 6]
	NPV% 95% CI: 100.0 (99.8-100.0) Clinically important traumatic brain injury – all of those this decision rule could be applied to (n=11,152) – **≥2 years** TP: 97 FP: 5987 TN: 5067 FN: 1 Sensitivity % 95% CI: 99.0 (94.4-100.0) Specificity% 95% CI: 45.8 (44.9-46.8) PPV% 95% CI: 1.6 (1.3-1.9) NPV% 95% CI: 100.0 (99.9-100.0) Clinically important traumatic brain injury – comparative population to compare three rules (n=5046) – **<2 years** TP: 42 FP: 2047 TN: 2957 FN: 0 Sensitivity % 95% CI: 100.0 (91.6-100.0) Specificity% 95% CI: 59.1 (57.7-60.5) PPV% 95% CI: 2.0 (1.5-2.7)

Reference	Babl 2017[5, 6]
	NPV% 95% CI: 100.0 (99.9-100.0) Clinically important traumatic brain injury – comparative population to compare three rules (n=13,867) – ≥**2 years** TP: 117 FP: 6606 TN: 7143 FN: 1 Sensitivity % 95% CI: 99.2 (95.4-100.0) Specificity% 95% CI: 52.0 (51.1-52.8) PPV% 95% CI: 1.7 (1.4-2.1) NPV% 95% CI: 100.0 (99.9-100.0) Traumatic brain injury on CT – comparative population to compare three rules (n=5046) – **<2 years** TP: 70 FP: 2019 TN: 2957 FN: 0 Sensitivity % 95% CI: 100.0 (94.9-100.0) Specificity% 95% CI: 59.4 (58.0-60.8) PPV% 95% CI: 3.4 (2.6-4.2)

Reference	Babl 2017[5, 6]
	NPV% 95% CI: 100.0 (99.9-100.0) <u>Traumatic brain injury on CT – comparative population to compare three rules (n=13,867) – ≥**2 years**</u> TP: 180 FP: 6543 TN: 7143 FN: 1 Sensitivity % 95% CI: 99.4 (97.0-100.0) Specificity% 95% CI: 52.2 (51.4-53.0) PPV% 95% CI: 2.7 (2.3-3.1) NPV% 95% CI: 100.0 (99.9-100.0) <u>Neurosurgery – comparative population to compare three rules (n=5046) – **<2 years**</u> TP: 6 FP: 2083 TN: 2957 FN: 0 Sensitivity % 95% CI: 100.0 (54.1-100.0) Specificity% 95% CI: 58.7 (57.3-60.0) PPV% 95% CI: 0.3 (0.1-0.6)

Reference	Babl 2017[5, 6]
	NPV% 95% CI: 100.0 (99.9-100.0) Neurosurgery – comparative population to compare three rules (n=13,867) – ≥**2 years** TP: 18 FP: 6705 TN: 7144 FN: 0 Sensitivity % 95% CI: 100.0 (81.5-100.0) Specificity% 95% CI: 51.6 (50.7-52.4) PPV% 95% CI: 0.3 (0.2-0.4) NPV% 95% CI: 100.0 (99.9-100.0) **CATCH** Need for neurological intervention – all of those this decision rule could apply to (n=4957) – **4 high risk predictors** TP: 20 FP: 779 TN: 4157 FN: 1 Sensitivity % 95% CI: 95.2 (76.2-99.9) Specificity% 95% CI: 84.2 (83.2 – 85.2)

Reference	Babl 2017[5, 6]
	PPV% 95% CI: 2.5 (1.5-3.8) NPV% 95% CI: 100.0 (99.9-100.0) <u>Brain injury on CT – all of those this decision rule could apply to (n=4957) – **7 high risk/medium risk predictors**</u> TP: 125 FP: 2100 TN: 2716 FN: 16 Sensitivity % 95% CI: 88.7 (82.2-93.4) Specificity% 95% CI: 56.4 (55.0-57.8) PPV% 95% CI: 5.6 (4.7-6.7) NPV% 95% CI: 99.4 (99.1-99.7) <u>Clinically important traumatic brain injury – comparative population to compare three rules (n=18,913)</u> TP: 147 FP: 5560 TN: 13193 FN: 13 Sensitivity % 95% CI: 91.9 (86.5-95.6) Specificity% 95% CI: 70.4 (69.7-71.0)

Reference	Babl 2017[5, 6]
	PPV% 95% CI: 2.6 (2.2-3.0) NPV% 95% CI: 99.9 (99.8-99.9) <u>Traumatic brain injury on CT – comparative population to compare three rules (n=18,913)</u> TP: 220 FP: 5487 TN: 13175 FN: 31 Sensitivity % 95% CI: 87.6 (82.9-91.5) Specificity% 95% CI: 70.6 (69.9-71.3) PPV% 95% CI: 3.9 (3.4-4.4) NPV% 95% CI: 99.8 (99.7-99.8) <u>Neurosurgery – comparative population to compare three rules (n=18,913)</u> TP: 23 FP: 5684 TN: 13205 FN: 1 Sensitivity % 95% CI: 95.8 (78.9-99.9) Specificity% 95% CI: 69.9 (69.2-70.6)

Reference	Babl 2017[5, 6]
	PPV% 95% CI: 0.4 (0.3-0.6) NPV% 95% CI: 100.0 (100.0-100.0) **CHALICE** Clinically significant intracranial injury – all of those this decision rule could apply to (n=20,029) TP: 370 FP: 4303 TN: 15,325 FN: 31 Sensitivity % 95% CI: 92.3 (89.2-94.7) Specificity% 95% CI: 78.1 (77.5-78.7) PPV% 95% CI: 7.9 (7.2-8.7) NPV% 95% CI: 99.8 (99.7-99.9) Clinically important traumatic brain injury – comparative population to compare three rules (n=18,913) TP: 148 FP: 4018 TN: 14735 FN: 12 Sensitivity % 95% CI: 92.5 (87.3-96.1)

Reference	Babl 2017[5, 6]
	Specificity% 95% CI: 78.6 (78.0-79.2) PPV% 95% CI: 3.6 (3.0-4.2) NPV% 95% CI: 99.9 (99.9-100.0) Traumatic brain injury on CT – comparative population to compare three rules (n=18,913) TP: 227 FP: 3939 TN: 14723 FN: 24 Sensitivity % 95% CI: 90.4 (86.1-93.8) Specificity% 95% CI: 78.9 (78.3-79.5) PPV% 95% CI: 5.4 (4.8-6.2) NPV% 95% CI: 99.8 (99.8-99.9) Neurosurgery – comparative population to compare three rules (n=18,913) TP: 22 FP: 4144 TN: 14745 FN: 2 Sensitivity % 95% CI: 91.7 (73.0-99.0)

Reference	**Babl 2017[5, 6]**
	Specificity% 95% CI: 78.1 (77.5-78.6) PPV% 95% CI: 0.5 (0.3-0.8) NPV% 95% CI: 100.0 (100.0-100.0)
Source of funding	Funded by grants from National Health and Medical Research Council, Murdoch Children's Research Institute, Emergency Medicine Foundation, Perpetual Philanthropic Services, Auckland Medical Research Foundation and A+ Trust, Townsville Hospital and Health Service Private Practice Research and Education Trust Fund. Supported by Victorian Government's Infrastructure Support Program. Two authors part funded by grant from either Royal Children's Hospital Foundation or Health Research Council of New Zealand.
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if consecutive or random sample enrolled, unclear if reference standard interpreted without knowledge of index test and not all had the same reference standard (CT). Indirectness (QUADAS 2 – applicability): • For the results in the comparative population: serious – rule is being used in the whole population, ignoring any inclusion/exclusion criteria specific to the rule (included for purposes of comparing between rules in the same study as slightly different outcome definitions used in rule-specific populations) • For the results for each decision rule in the population eligible for the specific decision rule: none
Comments	Note that an additional Babl 2018 paper includes results from this study specifically in the mild head injury subpopulation, which was not included and extracted separately as the review protocol does not specify mild head injury or include it as a subgrouping strategy.

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Reference	**Babl 2019[7]**
Study type	Prospective observational study (PREDICT study)
Study methodology	Data source: secondary analysis of prospective multicentre observational study that recruited children <18 years with head injury of any severity to 10 paediatric EDs in Australia and New Zealand between April 2011 and November 2014. Assesses NEXUS II whereas initial study looked at three other paediatric decision rules.
Number of patients	n = 20,109 (9.76% had CT scan in the ED)

Reference	**Babl 2019[7]**
Patient characteristics	Age, mean (SD): 5.7 (4.7) years *<3 years, 39.1%* *≥3 years, 60.9%* Gender: 63.7% male and 36.3% female GCS: not reported Ethnicity: not reported Setting: paediatric EDs in Australia and New Zealand Country: Australia and New Zealand Inclusion criteria: children <18 years; and presenting with head injury of any severity to paediatric EDs Exclusion criteria: trivial face injuries, refused participation, had neuroimaging prior to arrival in ED, did not wait to be seen or referred for care outside of the ED; and social issues preventing an approach of the patient or family. Children (<18 years) with head injury of any severity
Target condition(s)	Traumatic brain injury – head injury of any severity
Index test(s) and reference standard	Index test: NEXUS II Reference standard CT or systematic follow-up Enrolled by treating ED clinician who collected data report prior to any neuroimaging. Decision to obtain CT based on clinical judgement and own criteria with the study having to impact on this process. ED and hospital management data after visit recorded and telephone follow-up for people that did not have neuroimaging. Up to six follow-up attempts made up to 90 days after injury. Data of any representing to study hospitals and having a CT scan within follow-up period prior to the phone call were used to assess outcomes. Patients representing to other hospitals based on telephone follow-up had neuroimaging and neurosurgery reports requested where applicable. Research assistants not blinded to the purpose of the study. Assumption that those not undergoing CT scan were negative for the outcome based on telephone follow-up.

Reference	**Babl 2019[7]**
	Senior radiologist reports used to determine CT scan results.
Results	Outcomes: Clinically important intracranial injury – presence of ≥1 CT findings (substantial epidural or subdural haematoma; substantial cerebral contusion; extensive subarachnoid haemorrhage; signs of herniation; basal cistern compression or midline shift; haemorrhage in the posterior fossa; intraventricular haemorrhage; bilateral haemorrhage of any type; depressed or diastatic skull fracture; pneumocephalus; diffuse cerebral oedema; diffuse axonal injury). <u>Clinically important intracranial injury – NEXUS II rule – whole population of those with and without CT (n=20,109)</u> TP: 379 FP: 10406 TN: 9320 FN: 4 Sensitivity % 95% CI: 99.0 (97.3-99.7) Specificity% 95% CI: 47.2 (46.5-47.9) PPV% 95% CI: 3.5 (3.2-3.9) NPV% 95% CI: 100.0 (99.9-100.0) <u>Clinically important intracranial injury – NEXUS II rule – specific population of those with CT at any time (ED or follow-up; n=2087) – not used in analysis as larger population favoured (no reason to limit to those with CT)</u> TP: 379

Reference	Babl 2019[7]
	FP: 1497 TN: 207 FN: 4 Sensitivity % 95% CI: 99.0 (97.3-99.7) Specificity% 95% CI: 12.1 (10.6-13.8) PPV% 95% CI: 20.2 (18.4-22.1) NPV% 95% CI: 98.1 (95.2-99.5) <u>Clinically important intracranial injury – NEXUS II rule – specific population of those with CT at ED presentation (n=1962 – not used in analysis as larger population favoured (no reason to limit to those with CT)</u> TP: 373 FP: 1429 TN: 156 FN: 4 Sensitivity % 95% CI: 98.9 (97.3-99.7) Specificity% 95% CI: 9.8 (8.4-11.4) PPV% 95% CI: 20.7 (18.8-22.6) NPV% 95% CI: 97.5 (93.7-99.3)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if consecutive or random sample enrolled, unclear if reference standard interpreted without knowledge of index test and not all had the same reference standard (CT). Indirectness (QUADAS 2 – applicability): none

Reference	**Babl 2019[7]**
Comments	**-**

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Reference	**Berger 2016[9]**
Study type	Prospective cohort study
Study methodology	Data source: Enrolment across three children's hospitals in USA, starting on 1st October 2006, 1st June 2010 or 1st January 2011 depending on the hospital.
Number of patients	n = 1040 (n=862 with complete data analysed)
Patient characteristics	*Age, mean (SD): 4.7 (3.1) months* *Gender (male): 52% male* *GCS not reported* *Ethnicity*: 78% white *Setting*: three separate children's hospitals *Country*: USA *Inclusion criteria*: 30 to 364 days of age, well-appearing, and presented to a participating ED with a temperature <38.3°C, without a history of trauma and for evaluation of a symptom that is associated with an increased risk of abusive head trauma. *Exclusion criteria*: previously abnormal CT scan of the head. Infants (at least 30 days and <1 year) who appear well but have symptoms associated with an increased risk of abusive head trauma
Target condition(s)	Traumatic brain injury
Index test(s) and reference standard	Index test Pittsburgh Infant Brain Injury Score (PIBIS) – retrospectively derived based on data from 187 infants (150 without brain injury and 37 with mild abusive head trauma) presenting to tertiary care children's hospital for evaluation of non-specific symptoms. Looks separately at sensitivity and specificity for scores 0-5 separately.

Reference	Berger 2016[9]
	Reference (gold) standard: Neuroimaging (CT or MRI) and/or follow-up – those with normal neuroimaging or no neuroimaging at enrolment or during follow-up were considered to be reference standard negative. Those with abnormal neuroimaging at enrolment or during follow-up were considered to be reference standard positive. Follow-up: medical record review for 6 months after enrolment or up to 1 year of age, whichever occurred later. Aim of follow-up was to identify subjects with abnormal neuroimaging during the follow-up period and/or those who had neuroimaging performed to follow up on symptoms at enrolment. CTs and MRIs interpreted as part of clinical care and by study neurologist – difference in interpretations solved by consulting with a paediatric neurosurgeon. 722/1040 (69.4%) had CT and/or MRI at enrolment or during follow-up.
Results	Outcomes: Abnormal neuroimaging at enrolment or during follow-up. 81% had data available for all variables in the clinical prediction rule, with the proportion with missing data differing between groups (11% with normal neuroimaging, 3% with abnormal neuroimaging and 41% of those without neuroimaging). Accuracy data calculated for **862 subjects** with complete data. Abnormal neuroimaging at enrolment or during follow-up PIBIS score of 0 TP: unclear FP: unclear TN: unclear FN: unclear Sensitivity % 95% CI: 100 (CIs not reported) Specificity% 95% CI: 0 (CIs not reported)

Reference	Berger 2016[9]
	<u>PIBIS score of 1</u> TP: unclear FP: unclear TN: unclear FN: unclear Sensitivity % 95% CI: 99 (CIs not reported) Specificity% 95% CI: 12 (CIs not reported) <u>PIBIS score of ≥2 – only this score threshold presented in the evidence, as limited data provided for all other scores</u> TP: 196 FP: 306 TN: 345 FN: 14 Sensitivity % 95% CI: 93 (89-96) Specificity% 95% CI: 53 (49-57) PPV% 95% CI: 39.0 (34.8-43.6) NPV% 95% CI: 96.0 (93.6-97.9) <u>PIBIS score of 3</u> TP: unclear

Reference	Berger 2016[9]
	FP: unclear TN: unclear FN: unclear Sensitivity % 95% CI: 81 (CIs not reported) Specificity% 95% CI: 75 (CIs not reported) <u>PIBIS score of 4</u> TP: unclear FP: unclear TN: unclear FN: unclear Sensitivity % 95% CI: 45 (CIs not reported) Specificity% 95% CI: 90 (CIs not reported) <u>PIBIS score of 5</u> TP: unclear FP: unclear TN: unclear FN: unclear Sensitivity % 95% CI: 12 (CIs not reported)

Reference	**Berger 2016[9]**
	Specificity% 95% CI: 100 (CIs not reported)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Sample was not consecutive or random, unclear if index test interpreted without knowledge of reference standard and concerns about flow and timing, as not all were included in the analysis, the same reference standard was not used for all infants and the gap between index and reference standard was unclear. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Bertsimas 2019[10]**
Study type	Retrospective, secondary analysis of prospective cohort
Study methodology	Data source: prospective cohort of 42,412 children with head trauma and without severely altered mental status examined between 1st June 2004 and 30th September 2006 in EDs of North American participating in PECARN. Data analysis conducted between 15th September 2016 and 18th December 2018. As dataset was anonymised, same development and validation cohorts as original analysis could not be used. Therefore, randomly split into classifier development and validation cohorts.
Number of patients	n = 42,412 (35.3% in total had CT, though this is for development and validation cohorts combined and across decision rules. Proportion unclear for each specific cohort)
Patient characteristics	Age, mean (SD): 7.1 (5.5) years *<2 years, 25.3%* *≥2 years, 74.7%* Gender: 37.7% females and 62.3% males GCS: *15, 96.8%* Ethnicity: not reported Setting: data obtained from 25 North American EDs

Reference	**Bertsimas 2019[10]**
	Country: USA Inclusion criteria: children <18 years; and presenting to ED within 24 h of head trauma Exclusion criteria: underwent imaging before admission; trivial injury mechanisms; conditions complicating assessment (e.g. known brain tumours); GCS ≤13; ventricular shunts; and bleeding disorders. Children (<18 years) with head trauma (GCS 14-15)
Target condition(s)	Traumatic brain injury – head trauma with GCS 14-15
Index test(s) and reference standard	Index test: PECARN Also reports results for a machine learning OCT developed in the paper but this was not included as it was a machine learning approach rather than a specific clinical decision rule. Reference standard CT and/or follow-up (35.3% had CT) Medical records and CT scan results reviewed for those admitted. For those discharged, telephone survey 7 to 90 days after the ED visit, and medical records and county morgue records check for those uncontactable.
Results	Outcomes: Clinically important traumatic brain injury – defined as death from traumatic brain injury, neurosurgery, intubation for more than 24 hours, or hospital admission for at least 2 nights in patients with traumatic brain injury-related CT scan findings. **Development – PECARN** Clinically important traumatic brain injury – <2 years (n=8502) TP: 72

Reference	Bertsimas 2019[10]
	FP: 3886 TN: 4543 FN: 1 Sensitivity % calculated using excel sheet: 99.0 – reported to be 96.5 (90.8-99.2) in the paper but does not match what is calculated based on raw data Specificity% 95% CI: 53.9 (52.8-55.0) PPV% 95% CI: 1.8 (1.7-1.8) NPV% 95% CI: 99.9 (99.9-100.0) <u>Clinically important traumatic brain injury – ≥2 years (n=25,283)</u> TP: 208 FP: 10590 TN: 14478 FN: 7 Sensitivity % calculated using excel sheet: 97.0 – reported to be 96.0 (92.9-98.1) in the paper but does not match what is calculated based on raw data Specificity% 95% CI: 57.8 (57.1-58.4) PPV% 95% CI: 1.9 (1.8-2.0) NPV% 95% CI: 99.9 (99.9-100.0)

Reference	Bertsimas 2019[10]
	<u>Validation – PECARN</u> <u>Clinically important traumatic brain injury – <2 years (n=2216)</u> TP: 25 FP: 1033 TN: 1158 FN: 0 Sensitivity % calculated using excel sheet: 100.0 – reported to be 94.1 (81.7-99.1) in the paper but does not match what is calculated based on raw data Specificity% 95% CI: 52.8 (50.8-54.9) PPV% 95% CI: 2.2 (1.9-2.4) NPV% 95% CI: 99.9 (99.6-100.0) <u>Clinically important traumatic brain injury – ≥2 years (n=6411)</u> TP: 61 FP: 2692 TN: 3656 FN: 2 Sensitivity % calculated using excel sheet: 97.0 – reported to be 94.5 (87.3-98.3) in the paper but does not match what is calculated based on raw data Specificity % 95% CI: 57.6 (56.4-58.8) PPV% 95% CI: 2.2 (2.0-2.3)

Reference	**Bertsimas 2019[10]**
	NPV% 95% CI: 99.9 (99.8-100.0)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if consecutive or random sample enrolled, not all had the same reference standard and unclear time interval between index test and reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Bozan 2019[12]**
Study type	Prospective cohort study
Study methodology	Data source: education and research hospital in Istanbul, Turkey between 01/01/2016 and 30/04/2016.
Number of patients	n = 256
Patient characteristics	Age, median (IQR): 3.0 (1.0-7.75) years Gender: 59.8% male and 40.2% female GCS: *14, 12.1%* *15, 87.9%* Ethnicity: not reported

Reference	**Bozan 2019[12]**
	Setting: single hospital in Turkey Country: Turkey Inclusion criteria: <18 years; admitted with isolated blunt head trauma; GCS >13; and parental permission to participate in the study Exclusion criteria: ≥18 years; penetrating head trauma or trauma to other systems; those with GCS ≤13; incomplete data; and parents did not agree to participate in the study Children (<18 years) with minor blunt head trauma
Target condition(s)	Traumatic brain injury – minor blunt head trauma
Index test(s) and reference standard	Index test: PECARN CATCH Reference standard CT scan (all had CT) CT performed on all admitted to ED with an indication for a CT according to PECARN or CATCH clinical decision rules or for any other reason according to clinician's decision. Decision made by emergency medical specialist. Results reported by a radiologist blind to the study.
Results	Outcomes: Intracranial pathology on CT – linear fracture, skull base fracture, epidural haematoma, compression fracture, parenchymal haemorrhage, contusion, and subdural haematoma. Referred to as scalp fracture and/or intracranial bleeding in CBT. Clinically significant intracranial pathologies considered to be: >4 mm subdural haematoma, any epidural haematoma, depressed fractures, subarachnoid haemorrhage >1 mm thick, >5 mm cerebral contusion and intraventricular haemorrhage. Intracranial pathology on CT (scalp fracture and/or intracranial bleeding) – PECARN

Reference	Bozan 2019[12]
	TP: 18 FP: 111 TN: 126 FN: 1 Sensitivity % 95% CI: 95.0 (72.0-100.0) Specificity% 95% CI: 53.0 (47.0-60.0) PPV% 95% CI: 14.0 (9.0-21.0) NPV% 95% CI: 99.0 (95.0-100.0) <u>Intracranial pathology on CT (scalp fracture and/or intracranial bleeding) – CATCH</u> TP: 9 FP: 38 TN: 199 FN: 10 Sensitivity % calculated using excel sheet: 47.0 – reported to be 48.0 (25.0-71.0) in the paper but does not match what is calculated based on raw data Specificity% calculated using excel sheet: 84.0 – reported to be 83.0 (79.0-88.0) in the paper but does not match what is calculated based on raw data PPV% 95% CI: 19.0 (1.0-34.0) NPV% 95% CI: 95.0 (91.0-98.0)
Source of funding	Not reported

Reference	**Bozan 2019[12]**
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if consecutive or random sample enrolled, unclear if index test applied without knowledge of the reference standard and unclear time interval between index test and reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Easter 2014[23]**
Study type	prospective cohort study
Study methodology	Data source: prospective cohort study of children <18 years of age presenting to the ED at Denver Health Medical Centre with minor head injury from January 15, 2012 through June 15, 2013.
Number of patients	n = 1009 (19% had CT)
Patient characteristics	*Age, median (IQR): 6.1 (2.6-13.7)* *Gender (male): 650 (64%)* GCS 13: 4(0.4%) GCS 14: 40 (4%) GCS 15: 961 (95%) *Ethnicity*: not reported *Setting*: Medical health centre *Country*: USA *Inclusion criteria*: included children <18 years of age with: (1) a history or signs of blunt injury to the head; (2) GCS scores ≥13; (3) injury within the previous 24 hours prior to presentation to the ED; and (4) physician concern for potential TBI.

Reference	**Easter 2014[23]**
	Exclusion criteria: children known to be at heightened risk of TBI, including those with GCS scores <13, brain tumors, ventricular shunts, anticoagulant therapy, or bleeding disorders. Children presenting >24 hours after injury were also excluded as the risk of clinically important TBI decreases with time. Children <18 years of age with minor head injury (Glasgow Coma Scale 13 – 15) presenting within 24 hours of their injuries.
Target condition(s)	Traumatic brain injury
Index test(s) and reference standard	Index test PECARN CATCH CHALICE Reference (gold) standard: CT Follow-up: for patients who did not undergo CT, follow-up at the ED or outpatient clinic. This entailed a standardised telephone interview with patients' guardians to determine if patients exhibited any signs or symptoms of clinically important TBI. Patients with concerning symptoms were instructed to return for re-evaluation, and their subsequent medical records and imaging were reviewed.

Reference	**Easter 2014[23]**
Results	Outcomes: TBI requiring neurosurgery (CATCH, PECARN) and any TBI visible on CT (CATCH, PECARN, CHALICE). Need for neurosurgery included craniotomy, elevation of skull fracture, monitoring of intracranial pressure, or intubation for elevated intracranial pressure. The outcome measure was determined for 90% of patients through follow-up or CT. Follow-up was obtained on 717/821 (87%) patients who did not undergo CT, with 412/717 (57%) being evaluated by a physician in the ED or outpatient clinic and 305/717 (43%) through telephone follow-up. Complete data were obtained for 981/1,009 (97%) patients with PECARN, 1,002/1,009 (99%) with CATCH, and 858/1,009 (85%) with CHALICE. <u>Clinically important TBI</u> **PECARN** TP: 21 FP: 361 TN: 599 FN: 0 Sensitivity % 95% CI: 100 (84-100) Specificity% 95% CI: 62 (59-66) **CATCH**

Reference	Easter 2014[23]
	TP: 19 FP: 550 TN: 431 FN: 2 Sensitivity % calculated using excel sheet: 90.0 – reported to be 91 (70-99) in the paper but does not match what is calculated based on the raw data Specificity % 95% CI: 44 (41-47) **CHALICE** TP: 16 FP: 128 TN: 711 FN: 3 Sensitivity % 95% CI: 84 (60-97) Specificity% 95% CI: 85 (82-87) <u>Injury requiring neurosurgical intervention</u> **PECARN** TP: 4

Reference	Easter 2014[23]
	FP: 378 TN: 599 FN: 0 Sensitivity % 95% CI: 100 (40-100) Specificity% 95% CI: 61 (58-64) **CATCH** TP: 3 FP: 566 TN: 432 FN: 1 Sensitivity % 95% CI: 75 (19-99) Specificity % 95% CI: 43 (40-46) **CHALICE** TP: 3 FP: 141 TN: 713 FN: 1

Reference	Easter 2014[23]
	Sensitivity % 95% CI: 75 (19-99) Specificity% calculated using excel sheet: 83.0 – reported to be 84 (81-86) in the paper but does not match what is calculated based on raw data Any injury on CT **PECARN** TP: 51 FP: 399 TN: 598 FN: 1 Sensitivity % 95% CI: 98 (89-100) Specificity% calculated using excel sheet: 60.0 – reported to be 64 (61-67) in the paper but does not match what is calculated based on raw data **CATCH** TP: 47 FP: 522 TN: 428

Reference	**Easter 2014[23]**
	FN: 5 Sensitivity % 95% CI: 90 (79-97) Specificity % 95% CI: 45 (42-48) **CHALICE** TP: 25 FP: 119 TN: 700 FN: 14 Sensitivity % 95% CI: 64 (47-79) Specificity% calculated using excel sheet: 85.0 – reported to be 86 (83-88) in the paper but does not match what is calculated based on raw data
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Method of patient selection is not reported. Unclear if consecutive or random selection of patients enrolled. Not all patients enrolled, potentially leading to selection bias. Reference standard length of follow-up not specified. Indirectness (QUADAS 2 – risk of applicability): serious. If people had not been evaluated by follow-up, a proxy outcome assessment tool that was adapted from a validated follow-up tool used for minor head injury was used.
Comments	-

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Reference	**Ferrara 2016[26]**
Study type	Retrospective cohort (some prospective data but not for diagnostic accuracy)

Reference	**Ferrara 2016[26]**
Study methodology	Data source: children presenting to the ED and Paediatrics and Neonatology Ward of single hospital in Italy. Children admitted between January 2007 and December 2014 at the hospital and between January 2012 and December 2014 at the ED. For the retrospective cohort (used for diagnostic accuracy), data collected using patent records including demographic and clinical information as well as imaging studies. Presence and absence of PECARN criteria assessed. For the prospective cohort (outcome assessment), information obtained by telephone and questioning the caregivers of the child.
Number of patients	n = 38 (71% had CT)
Patient characteristics	Age, mean (SD): not reported *<2 years, 36.8%* *≥2 years, 63.2%* Gender: *Male, 67% and 43% in <2- and ≥2-year subgroups* *Female, 33% and 57% in <2- and ≥2-year subgroups* GCS: not reported Ethnicity: not reported Setting: ED and Paediatric/Neonatology ward of a single hospital in Italy Country: Italy Inclusion criteria: children between 0 and 14 years; and diagnosis of traumatic brain injury (mild-severe according to GCS). Exclusion criteria: children presenting with premorbid status (such as cognitive or motor impairments and seizures). Children (≤14 years) with traumatic brain injury of any severity
Target condition(s)	Traumatic brain injury – traumatic brain injury of any severity
Index test(s) and reference standard	Index test: PECARN Reference standard

Reference	Ferrara 2016[26]
	CT (71% had CT) For those without CT, method of confirming no positive CT was unclear as follow-up process/duration not mentioned in the paper.
Results	Outcomes: Positive CT scan – no definition provided. <u>Positive CT scan – PECARN - <2 years (n=14)</u> TP: unclear FP: unclear TN: unclear FN: unclear Sensitivity % 95% CI: 99.9 (15.8-100.0) Specificity% 95% CI: 62.5 (24.5-91.5) PPV% 95% CI: 33.0 (CIs not reported) NPV% 95% CI: 99.0 (CIs not reported) Attempted to calculate TP, FP, TN and FN using accuracy measures reported but statistics do not match total number included. <u>Positive CT scan – PECARN - ≥2 years (n=24)</u>

Reference	**Ferrara 2016[26]**
	TP: unclear FP: unclear TN: unclear FN: unclear Sensitivity % 95% CI: 99.9 (15.8-100.0) Specificity% 95% CI: 47.8 (16.3-67.7) PPV% 95% CI: 15.0 (CIs not reported) NPV% 95% CI: 99.0 (CIs not reported)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if a random or consecutive sample was enrolled, unclear if index test interpreted without knowledge of the reference standard, not all had the same reference standard of CT and follow-up for those without CT not described, and unclear time interval between index test and reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Gizli 2020[31]**
Study type	Retrospective cohort study
Study methodology	Data source: This study retrospectively examined the data of patients under the age of 18 years who were admitted to the Emergency Medicine Department of Uludag University Medical Faculty due to MHT (Glasgow Coma Scale [GCS] ⩾ 13) between the dates of 02 January 2014 and 12 December 2017 and subjected to CBT imaging
Number of patients	n = 530
Patient characteristics	*Age, mean (SD): 5.89 (4.89)*

Reference	Gizli 2020[31]
	Gender (male%): 62.60% The GCS was 14 in 1.1% of all patients, while it was 15 in 98.9%. *Ethnicity*: not reported *Setting*: ED *Country*: Turkey *Inclusion criteria*: Minor head trauma (MHT) patients younger than 18, GCS ⩾ 13, and MHT patients younger than 18 with blunt head trauma. *Exclusion criteria*: any trauma patients above the age of 18 years, GCS < 13, pregnant patients, haemorrhagic diathesis, using anticoagulants, patients with penetrant trauma, patients with priorly known brain tumour, and patients with neurological diseases.
Target condition(s)	Traumatic brain injury
Index test(s) and reference standard	Index test PECARN CATCH CHALICE Reference (gold) standard: Computerised brain tomography (CBT)

Reference	**Gizli 2020[31]**
	Abnormal CBT findings such as epidural bleeding, subdural bleeding, and all types of skull fractures were recorded as one group named “abnormal CT” group
Results	2X2 table calculated by NGC **PECARN n=158** TP: 17 FP: 61 TN: 73 FN: 7 Sensitivity % 95% CI: 72.4% Specificity% 95% CI: 54.5% **CATCH n=169** TP: 13 FP: 74 TN: 74 FN: 9 Sensitivity % 95% CI: 57.8%, Specificity % 95% CI: 50%,

Reference	**Gizli 2020[31]**
	CHALICE n=69 TP: 8 FP: 48 TN: 12 FN: 1 Sensitivity % 95% CI: 87.7%, Specificity % 95% CI: 20%,
Source of funding	no financial support for the research, authorship and/or publication of this article.
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: serious. Method of patient selection is not reported. Unclear if consecutive or random selection of patients enrolled. Indirectness*(QUADAS 2 – applicability)*: none
Comments	-

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Reference	**Gupta 2018[34]**
Study type	Prospective observational study

Reference	**Gupta 2018[34]**
Study methodology	Data source: planned secondary analysis of previously published derivation and validation studies (Mower 2005 and Mower 2017). These studies were originally in a population of all ages whereas this analysis focuses on those <18 years. Consecutive patients with blunt paediatric head injury presenting to one of four centres in California. Specifically chosen to provide broad representation from university and community hospitals, with and without residency programs, public and private hospitals and exposure to a broad range of communities, including urban, suburban and rural environments. Conducted between April 2006 and December 2015.
Number of patients	n = 1018
Patient characteristics	Age, median (IQR): 11.9 (4.5-15.5) years, range 0.01-17.9 years Gender: 75% female and 35% male GCS: not reported Ethnicity: *Hispanic, 30.0%* *Non-Hispanic, 70.0%* Race: *Asian, 4.0%* *Black, 16.3%* *Middle Eastern, 1.8%* *Native American, 0.1%* *Other, 5.4%* *White, 72.3%* *Unknown, 0.1%* Setting: four university and community hospitals in California Country: USA Inclusion criteria: acute blunt head trauma; aged <18 years; and underwent CT head imaging at participating centres Exclusion criteria: penetrating trauma; delayed presentations (>24 h after injury); undergoing imaging for reasons unrelated to trauma; and transferred to a participating centre with known intracranial injuries. Children (<18 years) with acute blunt head trauma

Reference	**Gupta 2018[34]**
Target condition(s)	Traumatic brain injury – acute blunt head trauma
Index test(s) and reference standard	Index test: NEXUS II Head CT decision instrument Reference standard CT (all had CT) CT would not be performed until decision criteria had been assessed and recorded. Clinicians cautioned against using decision instruments as determinants in making imaging decisions. Ultimate decision made at discretion of treating provider and not dictated by study protocol. This could be bypassed to obtain immediate imaging on any patients where clinician felt they may be harmed by even minimal delay. These were labelled as 'unstable' and clinicians instructed to complete assessments of criteria as soon as possible and before imaging results were available. Formal radiographic interpretations and outcome assignments completed without knowledge of criteria assessments for each patient.
Results	Outcomes: Need for neurosurgical intervention – death due to head injury, need for craniotomy, elevation of skull fracture, intubation related to head injury or intracranial pressure monitoring within 7 days of head injury Clinically significant head injury evident on CT imaging – all injuries evident on CT head imaging apart from the following in neurologically intact individuals: solitary small contusions, localized subarachnoid haemorrhage less than 1 mm thick, thin subdural hematomas less than 4 mm thick, isolated pneumocephaly, and closed depressed skull fractures that did not violate the inner table Need for neurosurgical intervention – NEXUS II: TP: 27 FP: 661 TN: 330

Reference	Gupta 2018[34]
	FN: 0 Sensitivity % 95% CI: 100.0 (87.2-100.0) Specificity% 95% CI: 33.3 (30.3-36.3) PPV% calculated using excel sheet: 4.0 NPV% 95% CI: 100.0 (99.6-100.0) <u>Clinically significant head injury evident on CT imaging – NEXUS II:</u> TP: 48 FP: 640 TN: 329 FN: 1 Sensitivity % 95% CI: 98.0 (89.1-99.9) Specificity% 95% CI: 34.0 (31.0-37.0) PPV% calculated using excel sheet: 7.0 NPV% 95% CI: 99.7 (98.3-100.0)
Source of funding	Funded in part by grants from Agency for Health Care Research and Quality, National Center for Injury Prevention and Control and UC Center for Health Quality and Innovation.
Limitations	Risk of bias (QUADAS 2 – risk of bias): none Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Ide 2017[45]**
Study type	retrospective cohort study
Study methodology	Data source: Japanese children with minor head trauma in ED part of a tertiary care pediatric hospital in Japan,
Number of patients	n = 2,208 children . < 2-Year-Old Group (n = 792, 12.2% with CT) ≥2-Year-Old Group (n = 1,416, 14.1% with CT)
Patient characteristics	*Age, mean (SD):* *Months (<2 years)* *13 (7–18)* *Months (>2 years old)* 54 (36–88) *Gender (male):* < 2years 56.2% >2 years 67.5% GCS: < 2years GCS = 15 754 (95.2) GCS = 14 38 (4.8) >2years GCS = 15 1379 (97.3) GCS = 14 37 (2.7) *Ethnicity*: not reported

Reference	**Ide 2017[45]**
	Setting: ED part of a tertiary care paediatric hospital *Country*: Japan *Inclusion criteria*: 1) all children younger than 18 years of age with a reported history of blunt head trauma between January and December 2013, 2) children who presented to the ED within 24 hours of injury, and 3) children with an initial Glasgow Coma Scale (GCS) ≥ 14 in the ED. *Exclusion criteria*: children with neuroimaging performed at another hospital before transfer, coagulopathy, known brain tumors, pre-existing neurological disorders which can complicate assessment or those who were missing the primary endpoint.
Target condition(s)	Traumatic brain injury
Index test(s) and reference standard	Index test PECARN Reference (gold) standard: Presence of clinically important TBI (ci TBI) evaluated by CT Follow—up Each case of a return visit within 4 weeks after the initial evaluation was examined to identify possible missed clinically important TBI (ciTBI) ciTBI defined as death from head trauma, neurosurgery, intubation > 24 hours, or hospital admission ≥ 2 nights
Results	There were 14 patients with ciTBI in the <2-year-old group and 10 in the ≥2-year-old group.

Reference	Ide 2017[45]
	There were 16 cases of physically abused children (<2 years old, 10 patients; ≥2 years old, six patients confirmed by the Suspected Child Abuse and Neglect Team. All children included in the analysis. < 2 year old group (including all children): n=792. 2X2 table calculated by NGC. Sensitivity and specificity reported by the paper. TP: 12 FP: 206 FN: 2 TN: 572 Sensitivity % 95% CI: 85.7 (57.2–98.2) Specificity% 95% CI: 73.5 (70.3–76.6) Positive predictive value: 5.5 (2.9–9.4) Negative predictive value: 99.7 (98.7–100) >2 year old group (including all children): n=1416. 2X2 table calculated by NGC. Sensitivity and specificity reported by the paper TP: 10 FP: 374 FN: 0 TN: 1032

Reference	**Ide 2017[45]**
	Sensitivity % 95% CI: 100 (58.7–100) Specificity % 95% CI: 73.4 (71.0–75.7) Positive predictive value: 2.6 (1.3–4.7) Negative predictive value: 100 (99.5–100)
Source of funding	Not reported
Limitations	Risk of bias: serious. Method of patient selection is not reported. Unclear if consecutive or random selection of patients enrolled. Indirectness: None
Comments	-

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Reference	**Ide 2020[44]**
Study type	Prospective cohort study
Study methodology	Data source: EDs at three freestanding children's hospitals, two general hospitals and one paediatric ED within a general hospital. Patients enrolled between June 2016 and September 2017. Enrolled by treating ED physicians, with clinical data collected before neuroimaging performed.
Number of patients	n = 6585 (split into <2 years old and ≥2 years old, n=2237 and n=4348, respectively)
Patient characteristics	Age, median (IQR): 13 (7-18) months for <2-year group and 56 (37-90) months for ≥2-year group Gender: not reported GCS: *15, 98.9% and 99.0% for* <2- *and* ≥2-year groups, respectively *14, 1.1% and 1.0% for* <2- *and* ≥2-year groups, respectively Ethnicity: not reported Setting: six EDs of general hospitals/children's hospitals in Japan

Reference	**Ide 2020[44]**
	Country: Japan Inclusion criteria: children <16 years; minor head trauma (GCS ≥14); and presenting within 24 h of their injuries. Included children with trivial injury mechanisms who were excluded in original PECARN study. Exclusion criteria: penetrating trauma; known brain tumours; pre-existing neurological disorders which can complicate assessment; neuroimaging performed at another hospital prior to ED consultation; bleeding disorders; GCS <14; suspected non-accidental trauma; severe injuries to other parts of the body; and past history of any intracranial lesions. Children (<16 years) with minor head trauma
Target condition(s)	Traumatic brain injury – minor head trauma
Index test(s) and reference standard	Index test: PECARN Reference standard CT and/or follow-up – CT performed in 5.5% those <2 years and 7.8% those ≥2 years. Follow-up or CT scan performed in 43.5% and 47.1%, respectively. Study reports that lead site investigators or research assistants at each site collected outcome data from electronic health records at least two weeks after first examination. Outcomes of any patients that had transferred to other hospitals could be requested. Enrolled by treating ED physicians, with clinical data collected before neuroimaging performed. ED physicians able to obtain head CT in accordance with their own clinical decisions. Management and follow-up of children was in accordance with institutional rules at each site. CT scans reviewed independently by onsite staff radiologists for confirmation of traumatic brain injury on CT.
Results	Outcomes: Clinically important traumatic brain injury – death, neurosurgery, intubation for >24 h for traumatic brain injury or hospital admission for two nights or more associated with traumatic brain injury on CT. Confirmed traumatic brain injury on CT was defined as any of the following: intracranial haemorrhage or contusion, cerebral oedema, traumatic infarction, sigmoid sinus

Reference	Ide 2020[44]
	thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus, or depressed skull fracture. **PECARN, <2 years** Clinically important traumatic brain injury – all included children (n=2237) TP: 13 FP: 641 TN: 1581 FN: 2 Sensitivity % 95% CI: 88.67 (59.54-98.34) Specificity% 95% CI: 71.15 (69.22-73.02) PPV% 95% CI: 1.99 (1.06-3.38) NPV% 95% CI: 99.87 (99.54-99.98) **PECARN, ≥2 years** Clinically important traumatic brain injury – all included children (n=4348) TP: 8 FP: 882 TN: 3458 FN: 0 Sensitivity % 95% CI: 100.00 (63.06-100.00)

Reference	**Ide 2020[44]**
	Specificity% 95% CI: 79.68 (78.45-80.87) PPV% 95% CI: 0.90 (0.39-1.76) NPV% 95% CI: 100.00 (99.89-100.00) Note the study also reports results separately for an analysis where those with trivial injury mechanisms are excluded, in line with the original PECARN study (falls from ground level and running/walking into something), but this was not extracted as not a separate group that would be relevant to review protocol
Source of funding	Supported by the Foundation for Growth Science
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if a random or consecutive sample was enrolled, unclear if the reference standard was interpreted without knowledge of the index test, unclear time interval between index test and reference standard, and very few of those included had CT – although two week follow-up using medical records was mentioned, the study states that <50% had CT or follow-up, suggesting follow-up different across participants. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Kim 2020[48]**
Study type	retrospective cohort study
Study methodology	Data source: The medical records of the children were reviewed in the ED of a University-affiliated Training Hospital from January 2013 to December 2015. The hospital is a regional level 1 trauma centre for both adult and paediatric patients
Number of patients	n = 433 children below 2years
Patient characteristics	*Age, mean (SD) in months: 11.6 (5.5)* *Gender (male): 277 (63.9)* *Ethnicity*: not reported *Setting*: ED of a training hospital

Reference	Kim 2020[48]
	Country: Korea *Inclusion criteria*: Children below 2 years with minor head trauma (GCS 14– 15) who presented to ED within 24 h of their injuries were included. We used the paediatric GCS score for preverbal children, age-appropriate modifications to account for developmental differences in verbal, motor, and cognitive abilities. *Exclusion criteria*: Children with penetrating trauma, known brain tumours, pre-existing neurological disorders, and who died prior to admission to the emergency ward were excluded. In addition, suspected cases of non-accidental trauma, insignificant facial injury only, or serious injuries to other body parts were excluded
Target condition(s)	Traumatic brain injury
Index test(s) and reference standard	Index test PECARN prediction rule (< 2 years) PECARN TBI prognostic rule is a scoring system for predicting the requirement for cranial CT scan in children with minor blunt head trauma described by GCS scores of 14– 15. This rule comprises two age-based criteria as follows: children below 2 years and the ones between ages of 2 and 18. A clinically important TBI (ciTBI) is described as a head injury resulting in one or more of the following: death, neurosurgery, intubation for a period beyond 24 h, and TBI-related admission for two or more nights in the hospital. The predictor variables for children below 2 years were as follows: GCS score of 14, other prognostics of altered mental status (agitation, somnolence, repetitive questioning, slow response to verbal communication), palpable skull fracture, non-frontal hematoma, history of impaired consciousness ⩾5s, serious mechanisms of injury (automobile crash with patient ejection, death of another passenger, or a rolled-over pedestrian/bicyclist without helmet struck by motorized vehicle, falls >90cm, and head struck by high-impact objects), and not acting normally per parent. Reference (gold) standard: CT

Reference	**Kim 2020[48]**
	Cranial CT scan was performed in accordance with the clinical discretion of the ED physician. In particular, in the intermediate risk group, CT scan was recommended on the basis of other clinical factors including the experience of the physician, multiple versus isolated findings (isolated loss of consciousness, isolated headache, isolated vomiting and certain types of isolated scalp hematomas in infants older than 3months), worsening symptoms or signs after ED observation, age < 3 months and parental preference. CT scans were interpreted by radiologists, and positive findings on the CT scan were defined by any the descriptions as follows: intracranial haemorrhage, brain contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift or herniation, diastasis of the skull, traumatic pneumocephalus, or depressed skull fracture in line with the PECARN study.
Results	Outcome: Practically important traumatic brain injury (piTBI) is a clinically essential traumatic brain injury including all cranial abnormalities (e.g. skull fracture) detected by computed tomography. 191 (44.1%) children were not subjected to any imaging studies. Of 224 children who underwent cranial CT scanning, positive findings were observed in 35 (15.6%) (20 and 15 children with skull fracture and intracranial haemorrhage, respectively), who were further categorized as piTBI. Only a patient underwent neurosurgery (0.2%). Notably, none of 408 (94.2%) children who were discharged from ED revisited the hospital. Diagnostic accuracy of the PECARN rules for the prediction of piTBI: (n=224) TP: 33 FP: 111 TN: 78 FN: 2 Sensitivity % 95% CI: 94.3 (80.8–99.3) Specificity% 95% CI: 41.3 (34.2–48.6)

Reference	**Kim 2020[48]**
Source of funding	Not reported
Limitations	Risk of bias: serious. Method of patient selection is not reported. Unclear if patients were selected consecutively or randomly, therefore there is potential patient selection bias. Indirectness: None
Comments	-

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Reference	**Li 2022[53]**
Study type	Retrospective cohort study
Study methodology	Data source: electronic health record system collected at Stanford Health Care's emergency department (ED).
Number of patients	n = 462
Patient characteristics	Age, mean (SD) years: 50.8 (22.7) Gender: 61.8% male and 38.2% female GCS (median Q1, Q3): *15, (14,15)*

Reference	**Li 2022[53]**
	Ethnicity: not reported Setting: Emergency Department Country: USA Inclusion criteria: children 18 years and over; presenting to ED within suspected TBI; and have a blood draw as part of the standard of care. Exclusion criteria: Non-English speaking patients; patients without the capacity to consent (including altered mental status and hearing impairments) if no legal authorised representative was available. Children (<16 years) with minor head trauma
Target condition(s)	Traumatic brain injury – minor head trauma
Index test(s) and reference standard	Index test The Canadian CT Head Rule, the New Orleans Criteria, the NEXUS II rule and ACEP Clinical Policy. Reference standard Non-contrast CT scan (all patients) Blood biomarkers were also studied within the review but were not relevant to this protocol.
Results	Outcomes: Traumatic brain injury – closed head injuries including skull fracture (6.7%), pneumocephalus (2.2%), intracranial hemorrhage (24.6%), mass effect (5.2%), and brain parenchymal injuries (7.8%). CT scans were independently reviewed for TBI imaging common data elements as defined by the National Institute of health. 2 experienced neuroradiologists assessed presence/absence of closed head. The volumes of each type of hematoma or contusion, as well as the extent of midline shift, were quantified as continuous variables, while the extent of subarachnoid hemorrhage, intraventricular hemorrhage, brain edema/swelling, cisternal compression and hydrocephaulus was characterised on ordinal scales.

Reference	Li 2022[53]
	Traumatic brain injury – Canadian TP: 111 FP: 230 TN: 111 FN: 11 Sensitivity% 91% Specificity% 33% PPV% 33% NPV% 91% Traumatic brain injury – New Orleans TP: 119 FP: 210 TN: 131 FN: 3 Sensitivity % 98% Specificity% 38% PPV% 36% NPV% 98%

Reference	Li 2022[53]
	<u>Traumatic brain injury – NEXUS II</u> TP: 120 FP: 260 TN: 81 FN: 2 Sensitivity% 98% Specificity% 24% PPV% 32% NPV% 98% <u>Traumatic brain injury – ACEP</u> TP: 119 FP: 269 TN: 3 FN: 72 Sensitivity% 98% Specificity% 21% PPV% 31% NPV% 96%
Source of funding	No financial support was received.

Reference	**Li 2022[53]**
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if a random or consecutive sample was enrolled, unclear if the index test results were interpreted without knowledge of the results of the reference standard, unclear time interval between index test and reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Lorton 2016[55]**
Study type	Prospective cohort study
Study methodology	Data source: multicentre, prospective cohort study of patients with minor head trauma presenting to three EDs in France. Enrolled patients between May 2013 and May 2014 in paediatric ED of Nantes University Hospital and between June 2014 and October 2015 in the EDs of two general hospitals located in Saint-Nazaire and La Roche-sur-Yon.
Number of patients	n = 1499 (5.1% had CT in whole population, proportion for <2 and >2 year groups unclear)
Patient characteristics	Age, median (IQR): 3 (1.7-6.0) years *<2 years, 28%* *≥2 years, 72%* Gender: 64% male and 36% female GCS: *15, 98.5%* *14, 1.5%* Ethnicity: not reported Setting: EDs of three hospitals in France Country: France Inclusion criteria: children <16 years; presenting to ED within 24 h of blunt head trauma; and initial GCS ≥14.

Reference	**Lorton 2016[55]**
	Exclusion criteria: GCS <14; trivial injury mechanisms (ground level falls, walking into stationary objects; and no signs or symptoms of head trauma other than scalp abrasions or lacerations); patients receiving a CT scan prior to ED consultation; penetrating trauma, pre-existing neurologic disorders including brain tumours; and bleeding disorders. Children (<16 years) with minor head trauma
Target condition(s)	Traumatic brain injury – minor head trauma
Index test(s) and reference standard	Index test: PECARN Reference standard CT or follow-up Paediatricians, emergency medicine physicians or residents completed all study forms prospectively when children first examined in ED. Clinical and radiological characteristics recorded and predictors of clinically important traumatic brain injury assessed. Decision to have CT was based on the index test itself. High risk had a CT scan, intermediate placed under observation and had a CT if they had multiple predictors of a clinically important traumatic brain injury and those in the very low risk group were discharged. Those without CT parents advised that should monitor wellbeing over next 48 h. To identify missed traumatic brain injuries in those discharged, parents contacted by telephone from 30-90 days after hospital visit using standardised interview. Identify those having any neuroimaging or had needed any secondary clinical interventions for the management of their head injury. If any indication that an important injury had been missed, clinical and medical records were obtained. For those without CT, follow-up was completed for 94%.
Results	Outcomes: Clinically important traumatic brain injury – death, neurosurgery, intubation induced due to the traumatic brain injury for >24 h or a hospital admission of at least two nights or more associated with a traumatic brain injury seen on CT.

Reference	Lorton 2016[55]
	CT scans interpreted by onside radiologists and traumatic brain injury on CT defined as presence of any of the following: diastasis of the skull and/or skull fracture, pneumocephalus, intracranial haemorrhage or contusion, sigmoid sinus thrombosis, traumatic infarction, diffuse axonal injury or signs of herniation. <u>Clinically important traumatic brain injury – PECARN – <2 years</u> TP: 3 FP: 151 TN: 267 FN: 0 Sensitivity % 95% CI: 100.0 (29.0-100.0) Specificity% 95% CI: 64.0 (59.0-69.0) PPV% 95% CI: 2.0 (0.0-6.0) NPV% 95% CI: 100.0 (99.0-100.0) <u>Clinically important traumatic brain injury – PECARN – ≥2 years</u> TP: 6 FP: 298 TN: 774 FN: 0 Sensitivity % 95% CI: 100.0 (54.0-100.0) Specificity% 95% CI: 72.0 (69.0-75.0)

Reference	**Lorton 2016[55]**
	PPV% 95% CI: 2.0 (1.0-4.0) NPV% 95% CI: 100.0 (99.0-100.0) Clinically important traumatic brain injury – PECARN – overall (< and ≥2 years combined) – not used in analysis given they give results for <2 and ≥2 year groups separately and this is the way it was designed to be presented, with most other studies reporting it this way TP: 9 FP: 449 TN: 1041 FN: 0 Sensitivity % 95% CI: 100.0 (66.0-100.0) Specificity% 95% CI: 70.0 (68.0-72.0) PPV% 95% CI: 2.0 (1.0-4.0) NPV% 95% CI: 100 (99.0-100.0)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if a random or consecutive sample was enrolled, reference standard not interpreted without knowledge of index test as decision to have CT or follow-up only was based on the index test itself, unclear time interval between index test and reference standard and not all received the same reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Mihindu[59]**
Study type	Retrospective review of registry

Reference	**Mihindu[59]**
Study methodology	Data source: records of those undergoing head CT at level I trauma centre after blunt head trauma between July 2008 and July 2010 retrieved from records in trauma registry.
Number of patients	n = 493
Patient characteristics	Age, mean (SD): not reported Gender: not reported GCS: 14-15 Ethnicity: not reported Setting: single level 1 trauma centre in USA Country: USA Inclusion criteria: children with GCS 14 and 15 after blunt head trauma; and had undergone a head CT. Exclusion criteria: not reported Children (<18 years) with mild traumatic brain injury
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: PECARN Reference standard CT (all had CT)

Reference	**Mihindu[59]**
Results	Outcomes: Clinically important traumatic brain injury – positive CT findings, significant clinical events and all neurosurgical interventions directed at head injury. Clinically important findings on CT included intracerebral haemorrhage, subarachnoid haemorrhage, subdural haematoma, epidural haematoma and diffuse axonal injury. Clinical events used by PECARN were used to define clinically important traumatic brain injury ((death attributable to TBI, neurosurgical intervention, and intubation for more than 24 hours) but not hospital stay for greater than two nights secondary to traumatic brain injury. <u>Clinically important traumatic brain injury – PECARN</u> TP: 46 FP: 269 TN: 178 FN: 0 Sensitivity % calculated using excel sheet: 100.0 Specificity % calculated using excel sheet: 40.0 PPV% calculated using excel sheet: 15.0 NPV% calculated using excel sheet: 100.0
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): serious. Unclear if random or consecutive sample enrolled, unclear if index test interpreted without knowledge of the reference standard result and unclear time interval between index test and reference standard measurements. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Nakhjavan-Shahraki 2017[63]**
Study type	Prospective cross-sectional study
Study methodology	Data source: children with mild traumatic brain injury taken to the emergency ward of two healthcare centres in Tehran, Iran. Convenience sampling method used.
Number of patients	n = 594 (55.4% had a CT in whole population, proportion for <2 year and >2 year groups unclear)
Patient characteristics	Age, mean (SD): 7.9 (5.3) years *<2 years, 19.2%* *≥2 years, 80.8%* Gender: 79.3% male and 20.7% female GCS: 14-15 Ethnicity: not reported Setting: emergency wards of two healthcare centres in Iran Country: Iran Inclusion criteria: patients taken to emergency ward with mild traumatic brain injury; <18 years; and GCS 14-15. Exclusion criteria: death before admission to emergency ward; referral to emergency ward 24 h after injury; brain tumour; and advanced neurologic failure. Children (<18 years) with mild traumatic brain injury
Target condition(s)	Traumatic brain injury – mild traumatic brain injury
Index test(s) and reference standard	Index test: PECARN Reference standard CT and/or follow-up for 2 weeks

Reference	**Nakhjavan-Shahraki 2017[63]**
	CT scanning done based on physician's opinion. Protocol did not have any interference with patient's routine care and PECARN checklist was filled in by an emergency medicine physician that was not in charge of the management of the patient.
Results	Outcomes: Clinically important traumatic brain injury – death from traumatic brain injury, need for neurosurgery, intubation >24 h, traumatic brain injury-related admission to hospital for at least two nights. Positive CT finding defined as presence of intracranial haemorrhage, brain contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift or herniation, diastase of skull and traumatic pneumocephalus. Skull fracture was considered a lesion if it was depressed by at least the width of the table of the skull. CT scans were interpreted by radiologists who were blinded regarding the study. All patients were followed for 2 weeks by phone to assess their outcome status. <u>Clinically important traumatic brain injury – PECARN - <2 years (n=114)</u> TP: 12 FP: 60 TN: 41 FN: 1 Sensitivity % 95% CI: 92.3 (62.1-99.6) Specificity% 95% CI: 40.6 (31.1-50.8) PPV% 95% CI: 16.7 (9.3-27.7) NPV% 95% CI: 97.6 (85.9-99.9)

Reference	**Nakhjavan-Shahraki 2017[63]**
	Clinically important traumatic brain injury – PECARN - ≥2 years (n=480) TP: 42 FP: 185 TN: 253 FN: 0 Sensitivity % 95% CI: 100.0 (89.6-100.0) Specificity% 95% CI: 57.8 (53.0-52.4) PPV% 95% CI: 18.5 (13.8-24.3) NPV% 95% CI: 100.0 (98.1-100.0)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Consecutive or random sample was not enrolled, time interval between index test and reference standard unclear and not all received the same reference standard. Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Osmond, 2018 [72]**
Study type	Prospective multi-centre cohort study
Study methodology	Data source: Between April 2006 and December 2009, a total of 6525 eligible patients were seen in the 9 study hospitals. Of these, 4494 (68.9%) were enrolled. Of the 4494 enrolled, 4060 (90.3%) had data forms completed by physicians and complete outcome assessments documented. The remaining 434 (9.7%) patients had no CT scan and no proxy outcome measure as they could not be reached for follow-up by telephone despite multiple attempts.
Number of patients	n = 4494 (9 Canadian paediatric emergency departments in Canada)

Reference	**Osmond, 2018** [72]
Patient characteristics	*Age, mean (SD):* 9.7 ± 4.8 *Patients ranged in age from 1 month to 16 years with a mean age of 9.7 years, and 464 (11.4%) were younger than 2 years.* *Gender (male): male 2618 (64.5%)* Initial GCS score: 15: 3706 (91.3%) 14: 263 (6.5%) 13: 91 (2.2%) *Ethnicity*: not reported *Setting*: ED in paediatric Emergency Research Canada (PERC) member hospitals *Country*: Canada *Inclusion criteria*: Children (aged 0–16 yr) with acute head injury were eligible for enrolment if they had all of the following: blunt head trauma resulting in witnessed loss of consciousness, amnesia, disorientation, persistent vomiting (2 episodes of vomiting 15 min apart) or persistent irritability for children 2 years of age or younger; initial emergency department GCS score of 13 or greater; and injury within the past 24 hours. *Exclusion criteria*: if children had obvious penetrating skull injury or depressed fracture; they had acute focal neurologic deficit; they had chronic generalised developmental delay; child abuse was suspected; they returned for reassessment of the same head injury; or they were pregnant.
Target condition(s)	Traumatic brain injury Outcomes: Neurosurgical intervention: defined as either death within 7 days secondary to head injury or the need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, intracranial pressure monitoring or intubation for head injury.

Reference	Osmond, 2018 [72]
	Brain injury on CT: defined as any acute intracranial finding on CT attributable to acute trauma. This included closed depressed skull fractures (depressed past the inner table) and pneumocephalus, but excluded nondepressed skull fractures and basilar skull fractures
Index test(s) and reference standard	Index test Canadian Assessment of Tomography for Childhood Head injury (CATCH) rule CT of the head is required for children with minor head injury and any 1 of these findings: High risk for neurosurgical intervention GCS score < 15 at 2 hours after injury Suspected open or depressed skull fracture History of worsening headache Irritability on examination Medium risk for brain injury on CT Any sign of basal skull fracture Large, boggy hematoma of the scalp Dangerous mechanism of injury 2 index tests: 7-item CATCH rule 8-item CATCH rule Reference (gold) standard: CT Follow-up by telephone Time between measurement of index test and reference standard: Not clear Final analysis, n=4060. Excluded n = 434 (lost to follow-up, no CT and no proxy outcome)

Reference	**Osmond, 2018** [72]
	CT of head performed: 1417 (34.9%) Cases with follow-up by telephone 2643 (65.1)
Results	**7 item CATCH rule** **Neurosurgical intervention:** TP: 21 FP: 1733 TN: 2304 FN: 2 Sensitivity % 95% CI: 91.3 (72.0–98.9) Specificity% 95% CI: 57.1 (55.5–58.6) **Brain injury on CT** TP: 192 FP: 1562 TN: 2301 FN: 5

Reference	Osmond, 2018 [72]
	Sensitivity % 95% CI: 97.5 (94.2–99.2) Specificity % 95% CI: 59.6 (58.0–61.1) **8 item CATCH rule** **Neurosurgical intervention:** TP: 23 FP: 2191 TN: 1846 FN: 0 Sensitivity % 95% CI: 100 (85.2–100) Specificity % 95% CI: 45.7 (44.2–47.3) **Brain injury on CT** TP: 196 FP: 2018 TN: 1845 FN: 1 Sensitivity % 95% CI: 99.5 (97.2–100)

Reference	**Osmond, 2018** [72]
	Specificity % 95% CI: 47.8 (46.8–49.4)
Source of funding	Not reported
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: serious. Method of patient selection is not reported. Unclear if consecutive or random selection of patients enrolled. Indirectness *(QUADAS 2 – risk of applicability)*: None
Comments	-

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Reference	**Schonfeld 2014**[80]
Study type	Prospective/retrospective cross-sectional study
Study methodology	Data source: children with minor blunt head trauma presenting to the ED for evaluation at two paediatric EDs located in Boston (USA) and Padova (Italy). In Boston, prospective cross-sectional cohort done between April 2011 and July 2013. In Padova, prospective cross-sectional study performed between June 2010 and November 2010 which was immediately followed by retrospective data collection (December 2010 to May 2011). Data collection: paediatric emergency medicine or general paediatrics attendings (Boston and Padova), paediatric emergency medicine fellows (Boston) or senior residents (Padova) completed all study forms for the two prospective cohorts. For the retrospective cohort, a trained researcher reviewed medical records and charts but was not blinded to outcome. Study forms were completed for all patients to capture the presence or absence of each of the six PECARN age-based traumatic brain injury predictors. For retrospective and prospective Padova cohort, children discharged from ED without CT scan were contacted by telephone for clinical follow-up ~2 weeks after initial evaluation. For Boston prospective cohort, clinical follow-up limited to complete hospital medical record review for 2 weeks from initial ED evaluation to determine if a patient had any neuroimaging performed or any clinical interventions for management of their head injury. Children who had either cranial MRI or CT were included in the CT group.
Number of patients	n = 2439 (15% had CT and 0.1% had MRI – overall imaging rate 15.0%, proportions unclear for >2 and <2 year groups specifically)
Patient characteristics	Age, mean (SD): *<2 years, 39.0%*

Reference	**Schonfeld 2014[80]**
	≥2 years, 61.0% Gender: 59.0% male and 41.0% female GCS: 14-15 Ethnicity: not reported Setting: EDs of one hospital in Boston, USA and one hospital in Padova, Italy Country: USA and Italy Inclusion criteria: children (<18 years in Boston and <15 years in Padova) with blunt head trauma and initial GCS ≥14; presenting to ED within 24 h of injury Exclusion criteria: trivial injury mechanism (e.g. ground-level falls or running into stationary objects with no signs of traumatic brain injury other than scalp abrasions and lacerations); those with neurological comorbidities, bleeding disorders or suspected child abuse; neuroimaging performed prior to ED physician evaluation; and children with neuroimaging performed prior to study form completion for the prospective cohorts in the study. Children (<18 years or <15 years depending on site) with minor blunt head trauma
Target condition(s)	Traumatic brain injury – minor blunt head trauma
Index test(s) and reference standard	Index test: PECARN Reference standard Neuroimaging (CT or MRI, vast majority CT) or follow-up only, up to 2 weeks For retrospective and prospective Padova cohort, children discharged from ED without CT scan were contacted by telephone for clinical follow-up ~2 weeks after initial evaluation. For Boston prospective cohort, clinical follow-up limited to complete hospital medical record review for 2 weeks from initial ED evaluation to determine if a patient had any neuroimaging performed or any clinical interventions for management of their head injury. Children who had either cranial MRI or CT were included in the CT group. 81% of those without CT in the Padova cohort completed clinical follow-up.

Reference	**Schonfeld 2014[80]**
	Clinicians in Boston had available head trauma guideline that was based on the PECARN traumatic brain injury rules. These rules were introduced into clinical practice in May 2010 in the Padova centre of this study.
Results	Outcomes: Clinically important traumatic brain injury – death, intubation >24 h, neurosurgery or two or more nights in the hospital for management of the head injury. Positive CT scan – defined as any of the following: intracranial haemorrhage or contusion, traumatic infarction, sigmoid sinus thrombosis, diffuse axonal injury, pneumocephalus, midline shift or signs of brain herniation, diastasis of the skull, and/or skull fracture. <u>Clinically important traumatic brain injury – PECARN - <2 years (n=956)</u> TP: 6 FP: 404 TN: 546 FN: 0 Sensitivity % 95% CI: 100.0 (64.3-100.0) Specificity % calculated using excel sheet: 57.0 – reported in paper but appear to have used incorrect numbers in calculation of specificity PPV% 95% CI: 1.7 (0.6-3.2) NPV% 95% CI: 100.0 (99.4-100.0) <u>Clinically important traumatic brain injury – PECARN - ≥2 years (n=1472)</u>

Reference	Schonfeld 2014[80]
	TP: 13 FP: 692 TN: 767 FN: 0 Sensitivity % 95% CI: 100.0 (79.4-100.0) Specificity % calculated using excel sheet: 53.0 – reported in paper but appear to have used incorrect numbers in calculation of specificity PPV% 95% CI: 2.0 (1.1-3.2) NPV% 95% CI: 100.0 (99.8-100.0) – incorrect numerator/denominator given in table but assume error only in these and not NPV and 95% CI reported Clinically important traumatic brain injury – PECARN – overall population (<2 years and ≥2 years, n=2428) – not used in analysis given they give results for <2 and ≥2 year groups separately and this is the way it was designed to be presented, with most other studies reporting it this way TP: 19 FP: 1096 TN: 1313 FN: 0 Sensitivity % 95% CI: 100.0 (83.2-100.0) Specificity % 95% CI: 55.0 (52.5-56.6) PPV% 95% CI: 1.8 (1.1-2.7) NPV% 95% CI: 100.0 (99.6-100.0)

Reference	Schonfeld 2014[80]
	Positive finding on CT – PECARN - <2 years (n=121, those with CT performed) TP: 36 FP: 68 TN: 15 FN: 2 Sensitivity % calculated using excel sheet: 95.0 Specificity % calculated using excel sheet: 18.0 PPV% calculated using excel sheet: 35.0 NPV% calculated using excel sheet: 88.0 Positive finding on CT – PECARN - ≥2 years (n=251, those with CT performed) TP: 30 FP: 204 TN: 17 FN: 0 Sensitivity % calculated using excel sheet: 100.0 Specificity % calculated using excel sheet: 8.0 PPV% calculated using excel sheet: 13.0 NPV% calculated using excel sheet: 100.0

Reference	**Schonfeld 2014[80]**
	Positive finding on CT – PECARN – overall population (<2 years and ≥2 years, those with CT performed, n=372) – not used in analysis given they give results for <2 and ≥2 year groups separately and this is the way it was designed to be presented, with most other studies reporting it this way TP: 66 FP: 272 TN: 32 FN: 2 Sensitivity % 95% CI: 97.1 (90.0-99.2) Specificity % 95% CI: 10.5 (7.6-14.5) PPV% calculated using excel sheet: 20.0 NPV% 95% CI: 94.1 (80.9-98.4)
Source of funding	Not reported
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if consecutive or random sample enrolled and some included prospectively while others retrospectively, reference standard not interpreted without knowledge of index test as decision to have imaging was based on the index test itself, unclear time interval between index test and reference standard, and reference standard was different across participants (small proportion had CT, two had MRI and others follow-up only). Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Sert 2020[81]**
Study type	Retrospective cohort study
Study methodology	Data source: records for those <18 years admitted to ED and undergoing CBT imaging between 1st January 2013 and 31st December 2017 scanned from hospital electronic database.

Reference	**Sert 2020[81]**
Number of patients	n = 2490
Patient characteristics	*Age, mean (SD) years: 6.6 (4.5)* *Gender (male): 1733 (69.9%)* *Gender (female): 757 (30.4%)* *Ethnicity*: not reported *Setting*: single ED of university-affiliated training hospital. Level 1 trauma centre for adult and paediatric patients. *Country*: Turkey GCS 14: 248 (10.0%) GCS 15: 2242 (90.0%) *Inclusion criteria*: <18 years; admitted to ED and underwent CBT imaging; and blunt minor head trauma (GCS >13) *Exclusion criteria:* underwent CBT for non-trauma reasons; multi-trauma in addition to head trauma; penetrating trauma; GCS score ≤13; incomplete records in electronic database; repeated CBT scan due to worsening symptoms; and patients with uncertain injury time. Children (<18 years) with minor blunt head trauma
Target condition(s)	Traumatic brain injury – minor blunt head trauma
Index test(s) and reference standard	Index test CATCH (Canadian Assessment of Tomography for Childhood Head Injury) PECARN (Paediatric Emergency Care Applied Research Network) Reference (gold) standard: CT (all had CT)

Reference	**Sert 2020[81]**
	Follow-up: unclear.
Results	Outcomes: New traumatic intracranial injury on CT: Defined as linear or non-linear skull fracture, any intracranial haemorrhage (epidural, subdural, subarachnoid, intracerebral), pneumocephalus, contusion or cerebral oedema Neurosurgical intervention or death: death due to head trauma or neurosurgical procedure, including invasive intracranial pressure measurement by any method, burr hole procedure, craniotomy, haematoma removal, surgical repair of displaced skull fracture and dura repair. **Intracranial injury** PECARN (n=2490 analysed) TP: 161 FP: 817 TN: 1505 FN: 7 Sensitivity % calculated using excel sheet: 96.0 Specificity % calculated using excel sheet: 65.0 PPV% calculated using excel sheet: 16.0 NPV% calculated using excel sheet: 100.0 CATCH (n=2490 analysed) TP: 154 FP: 795

Reference	Sert 2020[81]
	TN: 1527 FN: 14 Sensitivity % calculated using excel sheet: 92.0 Specificity % calculated using excel sheet: 66.0 PPV% calculated using excel sheet: 16.0 NPV% calculated using excel sheet: 99.0 **Neurosurgical intervention or death:** PECARN (n=2490 analysed) TP: 21 FP: 957 TN: 1512 FN: 0 Sensitivity % calculated using excel sheet: 100.0 Specificity % calculated using excel sheet: 61.0 PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0 CATCH (n=2490 analysed) TP: 21

Reference	**Sert 2020[81]**
	FP: 928 TN: 1541 FN: 0 Sensitivity % calculated using excel sheet: 100.0 Specificity % calculated using excel sheet: 62.0 PPV% calculated using excel sheet: 2.0 NPV% calculated using excel sheet: 100.0
Source of funding	Not reported
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: serious. Unclear if consecutive or random sample enrolled, unclear if index tests and reference standards were interpreted without knowledge of the other and unclear time interval between index test and reference standard. Indirectness *QUADAS 2 – applicability)*: None
Comments	-

98

Reference	**Thiam 2015[93]**
Study type	Prospective observational cohort study
Study methodology	Data source: data prospectively collected from children with head injury presenting at paediatric ED of KK Women's and Children's Hospital between April 2014 and July 2014.
Number of patients	n = 1179 (1.02% had CT, n=12)
Patient characteristics	Age, mean (SD): 4.4 (NR) years *<2 years, 32.8%* *≥2 years, 67.2%* Gender: 74.6% male and 25.4% female GCS:

Reference	**Thiam 2015[93]**
	13, 0.1% *14, 1.4%* *15, 98.2%* Ethnicity: not reported Setting: single ED in Singapore Country: Singapore Inclusion criteria: aged <16 years; had a presenting complaint of head injury; and presented to the ED within 72 hours after injury. Exclusion criteria: children ≥16 years; presentation to ED more than 72 hours after injury; bleeding disorders or usage of anticoagulants; brain tumours; ventricular shunts; and previous neuroimaging. Children (<16 years) with head injury of any severity
Target condition(s)	Traumatic brain injury – head injury of any severity
Index test(s) and reference standard	Index test: CATCH CHALICE PECARN Clinical decision rules retrospectively applied to cohort to determine if they would be considered positive for recommending a CT. Reference standard CT (only 1.02% had CT) and/or follow-up of 72 h Decisions on neuroimaging and subsequent disposition of the patients were made at the discretion of the physician. Follow-up: follow-up call was given to patients discharged from the ED after 72 h, to assess for any evolution of symptoms or attendance at another hospital.

Reference	Thiam 2015[93]
Results	Outcomes: Positive findings on CT – epidural haemorrhage, subdural haemorrhage, subarachnoid haemorrhage, intraparenchymal haematoma, cerebral oedema, depressed fracture and contusion. <u>Positive findings on CT – CATCH</u> TP: 6 FP: 231 TN: 942 FN: 0 Sensitivity % 95% CI: 100.0 (54.1-100.0) Specificity% 95% CI: 80.3 (77.9-82.5) PPV% 95% CI: 2.5 (0.9-5.4) NPV% 95% CI: 100.0 (99.6-100.0) <u>Positive findings on CT – CHALICE</u> TP: 5 FP: 277 TN: 896 FN: 1 Sensitivity % 95% CI: 83.3 (35.9-99.6)

Reference	Thiam 2015[93]
	Specificity% 95% CI: 76.4 (73.8-78.8) PPV% 95% CI: 1.8 (0.6-4.1) NPV% 95% CI: 99.9 (99.4-100.0) <u>Positive findings on CT – PECARN high- and intermediate-risk</u> TP: 6 FP: 450 TN: 723 FN: 0 Sensitivity % 95% CI: 100.0 (54.1-100.0) Specificity% 95% CI: 61.6 (58.8-64.4) PPV% 95% CI: 1.3 (0.5-2.8) NPV% 95% CI: 100.0 (99.5-100.0) <u>Positive findings on CT – PECARN high-risk only</u> TP: 6 FP: 39 TN: 1134 FN: 0 Sensitivity % 95% CI: 100.0 (54.1-100.0)

Reference	**Thiam 2015[93]**
	Specificity% 95% CI: 96.7 (95.5-97.6) PPV% 95% CI: 13.3 (5.1-26.8) NPV% 95% CI: 100.0 (99.7-100.0)
Source of funding	Supported by the Paediatrics Academic Clinical Program (Paeds ACP) Young Researcher Pilot Grant.
Limitations	Risk of bias (QUADAS 2 – risk of bias): very serious. Unclear if random or consecutive sample enrolled, unclear if index test interpreted without knowledge of reference standard, not all received the same reference standard, unclear time interval between index test and reference standard, and follow-up duration for those without CT was 72 h rather than 1 month specific in the protocol Indirectness (QUADAS 2 – applicability): none
Comments	-

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Reference	**Kwon 2021[51]**
Study type	Retrospective cohort study
Study methodology	Data source: records for those 0-5 years old with blunt head trauma and GCS 14 and over, admitted to ED within 24 hours of injury; between August 2015 and August 2018.
Number of patients	n = 271
Patient characteristics	*Age, mean (range) months: < 2 years old group (n=78): 12 (1-23); 2-5 years old group (n=173): 48 (24-71).* *Gender (male): < 2 years old group: 47 (60%); 2-5 years old group: 111 (64%)* *Gender (female): < 2 years old group: 31 (40%); 2-5 years old group: 62 (36%)* *Ethnicity*: not reported

Reference	**Kwon 2021[51]**
	Setting: education and research hospital in Gunpo, outside of Seoul, South Korea. *Country*: South Korea GCS 14: <2 years old group: 7(8.9%); 2-5 years old group: 15 (8.7%) GCS 15: <2 years old group: 71 (91%); 2-5 years old group: 158 (91.3%) *Inclusion criteria*: 0-5 years old with acute head injury were included if they had blunt head trauma and GCS of 14 or over admitted to the ED within 24 hours of injury. *Exclusion criteria: patients with a GCS of <14, penetrating head trauma and depressed fracture, bleeding disorder, trivial injury, or incomplete data were ineligible for the study.*
Target condition(s)	Traumatic brain injury – minor blunt head trauma
Index test(s) and reference standard	Index test PECARN (Paediatric Emergency Care Applied Research Network) CATCH2 (Canadian Assessment of Tomography for Childhood Head Injury 2) Reference (gold) standard: CT (all had CT) Follow-up: unclear.

Reference	Kwon 2021[51]
Results	Outcomes: Clinically important traumatic brain injury on CT. **Clinically important traumatic brain injury** **< 2 years old group** PECARN (n=78 analysed) TP: 6 FP: 58 TN: 13 FN: 1 Sensitivity %: 85.71 (42.13-99.64) Specificity %: 18.31 (10.13-29.27) PPV%: 2.10 (1.53-2.87) NPV%: 98.43 (90.55-99.76) CATCH2 (n=78 analysed) TP: 7 FP: 57 TN: 14 FN: 0

Reference	Kwon 2021[51]
	Sensitivity %: 100 (59.04-100) Specificity %: 19.72 (11.22-30.86) PPV%: 2.48 (2.22-2.77) NPV%: 100 **2-5 years old group** PECARN (n=173 analysed) TP: 6 FP: 111 TN: 54 FN: 2 Sensitivity %: 75 (34.91-96.81) Specificity %: 32.73 (25.64-40.45) PPV%: 2.22 (1.48-3.33) NPV%: 98.46 (94.98-99.54) CATCH2 (n=173 analysed) TP: 8 FP: 143 TN: 22

Reference	Kwon 2021[51]
	FN: 0 Sensitivity %: 100 (63.06-100) Specificity %: 13.3 (8.55-19.49) PPV%: 2.30 (2.17-2.44) NPV%: 100 **Total of above: 0-5 years** PECARN (n=251 analysed) TP: 12 FP: 169 TN: 67 FN: 3 Sensitivity %: 80 (51.91-95.67) Specificity %: 28.39 (22.73-34.60) PPV%: 2.23 (1.72-2.89) NPV%: 98.58 (96.12-99.49) CATCH2 (n=251 analysed) TP: 15 FP: 200

Reference	**Kwon 2021[51]**
	TN: 36 FN: 0 Sensitivity %: 100 (78.20-100) Specificity %: 15.25 (10.92-20.49) PPV%: 2.35 (2.23-2.48) NPV%: 100
Source of funding	Not reported
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: very serious. Unclear if consecutive or random sample enrolled, unclear if index tests and reference standards were interpreted without knowledge of the other and unclear time interval between index test and reference standard. Very few had ciTBI therefore was underpowered to detect significance. Indirectness *QUADAS 2 – applicability)*: None
Comments	-

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Reference	**Cho 2022[14]**
Study type	Retrospective cohort study
Study methodology	Data source: registry data from an ED-based Injury In-depth Surveillance System (nationwide database of injured patients visiting EDs) in 2 hospitals in Korea between August 2015 and August 2016.
Number of patients	n = 448
Patient characteristics	*Age, mean (IQR) months: 2.7 (0-4)* *Gender (male): 260 (58%)* *Gender (female): 188 (42%)*

Reference	**Cho 2022[14]**
	Ethnicity: not reported *Setting*: 2 paediatric emergency departments in Seoul. *Country*: South Korea GCS 14: 2 (0.4) *Inclusion criteria*: <19 years presenting with head trauma within 24 hours of the injury to 2 paediatric EDs. *Exclusion criteria: Patients with a GCS <14; previous history of neurological disease, or trivial injury mechanism (ground level fall, collision with a stationary object, no signs or symptoms of head trauma other than scalp abrasians and lacerations).*
Target condition(s)	Clinically important Traumatic Brain Injury (defined as death from traumatic brain injury, neurosurgical intervention for TBI, intubation of more than 24 h for TBI and hospital admission of 2 nights or more for traumatic brain injury in association with evidence of TBI on CT.
Index test(s) and reference standard	Index test PECARN (Paediatric Emergency Care Applied Research Network) Reference (gold) standard: 14.7% had CT (If the child's risk of ciTBI was high by PECARN algorithm, CT scan was performed; if the risk of ciTBI was intermediate, performing a CT scan was based on physician's judgement, but sufficient information was provided to the parents and final decision about CT scan made after discussion. Low risk of ciTBI CT was not recommended. Follow-up: between 7 days and 90 days after discharge, to ensure no missing TBI, a follow-up phone call was made by a designated nurse and asked whether the patient was diagnosed with TBI after being discharged from the ED.

Reference	Cho 2022[14]
Results	Outcomes: Clinically important traumatic brain injury on CT or follow-up. **Clinically important traumatic brain injury** **<2 years** PECARN (n=448 analysed) TP: 2 FP: 41 TN: 176 FN: 0 Sensitivity %: 100% (19.8-100) Specificity %: 81.1% (75.1-86) PPV%: 4.7% (0.8-17.1) NPV%: 100% (97.2-100) **2 years or over** PECARN (n=448 analysed) TP: 1 FP: 57 TN: 171

Reference	Cho 2022[14]
	FN: 0 Sensitivity %: 100% (5.1-100) Specificity %: 74.6% (68.4-80.1) PPV%: 1.7% (0.1-10.5) NPV%: 100 (97.2-100) Total of above: PECARN (n=448 analysed) TP: 3 FP: 98 TN: 347 FN: 0 Sensitivity %: 100% (31.0-100) Specificity %: 78% (73.8-81.7) PPV%: 3 (0.8-9.1) NPV%: 100 (98.6-100)
Source of funding	Not reported
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: very serious. Unclear if consecutive or random sample enrolled, unclear if index tests and reference standards were interpreted without knowledge of the other and unclear time interval between index test

Reference	**Cho 2022[14]**
	and reference standard, and follow-up duration was 7-90 days which was higher than the 2 weeks stated in the protocol. There was a very small number with ciTBI so was underpowered to detect any significance. Indirectness *QUADAS 2 – applicability)*: None
Comments	Only 3 patients had ciTBI.

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Reference	**Gambacorta 2022[30]**
Study type	Retrospective cohort study
Study methodology	Data source: Data of children with MHI admitted to the ED of A. Gemelli Hospital in Rome between July 2015 and June 2020.
Number of patients	n=3832 study cohort
Patient characteristics	*Age, mean (SD): 5.3 years (4.8)* *Gender (male): 2381 (65.13%)* *Gender (female): 1451(60.9%)* *Ethnicity*: not reported *Setting*: Hospital in Rome *Country*: Italy GCS <14: 11 *Inclusion criteria*: <18 years of age presenting to the ED within 24 hours of head trauma with GCS of 14 or over. *Exclusion criteria: children with severe head trauma; those with trauma that occurred patients who did not wait for the evaluation or refused clinical observation; patients who lacked the necessary data for the application of the PR.*
Target condition(s)	Clinically important Traumatic Brain Injury (defined as: death from TBI; neurosurgical intervention for TBI; intubation of more than 24 hours for TBI; hospital admission of 2 nights or more for the TBI in association with TBI on CT.

Reference	**Gambacorta 2022[30]**
Index test(s) and reference standard	Index test PECARN (Paediatric Emergency Care Applied Research Network) Reference (gold) standard: CT scan Follow-up: not reported
Results	Outcomes: **Clinically important traumatic brain injury** **2 years or over:** PECARN (n= 2613), 455 received a CT scan, 40/455 (8.8%) were abnormal, n=10 defined as ciTBI) TP: FP: TN: FN: Sensitivity %: 97.5 (86.8-99.9) Specificity %: 33.5 (29-38.3) PPV%: NPV%: **< 2 years** PECARN (n=1219 analysed, n=96 received CT scan, 3 had ci-TBI)

Reference	**Gambacorta 2022[30]**
	TP: FP: TN: FN: Sensitivity %: 97.96 (89.1-99.9) in identifying patients with CT scan abnormalities Specificity %: 48.94 (34.1-63.9) in identifying patients with CT scan abnormalities PPV%: NPV%:
Source of funding	Not reported
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: very serious. Unclear if consecutive or random sample enrolled, unclear if index tests and reference standards were interpreted without knowledge of the other and unclear time interval between index test and reference standard. Reference standard was CT and/or observation. There was a very small number with ciTBI so was underpowered to detect any significance. Indirectness *QUADAS 2 – applicability)*: None
Comments	Only 3 patients had ciTBI.

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Reference	**Meral Atis 2022[58]**
Study type	Prospective cohort study
Study methodologyalmer	Data source: between October 1st 2019 and March 8th 2020.
Number of patients	n = 1004

Reference	**Meral Atis 2022[58]**
Patient characteristics	*Age, n (%):* *<2: 290 (28.9)* *2-14: 676 (67.3)* *15-18: 38 (3.8)* *Gender (male): 657 (65.4)* *Gender (female): 347 (34.6%)* *Ethnicity*: not reported *Setting*: Emergency Neurosurgery Outpatient Clinic at Health Sciences University Okmeydani Training and Research Hospital. *Country*: Turkey GCS 13: 2 (0.2) GCS 14: 3 (0.3) GCS 15: 999 (99.5) *Inclusion criteria*: <18 years of age, presenting to the Emergency Neurosurgery Outpatient Clinic, with a GCS score of 13 or higher for whom the attending physician decided to order computed tomography scans of the head and the legal representative provided informed consent for inclusion. *Exclusion criteria: 18 years or older, GCS score <13, presenting with penetrating head trauma or trauma to the other body systems, patients with isolated mild facial trauma.*
Target condition(s)	Head CT positivity and/or the need for hospitalisation.
Index test(s) and reference standard	Index test PECARN (Paediatric Emergency Care Applied Research Network) CATCH (Canadian Assessment of Tomography for Childhood Head Injury) CHALICE (Children's Head Injury Algorithm for the Prediction of Important Clinical Events

Reference	**Meral Atis 2022[58]**
	Reference (gold) standard: CT results (absence or presence of a pathological finding requiring treatment or follow-up). Linear fracture, burst fracture, comminuted fracture, epidural hematoma, subdural hematoma, traumatic subarachnoid hemorrhage, and the presence of contusion were considered to be positive findings on head CT scans. Pediatric GCS score was used in the patient group aged 5 years and younger. Follow-up: not reported.
Results	Outcomes: Head CT positivity and/or the need for hospitalisation. Hospitalisation decision was made by the clinical decision of the neurosurgeon at the Emergency Neurosurgery Outpatient Clinic. **Presence of a pathology in head CT scans:** PECARN (n= 1004 analysed) TP: 24 (82.8%) FP: 536 (55%) TN: 439 (45%) FN: 5 (17.2%) Sensitivity %: 82.76% (64.23 to 94.15%) Specificity %: 45.03 (41.87 to 48.21%) PPV%: not reported NPV%: not reported CATCH (n= 966 analysed)

Reference	Meral Atis 2022[58]
	TP: 25 (89.3%) FP: 493 (52.6%) TN: 445 (47.4%) FN: 3 (10.7%) Sensitivity %: 89.29 (71.77 to 97.73%) Specificity %: 47.44 (44.2-50.69%) PPV%: not reported NPV%: not reported CHALICE (n= 966 analysed) TP: 2 (0.2%) FP: 82 (8.5%) TN: 856 (89%) FN: 26 (2.7%) Sensitivity %: 7.14% (0.88 to 23.50%) Specificity %: 91.26% (89.26-92.99%) PPV%: not reported NPV%: not reported

Reference	Meral Atis 2022[58]
	Hospitalisation: PECARN (n= 1004 analysed) TP: 26 (83.9%) FP: 534 (54.9%) TN: 5 (16.1%) FN: 439 (45.1%) Sensitivity %: 83.87% (66.27-94.55) Specificity %: 45.12% (41.96-48.31) PPV%: not reported NPV%: not reported CATCH (n= 1004 analysed) TP: 27 (90%) FP: 491 (52.5%) TN: 445 (47.5%) FN: 3 (10%) Sensitivity %: 90% (73.47-97.89) Specificity %: 47.54% (44.3-50.80) PPV%: not reported NPV%: not reported

Reference	Meral Atis 2022[58]
	CHALICE (n= 1004 analysed) TP: 3 (10%) FP: 81 (8.7%) TN: 855 (91.3%) FN: 27 (90%) Sensitivity %: 10% (2.11-25.53%) Specificity %: 91.35% (89.36-93.07%) PPV%: not reported NPV%: not reported
Source of funding	Not reported
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: serious. Unclear if index tests and reference standards were interpreted without knowledge of the other and unclear time interval between index test and reference standard. Indirectness *QUADAS 2 – applicability)*: None
Comments	Only 3 patients had ciTBI.

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Reference	Yogo 2021
Study type	Retrospective cohort study
Study methodology	Data source: patients <16 years of age with head trauma, who were admitted to 5 EDs in Japan. Data was collected from each patient's electronic medical record from the data centre. Derivation population enrolled April 2014 to December 2015; validation population from January 2016 to March 2018.

Reference	**Yogo 2021**
Number of patients	n = 645
Patient characteristics	*Age (years), median (IQR):* *5 (2-9)* *Gender (male): n (%): 439 (68)* *Gender (female): n (%): 206 (32)* *Ethnicity*: not reported *Setting*: Under 16 years with head trauma, who were admitted to five EDs in district general hospitals in Japan. The derivation population was enrolled from April 2014 to December 2015; and the validation population from January 2016 to March 2018. *Country*: Japan GCS <15: 72 (11%) *Inclusion criteria*: <16 years of age, history of blunt head injury within 24 hours before admission to the ED; and undergoing a head CT scan for the first time in ED. *Exclusion criteria: Patients transferred from another hospital after undergoing neuroimaging and those who refused consent for treatment were excluded from this study.*
Target condition(s)	Clinically important Traumatic Brain Injury
Index test(s) and reference standard	Index test PECARN (Paediatric Emergency Care Applied Research Network) CATCH (Canadian Assessment of Tomography for Childhood Head Injury) CHALICE (Children's Head Injury Algorithm for the Prediction of Important Clinical Events Reference (gold) standard: CT scan.

Reference	Yogo 2021
	Follow-up: not reported.
Results	Outcomes: **Clinically important traumatic brain injury** Simplified CDR (n= 306 analysed) TP: 31 FP: 8 TN: 136 FN: 131 Sensitivity %: 79.5 (65.5-89) Specificity %: 50.9 (48.9-52.3) PPV%: 19.1 (15.8-21.4) NPV%: 94.4 (90.6-97) CATCH (n= 306 analysed) TP: 33 FP: 6 TN: 163 FN: 104 Sensitivity %: 84.6 (71.2-92.6)

Reference	Yogo 2021
	Specificity %: 61 (59.1-62.2) PPV%: 24.1 (20.3-26.4) NPV%: 96.4 (93.4-98.3) CHALICE (n= 306 analysed) TP: 25 FP: 14 TN: 161 FN: 106 Sensitivity %: 64.1 (49.5-76.7) Specificity %: 60.3 (58.2-62.1) PPV%: 19.1 (14.7-22.8) NPV%: 92 (88.7-94.8) PECARN (n= 306 analysed) TP: 35 FP: 4 TN: 106 FN: 161 Sensitivity %: 89.7 (77.3-95.9)

Reference	**Yogo 2021**
	Specificity %: 39.7 (37.6-40.4) PPV%: 17.9 (15.4-19.1) NPV%: 96.3 (91.9-98.5)
Source of funding	Not reported
Limitations	Risk of bias *(QUADAS 2 – risk of bias)*: serious. Unclear if consecutive or random sample enrolled, unclear if index tests and reference standards were interpreted without knowledge of the other and unclear time interval between index test and reference standard. Indirectness *QUADAS 2 – applicability)*: None
Comments	

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D.4 Children/infants – studies previously included in the review

106 **Studies extracted previously as part of the guideline (not reproduced from HTA)**

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Fabbri 2011[25]	Prospective diagnostic cohort	N = 2391 Inclusion criteria:	Age, Median (range) = 3 (IQR, 1-5) Sex, male =	Review of all children with documented intracranial lesions in medical databases.	Intracranial lesion (NEXUS)	TP = 16 FP = 963 FN= 2 TN = 1410	Source of funding: None reported

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
	(validation of NEXUS and derivation of a new rule) Setting: Multicenter study, Italy	Consecutively triaged children within 24h after injury, aged ≤10 years. Exclusion criteria: Head injuries needing sedation for intubation before emergency department admission, multiple injuries, severe hypotension caused by extracranial injuries and penetrating injuries.	2502 (64.8%) Initial score on GCS 15 = 3489 (90.2%) 14 = 282 (7.3%) 13 = 95(2.5%) Received CT = 2043 (52.8%) 1823 = discharged directly from emergency department	A member of the emergency department then contacted all cases by means of a structured telephone interview to evaluate the outcome by GCS at 6 months follow up. Main outcome was post traumatic lesion on CT scan within 7 days after injury. Posttraumatic lesions requiring admission to hospital and follow-up included: intracerebral hematoma or brain contusion, traumatic subarachnoid haemorrhage, subdural haemorrhage, epidural hematoma, intraventricular haemorrhage and a depressed skull fracture. NEXUS II rule used or Italian proposal, which consisted of: Abnormal GCS, evidence of skull or base fracture, abnormal neurologic examination, vomiting, loss of consciousness, drowsiness or amnesia, headache, impact seizure.		Sensitivity = 88.9 (63.9 - 95.6) Specificity = 59.4 (57.4 – 61.3) NPV = 99.9	Risk of bias – very serious – unclear if index test and reference standard interpreted without knowledge of the other, unclear time interval between index test and reference standard and not all had the same reference standard Indirectness - none
					Intracranial lesion (Italian proposal)	TP = 18 FP = 566 FN= 0 TN = 1807 Sensitivity = 1.00 [78.1 – 99.7] Specificity = 76.1 [74.4 – 77.8] NPV= 100	

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Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Fuller 2011[28]	Prospective cohort (retrospective database search) Validation of PECARN in CHALICE data set. Setting: UK	N = 22,772 (10415 suitable for PECARN rule 5 - 16 years, 4717 suitable for < 2 years) Inclusion criteria: Children 5 - 16 years presenting to the emergency department of 10 northwest England hospitals with head injury. Additional information from authors: Children <2 years from CHALICE cohort. Exclusion criteria: None reported	Entire cohort: Age, mean = 5.7 years Sex, male = 65%	CHALICE patients >5 years were categorised according to PECARN CDR predictors and outcomes (clinically important head injury: death from head injury, neurosurgery, intubation >24h, hospital admission >2 nights with positive CT head).	Intracranial lesion (5 - 16 years)	Sensitivity = 95 (91 - 97) Specificity = 75 (74 - 76) NPV = 99.8 (99.7 - 99.9)	Source of funding: None reported Risk of bias – very serious – unclear if consecutive sample enrolled and exclusion criteria unclear, unclear if index test and reference standard were interpreted without knowledge of the other, unclear if reference standard is likely to diagnose the target condition, unclear time interval between index test and reference standard,
					Additional information from authors: (5 - 16 years)	TP = 234 FP = 2544 FN= 12 TN = 7625 PPV = 8.4 (7.4 - 9.5)	
					Additional information from authors: Intracranial lesion (<2 years)	TP = 17 FP = 1750 FN= 0 TN = 2950 Sensitivity = 100 (80.5 - 100) Specificity = 62.8 (61.4 - 64.2) NPV = 100 (99.9 - 100 PPV = 0.96 (0.6 - 1.5)	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
							unclear if all received the same reference standard and unclear if all patients were included in the analysis Indirectness - none

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Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Osmond 2010[71] Linked to Osmond 2006[70] (abstract only) Validation provided in Osmond 2012[69] (abstract only)	Prospective diagnostic cohort (derivation of the CATCH decision rule) Setting: 10 Canadian paediatric teaching institutions	N = 3866 Inclusion criteria: 1) Consecutive children enrolled, 0 – 16 years 2) Blunt trauma to the head resulting in witnessed loss of consciousness, definite amnesia, witnessed disorientation, persistent vomiting (≥2 more distinct episodes of	Consecutive children enrolled, 0 – 16 years Age, Median (range) = 10 (0-16) Sex, male = 2502 (64.8%) Initial score on GCS 15 = 3489 (90.2%)	Patients underwent clinical examination, treating physician determined whether a CT of the head was required. Radiologists interpreted CT blinded to data collection form. Patients who did not receive a CT were classified as not having a clinically important brain injury after follow up at 14 days by telephone interview (headache absent or mild, no memory or concentration problems, no seizures and retuned to usual daily activities e.g. feeding,	Brain injury - high and medium risk (any acute intracranial finding revealed on CT that was attributable to acute injury, including closed depressed skull fracture and pneumocephalus, but excluding non depressed skull fractures and basilar skull fractures.)	24 (0.6%) (underwent neurologically intervention) CATCH rule: TP = 156 FP = 1851 FN= 3 TN = 1856 Sensitivity = 98.1 [95, 100] Specificity = 50.1 [48, 52]	Quality assessment from 2022 update: Risk of bias – serious – unclear if reference standard interpreted without knowledge od index test and unclear time interval

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
		vomiting 15 mins apart) or persistent irritability in the emergency department (children <2 years). 3) Initial score of 13 GCS, in emergency department, as determined by the treating physician. 4) Injury within past 24 hours. <u>Exclusion criteria:</u> 1) Obvious penetrating skull injury or obvious depressed fracture, acute focal neurologic deficit, chronic generalised developmental delay or head injury secondary to suspected child abuse.	14 = 282 (7.3%) 13 = 95(2.5%) Received CT = 2043 (52.8%) 1823 = discharged directly from emergency department	sleeping, school, play, work). Patients who did not undergo CT and not reached for follow up were excluded from final analysis (n = 245). Variables (from history and physical examination) with the highest association with brain injury found on physical examination and a rule was derived using recursive partitioning analysis: Canadian Assessment of Tomography for Childhood Head Injury: the CATCH rule <u>High risk (need for neurologic intervention</u> 1) GCS <15 at 3 hours after injury 2) Suspected open or depressed skull fracture 3) History of worsening headache 4) Irritability on examination	Neurological intervention - high risk (death within 7 days secondary to head injury or need for craniotomy, elevation of skull fracture, monitoring of intracranial pressure or insertion of an endotrachial tube for treatment of head injury)	TP = 24 FP = 1144 FN= 0 TN = 2698 Sensitivity = 100 [86 - 100] Specificity = 70.2 [69 - 72]	between index test and reference standard Indirectness – none
					Validation of CATCH rule, n = 4060 <u>Neurological intervention - high risk</u>	CATCH rule: TP = 20 FP = 538 FN= 3 TN = 3487 Sensitivity = 87 [68 - 95] Specificity = 87 [86 - 86 - 88]	

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
		2) Patients returning for reassessment of a previously treated head injury and those who were pregnant.		Medium risk (brain injury on CT scan) 5) Any sign of basal skull fracture 6) Large, boggy haematoma of the scalp 7) Dangerous mechanism of injury	Validation of CATCH rule, n = 4060 Brain injury - high and medium risk	CATCH rule: TP = 193 FP = 1331 FN= 4 TN = 2520 Sensitivity = 98 [95 - 99] Specificity = 65 [64 - 67]	

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110 **Summary of studies reproduced from HTA: decision rules for children and infants with mild head injury, definitions of outcomes and**
111 **reference standards**

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
Atabaki et al. 2008[4]	Atabaki et al. 2008	ICI: subdural, epidural, subarachnoid, intraparenchymal and intraventricular haemorrhages as well as contusion and cerebral oedema	CT scan	1000/1000 (100%)	Neurosurgery, including craniotomy, craniectomy, evacuation or intracranial pressure monitoring	Medical record review (unclear when performed)	Risk of bias based on checklist in HTA: serious – based on limitations described in table on page 38 of HTA paper Indirectness - none
Buchanich 2007[13]	Buchanich 2007	ICI: intracranial haematoma, intracranial haemorrhage, cerebral contusion	CT scan Follow-up questionnaire/ telephone interview	97/97 (100%)	NA	NA	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		and/or cerebral oedema					page 38 of HTA paper Indirectness - none
Da Dalt et al. 2006[16]	Da Dalt et al. 2006	ICI: identified on CT either at initial ER presentation or during any hospital admission or readmission	CT scan obtained at discretion of treating physician All children discharged immediately from ER or after short observation received a follow-up telephone interview approximately 10 days later. Hospital records were checked for readmissions for 1 month after conclusion of study	79/3806 (2%)	NA	NA	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 38 of HTA paper Indirectness - none
Dietrich et al. 1993[20]	Dietrich et al. 1993	Intracranial pathology: epidural or subdural haematoma, cerebral contusions or lacerations, intraventricular haemorrhage pneumocephaly or cerebral oedema, with or without skull fracture	CT scan	166/166 (100%) 71/71 (100%)[a]	NA	NA	Risk of bias based on checklist in HTA: serious – based on limitations described in table on page 38 of HTA paper Indirectness - none

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
Dunning et al. 2006[21, 22]	CHALICE, RCS guidelines	Clinically significant ICI: death as a result of head injury, requirement for neurosurgical intervention or marked abnormalities on the CT scan	All patients treated according to RCS guidelines. This recommends admission for those at high risk and CT scan for those at highest risk Follow-up: all patients who were documented as having had a skull radiograph, admission to hospital, CT scan or neurosurgery were followed up	744/22,772 (3.3%)	NR	NR, assume as the same for ICI	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 38 of HTA paper Indirectness - none
Greenes and Schutzman 1999[32], 2001[33]	Greenes and Schutzman 1999, 2001	Greenes and Schutzman 1999 ICI: acute intracranial haematoma, cerebral contusion and/or diffuse brain swelling evident on head CT Greenes and Schutzman 2001 ICI: cerebral contusion, cerebral oedema or intracranial haematoma noted on CT	Greenes and Schutzman 1999 CT scan, follow-up calls, review of medical records Greenes and Schutzman 2001 CT scan	188/608 (31%). 73 symptomatic patients did not receive CT [b]172/172 (100%)	NA	NA	Risk of bias based on checklist in HTA: serious – based on limitations described in table on page 38 of HTA paper Indirectness - none

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
Guzel et al. 2009[35]	Guzel et al. 2009	Positive CT scan: definition NR	CT scan	337/337 (100%)	NA	NA	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 38 of HTA paper Indirectness - none
Haydel and Schembekar 2003[39]	NOC	ICI on head CT: any acute traumatic intracranial lesion, including subdural epidural or parenchymal haematoma, subarachnoid haemorrhage, cerebral contusion or depressed skull fracture	CT scan	175/175 (100%)	Need for neurosurgical or medical intervention in patients with ICI on CT	All patients with abnormal CT scan admitted and followed until discharge	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 38 of HTA paper Indirectness - none
Kupperman et al. 2009[50]	Kupperman et al. 2009	Clinically important brain injury: death from TBI, neurosurgery, intubation for > 24 hours for TBI, or hospital admission of two nights or more associated with TBI on CT. Brief intubation for imaging and overnight stay for	CT scans, medical records, and telephone follow-up. Those admitted: medical records, CT scan results Those discharged: telephone survey 7 to 90 days after the ED visit, and medical records and county morgue	9420/25,283 (37.3%)[c] 2632/8502 (31.0%)[c] 2223/6411 (34.7%)[c] 694/2216 (31.3%)[c]	NR	NR for neurosurgery. Assume as for ICI	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 38 of HTA paper Indirectness - none

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		minor CT findings not included	records check for those uncontactable				
Oman 2006[66]; [a]Sun et al. 2007[91]	NEXUS II, pilot PECARN	Clinically important/ significant ICI: any injury that may require neurosurgical intervention, lead to rapid clinical deterioration, or result in significant long-term neurological impairment	CT scan	1666/1666 (100%)[d] 309/309 (100%)[d] 208/208 (100%)	NA	NA	Risk of bias based on checklist in HTA: serious – based on limitations described in table on page 38 of HTA paper Indirectness - none
Osmond et al. 2006[70]	CATCH	Brain injury	CT scan 14-day telephone interview	NR	Neurosurgery: craniotomy, elevation of skull fracture, intubation, intracranial pressure monitor and/or anticonvulsants within 7 days[e]	NR	See Osmond 2010 evidence table
Palchak et al. 2003[73]	Pilot PECARN	TBI identified on CT scan or TBI requiring acute intervention or intervention by one or more of: neurosurgical procedure, ongoing antiepileptic pharmacotherapy beyond 7 days, the presence of a neurological deficit	CT or performance of intervention	1271/2043 (62.2%) 1098/1098 (100%) 194/194 (100%)	Need for neurosurgical intervention	NR	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 38 of HTA paper Indirectness - none

Study	Rule(s) tested	Definition of ICI	Reference standard used for ICI	Patients who had CT (n)	Definition of need for neurosurgery	Reference standard used for need for neurosurgery	Risk of bias and indirectness
		that persisted until discharge from the hospital, or two or more nights of hospitalisation because of treatment of the head injury					
Quayle et al. 1997[77]	Quayle et al. 1997	ICI: definition NR	CT scan	321/321 (100%)	NA	NA	Risk of bias based on checklist in HTA: very serious – based on limitations described in table on page 38 of HTA paper Indirectness - none

CATCH, Canadian Assessment of Tomography for Childhood Injury; Cs, consecutive; Cv, convenience; NA, not applicable; NEXUS II, National Emergency X-Radiography Utilization Study II; NR, not reported; P, prospective; PECARN, Paediatric Emergency Care Applied Research Network; R,retrospective; RCS, Royal College of Surgeons; UCD, University of California–Davis rule.
(a) Dietrich et al.: large cohort was split into two separate cohorts of different ages.
(b) Greenes and Schutzman derived rule for asymptomatic subset of original cohort reported in Greenes and Schutzman, using only thosewith CT.
(c) Kupperman et al. report two separate cohorts of patients, with each cohort split into two groups of different ages.
(d) Oman and Sun et al. use a subset of the NEXUS II derivation cohort; all cohorts reported here are subgroups with overlapping patients.
(e) From Mehta.

Decision rules for children and infants with mild head injury reproduced from HTA

Criteria / Decision rule	Atabaki et al 2008	Buchanich 2007	Da Dalt et al 2006	Dietrich et al 1993	CHALICE	CATCH Medium risk	CATCH high risk	Greenes and Schutzman 1999	Greenes and Schutzman 2001	Guzel et al 2009
Version of rule						Medium-risk factors	High-risk factors	Decision rule	Scoring system	

Criteria / Decision rule	Atabaki et al 2008	Buchanich 2007	Da Dalt et al 2006	Dietrich et al 1993	CHALICE	CATCH Medium risk	CATCH high risk	Greenes and Schutzman 1999	Greenes and Schutzman 2001	Guzel et al 2009
Eligibility criteria	<21 years all severity	<3 years, GCS 14-15	<16 years, all severity, some exclusions	>2 years to 20 years, all severity, some exclusions	< 16 years, all severity	< 16 years, GCS 13-15, with clinical characteristics	<16 years, GCS 13-15, with clinical characteristics	<2 years, all severity	Asymptomatic < 2 years	<16 years, GCS 13-15
Mental status	GCS <15		Abnormal GCS	GCS <15	Abnormal GCS <14 or GCS <15 if <1 year old			Depressed		
Focal/neurological status	Sensory deficit		Abnormal neurological examination	Focal neurological deficits				Abnormal vital signs indicating possible increased intracranial pressure or focal neurological findings		
Skull fracture	Defect or signs of basilar skull fracture		Clinical signs in risk area, skull base fracture		Clinical signs of skull fracture	Signs of basal skull fractureb		Abnormal vital signs indicating possible increased intracranial pressure or focal neurological findings		
LOC			Prolonged	LOC	LOC			LOC		LOC

Criteria / Decision rule	Atabaki et al 2008	Buchanich 2007	Da Dalt et al 2006	Dietrich et al 1993	CHALICE	CATCH Medium risk	CATCH high risk	Greenes and Schutzman 1999	Greenes and Schutzman 2001	Guzel et al 2009
Vomiting		Vomiting		Vomiting	Vomiting			Two or more		Vomiting
Age	<2 years								Risk factorc	
Amnesia			Persistent	For the event	Amnesia					PTA
Coagulopathy										
Seizures				Seizures	Seizures					Seizures
Visible injury		Scalp lacerations			Scalp trauma	Large boggy scalp haematoma			Scalp haematoma location and size[c]	
Behaviour		Inconsolable	Persistent drowsiness			b	Irritability on examination	Lethargy or irritability		
Headache		Persistent	Headache			b	Worsening headache			Headache
Previous neurosurgery										
Failure to improve						b	Failure to reach GCS 15 in 2 hours			
Mechanism of injury	Bicycle-related injury				High speed road traffic, or high speed or fall >3 m	Dangerous				

Criteria / Decision rule	Atabaki et al 2008	Buchanich 2007	Da Dalt et al 2006	Dietrich et al 1993	CHALICE	CATCH Medium risk	CATCH high risk	Greenes and Schutzman 1999	Greenes and Schutzman 2001	Guzel et al 2009
Deterioration in mental status	Mental status change									
Other	Dizziness	Vision changes, gender, area of residence			Suspicion of non-accidental injury			Bulging fontanelle		Blurred vision

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125 **Decision rules for children and infants with mild head injury reproduced from HTA continued**

Criteria / Decision rule	NEXUS II	NOC	PECARN (>2 years to 18 years)	PECARN (<2 years)	Quayle et al 1997	RCS[a] guidelines	UCD - neurosurgery	UCD – intervention or brain injury	UCD - TBI
Version of rule			≥ 2 years to <18	<2 years			Neurosurgery	Intervention or brain injury	TBI
Eligibility criteria[b]	All ages, blunt head trauma	5 – 17 years, GCS 15 with clinical characteristics, some exclusion	≥2 years to < 18 years, GCS 14-15, some exclusions (e.g. trivial injury)	<2 years, GCS 14-15, some exclusions (e.g. trivial injury	<18 years, non-trivial injury (with clinical characteristics)	All severities and ages,[a] with additional protocol for children	<18 years, non-trivial head injury, with clinical characteristics, some exclusions	<18 years, not trivial head injury, with clinical characteristics, some exclusions	<18 years, GCS 14-15, non-trivial, with clinical characteristics, some exclusions
Mental status	Altered level of alertness		Altered	Altered	Altered		Abnormal[c]	Abnormal[c]	Abnormal[c]
Focal/neurological status	Neurological deficit				Focal neurological deficit		Focal neurological deficit		

Criteria Decision rule	NEXUS II	NOC	PECARN (>2 years to 18 years)	PECARN (<2 years)	Quayle et al 1997	RCS[a] guidelines	UCD - neurosurgery	UCD – intervention or brain injury	UCD - TBI
Skull fracture	Evidence of significant skull fracture	Clinically suspected skull fracture	Clinical signs of basilar skull fracture	Palpable or unclear	Signs of basilar skull fracture			Clinical signs of skull fracture	Clinical signs of skull fracture
LOC			LOC	LOC		LOC[d]			
Vomiting	Persistent	Vomiting	Vomiting			Persistent[d]	Vomiting	Vomiting[e]	Vomiting
Age	N/A to children (≥65 years)								
Amnesia						Amnesia[d]			
Coagulopathy	Coagulopathy								
Seizures		PTS							
Visible injury	Scalp haematoma	Trauma above the clavicles[f]		Scalp haematoma		Scalp laceration, bruise or swelling[d] Significant maxillofacial injuries[d]		Scalp haematoma in a child ≤2 years	Scalp haematoma in a child ≤2 years
Intoxication		Drug or alcohol							
Behaviour	Abnormal behaviour			Acting abnormally according to parent					
Headache		Headache	Severe			Persistent[d]		Headache[e]	
Previous neurosurgery									
Failure to improve									

Criteria / Decision rule	NEXUS II	NOC	PECARN (>2 years to 18 years)	PECARN (<2 years)	Quayle et al 1997	RCS[a] guidelines	UCD - neurosurgery	UCD – intervention or brain injury	UCD - TBI
Mechanism of injury			Severe[g]	Severe[h]		Violent[d] fall from >1m[i] or on to hard surface[i]			
Deterioration in mental status									
Other		Short term memory deficits[j]				Tense fontanelle[i] Suspected non-accidental injury[i]			

MVC, motor vehicle collision; RCS, Royal College of Surgeons.

(a) RCS guidelines for all ages is in three parts: (1) Indications for referral to neurosurgeon and/or urgent CT: coma; deteriorating level of consciousness or progressive focal neurological deficit; fracture of the skull if with confusion, deteriorating impairment of consciousness, fits, or neurological symptoms or signs; open injury (depressed compound fracture of skull vault, base of skull fracture or penetrating injury); patient fulfils criteria for CT of the head within referring hospital but this cannot be performed within a reasonable time (e.g. 2–4 hours). (2) Indications for CT of the head prior to referral to neurosurgeons: full consciousness but with a skull fracture; fits without a skull fracture; confusion or neurological symptoms/signs persisting after initial assessment and resuscitation; unstable systemic state precluding transfer to neurosurgery, diagnosis uncertain; tense fontanelle or suture diastasis in a child; significant head injury requiring general anaesthesia. (3) Indications for referral to neurosurgeons after CT of the head: abnormal CT scan (after neurosurgical opinion on images transferred electronically) or normal CT scan but unsatisfactory progress.

(b) Eligibility criteria are either the inclusion criteria of the derivation cohort or the patients for whom the rule was intended if there is no derivation cohort.

(c) Abnormal mental status present if GCS < 15, if patient confused, somnolent, repetitive or slow to respond to verbal communication.

(d) Indications for skull radiography in children. If skull radiograph is positive, CT required. Other indications for all ages also apply.a

(e) Definition used by Sun et al.; high-risk vomiting, severe or progressive headache.

(f) Contusions, abrasions, lacerations, haematoma, deformity, clinically suspected facial or skull fracture.

(g) Severe mechanism defined as MVC with patient ejection, death of another passenger, or rollover, pedestrian or bicyclist without helmet struck by a motorised vehicle, falls of > 1.5 m, head struck by a high-impact object

(h) Motor vehicle collision with patient ejection, death of another passenger, or rollover, pedestrian or bicyclist without helmet struck by a motorised vehicle, falls of > 0.9 m, head struck by a high-impact object.

(i) Indications for skull radiography in infants. If skull radiograph is positive, CT required. Other indications for all ages also apply.a

(j) Defined by persistent anterograde amnesia and normal GCS, to three-object recall.

D.5 HTA report

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
Pandor 2011[65] Only data relating to decision rules presented here. HTA report also reviews studies relating to bio-markers, individual patient characteristics	Health Technology Assessment systematic review of diagnostic cohort studies (prospective or retrospective) with a minimum of 20 patients **Excluded:** Case control studies, animal studies, narrative reviews, editorials, opinions, non-English language papers, reports in which insufficient methodological details reported to allow critical	Adults N = 19 studies reporting data for 25 decision rules, 11 were evaluated in more than one dataset 6 also stratified into two categories, one to identify those needing neurosurgery (high risk) and one to identify those at risk of ICI (medium risk) 6 included coagulapathy as part of the decision rule (criteria varied between rules). Children N = 14 studies reporting data for 15 decision rules, 4 were evaluated in more than one dataset for ICI only	Inclusion criteria **Population:** All adults and children of any age with mild head injury (defined as patients with blunt head injury and a GCS of 13-15 at presentation. Studies with a broad range of head injury provided >50% had mild head injury. Exclusion criteria: **Population:** Moderate or severe head injury (defined as GCS of ≤12 at presentation)	**Index tests:** • Application of a clinical decision rule (defined as a decision making toll that incorporates 3 or more variables obtained from the history, physical examination or simple diagnostic tests) **Reference standard:** • CT scan • Combination of CT scan and follow-up for those without CT scan • MRI scan	The need for neurosurgical intervention Any intracranial injury	Each study tests their population against one or more decision rules. Results given in forest plots. Summary of studies and rules tested presented in Table 18 - Table 21 below.	Source of funding: National Institute for Health Research (NIHR) Health Technology Assessment programme

Reference	Study type	Number of patients	Patient characteristics	Intervention and comparison (Index test and reference standard)	Outcome measures	Effect sizes	Comments
	appraisal of the study quality.	4 presented more than one version of the rule	or no history of injury.				

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Appendix E – Forest plots

E.1 Coupled sensitivity and specificity forest plots

E.1.1 Adults – Any intracranial injury (definitions vary) – studies where all had CT

Figure 2: CCHR high and medium risk

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Arab 2015	12	128	6	221	0.67 [0.41, 0.87]	0.63 [0.58, 0.68]
Davey 2018	5	167	0	68	1.00 [0.48, 1.00]	0.29 [0.23, 0.35]
Ibanez 2004	71	505	12	513	0.86 [0.76, 0.92]	0.50 [0.47, 0.54]
Jones 2020	31	459	8	181	0.79 [0.64, 0.91]	0.28 [0.25, 0.32]
Kavalci 2014	14	88	7	66	0.67 [0.43, 0.85]	0.43 [0.35, 0.51]
Lamba 2021	16	46	0	39	1.00 [0.79, 1.00]	0.46 [0.35, 0.57]
Li 2022	111	230	11	111	0.91 [0.84, 0.95]	0.33 [0.28, 0.38]
Smits 2005	171	1105	34	718	0.83 [0.78, 0.88]	0.39 [0.37, 0.42]
Yang 2017	82	272	0	271	1.00 [0.96, 1.00]	0.50 [0.46, 0.54]

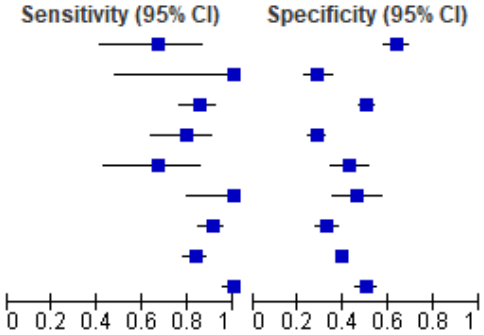

Figure 3: CCHR high and medium risk adapted to cohort

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Smits 2005	265	1731	47	1138	0.85 [0.80, 0.89]	0.40 [0.38, 0.41]

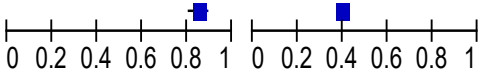

Figure 4: CCHR high and medium risk with cut-point ≥2

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Chobdari 2018	106	33	33	92	0.76 [0.68, 0.83]	0.74 [0.65, 0.81]

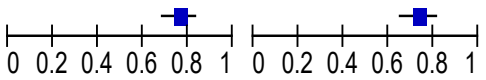

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Figure 5: NOC

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Haydel 2000	57	640	0	212	1.00 [0.94, 1.00]	0.25 [0.22, 0.28]
Ibanez 2004	79	828	4	190	0.95 [0.88, 0.99]	0.19 [0.16, 0.21]
Jones 2020	36	552	3	88	0.92 [0.79, 0.98]	0.14 [0.11, 0.17]
Kavalci 2014	12	143	7	66	0.63 [0.38, 0.84]	0.32 [0.25, 0.38]
Li 2022	119	210	3	131	0.98 [0.93, 0.99]	0.38 [0.33, 0.44]
Papa 2012	22	262	0	30	1.00 [0.85, 1.00]	0.10 [0.07, 0.14]
Smits 2005	115	1123	2	67	0.98 [0.94, 1.00]	0.06 [0.04, 0.07]
Yang 2017	82	336	0	207	1.00 [0.96, 1.00]	0.38 [0.34, 0.42]

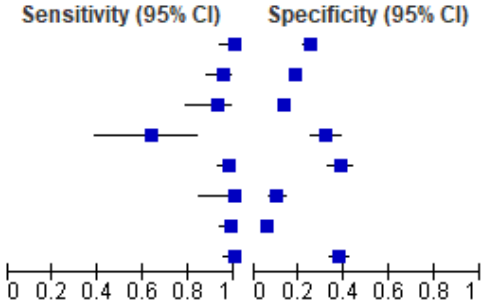

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Figure 6: NOC adapted to cohort

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Smits 2005	310	2777	2	92	0.99 [0.98, 1.00]	0.03 [0.03, 0.04]

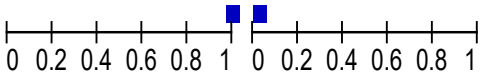

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Figure 7: NOC with cut-point ≥2

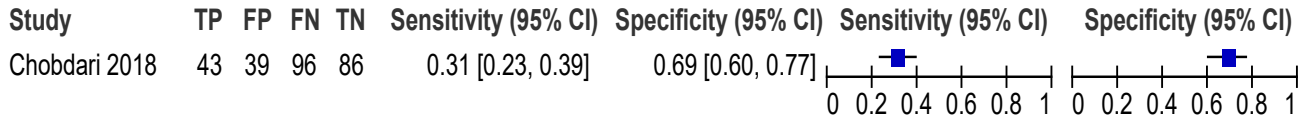

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Figure 8: NEXUS II

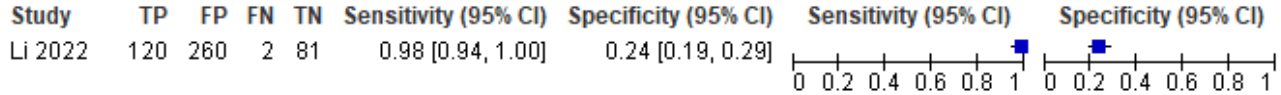

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Figure 9: CHIP simple decision rule

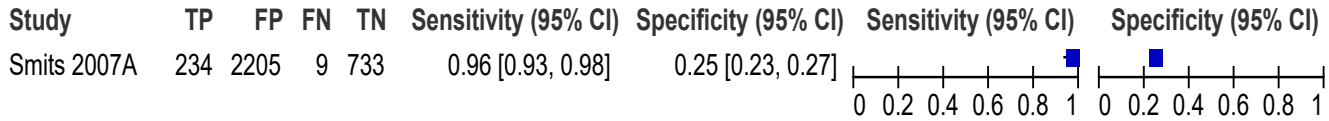

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Figure 10: NCWFNS high and medium risk

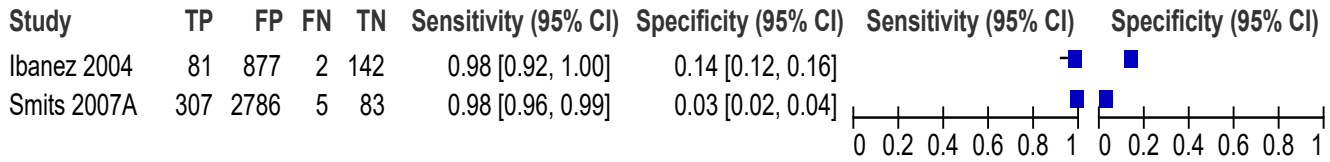

Figure 11: NICE lenient criteria (2003 and 2007 versions)

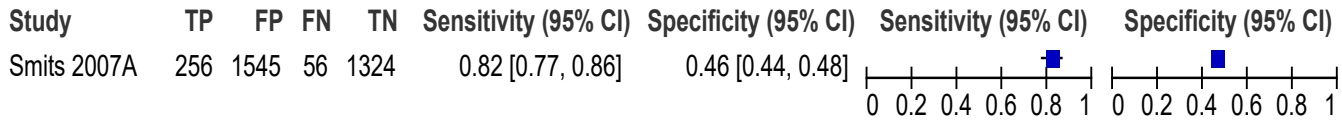

Figure 12: Scandinavian lenient criteria

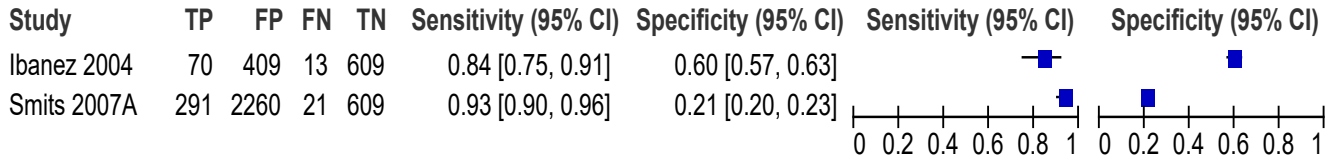

Figure 13: Arienta 1997 rule

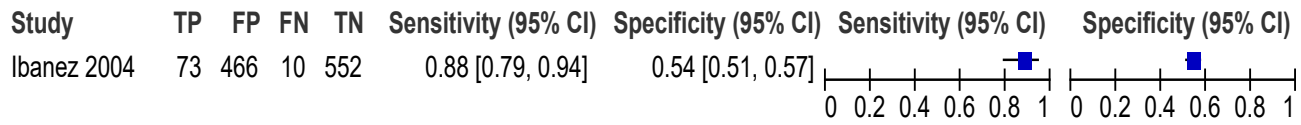

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Figure 14: Ono et al. 2007 rule

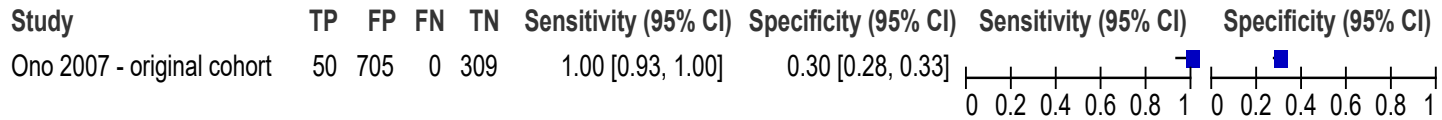

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Figure 15: SIGN CT urgently

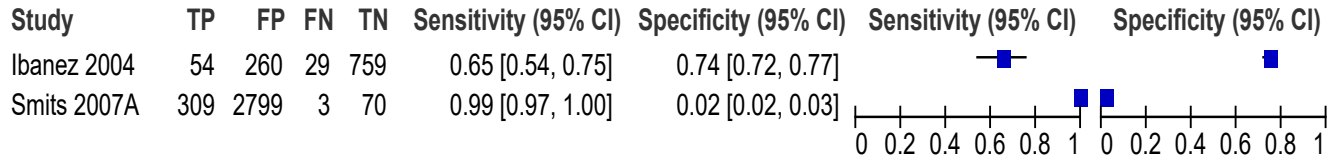

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Figure 16: EFNS recommended and mandatory

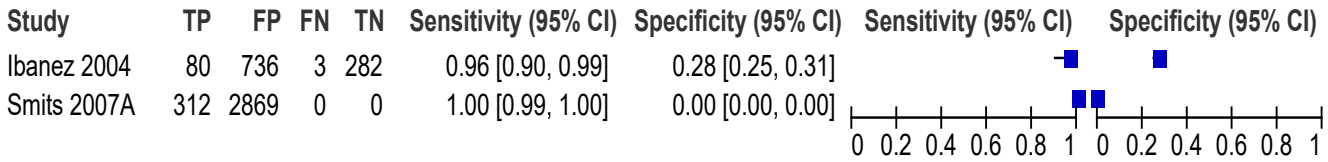

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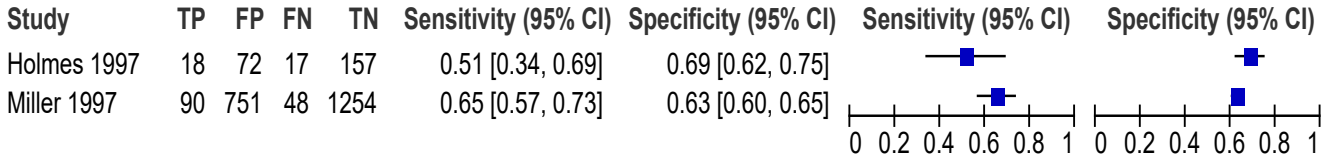
Figure 17: Miller et al. criteria



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E1102 Adults – Any intracranial injury (definitions vary) – studies where only a proportion had CT

Figure 18: NICE 2014 guideline

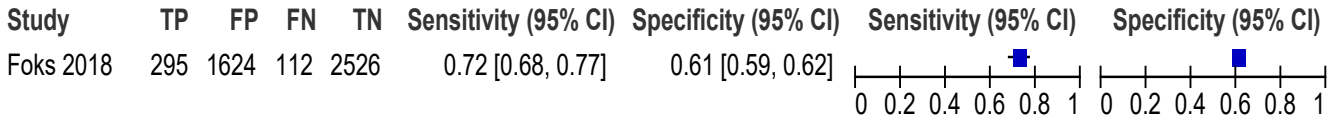

Figure 19: CCHR high and medium risk

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bouida 2013	207	472	11	892	0.95 [0.91, 0.97]	0.65 [0.63, 0.68]
Foks 2018 - original rule in subpop. designed for	209	821	47	606	0.82 [0.76, 0.86]	0.42 [0.40, 0.45]
Korley 2013	5	104	0	60	1.00 [0.48, 1.00]	0.37 [0.29, 0.44]
Stein 2009	526	3935	5	3489	0.99 [0.98, 1.00]	0.47 [0.46, 0.48]
Vaniyapong 2020	214	711	30	209	0.88 [0.83, 0.92]	0.23 [0.20, 0.26]

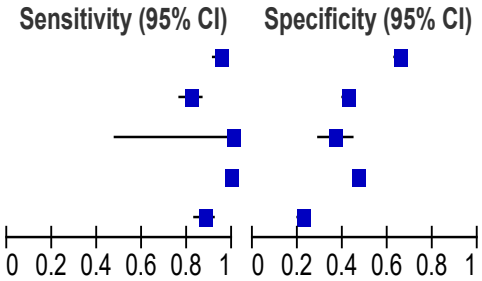

Figure 20: CCHR high and medium risk adapted to cohort

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Foks 2018 - adapted rule in whole population	333	2409	74	1741	0.82 [0.78, 0.85]	0.42 [0.40, 0.43]

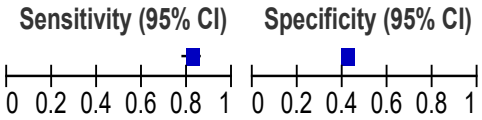

Figure 21: CCHR high risk

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Stein 2009	515	3638	16	3786	0.97 [0.95, 0.98]	0.51 [0.50, 0.52]

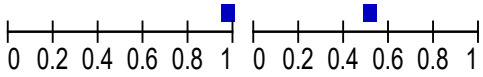

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Figure 22: NOC

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bouida 2013	187	976	31	388	0.86 [0.80, 0.90]	0.28 [0.26, 0.31]
Foks 2018 - original rule in subpop. designed for	137	973	2	35	0.99 [0.95, 1.00]	0.03 [0.02, 0.05]
Korley 2013	5	159	0	5	1.00 [0.48, 1.00]	0.03 [0.01, 0.07]
Stein 2009	526	4974	5	2450	0.99 [0.98, 1.00]	0.33 [0.32, 0.34]

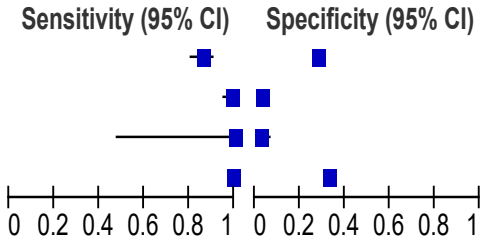

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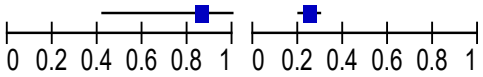
Figure 23: NOC – Yarlagadda 2019 study presented separately based on differences in population compared to other studies

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Yarlagadda 2019	6	244	1	81	0.86 [0.42, 1.00]	0.25 [0.20, 0.30]



Study specifically in those with inpatient falls and majority taking anticoagulation

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Figure 24: NOC adapted to cohort

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Foks 2018 - adapted rule in whole population	402	3984	5	166	0.99 [0.97, 1.00]	0.04 [0.03, 0.05]

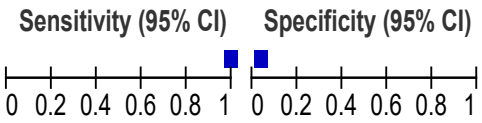

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Figure 25: NEXUS II

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Stein 2009	515	3935	16	3489	0.97 [0.95, 0.98]	0.47 [0.46, 0.48]

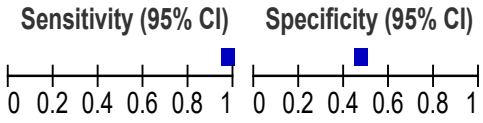

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Figure 26: CHIP simple decision rule

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Foks 2018	383	3253	24	897	0.94 [0.91, 0.96]	0.22 [0.20, 0.23]

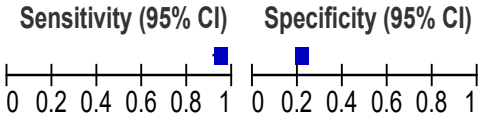

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Figure 27: NCWFNS high and medium risk

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fabbri 2005	530	4010	12	3403	0.98 [0.96, 0.99]	0.46 [0.45, 0.47]

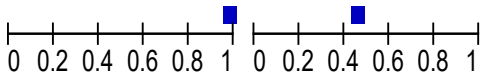

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Figure 28: NICE lenient criteria (2003 and 2007 versions)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fabbri 2005	507	2223	35	5190	0.94 [0.91, 0.95]	0.70 [0.69, 0.71]
Stein 2009	526	5123	5	2301	0.99 [0.98, 1.00]	0.31 [0.30, 0.32]

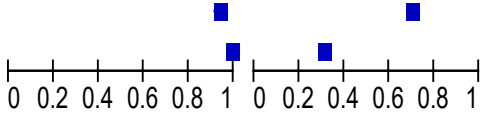

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Figure 29: Scandinavian lenient criteria

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Stein 2009	510	3489	21	3935	0.96 [0.94, 0.98]	0.53 [0.52, 0.54]

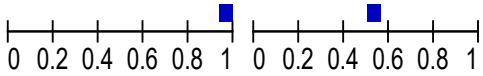

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Figure 30: Arienta et al. 1997 rule

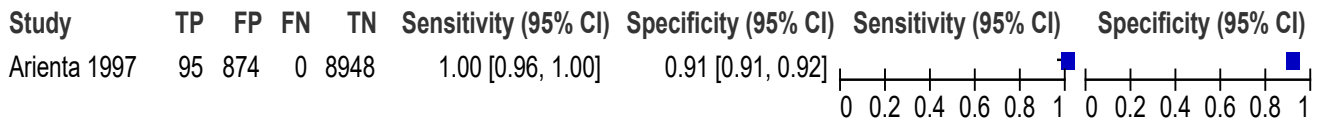

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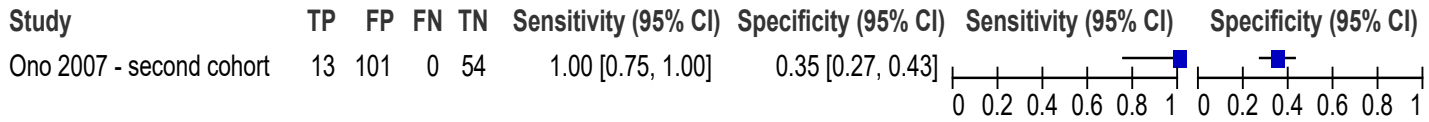
Figure 31: Ono et al. 2007 rule



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E183 **Adults – Clinically important/more serious injuries (definitions vary) – studies where all had CT**

Figure 32: CCHR high and medium risk

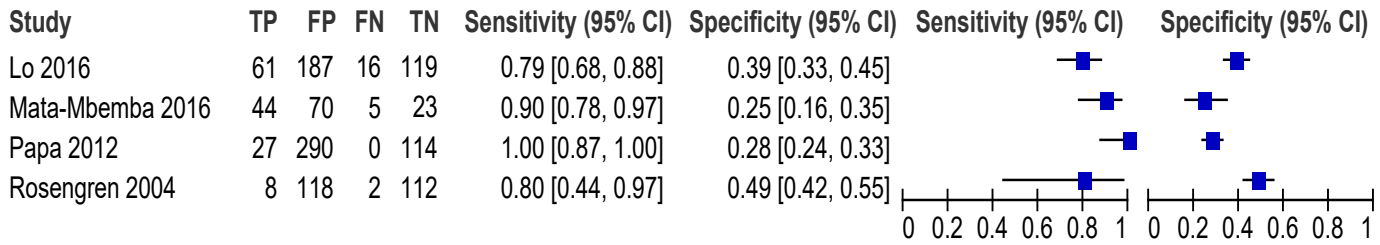

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Figure 33: CCHR high risk

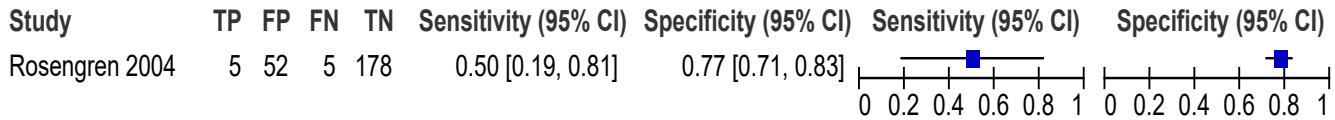

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Figure 34: CCHR moderate risk

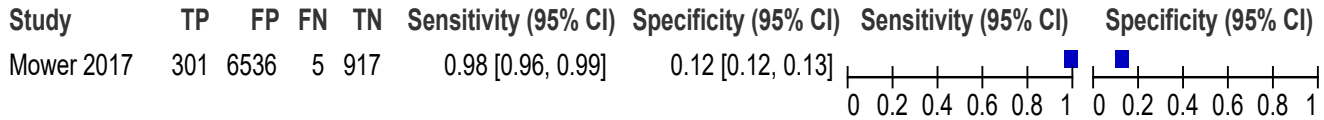

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Figure 35: NOC

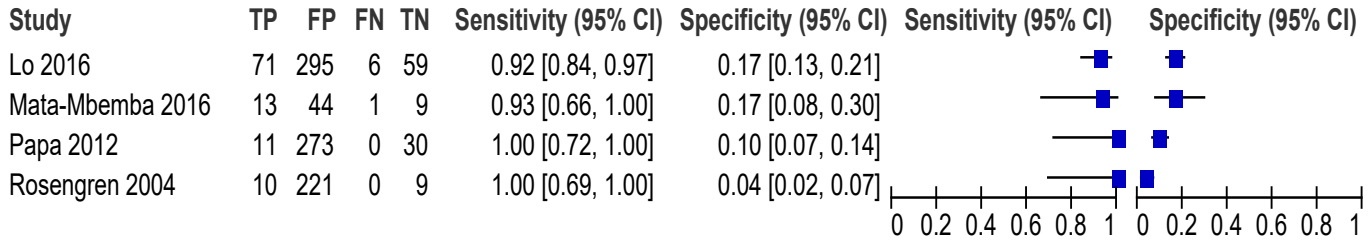

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Figure 36: NOC adapted to cohort

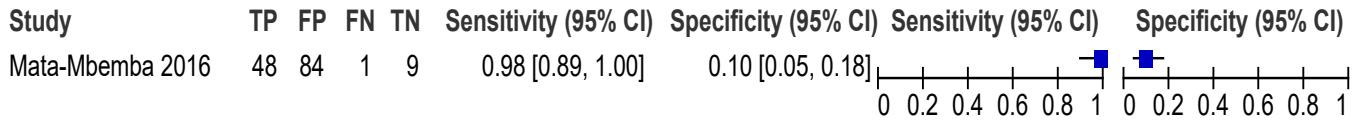

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Figure 37: NEXUS II

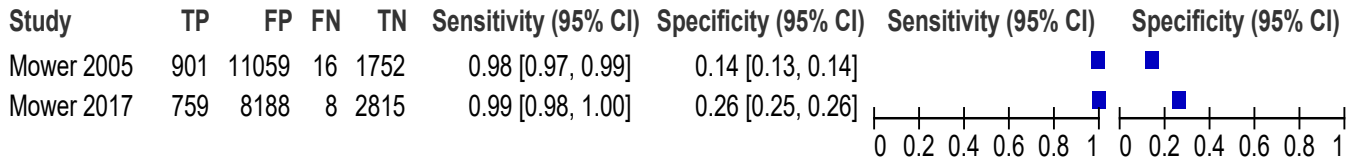

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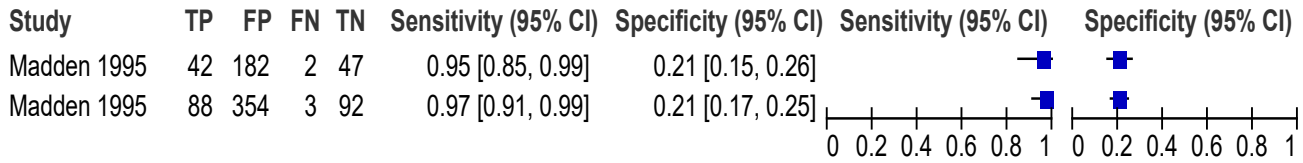
Figure 38: Madden et al. 1995 rule



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E1944 Adults – Clinically important/more serious injuries (definitions vary) – studies where only a proportion had CT

Figure 39: NICE 2014 guideline

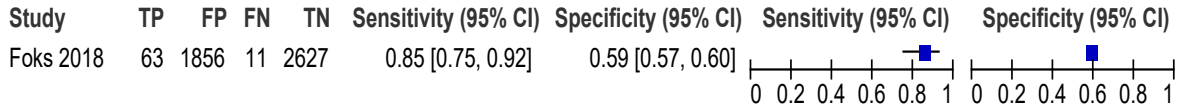

Figure 40: CCHR high and medium risk

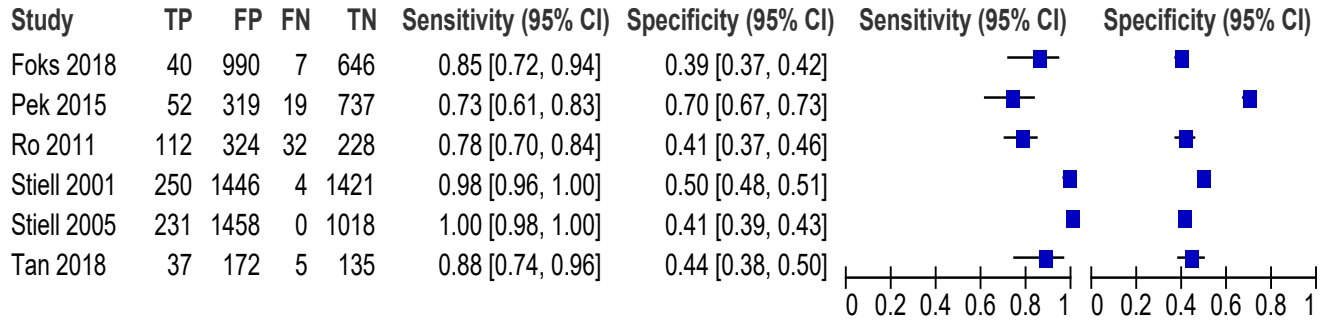

Figure 41: CCHR high and medium risk adapted to cohort

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Foks 2018 - adapted rule in whole population	65	2677	9	1806	0.88 [0.78, 0.94]	0.40 [0.39, 0.42]

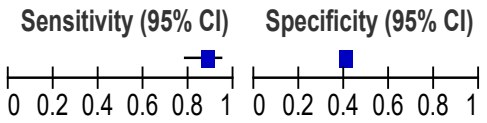

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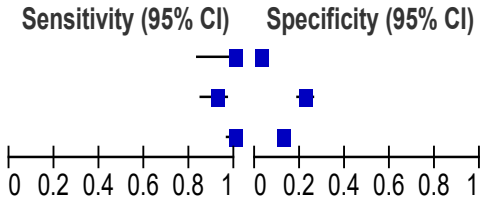
Figure 42: NOC

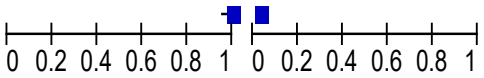
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Foks 2018 - original rule in subpop. designed for	20	1090	0	37	1.00 [0.83, 1.00]	0.03 [0.02, 0.04]
Ro 2011	91	433	8	125	0.92 [0.85, 0.96]	0.22 [0.19, 0.26]
Stiell 2005	97	1506	0	219	1.00 [0.96, 1.00]	0.13 [0.11, 0.14]



196

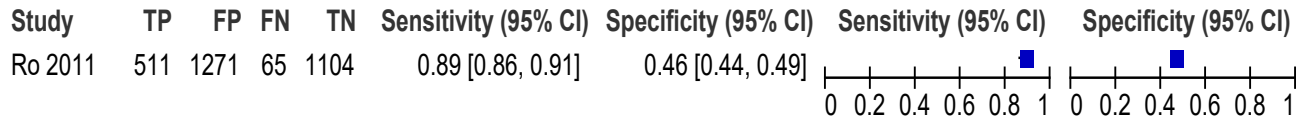
Figure 43: NOC adapted to cohort

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Foks 2018 - adapted rule in whole population	74	4312	0	171	1.00 [0.95, 1.00]	0.04 [0.03, 0.04]



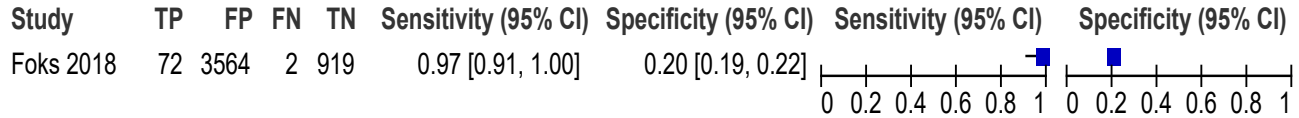
197

Figure 44: NEXUS II



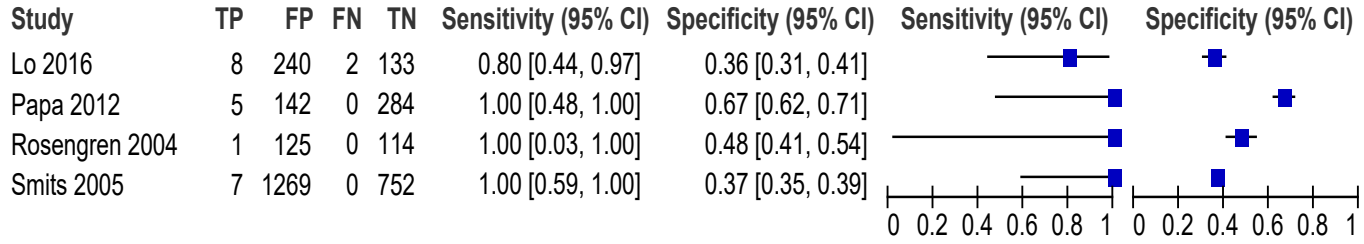
198

Figure 45: CHIP simple decision rule



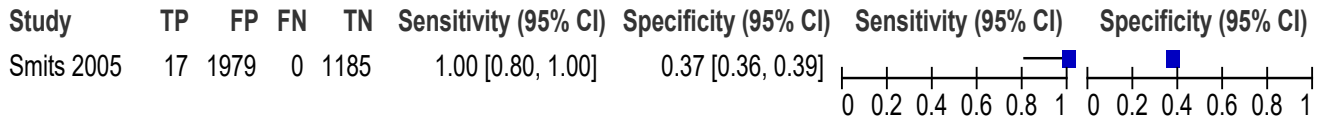
E195 **Adults – neurosurgery (definitions vary) – studies where all had CT**

Figure 46: CCHR high and medium risk



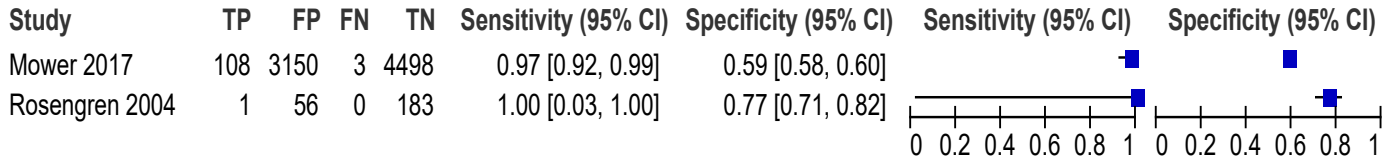
200

Figure 47: CCHR high and medium risk adapted to cohort



201

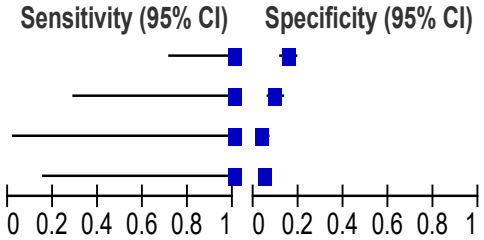
Figure 48: CCHR high risk



202

Figure 49: NOC

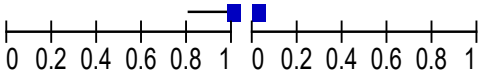
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Lo 2016	11	355	0	65	1.00 [0.72, 1.00]	0.15 [0.12, 0.19]
Papa 2012	3	281	0	30	1.00 [0.29, 1.00]	0.10 [0.07, 0.13]
Rosengren 2004	1	230	0	9	1.00 [0.03, 1.00]	0.04 [0.02, 0.07]
Smits 2005	2	1236	0	69	1.00 [0.16, 1.00]	0.05 [0.04, 0.07]



203

Figure 50: NOC adapted to cohort

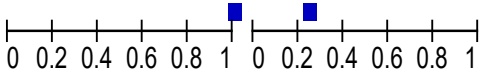
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Smits 2005	17	3070	0	94	1.00 [0.80, 1.00]	0.03 [0.02, 0.04]



204

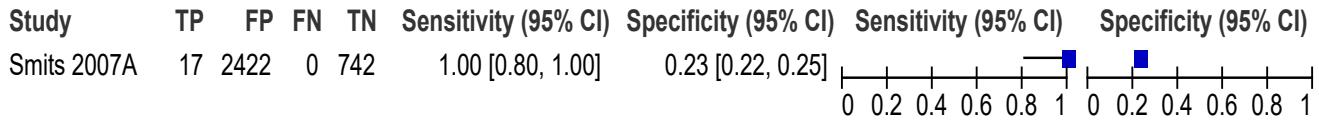
Figure 51: NEXUS II

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Mower 2017	420	8527	0	2823	1.00 [0.99, 1.00]	0.25 [0.24, 0.26]



205

Figure 52: CHIP simple decision rule



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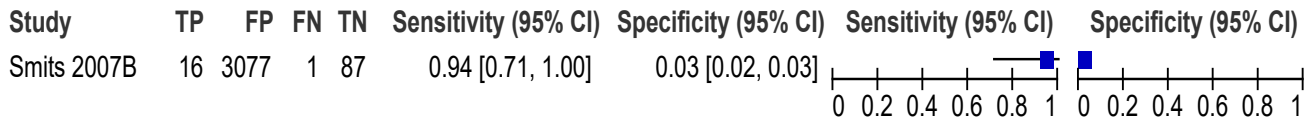
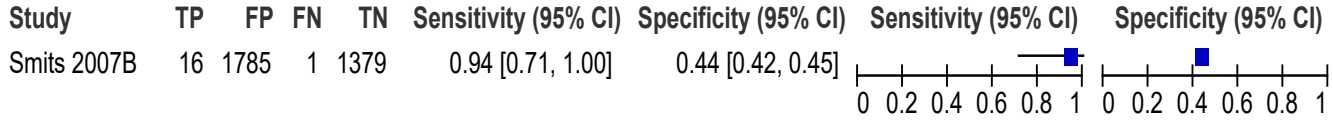
207

Figure 53: NCWFNS high and medium risk



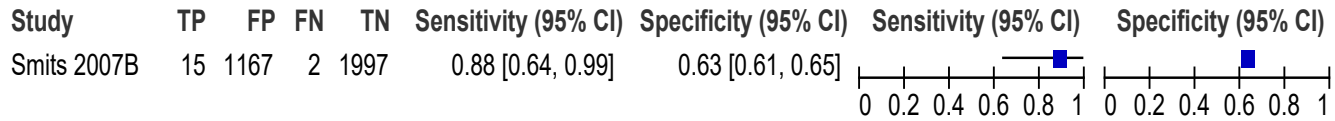
208

Figure 54: NICE lenient criteria (2003 and 2007 versions)



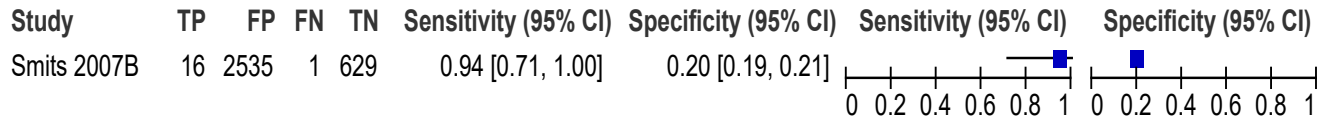
209

Figure 55: NICE strict (2003/2007 version? pre-2014)



210

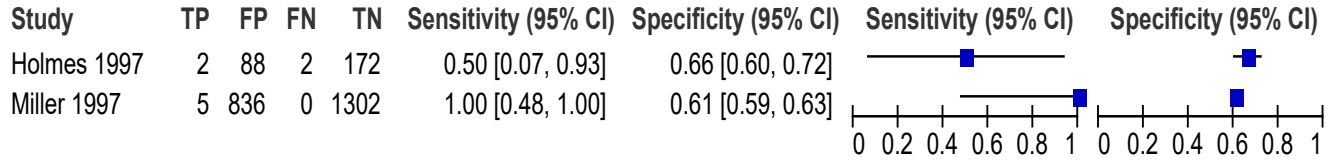
Figure 56: Scandinavian lenient criteria



211

212

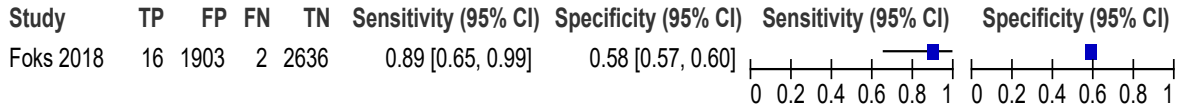
Figure 57: Miller et al. criteria



213

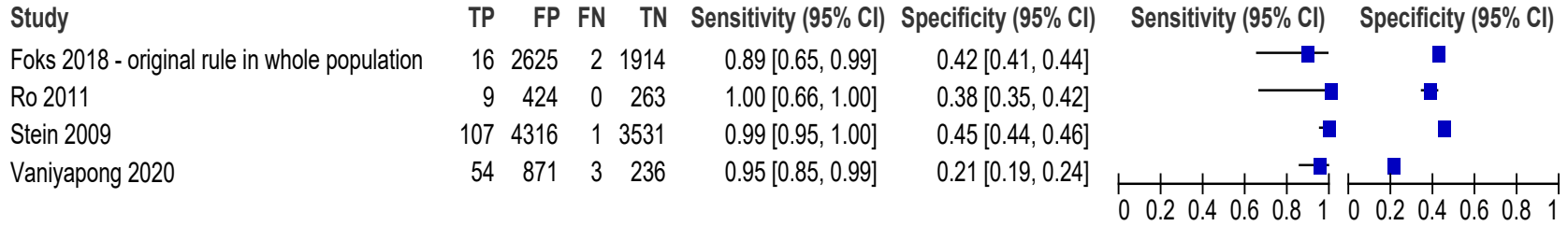
E2146 Adults – neurosurgery (definitions vary) – studies where only a proportion had CT

Figure 58: NICE 2014 guideline



215

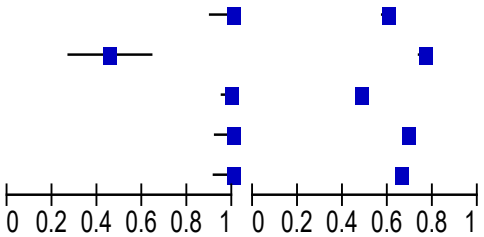
Figure 59: CCHR high and medium risk



216

Figure 60: CCHR high risk

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bouida 2013	34	622	0	926	1.00 [0.90, 1.00]	0.60 [0.57, 0.62]
Pek 2015	14	261	17	835	0.45 [0.27, 0.64]	0.76 [0.74, 0.79]
Stein 2009	107	4080	1	3767	0.99 [0.95, 1.00]	0.48 [0.47, 0.49]
Stiell 2001	44	962	0	2115	1.00 [0.92, 1.00]	0.69 [0.67, 0.70]
Stiell 2005	41	918	0	1748	1.00 [0.91, 1.00]	0.66 [0.64, 0.67]

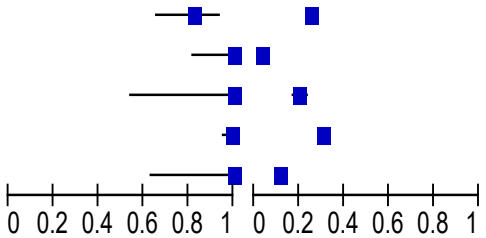


217

218

Figure 61: NOC

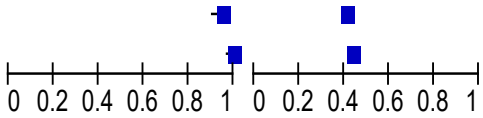
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bouida 2013	28	1152	6	396	0.82 [0.65, 0.93]	0.26 [0.23, 0.28]
Foks 2018 - original rule in whole population	18	4350	0	189	1.00 [0.81, 1.00]	0.04 [0.04, 0.05]
Ro 2011	6	518	0	133	1.00 [0.54, 1.00]	0.20 [0.17, 0.24]
Stein 2009	107	5414	1	2433	0.99 [0.95, 1.00]	0.31 [0.30, 0.32]
Stiell 2005	8	1595	0	219	1.00 [0.63, 1.00]	0.12 [0.11, 0.14]



219

Figure 62: NEXUS II

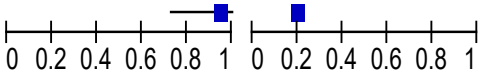
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Ro 2011	135	1646	7	1163	0.95 [0.90, 0.98]	0.41 [0.40, 0.43]
Stein 2009	108	4394	0	3453	1.00 [0.97, 1.00]	0.44 [0.43, 0.45]



220

Figure 63: CHIP simple decision rule

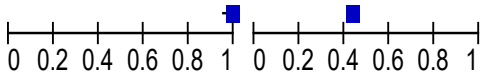
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Foks 2018	17	3619	1	920	0.94 [0.73, 1.00]	0.20 [0.19, 0.21]



221

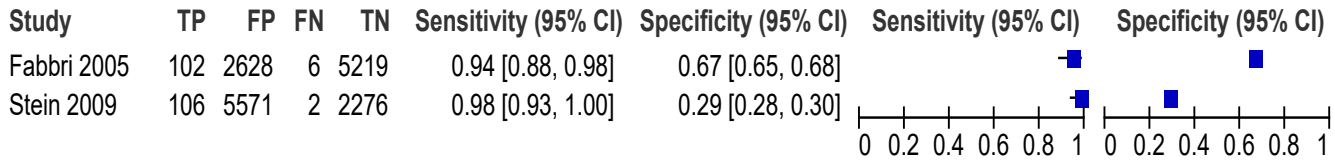
Figure 64: NCWFNS high and medium risk

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Fabbri 2005	107	4433	1	3414	0.99 [0.95, 1.00]	0.44 [0.42, 0.45]



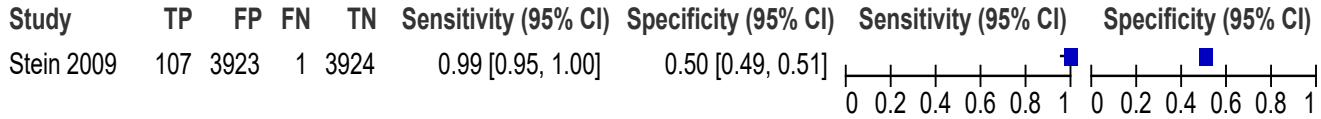
222

Figure 65: NICE lenient (2003 and 2007 guideline versions)



223

Figure 66: Scandinavian lenient criteria



E2147 Adults – Foks 2018 comparative Forest plots

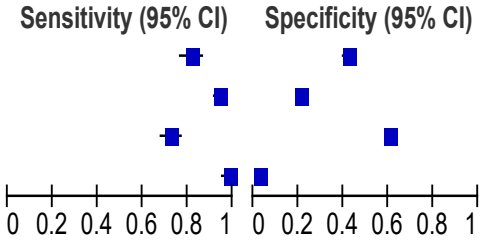
225 Note that the Forest plots below were presented to the committee for visual purposes to allow easier comparison of the decision rules in the Foks
226 2018 paper, which gave results for the NICE 2014 guideline recommendations and three other adult decision rules in the same paper. This study
227 used the same outcome definitions across decision rules and reported three separate outcomes: intracranial traumatic finding on CT, potential
228 neurosurgical lesion on CT and neurosurgical intervention, the definitions of which can be found in the evidence table in Appendix D. All of the data
229 in the plots presented here is already covered in earlier plots for each specific decision rule.

230 For CCHR and NOC rules, the analyses in the specific subpopulation the rule was developed for use in have been used where possible, rather
231 than an un-adapted version of the rule used in the whole population, as the latter means that the rules were used in some where the rule is not
232 usually used (based on inclusion/exclusion criteria for the rules when developed). The study does report results for adapted versions of these two
233 rules in the whole population, which are reported in earlier plots separate from the original CCHR and NOC rules. Data for neurosurgical
234 intervention in the rule-specific population was not available for CCHR and NOC rules, so the results for the un-adapted version used in the whole
235 population have therefore been used as this is all that was available for this outcome.

236

Figure 67: Foks 2018 Intracranial traumatic finding on CT - comparative plot of multiple tests

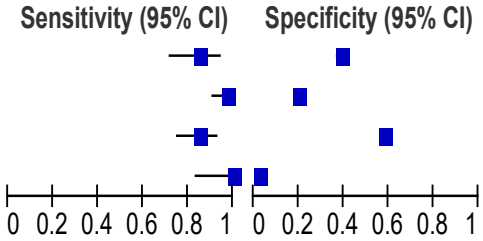
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CCHR - subpopulation rule developed using	209	821	47	606	0.82 [0.76, 0.86]	0.42 [0.40, 0.45]
CHIP	383	3253	24	897	0.94 [0.91, 0.96]	0.22 [0.20, 0.23]
NICE 2014 guideline	295	1624	112	2526	0.72 [0.68, 0.77]	0.61 [0.59, 0.62]
NOC - subpopulation rule developed using	137	973	2	35	0.99 [0.95, 1.00]	0.03 [0.02, 0.05]



237

Figure 68: Foks 2018 potential neurosurgical lesion - comparative plot of multiple tests

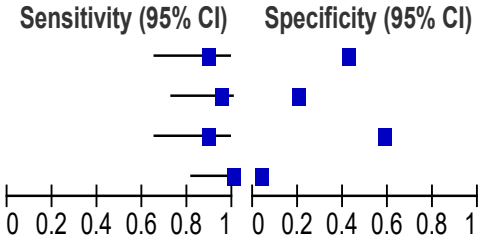
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CCHR - subpopulation rule developed using	40	990	7	646	0.85 [0.72, 0.94]	0.39 [0.37, 0.42]
CHIP	72	3564	2	919	0.97 [0.91, 1.00]	0.20 [0.19, 0.22]
NICE 2014 guideline	63	1856	11	2627	0.85 [0.75, 0.92]	0.59 [0.57, 0.60]
NOC - subpopulation rule developed using	20	1090	0	37	1.00 [0.83, 1.00]	0.03 [0.02, 0.04]



238

Figure 69: Foks 2018 Neurosurgical intervention - comparative plot of multiple tests

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CCHR - unadapted rule in whole population	16	2625	2	1914	0.89 [0.65, 0.99]	0.42 [0.41, 0.44]
CHIP	17	3619	1	920	0.94 [0.73, 1.00]	0.20 [0.19, 0.21]
NICE 2014 guideline	16	1903	2	2636	0.89 [0.65, 0.99]	0.58 [0.57, 0.60]
NOC - unadapted rule in whole population	18	4350	0	189	1.00 [0.81, 1.00]	0.04 [0.04, 0.05]



Note: results for CCHR and NOC tests are from un-adapted versions of the rules being used in the whole population, regardless of whether participants met the inclusion/exclusion criteria for these specific rules as the study did not report the outcome of neurosurgical intervention in the rule-specific population

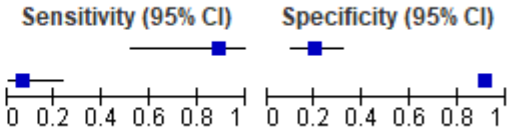
239

240

E24.8 Children – Any intracranial injury (definitions vary) – studies where all had CT

Figure 70: CHALICE

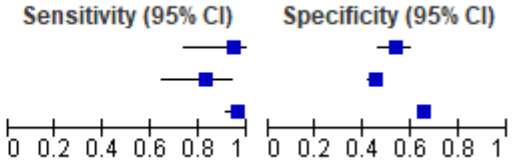
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gizli 2020	8	48	1	12	0.89 [0.52, 1.00]	0.20 [0.11, 0.32]
Meral Atis 2022	2	82	26	856	0.07 [0.01, 0.24]	0.91 [0.89, 0.93]



242

Figure 71: PECARN – not split into age groups

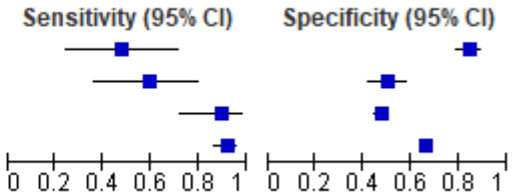
Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bozan 2019	18	111	1	126	0.95 [0.74, 1.00]	0.53 [0.47, 0.60]
Meral Atis 2022	24	536	5	439	0.83 [0.64, 0.94]	0.45 [0.42, 0.48]
Sert 2020	161	817	7	1505	0.96 [0.92, 0.98]	0.65 [0.63, 0.67]



243

Figure 72: CATCH – original 7-item version

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bozan 2019	9	38	10	199	0.47 [0.24, 0.71]	0.84 [0.79, 0.88]
Gizli 2020	13	74	9	74	0.59 [0.36, 0.79]	0.50 [0.42, 0.58]
Meral Atis 2022	25	493	3	445	0.89 [0.72, 0.98]	0.47 [0.44, 0.51]
Sert 2020	154	795	14	1527	0.92 [0.86, 0.95]	0.66 [0.64, 0.68]



244

Figure 73: Atabaki 2008 rule

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Atabaki 2008	62	478	3	457	0.95 [0.87, 0.99]	0.49 [0.46, 0.52]

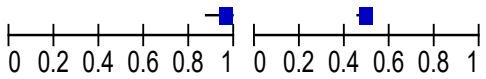


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Figure 74: Dietrich et al. 1993 rule

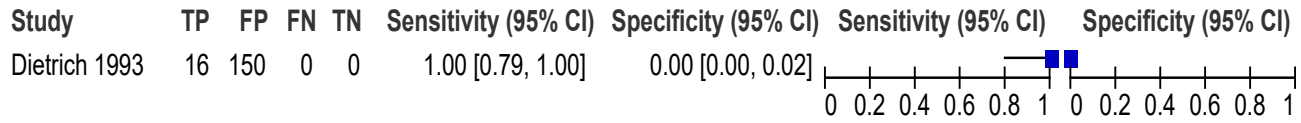

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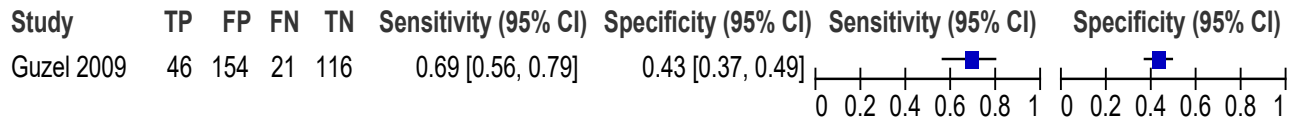
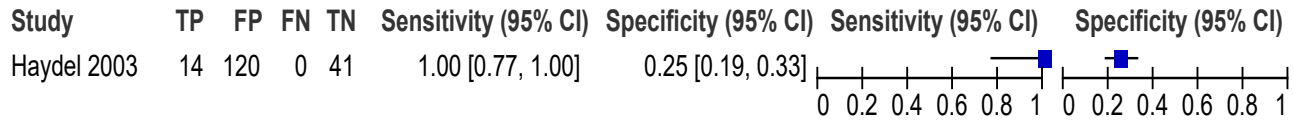
Figure 75: Guzel et al. 2009 rule



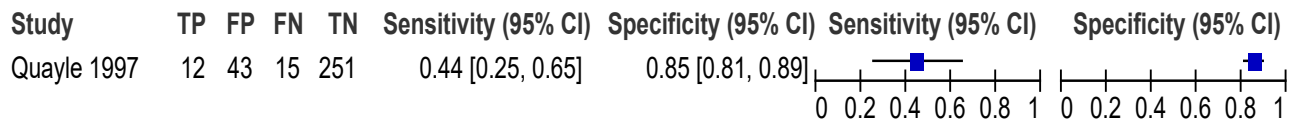
247

Figure 76: NOC



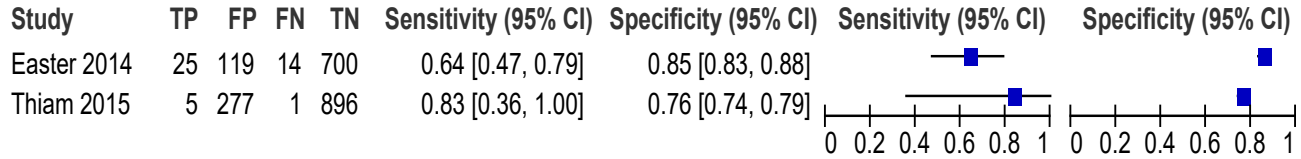
248

Figure 77: Quayle 1997 rule



E249 **Children – Any intracranial injury (definitions vary) – studies where only a proportion had CT**

Figure 78: CHALICE



250

Figure 79: CHALICE – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

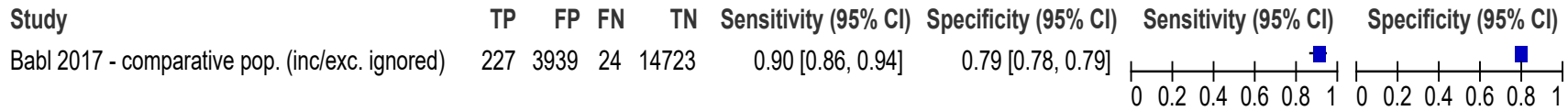


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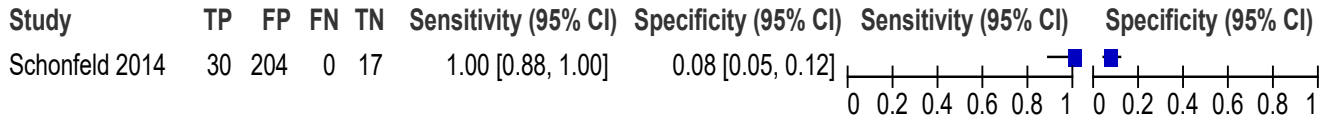
Figure 80: PECARN ≥2 years



Note: Ferrara 2016 also reports sensitivity and specificity for this rule to be 0.999 (0.158 to 1.000) and 0.478 (0.163 to 0.677) in a population of n=24, but could not be included in the Forest plot above as raw data could not be calculated from accuracy measures given, meaning there are possible errors or a result of the small sample size.

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Figure 81: PECARN ≥2 years – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

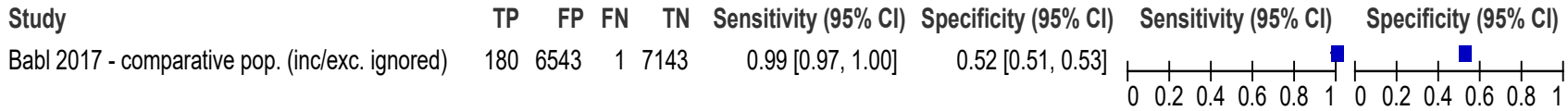

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Figure 82: PECARN not split into age groups

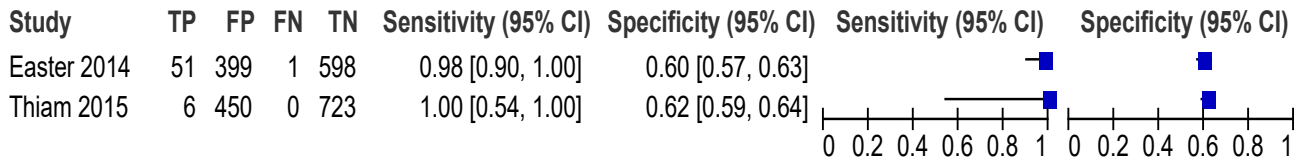

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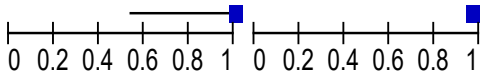
Figure 83: PECARN high risk, not split into age groups

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Thiam 2015	6	39	0	1134	1.00 [0.54, 1.00]	0.97 [0.95, 0.98]



255

Figure 84: CATCH – original 7-item rule – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Babl 2017 - rule-specific population	125	2100	16	2716	0.89 [0.82, 0.93]	0.56 [0.55, 0.58]
Easter 2014	47	522	5	428	0.90 [0.79, 0.97]	0.45 [0.42, 0.48]
Osmond 2006	167	1802	3	1809	0.98 [0.95, 1.00]	0.50 [0.48, 0.52]
Osmond 2010	156	1851	3	1856	0.98 [0.95, 1.00]	0.50 [0.48, 0.52]
Osmond 2012	193	1331	4	2520	0.98 [0.95, 0.99]	0.65 [0.64, 0.67]
Osmond 2018	192	1562	5	2301	0.97 [0.94, 0.99]	0.60 [0.58, 0.61]
Thiam 2015	6	231	0	942	1.00 [0.54, 1.00]	0.80 [0.78, 0.83]

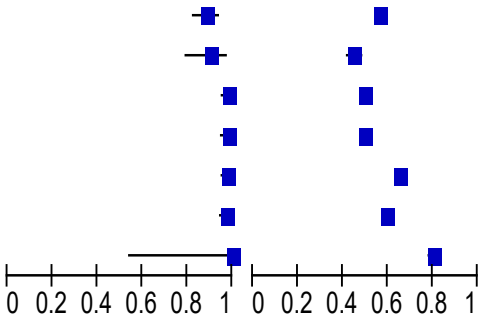


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Figure 85: CATCH – original 7-item rule

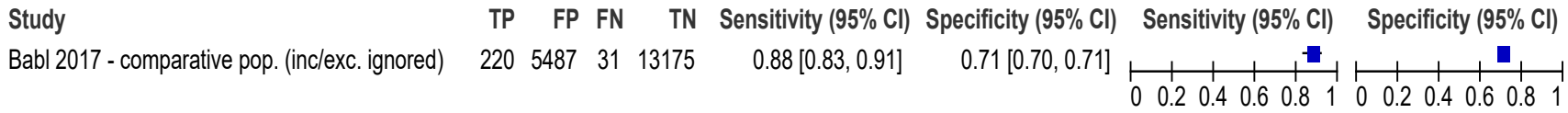

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Figure 86: CATCH – revised 8-item version

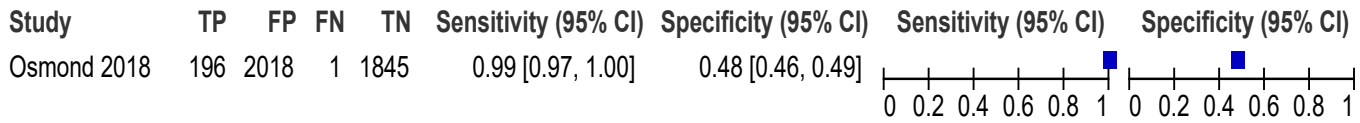

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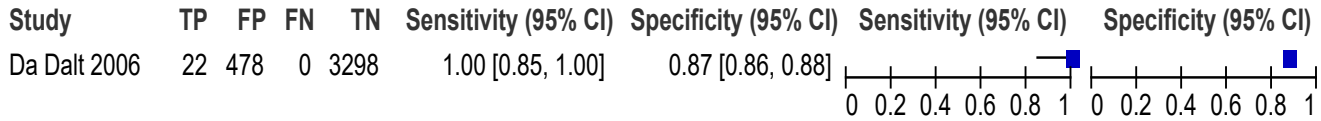
Figure 87: Da Dalt A+B vs. C+D



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E.2.10 Children – Clinically important/more serious injuries (definitions vary) – studies where all had CT

Figure 88: PECARN not split into age groups

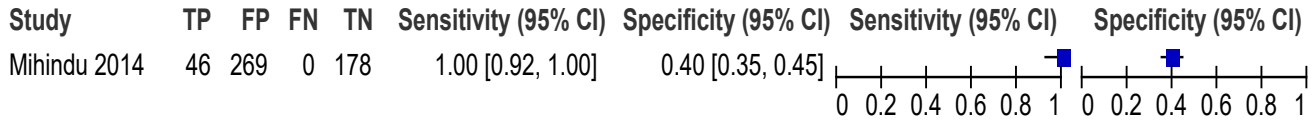

Figure 89: PECARN ≥2 years

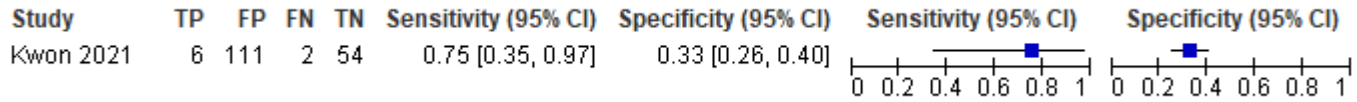

Figure 90: CATCH <2 years - revised 8-item version

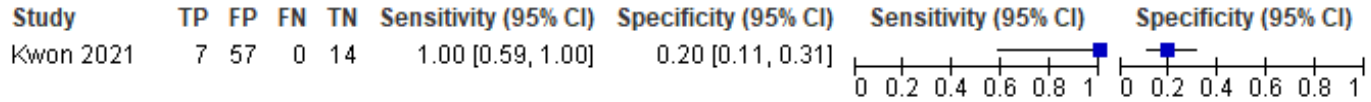

Figure 91: NEXUS II

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Gupta 2018	27	661	0	330	1.00 [0.87, 1.00]	0.33 [0.30, 0.36]
Oman 2006	136	1298	2	230	0.99 [0.95, 1.00]	0.15 [0.13, 0.17]

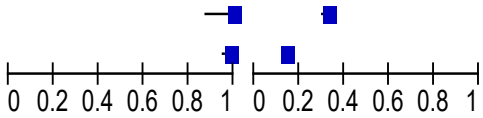

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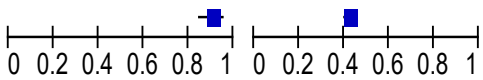
Figure 92: Pilot PECARN ≥2 years

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Sun 2007	125	876	13	652	0.91 [0.84, 0.95]	0.43 [0.40, 0.45]



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E.1261 Children – Clinically important/more serious injuries (definitions vary) – studies where only a proportion had CT

Figure 93: CHALICE

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Babl 2017 - rule-specific population	370	4303	31	15325	0.92 [0.89, 0.95]	0.78 [0.77, 0.79]
Dunning 2006	164	2853	4	19558	0.98 [0.94, 0.99]	0.87 [0.87, 0.88]
Easter 2014	16	128	3	711	0.84 [0.60, 0.97]	0.85 [0.82, 0.87]

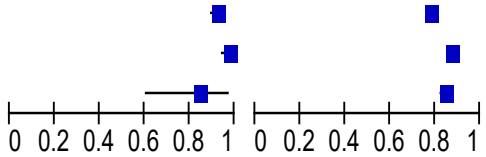

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Figure 94: CHALICE – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Babl 2017 - comparative pop. (inc/exc. ignored)	148	4018	12	14735	0.93 [0.87, 0.96]	0.79 [0.78, 0.79]

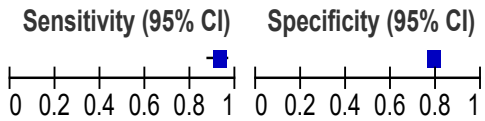

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Figure 95: PECARN ≥2 years

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Atabaki 2016	60	2614	2	3635	0.97 [0.89, 1.00]	0.58 [0.57, 0.59]
Babl 2017 - rule-specific population	97	5987	1	5067	0.99 [0.94, 1.00]	0.46 [0.45, 0.47]
Fuller 2011	234	2544	12	7625	0.95 [0.92, 0.97]	0.75 [0.74, 0.76]
Ide 2017	10	374	0	1032	1.00 [0.69, 1.00]	0.73 [0.71, 0.76]
Ide 2020	8	882	0	3458	1.00 [0.63, 1.00]	0.80 [0.78, 0.81]
Kupperman 2009 cohort 1	208	10412	7	14656	0.97 [0.93, 0.99]	0.58 [0.58, 0.59]
Kupperman 2009 cohort 2	61	2550	2	3798	0.97 [0.89, 1.00]	0.60 [0.59, 0.61]
Lorton 2016	6	298	0	774	1.00 [0.54, 1.00]	0.72 [0.69, 0.75]
Nakhjavan-Shahraki 2017	42	185	0	253	1.00 [0.92, 1.00]	0.58 [0.53, 0.62]
Schonfeld 2014	13	692	0	767	1.00 [0.75, 1.00]	0.53 [0.50, 0.55]

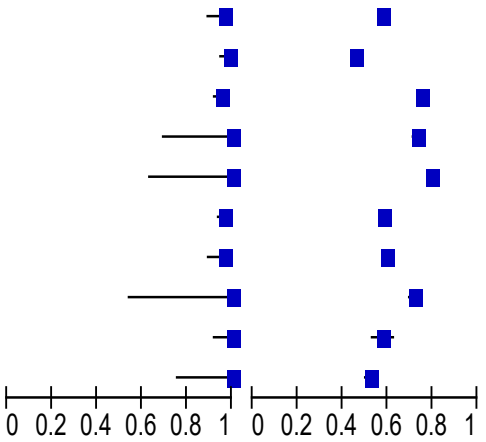

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Figure 96: PECARN ≥2 years – Bertsimas 2019 presented separately as re-analysis of same dataset used in Kupperman 2009

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bertsimas 2019 - development	208	10590	7	14478	0.97 [0.93, 0.99]	0.58 [0.57, 0.58]
Bertsimas 2019 - validation	61	2692	2	3656	0.97 [0.89, 1.00]	0.58 [0.56, 0.59]

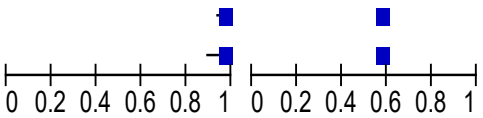

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Figure 97: PECARN ≥2 years – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Babl 2017 - comparative pop. (inc/exc. ignored)	117	6606	1	7143	0.99 [0.95, 1.00]	0.52 [0.51, 0.53]

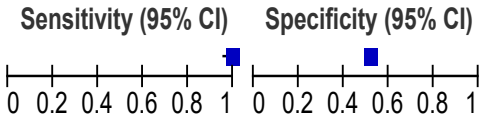

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Figure 98: PECARN, not split into age groups

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Easter 2014	21	361	0	599	1.00 [0.84, 1.00]	0.62 [0.59, 0.65]

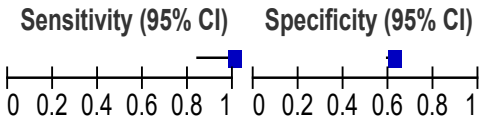

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Figure 99: CATCH – original 7-item rule

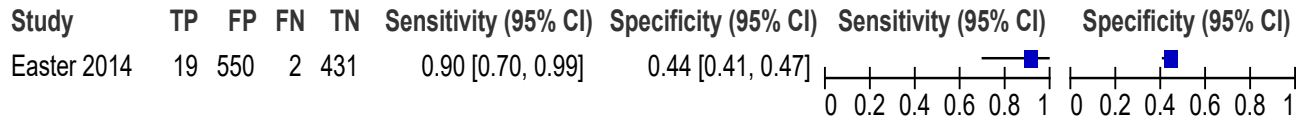

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Figure 100: CATCH – original 7-item rule – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

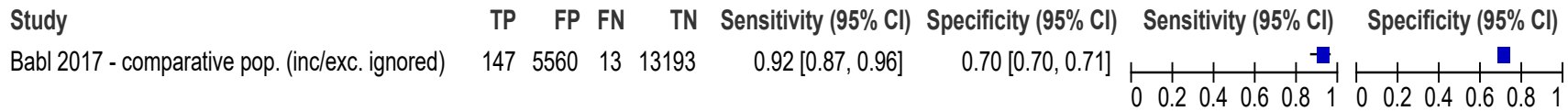

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Figure 101: NEXUS II

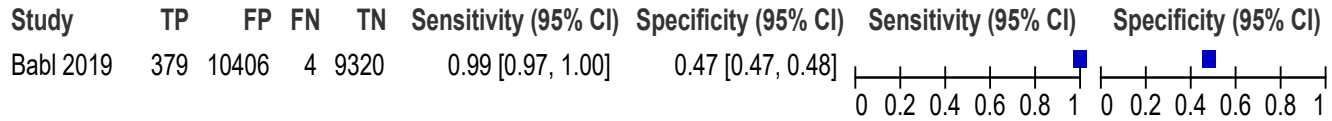

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Figure 102: Pilot PECARN ≥2 years

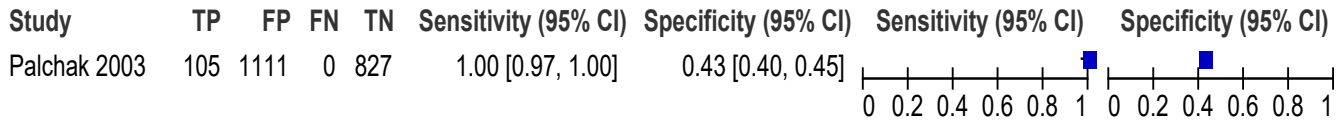

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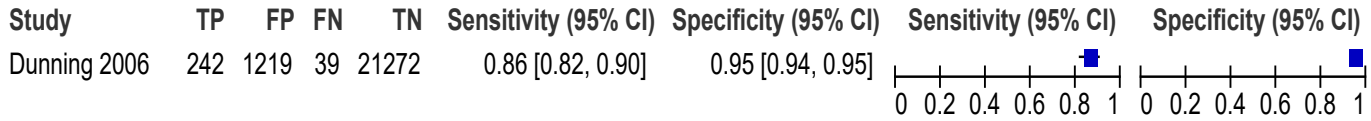
Figure 103: RCS guidelines



E.1.2 Children – neurosurgery (definitions vary) – studies where all CT

Figure 104: PECARN, not split into age groups

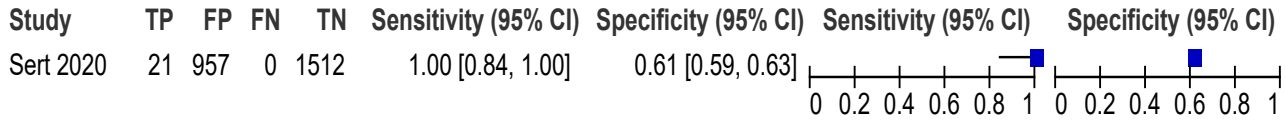


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Figure 105: CATCH – original 7-item version

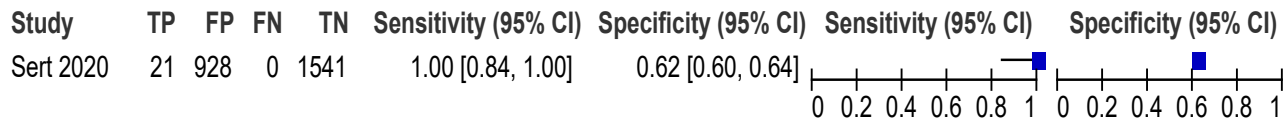

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Figure 106: NEXUS II

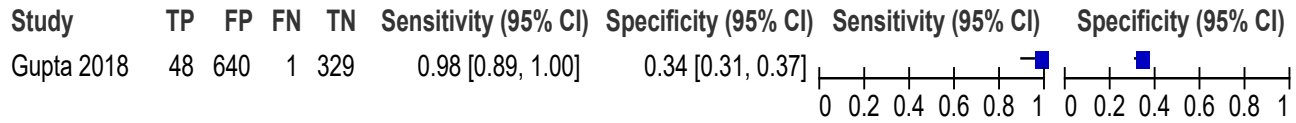

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Figure 107: Atabaki 2008 rule

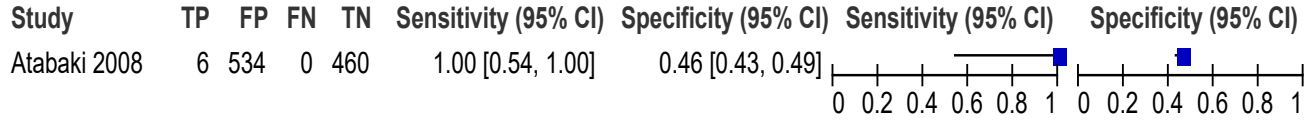

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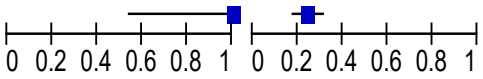
Figure 108: NOC

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Haydel 2003	6	128	0	41	1.00 [0.54, 1.00]	0.24 [0.18, 0.31]



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E.1.3 Children – neurosurgery (definitions vary) – studies where only a proportion had CT

Figure 109: CHALICE

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Babl 2017 - comparative pop. (inc/exc. ignored)	22	4144	2	14745	0.92 [0.73, 0.99]	0.78 [0.77, 0.79]
Dunning 2006	134	3076	3	19559	0.98 [0.94, 1.00]	0.86 [0.86, 0.87]
Easter 2014	3	141	1	713	0.75 [0.19, 0.99]	0.83 [0.81, 0.86]

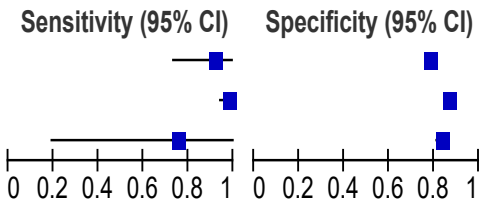

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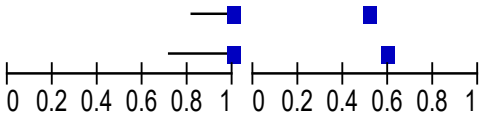
Figure 110: PECARN ≥2 years

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Babl 2017 - comparative pop. (inc/exc. ignored)	18	6705	0	7144	1.00 [0.81, 1.00]	0.52 [0.51, 0.52]
Kupperman 2009 cohort 2	11	2600	0	3800	1.00 [0.72, 1.00]	0.59 [0.58, 0.61]



287

Figure 111: PECARN, not split into age groups

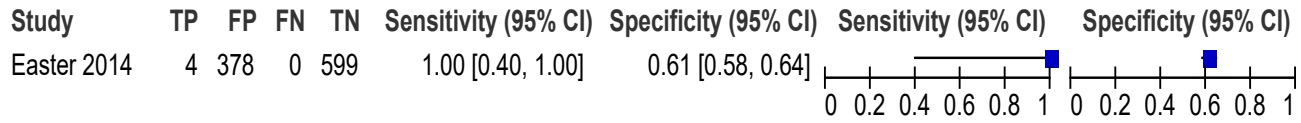


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Figure 112: CATCH – original 7-item version

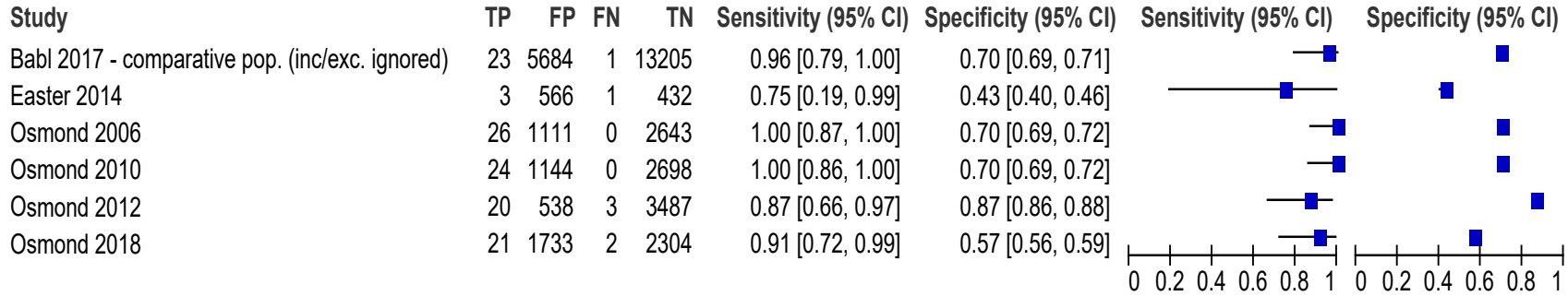

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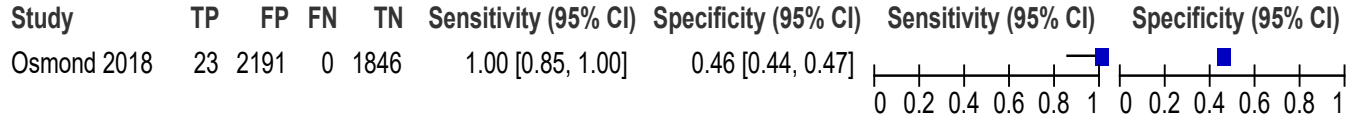
Figure 113: CATCH – revised 8-item version



290

Figure 114: CATCH – original 7-item rule – any of four high risk factors

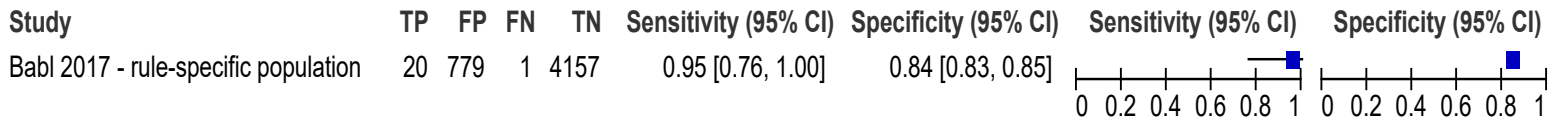


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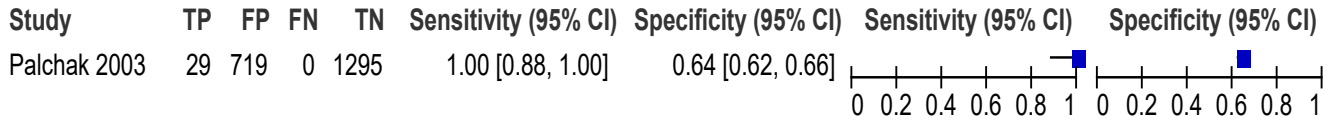
Figure 115: Pilot PECARN ≥2 years



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E.1914 Infants and young children – Any intracranial injury (definitions vary) – studies where all had CT

Figure 116: Dietrich et al. 1993 rule

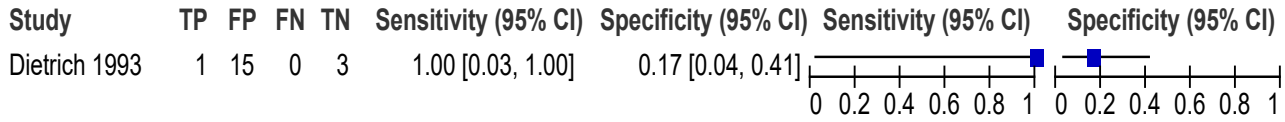

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Figure 117: Buchanich 2007 rule

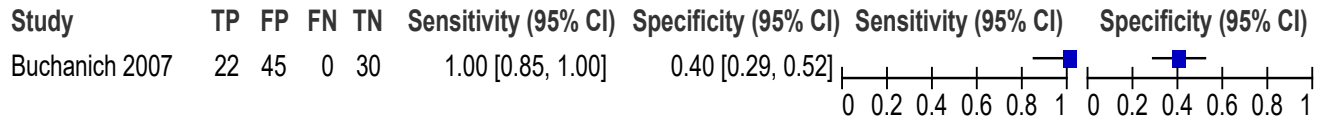

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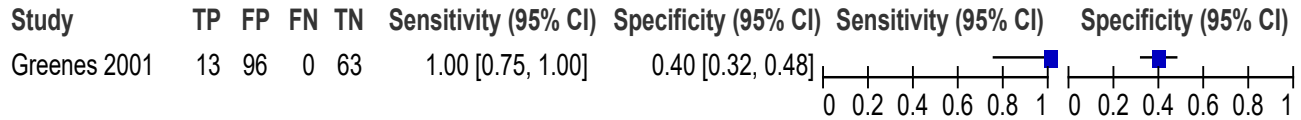
Figure 118: Greenes 2001 scoring system



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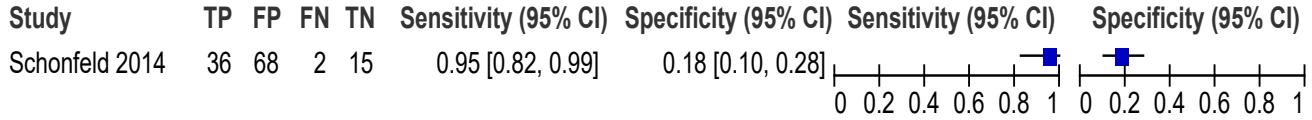
E.2.15 Infants and young children – Any intracranial injury (definitions vary) – studies where only a proportion had CT

Figure 119: PECARN <2 years



Note: Ferrara 2016 also reports sensitivity and specificity for this rule to be 0.999 (0.158 to 1.000) and 0.625 (0.245 to 0.915) in a population of n=14, but could not be included in the Forest plot above as raw data could not be calculated from accuracy measures given, meaning there are possible errors or a result of the small sample size

Figure 120: PECARN <2 years – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

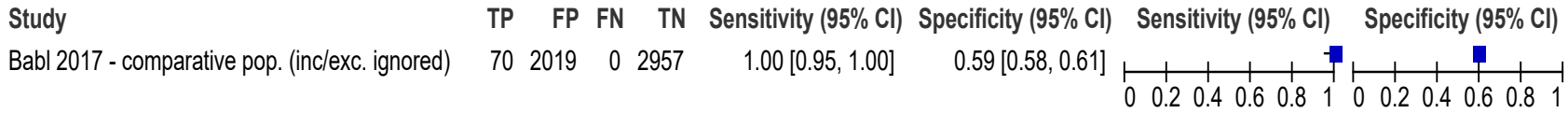


Figure 121: Pittsburgh Infant Brain Injury Score ≥2

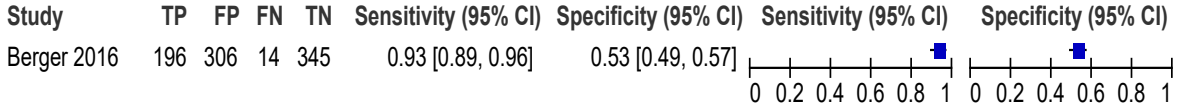


Figure 122: Greenes 1999 rule

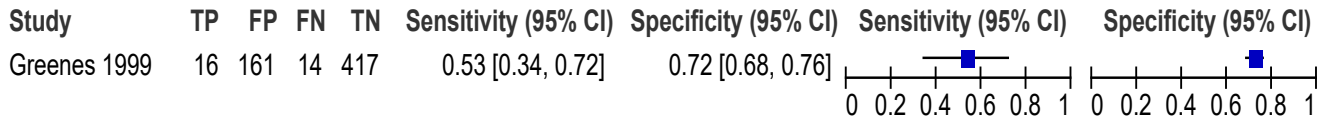


Figure 123: NEXUS II

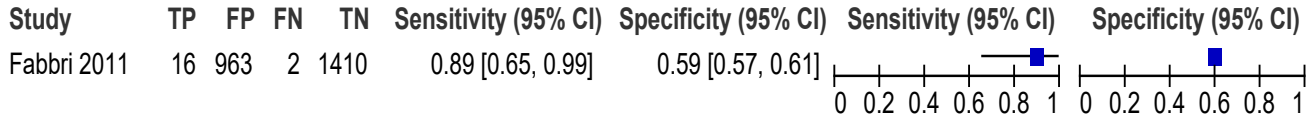
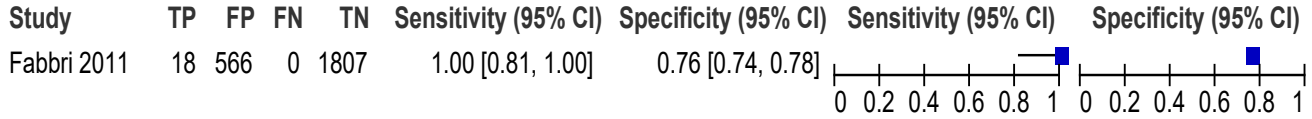


Figure 124: Fabbri et al. 2011 rule



E.1016 Infants and young children – Clinically important/more serious injuries (definitions vary) – studies where all had CT

Figure 125: PECARN <2 years

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Kim 2020	33	111	2	78	0.94 [0.81, 0.99]	0.41 [0.34, 0.49]
Kwon 2021	6	58	1	13	0.86 [0.42, 1.00]	0.18 [0.10, 0.29]

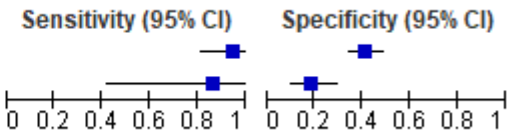


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Figure 126: Pilot PECARN

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Sun 2007	7	179	0	22	1.00 [0.59, 1.00]	0.11 [0.07, 0.16]

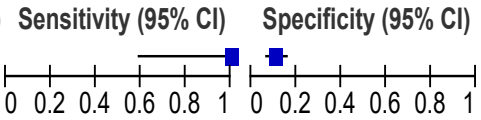

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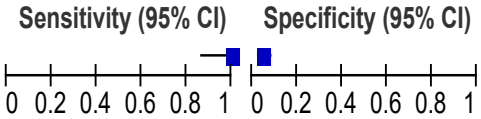
Figure 127: NEXUS II

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Oman 2006	25	269	0	15	1.00 [0.86, 1.00]	0.05 [0.03, 0.09]



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E.1307 Infants and young children – Clinically important/more serious injuries (definitions vary) – studies where only a proportion had CT

Figure 128: PECARN <2 years

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Atabaki 2016	25	1002	0	1158	1.00 [0.86, 1.00]	0.54 [0.51, 0.56]
Babl 2017 - rule-specific population	38	1834	0	2139	1.00 [0.91, 1.00]	0.54 [0.52, 0.55]
Cho 2022	2	41	0	171	1.00 [0.16, 1.00]	0.81 [0.75, 0.86]
Fuller 2011	17	1750	0	2950	1.00 [0.80, 1.00]	0.63 [0.61, 0.64]
Ide 2017	12	206	2	572	0.86 [0.57, 0.98]	0.74 [0.70, 0.77]
Ide 2020	13	641	2	1581	0.87 [0.60, 0.98]	0.71 [0.69, 0.73]
Kupperman 2009 cohort 1	72	3901	1	4528	0.99 [0.93, 1.00]	0.54 [0.53, 0.55]
Kupperman 2009 cohort 2	25	1015	0	1176	1.00 [0.86, 1.00]	0.54 [0.52, 0.56]
Lorton 2016	3	151	0	267	1.00 [0.29, 1.00]	0.64 [0.59, 0.68]
Nakhjavan-Shahraki 2017	12	60	1	41	0.92 [0.64, 1.00]	0.41 [0.31, 0.51]
Schonfeld 2014	6	404	0	546	1.00 [0.54, 1.00]	0.57 [0.54, 0.61]

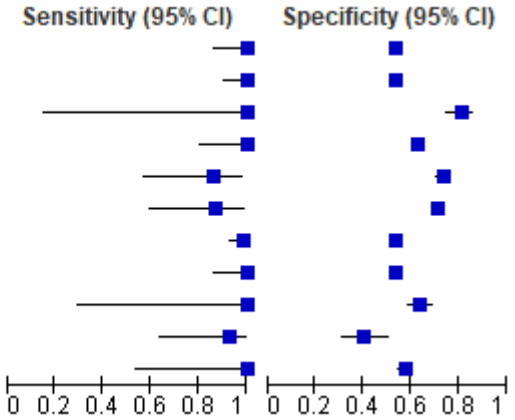

Figure 129: PECARN <2 years – Bertsimas 2019 presented separately as re-analysis of same dataset used in Kupperman 2009

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Bertsimas 2019 - development	72	3886	1	4543	0.99 [0.93, 1.00]	0.54 [0.53, 0.55]
Bertsimas 2019 - validation	25	1033	0	1158	1.00 [0.86, 1.00]	0.53 [0.51, 0.55]

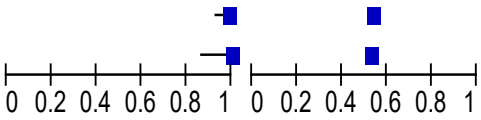

Figure 130: PECARN <2 years – Babl 2017 presented separately as reported in comparative population where inclusion/exclusion criteria of specific rules were ignored

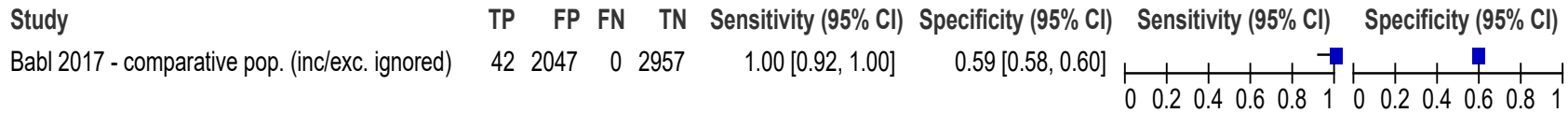

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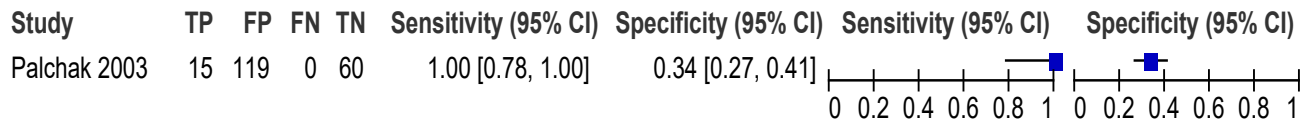
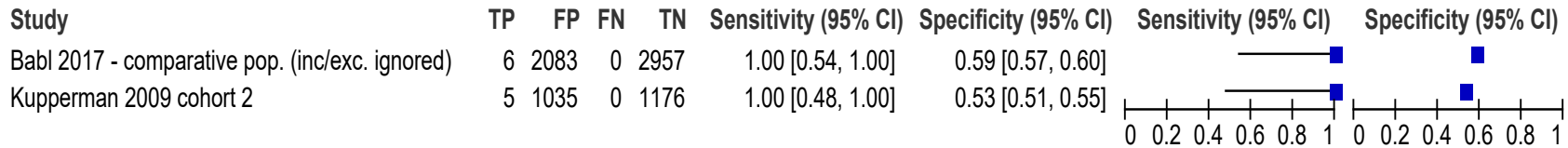
Figure 131: Pilot PECARN <2 years



E.1.1.8 Infants and young children – neurosurgery – studies where only a proportion had CT

Figure 132: PECARN <2 years rule



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E.1.19 Children/infants – Babl 2017 and 2019 comparative Forest plots

Note that the Forest plots below were presented to the committee for visual purposes to allow easier comparison of the decision rules in the Babl 2017 and 2019 papers, which gave results for the CHALICE rule (which the NICE 2014 recommendations were based on, with some amendments) and three other decision rules used in children in the same paper.

The 2019 paper reports data for the NEXUS II decision rule, which is not reported in the 2017 paper. Results are available across the two papers for all four decision rules in terms of outcomes as defined in each specific rule and in the rule-specific population (those meeting inclusion criteria and no criteria excluding them from the rule). In addition, the 2017 paper also provides results in a comparative population for three of the four rules (all apart from NEXUS II), which ignores inclusion and exclusion criteria for specific rules and uses all rules in the same group of people, and uses identical outcome definitions, to allow easier comparison. Although this analysis allows easier comparison, the use of the decision rules in some people that the rules were not designed for (i.e. in people that were excluded when the rule was developed) means the results may be less reliable than the results when used in the intended population for each rule. For this reason, separate Forest plots are presented below as follows:

- intracranial injury as specified by each rule (this could be any traumatic brain injury or clinically important injuries depending on the rule)
- any traumatic brain injury with the same outcome definition in the comparative population across rules
- clinically important traumatic brain injury with the same outcome definition in the comparative population across rules
- neurosurgery with the same outcome definition in the comparative population across rules

Definitions of outcomes according to specific decision rules and those used within the comparative population can be found in the evidence table for Babl 2017 and Babl 2019 in Appendix D. All of the data in the plots presented here is already covered in earlier plots for each specific decision rule.

Figure 133: Babl 2017/2019 - intracranial injury (any traumatic or clinically imp injury, rule-specific outcome)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CATCH	125	2100	16	2716	0.89 [0.82, 0.93]	0.56 [0.55, 0.58]
CHALICE	370	4303	31	15325	0.92 [0.89, 0.95]	0.78 [0.77, 0.79]
NEXUS II	379	10406	4	9320	0.99 [0.97, 1.00]	0.47 [0.47, 0.48]
PECARN 2 years and above	97	5987	1	5067	0.99 [0.94, 1.00]	0.46 [0.45, 0.47]
PECARN less than 2 years	38	1834	0	2139	1.00 [0.91, 1.00]	0.54 [0.52, 0.55]

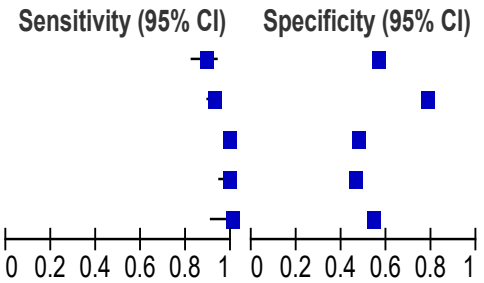


Figure 134: Babl 2017 - any injury (traumatic brain injury/brain injury on CT) in comparative population (inclusion/exclusion criteria ignored)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CATCH	220	5487	31	13175	0.88 [0.83, 0.91]	0.71 [0.70, 0.71]
CHALICE	227	3939	24	14723	0.90 [0.86, 0.94]	0.79 [0.78, 0.79]
PECARN 2 years and above	180	6543	1	7143	0.99 [0.97, 1.00]	0.52 [0.51, 0.53]
PECARN less than 2 years	70	2019	0	2957	1.00 [0.95, 1.00]	0.59 [0.58, 0.61]

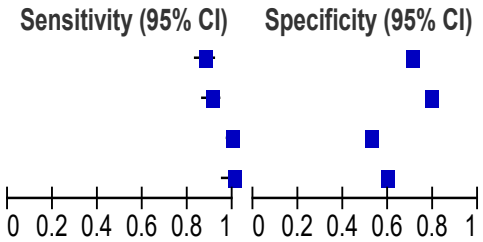


Figure 135: Babl 2017 - clinically important injury (more serious injuries) in comparative population (inclusion/exclusion criteria ignored)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CATCH	147	5560	13	13193	0.92 [0.87, 0.96]	0.70 [0.70, 0.71]
CHALICE	148	4018	12	14735	0.93 [0.87, 0.96]	0.79 [0.78, 0.79]
PECARN 2 years and above	117	6606	1	7143	0.99 [0.95, 1.00]	0.52 [0.51, 0.53]
PECARN less than 2 years	42	2047	0	2957	1.00 [0.92, 1.00]	0.59 [0.58, 0.60]

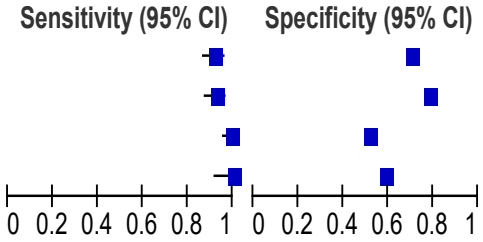
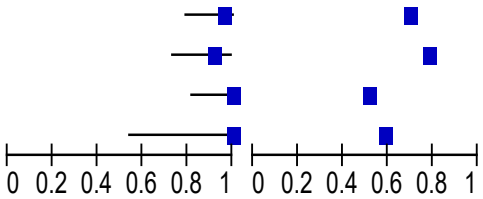


Figure 136: Babl 2017 - neurosurgery in comparative population (inclusion/exclusion criteria ignored)

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
CATCH	23	5684	1	13205	0.96 [0.79, 1.00]	0.70 [0.69, 0.71]
CHALICE	22	4144	2	14745	0.92 [0.73, 0.99]	0.78 [0.77, 0.79]
PECARN 2 years and above	18	6705	0	7144	1.00 [0.81, 1.00]	0.52 [0.51, 0.52]
PECARN less than 2 years	6	2083	0	2957	1.00 [0.54, 1.00]	0.59 [0.57, 0.60]



E.2 Sensitivity / 1-specificity plots

Please note that this section has been renamed from 'ROC curves'. ROC curves are of value when evaluating a single test over its many thresholds, allowing an overall summary evaluation of how well the test performs across its many thresholds, as denoted by the area under the ROC curve. In the plots below the intention is different – it is simply to summarise the overall pooled sensitivity and specificity across several studies for an individual test threshold. The dark circle represents the pooled result and the dotted line represents the 95% confidence region. Note that 95% confidence regions are not generally calculable if the number of studies is <4. Note that these are only presented for those analyses where meta-analysis was possible.

E.2.1 Adults

Figure 137: CCHR high and medium risk – any injury with all having CT – 9 studies

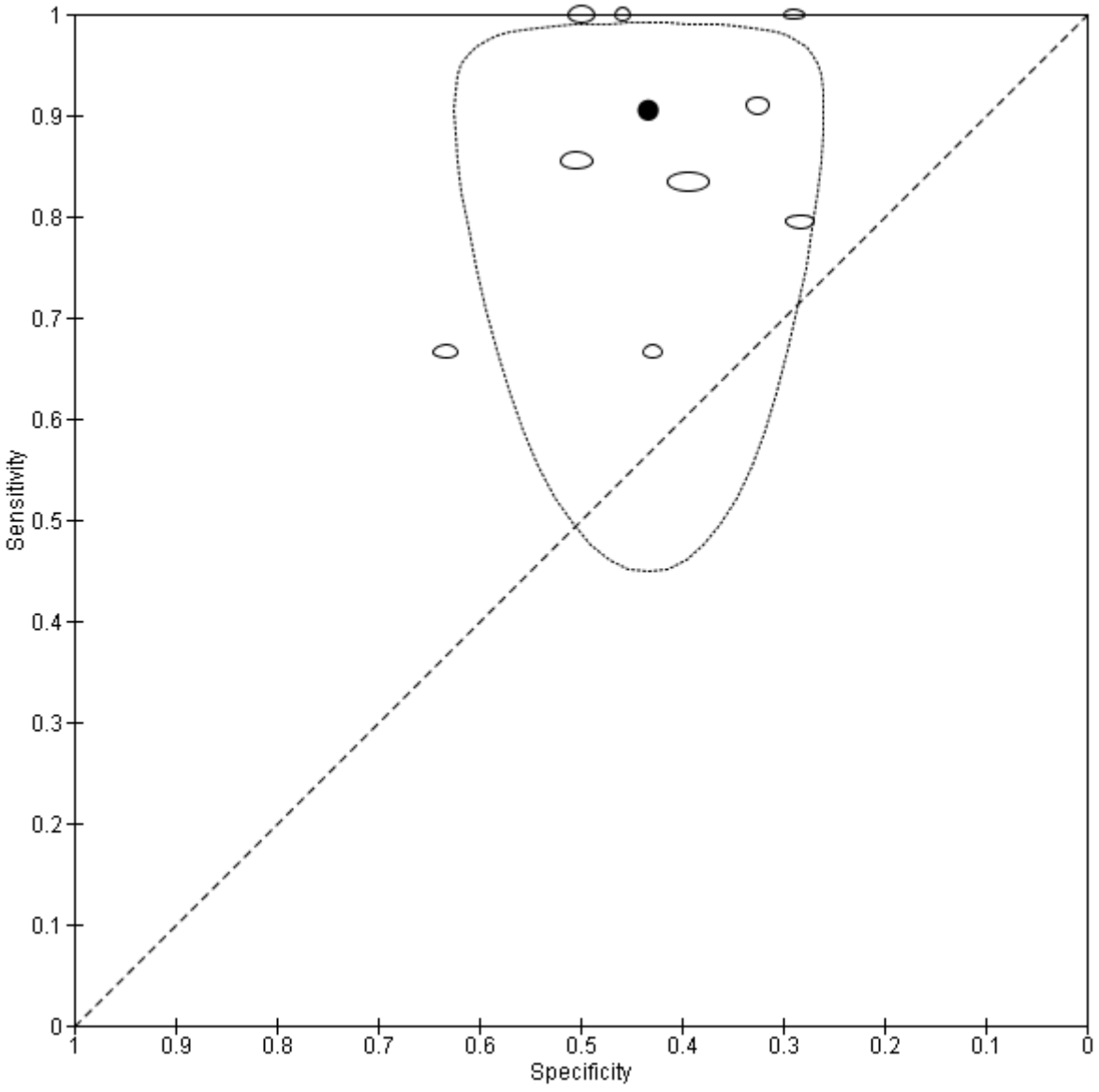


Figure 138: CCHR high and medium risk – any injury with only a proportion having CT – 5 studies

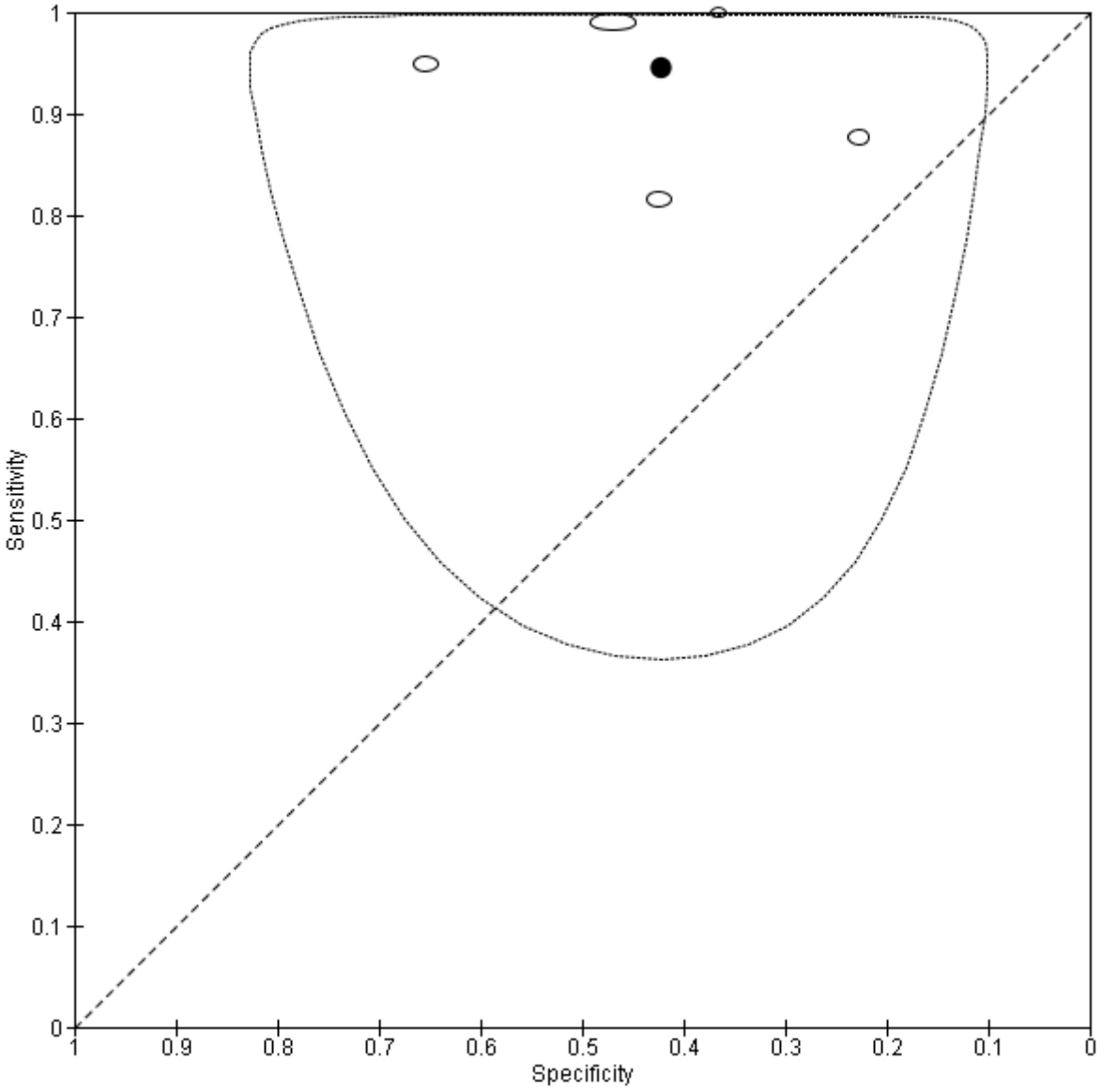


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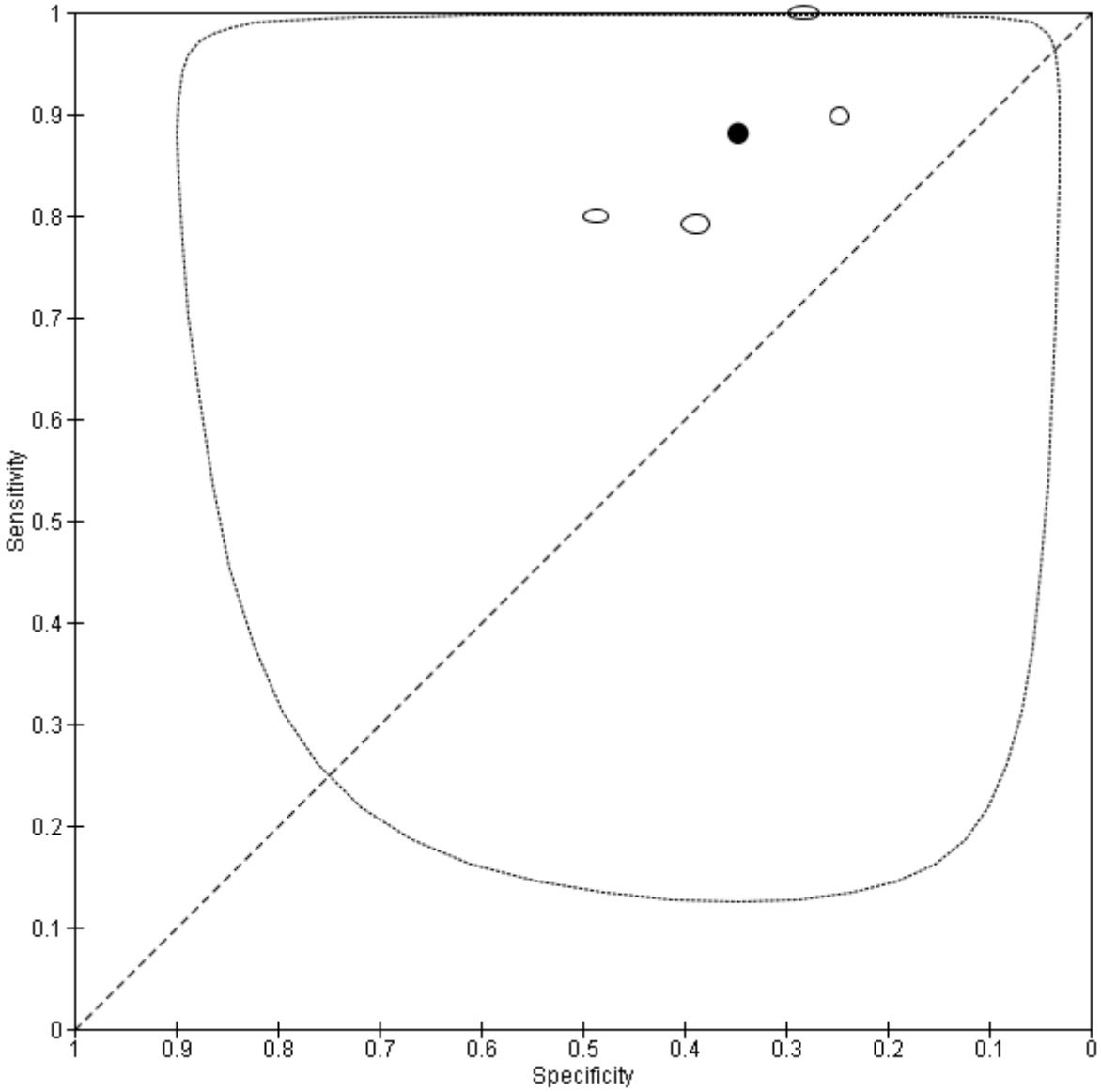
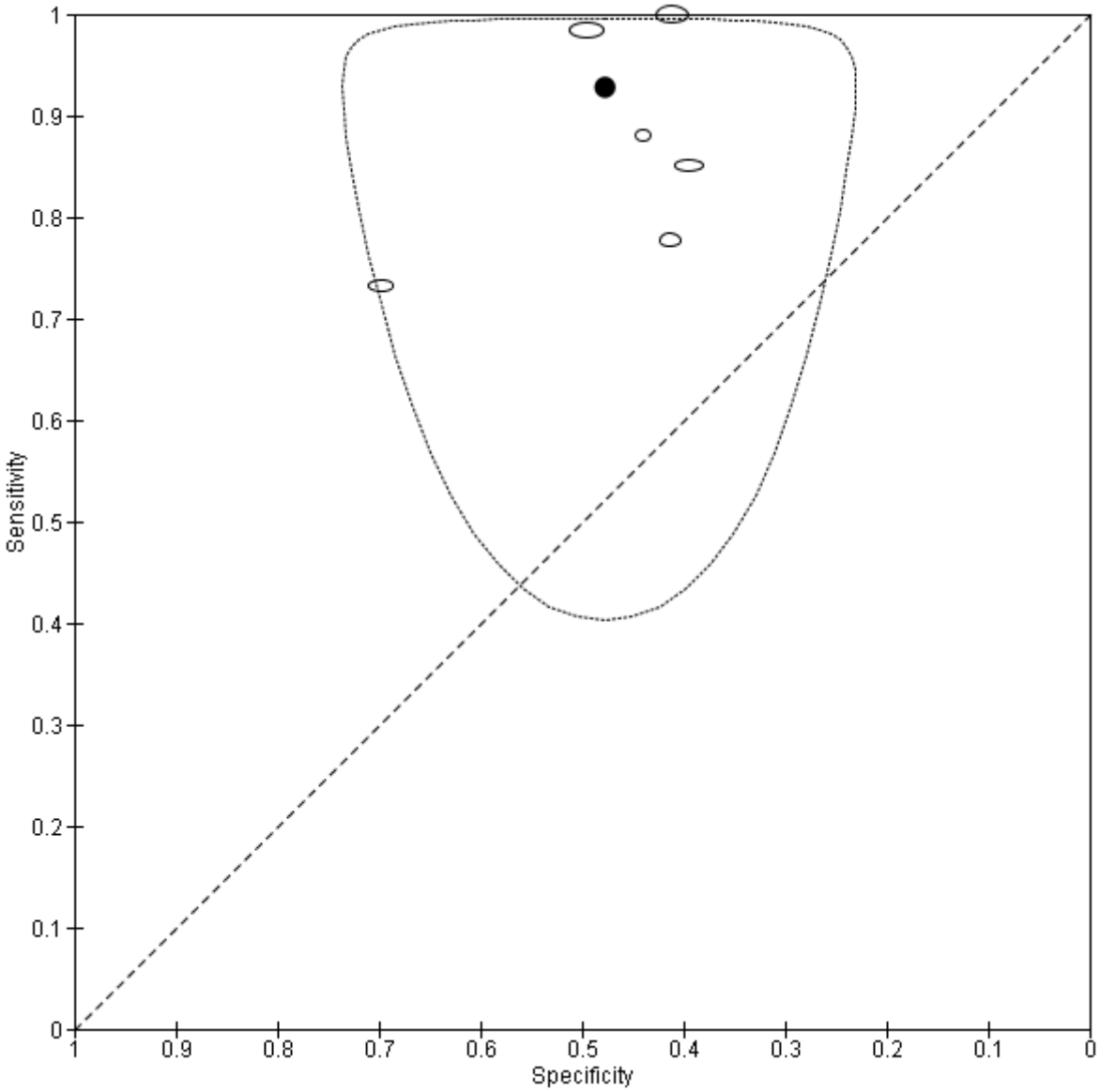
Figure 139: CCHR high and medium risk - clinically important/more serious injuries with all having CT – 4 studies



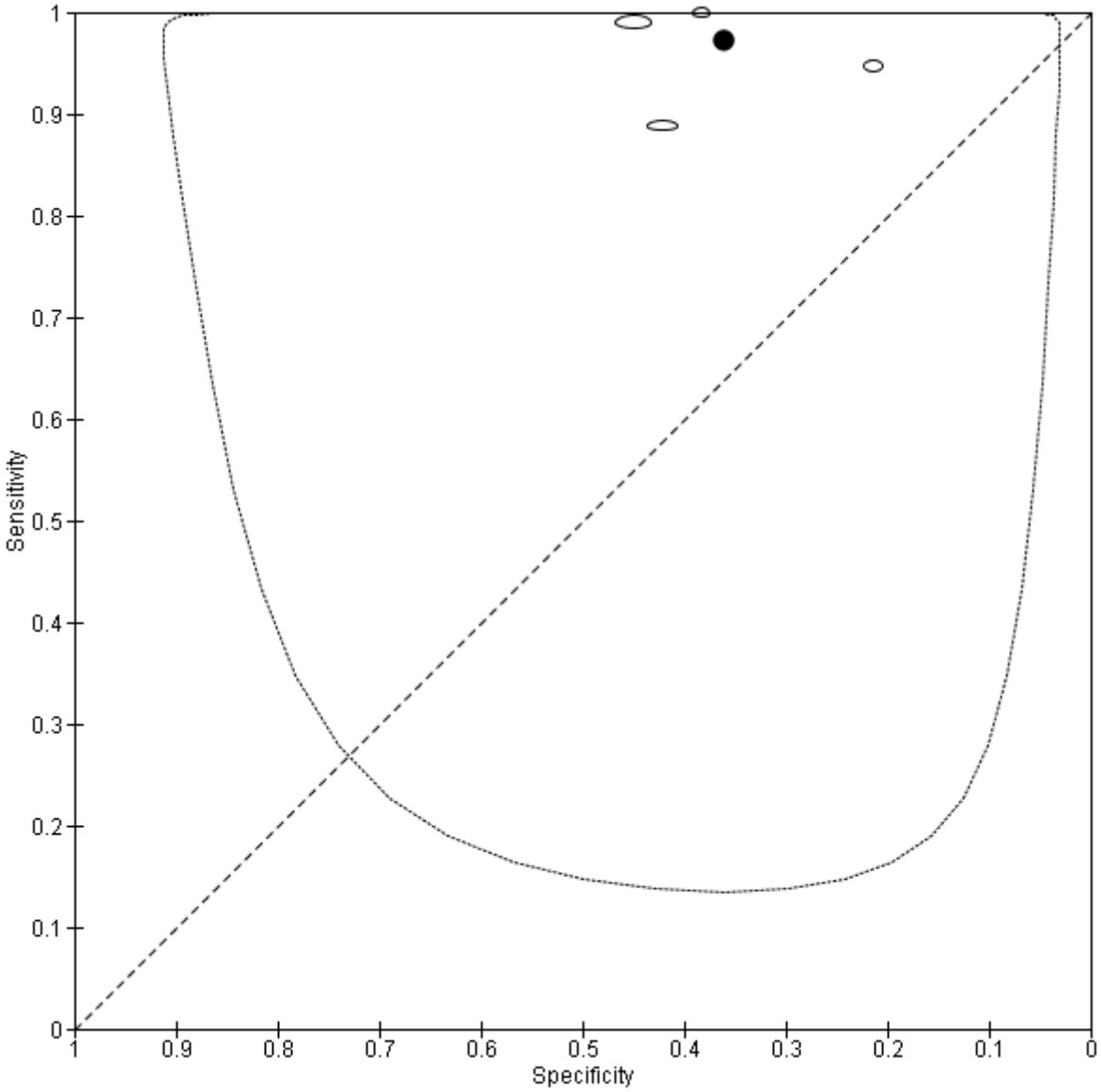
14

Figure 140: CCHR high and medium risk - clinically important/more serious injuries with only a proportion having CT – 6 studies



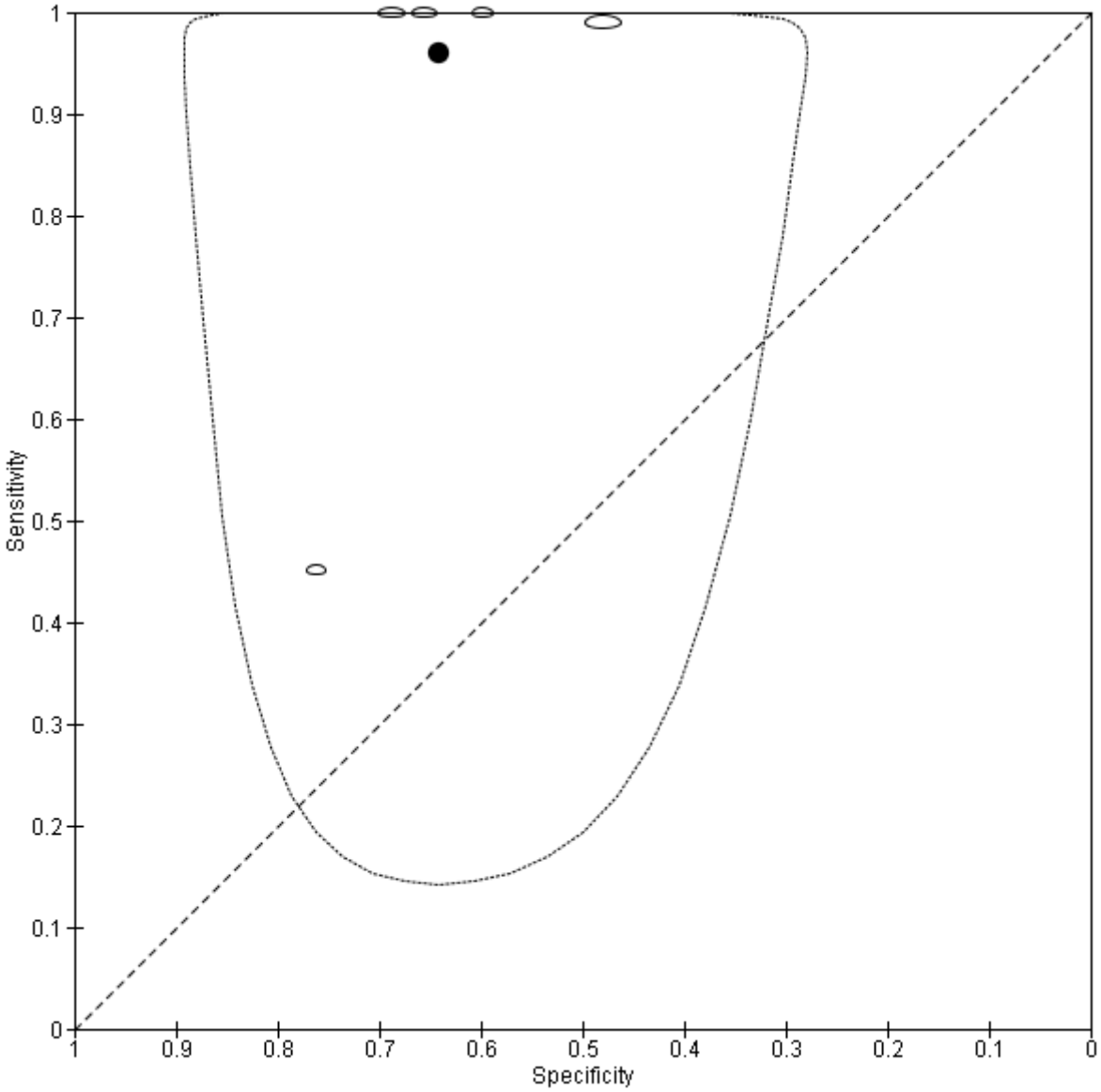
15

Figure 141: CCHR high and medium risk - neurosurgery (definitions vary) with only a proportion having CT – 4 studies



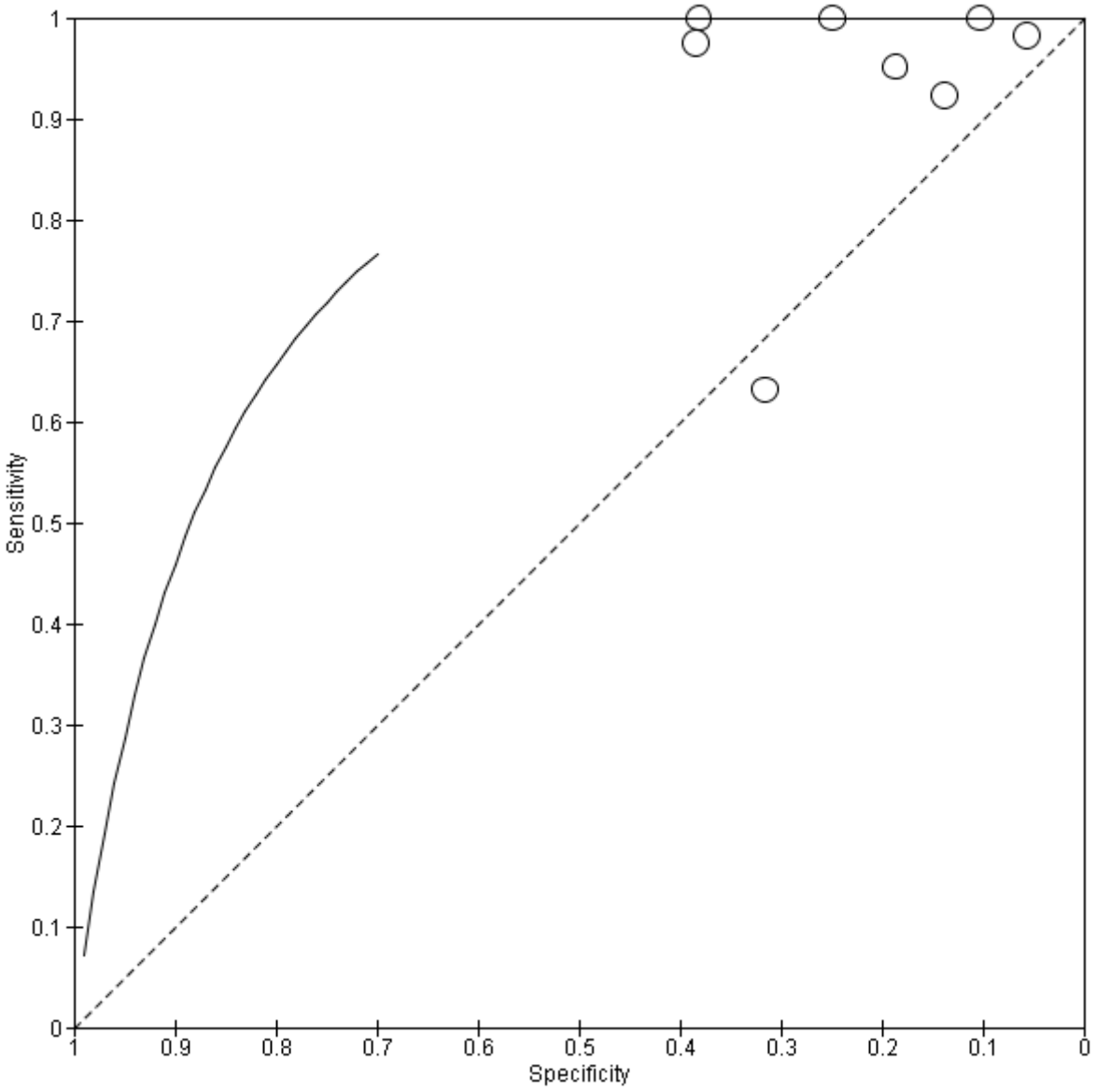
16

Figure 142: CCHR high risk - neurosurgery with only a proportion having CT – 5 studies



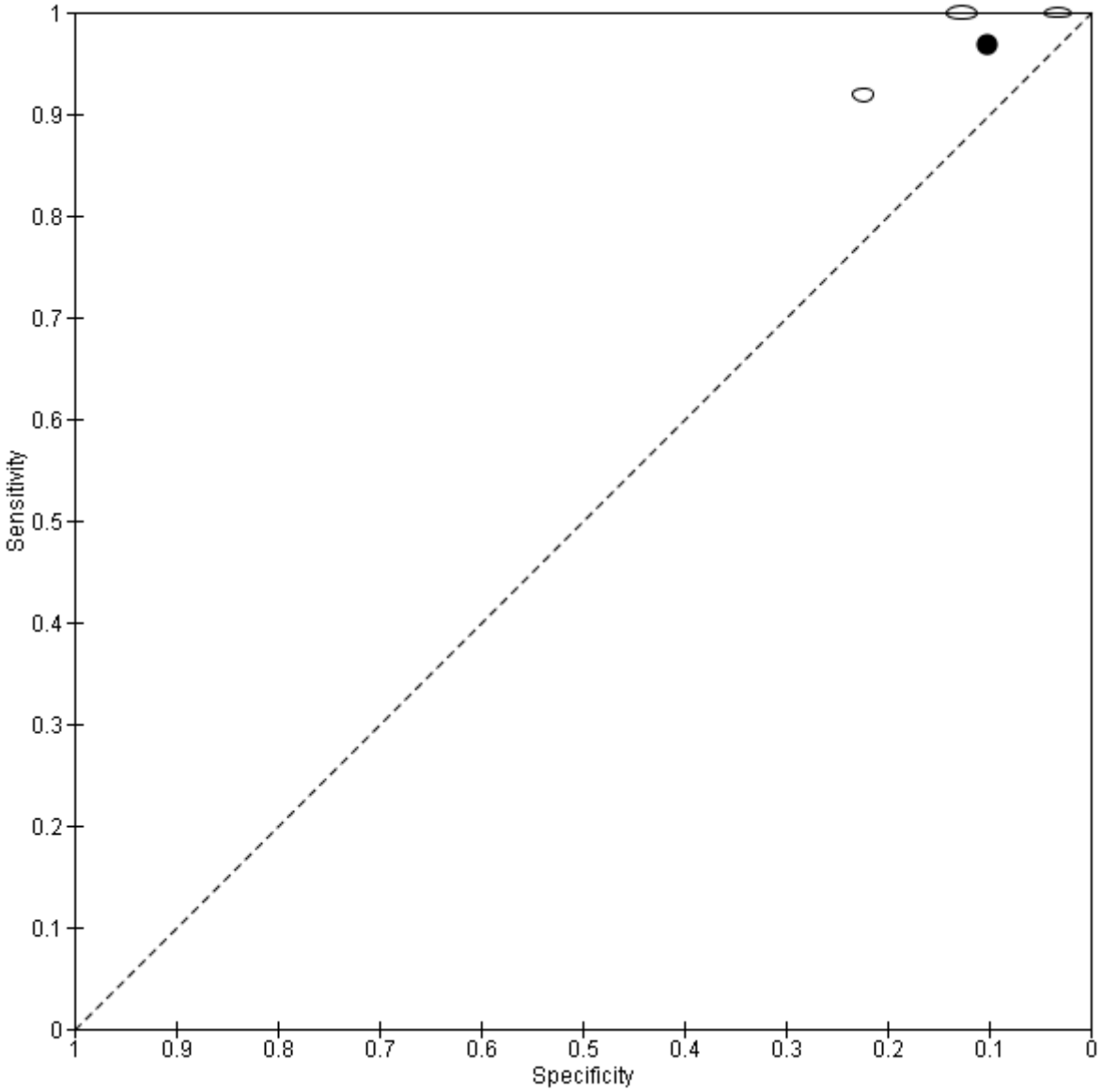
17

Figure 143: NOC - any injury (definitions vary) with all having CT – 8 studies



18

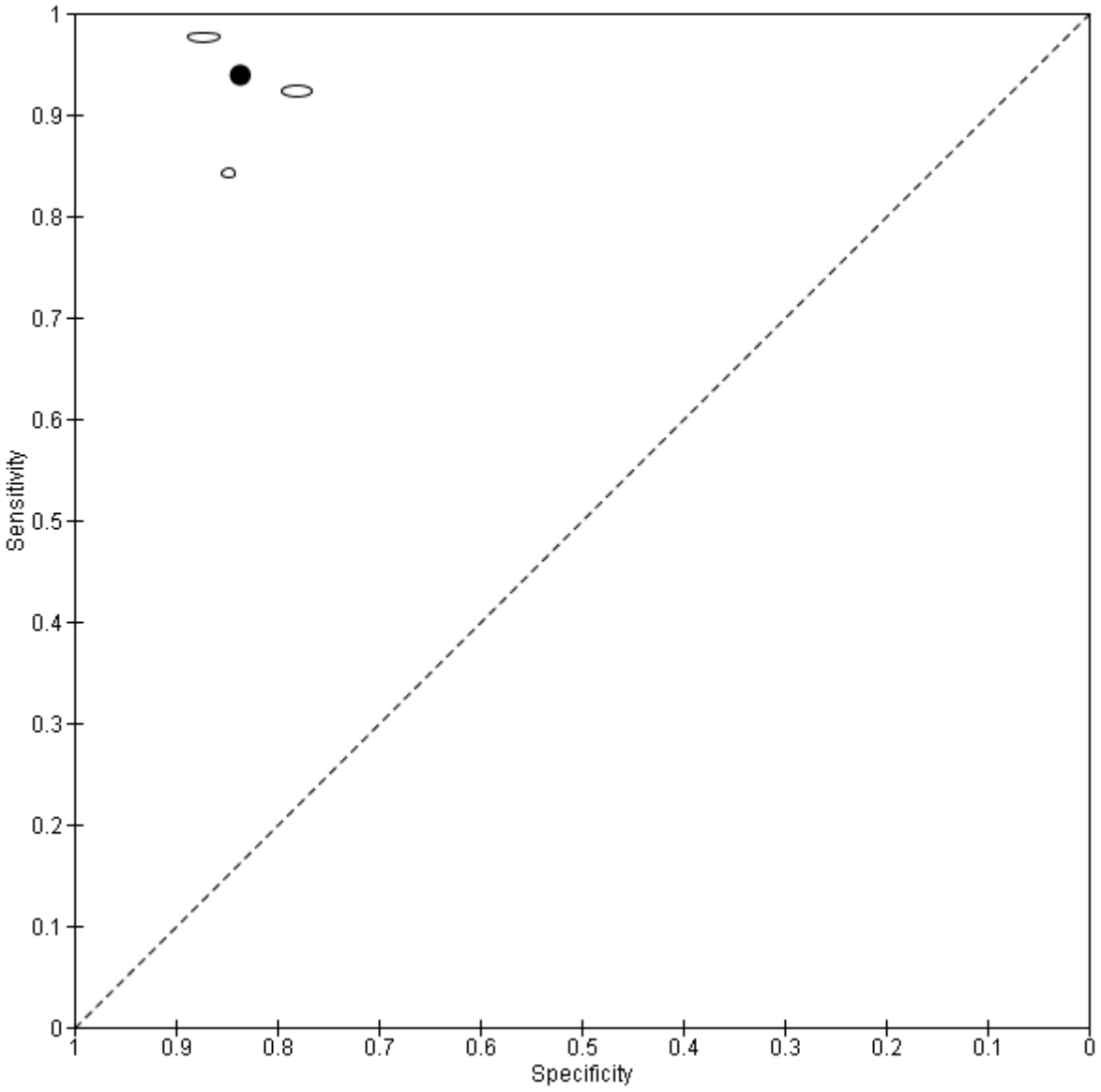
Figure 144: NOC - clinically important/more serious injuries (definitions vary) with only a proportion having CT – 3 studies



19

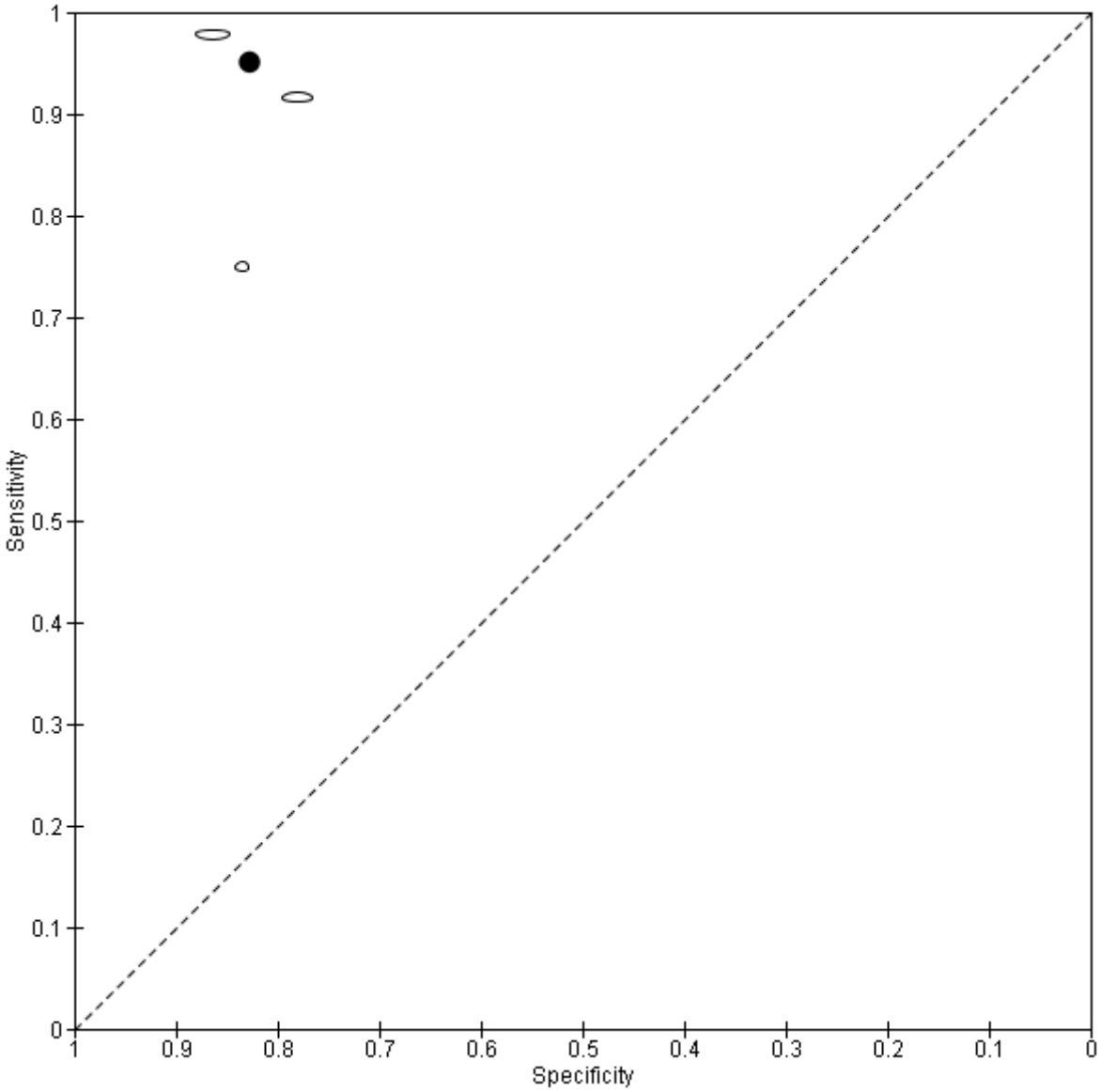
E.202 Children

Figure 145: CHALICE - clinically important/more serious injuries (definition varies) with only a proportion having CT – 3 studies



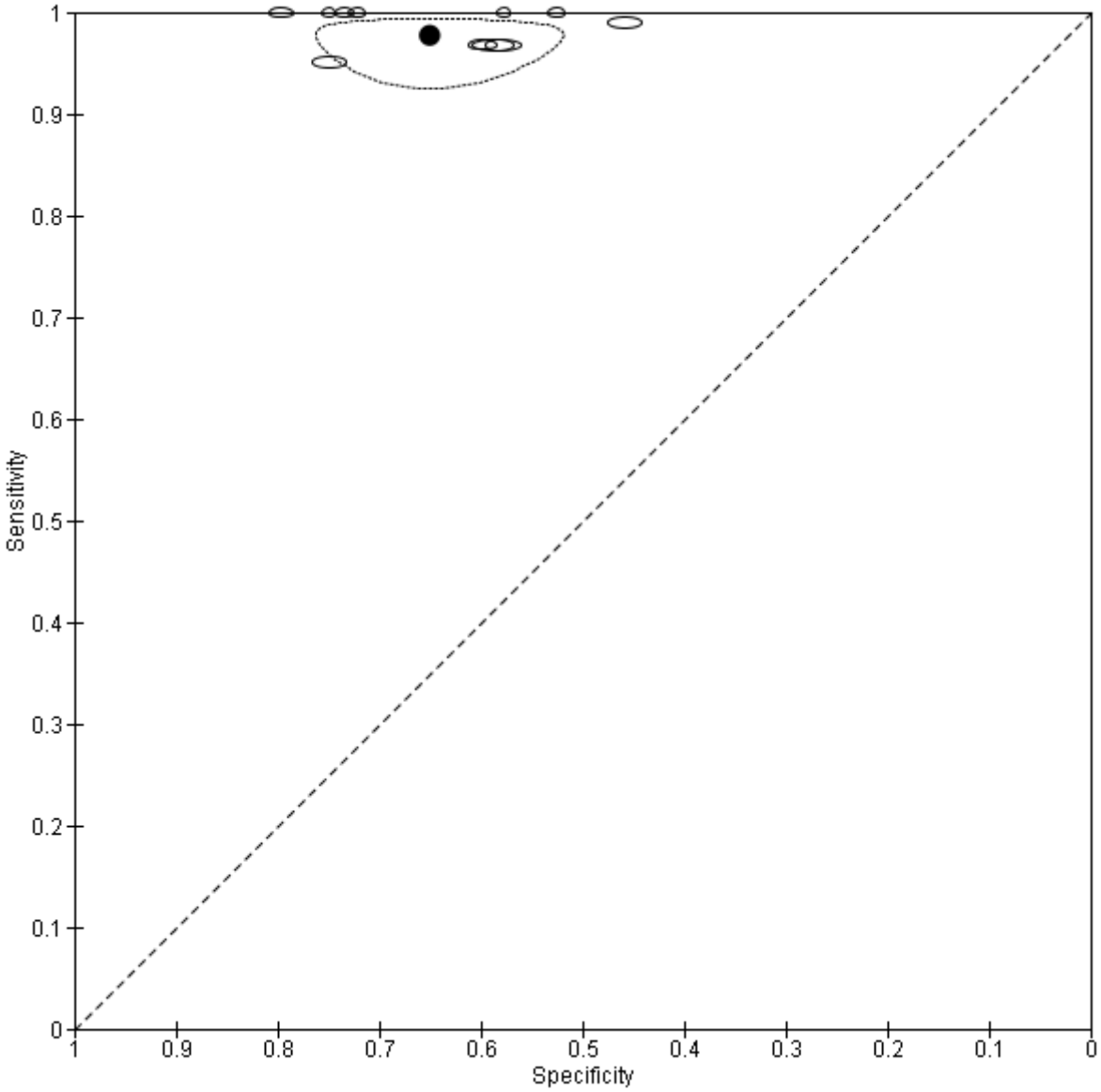
21

Figure 146: CHALICE - neurosurgery (definition varies) with only a proportion having CT – 3 studies



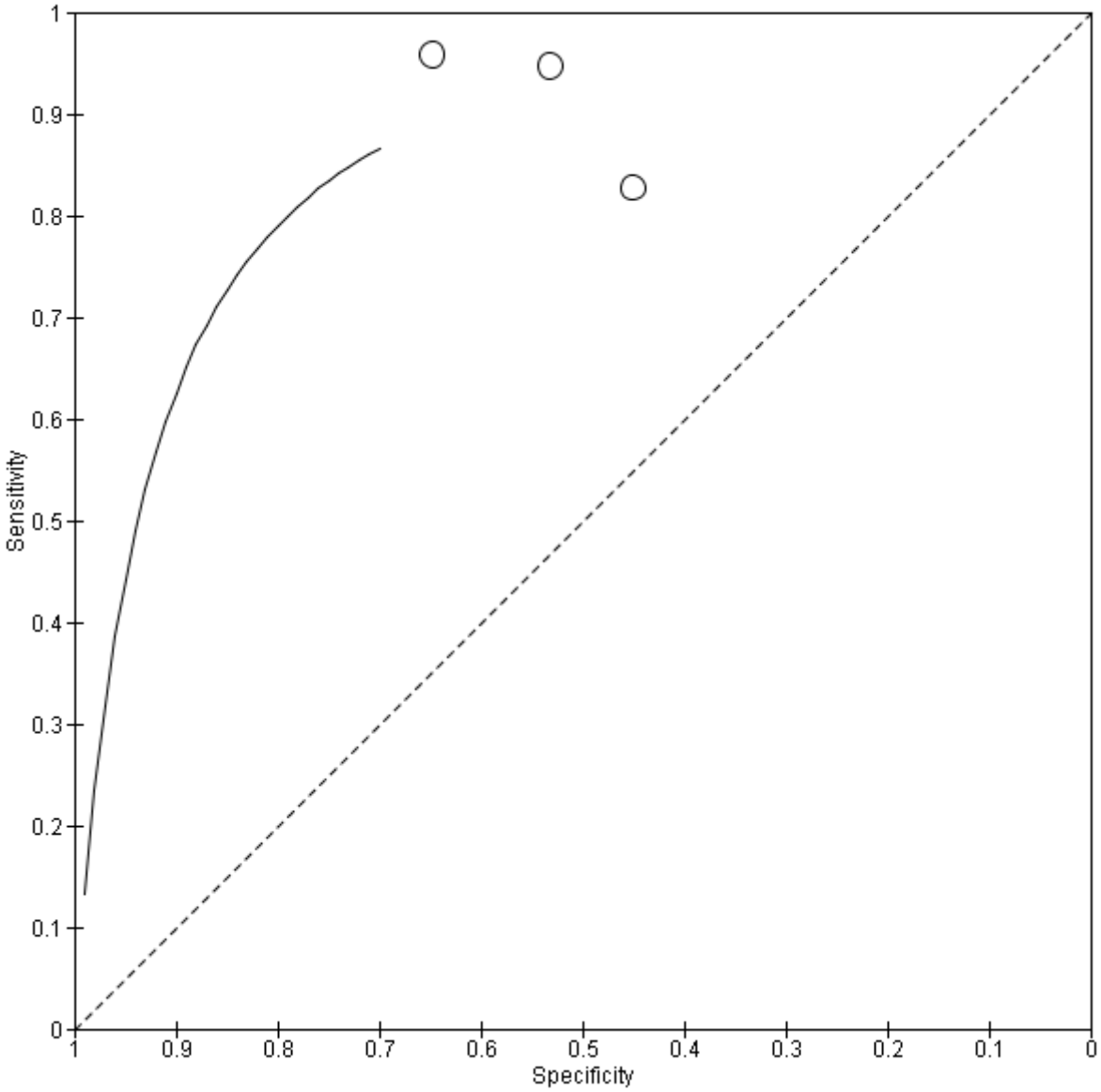
22

Figure 147: PECARN ≥2 years - clinically important/more serious injuries (definition varies) with only a proportion having CT – 11 studies/cohorts



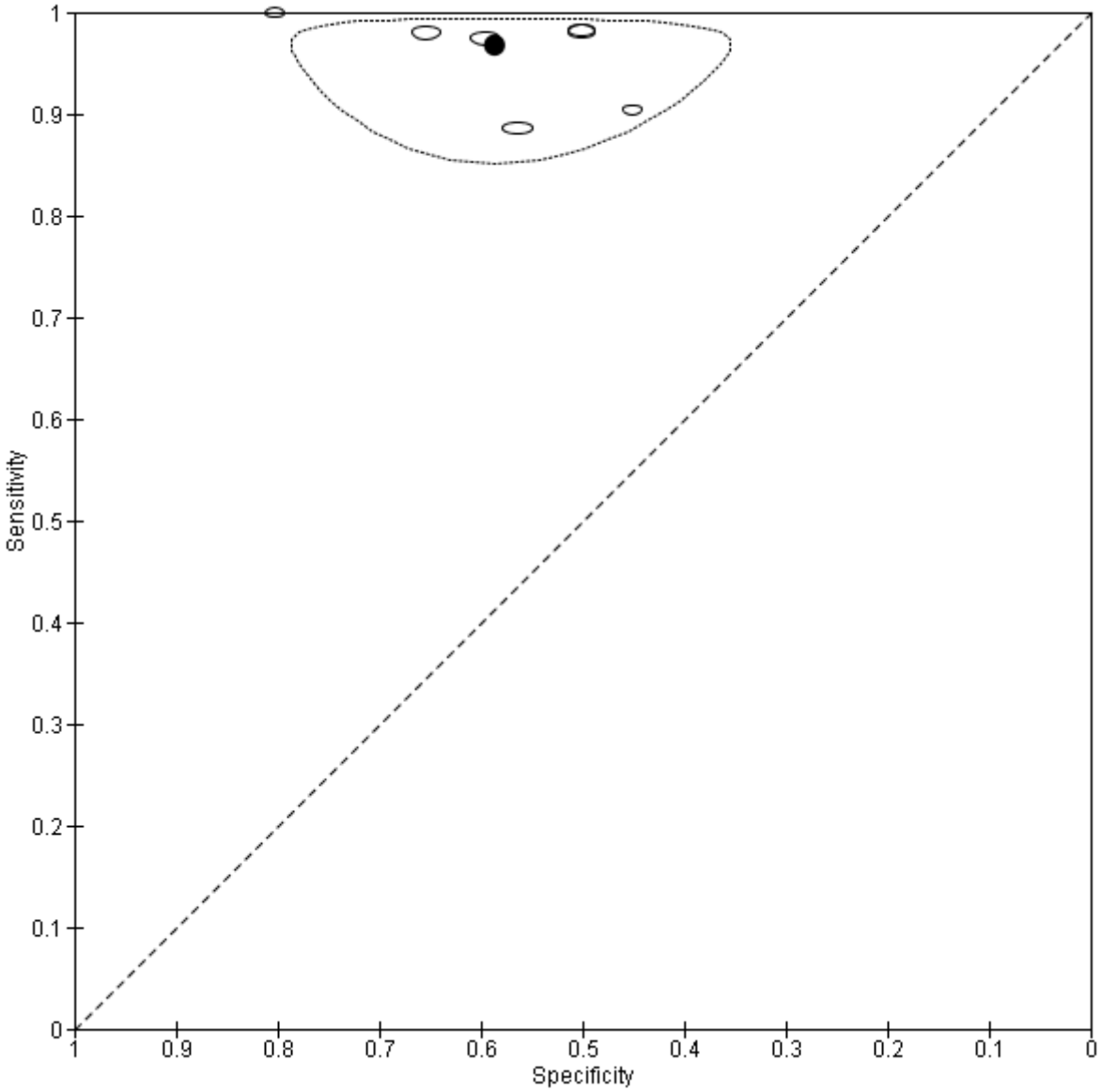
23
24

Figure 148: PECARN not split into age groups – any injury (definition varies) with all having a CT – 3 studies



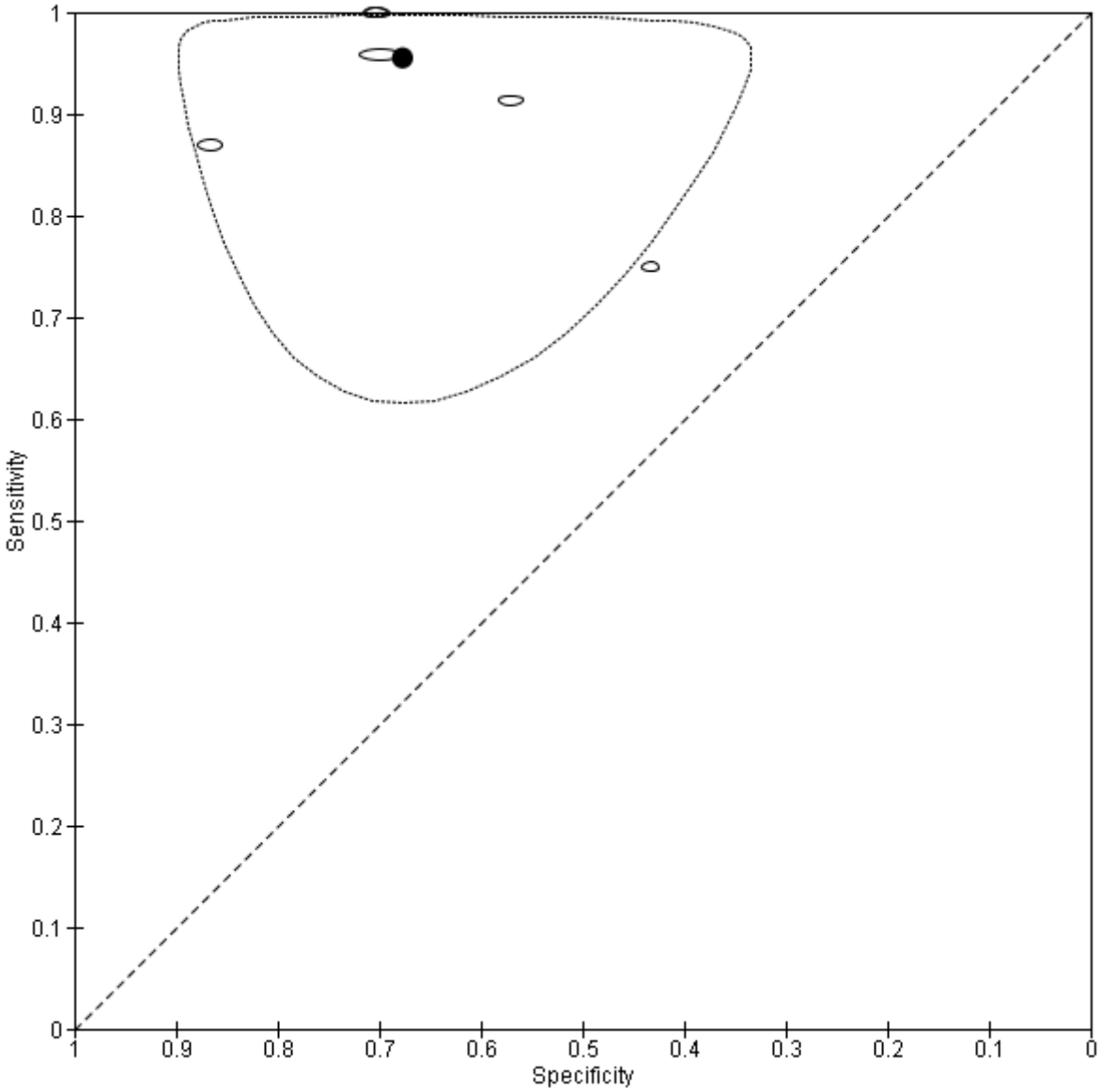
25

Figure 149: CATCH original 7-item rule - any injury (definition varies) with only a proportion having CT – 7 studies



26

Figure 150: CATCH original 7-item rule - neurosurgery (definition varies) with only a proportion having CT – 6 studies



Key:

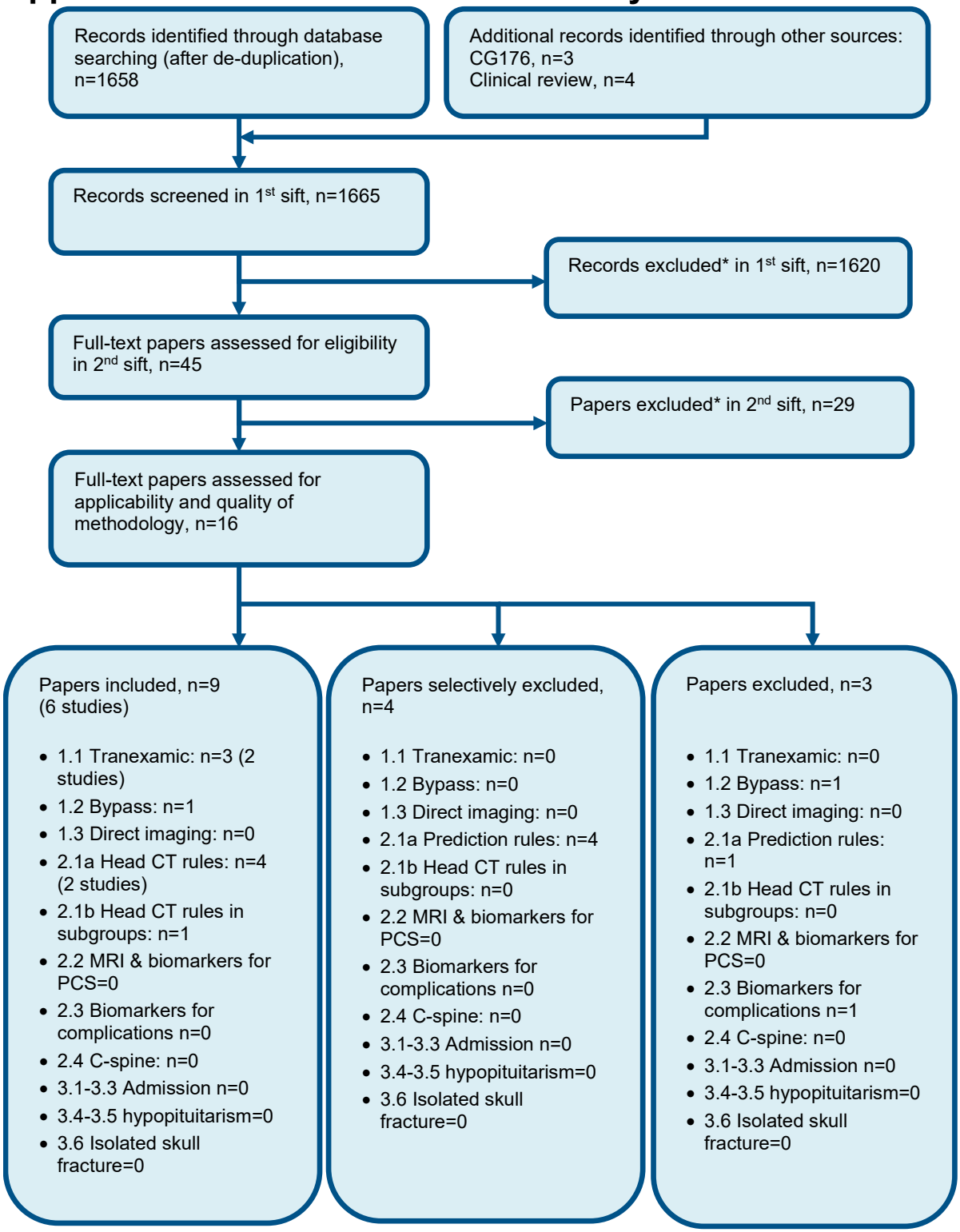
Solid line represents the ROC summary curve

Dotted line represents the 95% confidence region of the ROC

Solid circle represents pooled ROC

Clear circles represent ROC of individual studies

Appendix F – Economic evidence study selection



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

Appendix G – Economic evidence tables

Study	Dalziel 2019[17]			
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA (health outcome: QALYs) **Study design:** Patient-level simulation **Approach to analysis:** Usual care outcomes is based on APHIRST validation cohort (Babl 2017[5] and Babl 2019[7]) Outcomes in each decision rule were estimated by applying the corresponding computer algorithm. Effectiveness was calculated in terms of identified and missed brain injuries in each strategy. **Perspective:** Australian Medicare perspective **Time horizon:** Lifetime	**Population:** Children younger than 18 years with head injury and GCS 13-15 on presentation to ED. **Cohort settings:** Mean age: 5.7 Male: 63.8% **Intervention 1:** Australian and New Zealand usual care **Intervention 2:** CHALICE decision rule **Intervention 3:** PECARN decision rule **Intervention 2:** CATCH decision rule	**Total costs (mean per patient):** Intervention 1: £3,208 Intervention 2: £3,225 Intervention 3: £3,230 Intervention 4: £3,242 Incremental (2-1): £17 Incremental (3-1): £22 Incremental (4-1): £34 **Currency & cost year:** 2016 Australian dollars (presented here as 2019 UK pounds[(a)]) **Cost components incorporated:** ED, Emergency SSU, general ward, ICU, cranial CT scan, intubation, neurosurgery, GOS-E state cost of care, cancer cost	**QALYs (mean per patient):** Intervention 1: 16.97686 QALYs Intervention 2: 16.97567 QALYs Intervention 3: 16.97604 QALYs Intervention 4: 16.97581 QALYs Incremental (2-1): -0.00119 QALYs Incremental (3-1): -0.00082 QALYs Incremental (4-1): -0.00105 QALYs	Intervention 1 dominates interventions 2, 3 and 4 4 was dominated by 3 3 cost £13,514 per QALY compared with 2, although net health benefit at £20,000 per QALY was almost identical. **Analysis of uncertainty:** The probabilistic sensitivity analysis shows that usual care is dominant compared with CHALICE, PECARN and CATCH in 62%, 60% and 61% of the simulations, respectively. When intermediate risk in PECARN were allocated to low risk (no CT) the rule became close in cost, but not effectiveness to usual care. When intermediate risk people were allocated to high risk (receive CT) the rule became more effective but more costly. In none of these, usual care became less cost effective.

Discounting: Costs: 5% Outcomes: 5%				
Data sources				
Health outcomes: Baseline probabilities and outcomes in the usual care were estimated using APHIRST multi-centres observational study. To estimate probabilities in the three decision rule strategies, the algorithm of each decision rule was applied to each child and assessed as being high risk (receive CT) or low risk (be discharged). The effectiveness of the new strategies was calculated in terms of missed or correctly identified brain injury with the three decision rules compared to the observed usual care. People with missed brain injuries were assumed to re-present to the hospital. CT scan has a probability of causing cancer later in life taken from a meta-analysis and temporarily reduces the utility of the child. CT scan was assumed to be 100% accurate. **Quality-of-life weights:** Quality of life in the different COS stages were calculated through a standard gamble approach. **Cost sources:** Single specialist paediatric hospital in Melbourne for all immediate costs except CT scan, which was estimated through an Australian government source, and intubation cost that was taken from a published study. Published evidence were used to estimate COS stages and cancer costs.				
Comments				
Source of funding: The study was funded by grants from the National Health and Medical Research Council **Limitations:** Usual care was defined as defined as management by clinicians according to current, unstandardized, local practice in Australia and New Zealand. This may be considerably different than usual care in the UK considering that the proportion of children receiving CT in Australia and New Zealand seem to be relatively low compared to other settings. In addition, clinicians in different settings may be using different decision rules drawn from experience and training. PECARN algorithm is built to allow clinical discretion but this could not be implemented in the model. It is not clear how mortality was modelled for those in the different COS stages. Most of the immediate costs were calculated from a single centre in Melbourne. Quality of life scores in the different COS stages were calculated using a standard gamble approach instead of a validated questionnaire. **Other:** None				
Overall applicability:[c] Partially applicable **Overall quality:**[d] Potentially serious limitations				

(a) Abbreviations: 95% CI= 95% confidence interval; APHIRST= Australasian Pediatric Head Injury Rules Study, CATCH= Canadian Assessment of Tomography for Childhood Head Injury; CHALICE= Prediction of Important Clinical Events; CUA= cost utility analysis; CT = Computed tomography; GOS = Glasgow outcome scale; ICER= incremental cost-effectiveness ratio; NA = not applicable; NR= not reported; PECARN= Pediatric Emergency Care Applied Research Network; QALYs= quality-adjusted life years.

(b) Converted using 2018/19 purchasing power parities[68]

(c) Directly applicable / Partially applicable / Not applicable

(d) Minor limitations / Potentially serious limitations / Very serious limitations

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Pandor 2011[41, 42, 74]				
Study details	**Population & interventions**	**Costs** (with and without intracranial lesion)	**Health outcomes** (with and without intracranial lesion)	**Cost-effectiveness** (with and without intracranial lesion)
Economic analysis: CUA (health outcome = QALYs) **Study design:** Probabilistic decision analytical model **Approach to analysis:** Markov model estimating the cost-effectiveness of diagnostic strategies for mild head injury (MHI) for children and adults. Patients assumed to: i) have an intracranial lesion requiring neurosurgery (e.g. extradural haemorrhage); or ii) intracranial lesion not requiring surgery; or iii) no intracranial haemorrhage on admission to ED. Health states were modelled as Glasgow Outcome	**Population:** Adults and children admitted to ED with mild head injury (MHI). **Cohort settings:** Start age = decision rules evaluated for 1, 10, 40 and 75 years old **Decision rules for adults:** CT all (theoretical); "abnormal arrival" GCS; CCHR (high risk); CCHR (high or medium risk); NCWFNS; NOC; NEXUS II; NICE 2007; Scandinavian. **Decision rules for children:** CT all (theoretical option); CHALICE, PECAR, UCD and therule of Atabaki et al 2008.	**Total costs (mean per patient) for adults aged 40 years:** Discharge all: £3305 Abnormal arrival GCS: £2991. CT all: £2955. NCWFNS: £2911. Scandinavian: £2905. NEXUS II: £2908. NICE 2007: £2923. CCHR (high risk): £2918. NOC: £2922. CCHR (high or medium risk): £2909. **Total costs (mean per patient) for adults aged 75 years:** Discharge all: £1716 Abnormal arrival GCS: £1543 CT all: £1567 NCWFNS: £1523 NICE 2007: £1535 NEXUS II: £1520 Scandinavian: £1517 NOC: £1534 CCHR (high risk): £1521	**QALYs (mean per patient) for adults aged 40 years:** Discharge all: 18.6633 Abnormal arrival GCS: 18.6839 CT all: 18.6868 NCWFNS: 18.6878 Scandinavian: 18.6880 NEXUS II: 18.6880 NICE 2007: 18.6881 CCHR (high risk): 18.6882 NOC: 18.6884 CCHR (high or medium risk): 18.6888 **QALYs (mean per patient) for adults aged 75 years:** Discharge all: 7.8277 Abnormal arrival GCS: 7.8363 CT all: 7.8368 NCWFNS:7.8376 NICE 2007: 7.8376 NEXUS II: 7.8377 Scandinavian: 7.8377 NOC: 7.8378 CCHR (high risk): 7.8378 CCHR (high or medium risk): 7.8381	**Adults aged 40 years:** The following strategies were dominated: Discharge all; Abnormal arrival GCS; CT all; NCWFNS; NICE 2007, CCHR (high risk); NOC. The NEXUS II strategy was extendedly dominated. CCHR (high or medium risk) versus Scandinavian: £3879 per QALY gained (pa) Probability CCHR (high or medium risk) cost-effective for willingness –to-pay thresholds between £0 and £50,000 is 28-42% **Adults aged 40 years:** The following strategies were dominated: Discharge all; Abnormal arrival GCS; CT all; NCWFNS; NICE 2007; NEXUS II; NOC; CCHR (high risk). CCHR (high or medium risk) versus Scandinavian: £10,397 per QALY gained (pa) CI: Not reported Probability CCHR (high or medium risk) cost-effective for willingness –to-pay thresholds between £0 and £50,000 is 34-42% **Children aged 10 years:**

Scores (GOS) states over time. **Perspective:** UK NHS **Time horizon:** lifetime **Treatment effect duration:** GOS at 1 year were compared with outcomes at 5-7 years, with patients randomly assigned a time between 5 and 7 years at which point they change state, based on Whitnall et al. After that, patients were assumed to stay in that state for life as no further data were available. **Discounting:** Costs and outcomes discounted at a rate of 3.5%		CCHR (high or medium risk): £1521 **Total costs (mean per patient) for a child aged 10 years:** CHALICE: £3567 PECARN: £3611 UCD: £3608 Atabaki et all: £3621 CT all: £3666 Discharge all: £4115 **Total costs (mean per patient) for a child aged 1 year:** CHALICE: £3648 PECARN: £3699 UCD: £3700 Atabaki et all: £3713 CT all: £3771 Discharge all: £4206 **Currency & cost year:** 2008 UK pounds **Cost compoents incorporated:** ED visit; CT scan; admission with no deterioration or neurosurgery; neurosurgical intervention before deterioration; long-	**QALYs (mean per patient) for children aged 10 years:** CHALICE: 22.4156 PECARN: 22.4119 UCD: 22.4112 Atabaki et all: 22.4108 CT all: 22.4072 Discharge all: 22.3847 **QALYs (mean per patient) for children aged 1 year:** CHALICE: 22.9857 PECARN: 22.9787 UCD: 22.9760 Atabaki et all: 22.9764 CT all: 22.9663 Discharge all: 22.9549	CHALICE dominant strategy Probability CHALICE cost-effective for willingness –to-pay thresholds between £0 and £50,000 is 70-100% **Children aged 1 year:** CHALICE dominant strategy Probability CHALICE cost-effective for thresholds between £0 and £50,000 is 75-100% **Analysis of uncertainty:** Several sensitivity analyses were conducted. First, the deterministic findings for all patients groups were replicated using the prevalence estimates of neurosurgical and non-neurosurgical lesions in Stein et al. The CHALICE rule remained dominant for children, but the NEXUS II rule was dominant for adults (but the absolute cost and QALY differences between the CCHR and NEXUS II were very small in both analyses and attributable to small differences in point estimate of sensitivity). Univariate sensitivity analysis was conducted on several parameters using lowest and highest value of 95% CI – for all ages, no parameter change altered the decision on optimal strategy. The findings were also not

		term costs for patients with GOS 3 and 4; intensive care, rehabilitation, and nursing home costs for patients with GOS 2; costs of cancer (due to radiation exposure)		sensitive to changes in the discount rate (from 0 to 6%). When validation cohort data was used for children CHALICE was dominated by UCD and NEXUS II.
Data sources				
Health outcomes: To estimate outcomes, a systematic review and fixed-effect meta-analysis was conducted to estimate the proportion of patients in GOS states (from 1 to 5) after early intervention (i.e. neurosurgery). The adverse effect associated with late intervention was derived from two cohort studies – Haselsberger 1988[36] and Deverill 2007,[19] although how these studies were used was unclear. Movements between GOS states over time were estimated from a prospective cohort study by Whitnall 2006.[95] This determined the outcomes at 5-7 years compared with outcomes at 1 year. Types, prevalence and cost of radiation-induced cancers in children based on estimated in Stein 2008. [88] **Quality-of-life weights:** EQ5D from Smits 2010.[85] **Cost sources:** National Schedule of Reference Costs 2007-08; PSSRU Unit costs of health and social care 2009; Beecham 2009[8] for long term costs for GOS 4 and 3.				
Comments				
Source of funding: National Institute for Health Research - Health Technology Assessment programme **Limitations:** The following limitations were noted: 1) Estimating the benefit of treating neurosurgical and non-neurosurgical lesions relied upon observational data with small numbers. For example, the probabilities of GOS 2 and 3 are subject to great uncertainty, which in turn can affect the cost-effectiveness findings. The estimates were validated at the time by experienced neurosurgeons and emergency physicians who felt that the estimates were appropriate. However, the guideline committee felt that the proportion with GOS 2 (vegetative state) seemed a little high. 2) The model assumed that hospital admission and treatment provided no benefit for patients with a non-neurosurgical lesion that did not deteriorate or those with a normal CT scan, as no clear evidence was found for these benefits. 3) For children the evidence for validation of the prediction rules was very limited. **Other:** 95% confidence interval and p-values not reported for cost and QALY outcomes				
Overall applicability*: Directly applicable Overall quality: Potentially serious limitations**				

Abbreviations: CCA = cost-consequence analysis; CEA = cost-effectiveness analysis; CI = 95% confidence interval; CUA = cost-utility analysis; ED = Emergency Department; EQ-5D = Euroqol five dimensions (scale: 0.0 [death] to 1.0 [full health]; <0.0 = worse than death); GOS = Glasgow Outcome Scores ; ICER = incremental cost-effectiveness ratio; NR = not reported; pa = probabilistic analysis; PSA = Probabilistic Sensitivity Analysis; QALYs = quality-adjusted life years; SA = sensitivity analysis

** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious limitations / Very serious limitations*

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Appendix H – Health economic model

Modelling was not conducted for this review.

4 Appendix I – Excluded studies

5 Clinical studies

6 Table 59: Studies excluded from the clinical review

Study	Code [Reason]
Alzuhairy, A. K. A. (2020) Accuracy of Canadian CT Head Rule and New Orleans Criteria for Minor Head Trauma; a Systematic Review and Meta-Analysis. Archives of Academic Emergency Medicine 8(1): e79	- Systematic review used as source of primary studies
Arora, R., White, E. N., Niedbala, D. et al. (2020) Reducing Computed Tomography Scan Utilization for Pediatric Minor Head Injury in the Emergency Department: A Quality Improvement Initiative. Academic Emergency Medicine 27: 27	- Comparator in study does not match that specified in this review protocol
Atabaki, S. M., Jacobs, B. R., Brown, K. M. et al. (2017) Quality Improvement in Pediatric Head Trauma with PECARN Rules Implementation as Computerized Decision Support. Pediatric Quality & Safety 2(3): e019	- Comparator in study does not match that specified in this review protocol
Babl, F. E. and Bressan, S. (2015) Prediction rule: Physician practice and PECARN rule outperform CATCH and CHALICE rules based on the detection of traumatic brain injury as defined by PECARN. Evidence-Based Medicine 20(1): 33-34	- Secondary publication of an included study that does not provide any additional relevant information
Babl, F. E., Oakley, E., Dalziel, S. R. et al. (2018) Accuracy of Clinician Practice Compared With Three Head Injury Decision Rules in Children: A Prospective Cohort Study. Annals of Emergency Medicine 71(6): 703-710	- Secondary publication of an included study that does not provide any additional relevant information
Bent, C., Lee, P. S., Shen, P. Y. et al. (2015) Clinical scoring system may improve yield of head CT of non-trauma emergency department patients. Emergency Radiology 22(5): 511-6	- Population not relevant to this review protocol - Diagnostic test/factor not relevant to review protocol
Bezuidenhout, A. F., Hurter, D., Maydell, A. T. et al. (2013) The Kimberley Hospital Rule (KHR) for urgent computed tomography of the brain in a resource-limited environment. South African Medical Journal. Suid-Afrikaanse Tydskrif Vir Geneeskunde 103(9): 646-51	- Diagnostic test/factor not relevant to review protocol

Study	Code [Reason]
Bouida, W., Marghli, S., Souissi, S. et al. (2013) Prediction value of the Canadian CT head rule and the New Orleans criteria for positive head CT scan and acute neurosurgical procedures in minor head trauma: a multicenter external validation study. Annals of Emergency Medicine 61(5): 521-7	- Duplicate reference
Bressan, S., Berlese, P., Arpone, M. et al. (2021) Missed intracranial injuries are rare in emergency departments using the PECARN head injury decision rules. Childs Nervous System 37(1): 55-62	- Study design not relevant to this review protocol
Bressan, S., Eapen, N., Phillips, N. et al. (2021) PECARN algorithms for minor head trauma: Risk stratification estimates from a prospective PREDICT cohort study. Academic Emergency Medicine 28(10): 1124-1133	- Study design not relevant to this review protocol
Carnevale, T. J., Meng, D., Wang, J. J. et al. (2015) Impact of an emergency medicine decision support and risk education system on computed tomography and magnetic resonance imaging use. Journal of Emergency Medicine 48(1): 53-7	- Population not relevant to this review protocol - Diagnostic test/factor not relevant to review protocol
Coffey, Frank, Hewitt, Susanne, Stiell, Ian et al. (2011) Validation of the Canadian c-spine rule in the UK emergency department setting. Emergency Medicine Journal 28(10): 873-876	- Population not relevant to this review protocol
Covino, M., Gilardi, E., Manno, A. et al. (2019) A new clinical score for cranial CT in ED non-trauma patients: Definition and first validation. American Journal of Emergency Medicine 37(7): 1279-1284	- Population not relevant to this review protocol
Dalziel, K., Cheek, J. A., Fanning, L. et al. (2019) A Cost-Effectiveness Analysis Comparing Clinical Decision Rules PECARN, CATCH, and CHALICE With Usual Care for the Management of Pediatric Head Injury. Annals of Emergency Medicine 73(5): 429-439	- Secondary publication of an included study that does not provide any additional relevant information
Dayan, P. S., Ballard, D. W., Tham, E. et al. (2017) Use of Traumatic Brain Injury Prediction Rules With Clinical Decision Support. Pediatrics 139(4)	- Comparator in study does not match that specified in this review protocol

Study	Code [Reason]
	- Study design not relevant to this review protocol
Deakyne, S. J., Bajaj, L., Hoffman, J. et al. (2015) Development, Evaluation and Implementation of Chief Complaint Groupings to Activate Data Collection: A Multi-Center Study of Clinical Decision Support for Children with Head Trauma. Applied Clinical Informatics 6(3): 521-35	- Diagnostic test/factor not relevant to review protocol
Delefortrie, Q., Lejeune, F., Kerzmann, B. et al. (2018) Evaluation of the Roche R Elecsys and the Diasorin R Liaison S100 kits in the management of mild head injury in the emergency room. Clinical Biochemistry 52: 123-130	- Diagnostic test/factor not relevant to review protocol
Denver, D.; Shetty, A.; Unwin, D. (2015) Falls and Implementation of NEXUS in the Elderly (The FINE Study). Journal of Emergency Medicine 49(3): 294-300	- Diagnostic test/factor not relevant to review protocol - Reference standard not relevant to review protocol
De Wit, K., Mercuri, M., Clayton, N. et al. (2021) Which older emergency patients are at risk of intracranial bleeding after a fall? A protocol to derive a clinical decision rule for the emergency department. BMJ Open 11(7)	- Study design not relevant to this review protocol – protocol for a study
Dietrich, Ann M, Bowman, Mary Jo, Ginn-Pease, Margaret E et al. (1993) Pediatric head injuries: can clinical factors reliably predict an abnormality on computed tomography?. Annals of emergency medicine 22(10): 1535-1540	- Diagnostic test/factor not relevant to review protocol
Ding, J., Guo, Y., Chen, S. W. et al. (2011) Clinical study of routine repeat CT after traumatic brain injury. Journal of shanghai jiaotong university (medical science) 31(6): 793-796	- Study not reported in English
Ding, J., Yuan, F., Guo, Y. et al. (2012) A prospective clinical study of routine repeat computed tomography (CT) after traumatic brain injury (TBI). Brain injury 26(10): 1211-1216	- Diagnostic test/factor not relevant to review protocol

Study	Code [Reason]
Drexelius, N. (2006) Mild head injury: CT or observation? Zeitschrift fur allgemeinmedizin 82(12): 529	- Study not reported in English
Edalatfar, M., Piri, S. M., Mehrabinejad, M. M. et al. (2021) Biofluid Biomarkers in Traumatic Brain Injury: A Systematic Scoping Review. Neurocritical Care 05: 05	- Diagnostic test/factor not relevant to review protocol
Ellethy, Hanem; Chandra, Shekhar S; Nasrallah, Fatima A (2022) Deep Neural Networks Predict the Need for CT in Pediatric Mild Traumatic Brain Injury: A Corroboration of the PECARN Rule. Journal of the American College of Radiology: JACR 19(6): 769-778	- Study does not contain an intervention relevant to this review protocol
Engineer, R. S., Podolsky, S. R., Fertel, B. S. et al. (2018) A Pilot Study to Reduce Computed Tomography Utilization for Pediatric Mild Head Injury in the Emergency Department Using a Clinical Decision Support Tool and a Structured Parent Discussion Tool. Pediatric Emergency Care 15: 15	- No outcomes relevant to protocol reported
Faris, G., Byczkowski, T., Ho, M. et al. (2016) Prediction of Persistent Postconcussion Symptoms in Youth Using a Neuroimaging Decision Rule. Academic Pediatrics 16(4): 336-342	- Study design not relevant to this review protocol
Farris, C. W., Baghdanian, A., Takahashi, C. et al. (2021) Implementation of Institutional Triaging Algorithms Decreases Head and Neck MDCT Use in Blunt Trauma. Radiology 298(3): 622-629	- Comparator in study does not match that specified in this review protocol
Fisher, J. A. N. and Welle, C. G. (2018) Rapid detection and monitoring of brain injury using sensory-evoked responses. Neuromethods 139: 243-256	- Diagnostic test/factor not relevant to review protocol
Foster, S. M., Muller, A., Conklin, J. et al. (2019) Is clinician assessment accurate or is routine pan-body CT needed in the stable intoxicated trauma patient? American Journal of Surgery 218(4): 755-759	- Diagnostic test/factor not relevant to review protocol
Fournier, N., Gariepy, C., Prevost, J. F. et al. (2019) Adapting the Canadian CT head rule age	- Diagnostic test/factor not relevant to review protocol

Study	Code [Reason]
criteria for mild traumatic brain injury. Emergency Medicine Journal 36(10): 617-619	
Fulkerson, D. H., White, I. K., Rees, J. M. et al. (2015) Analysis of long-term (median 10.5 years) outcomes in children presenting with traumatic brain injury and an initial Glasgow Coma Scale score of 3 or 4. Journal of neurosurgery pediatrics16(4): 410-419	- Study design not relevant to this review protocol
Furtado, L. M. F., da Costa Val Filho, J. A., Dos Santos, A. R. et al. (2020) Pediatric minor head trauma in Brazil and external validation of PECARN rules with a cost-effectiveness analysis. Brain Injury 34(11): 1467-1471	- No useable diagnostic data
Garcia, C. M. and Cunningham, S. J. (2018) Role of clinical suspicion in pediatric blunt trauma patients with severe mechanisms of injury. American Journal of Emergency Medicine 36(1): 105-109	- Diagnostic test/factor not relevant to review protocol
Ghag, G. and Jagdale, A. (2018) Correlation of paediatric trauma score, revised trauma score and injury severity score with length of hospital stay in paediatric trauma patients. Journal of Clinical and Diagnostic Research 12(4): PC05-PC07	- Study design not relevant to this review protocol
Gimbel, R. W., Pirrallo, R. G., Lowe, S. C. et al. (2018) Effect of clinical decision rules, patient cost and malpractice information on clinician brain CT image ordering: a randomized controlled trial. BMC Medical Informatics & Decision Making 18(1): 20	- Study design not relevant to this review protocol
Gokharman, F. D., Aydin, S., Fatihoglu, E. et al. (2017) Pediatric Emergency Care Applied Research Network head injuryprediction rules: on the basis of cost and effectiveness. Turkish Journal of Medical Sciences 47(6): 1770-1777	- Study design not relevant to this review protocol
Gozt, A., Licari, M., Halstrom, A. et al. (2020) Towards the development of an integrative, evidence-based suite of indicators for the prediction of outcome following mild traumatic brain injury: Results from a pilot study. Brain Sciences 10 (1)	- Study design not relevant to this review protocol
Gravel, J., Gouin, S., Chalut, D. et al. (2015) Derivation and validation of a clinical decision	- Reference standard not relevant to review protocol

Study	Code [Reason]
rule to identify young children with skull fracture following isolated head trauma. CMAJ Canadian Medical Association Journal 187(16): 1202-1208	
Grubenhoff, J. (2021) PECARN blunt head-trauma prediction rule in infants <3 months old. Journal of Pediatrics 238: 338-342	- Study design not relevant to this review protocol – conference abstract of a study which was secondary analysis of the PECARN trial.
Guha, A. (2002) The Canadian C-Spine Rule for Radiography in alert and Stable Trauma Patients. Critical Care 6 (1)	- Diagnostic test/factor not relevant to review protocol
Güzel, Ahmet, Hiçdönmez, Tufan, Temizöz, Osman et al. (2009) Indications for brain computed tomography and hospital admission in pediatric patients with minor head injury: how much can we rely upon clinical findings? Pediatric neurosurgery 45(4): 262-270	- Components of the novel decision rule assessed are not clear
Harrison, D. A., Prabhu, G., Grieve, R. et al. (2013) Risk Adjustment In Neurocritical care (RAIN) - prospective validation of risk prediction models for adult patients with acute traumatic brain injury to use to evaluate the optimum location and comparative costs of neurocritical care: A cohort study. Health Technology Assessment 17(23): VII-XVII+1	- Study design not relevant to this review protocol
Hautala, M., Koskela, U., Pokka, T. et al. (2021) Efficacy of the implementation of the National Emergency X-Radiography Utilization Study II decision rule to clinical practice for paediatric head injury patients. Acta Paediatrica 28: 28	- Comparator in study does not match that specified in this review protocol
Hellstrom, J., Romanos Zapata, R., Libard, S. et al. (2019) Evaluation of the INTERPRET decision-support system: can it improve the diagnostic value of magnetic resonance spectroscopy of the brain? Neuroradiology 61(1): 43-53	- Population not relevant to this review protocol - Diagnostic test/factor not relevant to review protocol
Hess, E. P., Homme, J. L., Kharbanda, A. B. et al. (2018) Effect of the Head Computed Tomography Choice Decision Aid in Parents of Children With Minor Head Trauma: A Cluster Randomized Trial. JAMA Network Open 1(5): e182430	- Comparator in study does not match that specified in this review protocol

Study	Code [Reason]
Hess, E. P., Wyatt, K. D., Kharbanda, A. B. et al. (2014) Effectiveness of the head CT choice decision aid in parents of children with minor head trauma: study protocol for a multicenter randomized trial. Trials [Electronic Resource] 15: 253	- Comparator in study does not match that specified in this review protocol
Hinzpeter, R., Sprengel, K., Wanner, G. A. et al. (2017) Repeated CT scans in trauma transfers: An analysis of indications, radiation dose exposure, and costs. European Journal of Radiology 88: 135-140	- Study design not relevant to this review protocol
Holmes, M. W., Goodacre, S., Stevenson, M. D. et al. (2013) The cost-effectiveness of diagnostic management strategies for children with minor head injury. Archives of Disease in Childhood 98(12): 939-44	- Study design not relevant to this review protocol
Homme, J. J. L. (2018) Pediatric Minor Head Injury 2.0: Moving from Injury Exclusion to Risk Stratification. Emergency Medicine Clinics of North America 36(2): 287-304	- Review article but not a systematic review
Huisman, T. A. G. M. (2015) Prediction rule: CT should not be relied on for cases of isolated vomiting in children with blunt head trauma. Evidence-Based Medicine 20(1): 32	- Diagnostic test/factor not relevant to review protocol
Jannis, J. (2004) The use of brain CT Scan in craniocerebral trauma with Glasgow Coma Scale Scores of 13 - 15 in Dr. Cipto Mangunkusumo Hospital 1999-2001. Medical Journal of Indonesia 13(3): 156-160	- Diagnostic test/factor not relevant to review protocol
Joseph, B., Obaid, O., Dultz, L. et al. (2022) Validating The Brain Injury Guidelines (BIG): Results of An AAST Prospective Multi-Institutional Trial. The Journal of Trauma and Acute Care Surgery 03: 28	- Study design not relevant to this review protocol
Kadom, N., Vey, B. L., Frush, D. P. et al. (2018) Think a-head campaign of image gently: Shared decision-making in pediatric head trauma. American Journal of Neuroradiology 39(8): 1386-1389	- Review article but not a systematic review
Koiso, T., Goto, M., Terakado, T. et al. (2021) The effects of antithrombotic therapy on head	- Study design not relevant to this review protocol

Study	Code [Reason]
trauma and its management. Scientific Reports 11(1): 20459	
Kuczawski, M., Stevenson, M., Goodacre, S. et al. (2016) Should all anticoagulated patients with head injury receive a CT scan? Decision-analysis modelling of an observational cohort. BMJ Open 6(12): e013742	- Study design not relevant to this review protocol
Lagarde, E. (2015) New Clinical Decision Instruments Can and Should Reduce Radiation Exposure. PLoS Medicine 12 (10)	- Review article but not a systematic review
Langness, S., Ward, E., Halbach, J. et al. (2018) Plasma D-dimer safely reduces unnecessary CT scans obtained in the evaluation of pediatric head trauma. Journal of Pediatric Surgery 53(4): 752-757	- Diagnostic test/factor not relevant to review protocol
Laribi, S., Kansao, J., Borderie, D. et al. (2014) S100B blood level measurement to exclude cerebral lesions after minor head injury: the multicenter STIC-S100 French study. Clinical Chemistry & Laboratory Medicine 52(4): 527-36	- Diagnostic test/factor not relevant to review protocol
Leonard, J. C., Browne, L. R., Ahmad, F. A. et al. (2019) Cervical spine injury risk factors in children with blunt trauma. Pediatrics 144 (1)	- Reference standard not relevant to review protocol
Li, Q. and Zhou, Q. (2017) Relationship between CT features and serum GFAP, NSE and S100B protein in patients with severe traumatic brain injury. Biomedical Research (India) 28(22): 9926-9929	- Diagnostic test/factor not relevant to review protocol
Lodwick, D. L., Cooper, J. N., Lawrence, A. E. et al. (2019) Factors Affecting Emergency Department Computed Tomography Use in Children. Journal of Surgical Research 241: 294-301	- Study design not relevant to this review protocol - Population not relevant to this review protocol
Lugones, M., Parkin, G., Bjelosevic, S. et al. (2018) Blood biomarkers in paediatric mild traumatic brain injury: a systematic review. Neuroscience and Biobehavioral Reviews 87: 206-217	- Diagnostic test/factor not relevant to review protocol
Mahan, M. Y., Thorpe, M., Ahmadi, A. et al. (2019) Glial Fibrillary Acidic Protein (GFAP)	- Diagnostic test/factor not relevant to review protocol

Study	Code [Reason]
Outperforms S100 Calcium-Binding Protein B (S100B) and Ubiquitin C-Terminal Hydrolase L1 (UCH-L1) as Predictor for Positive Computed Tomography of the Head in Trauma Subjects. World Neurosurgery 128: e434-e444	
Marincowitz, C., Lecky, F. E., Allgar, V. et al. (2020) Development of a Clinical Decision Rule for the Early Safe Discharge of Patients with Mild Traumatic Brain Injury and Findings on Computed Tomography Brain Scan: A Retrospective Cohort Study. Journal of Neurotrauma 37(2): 324-333	- Population not relevant to this review protocol
Martin, G. E., Carroll, C. P., Plummer, Z. J. et al. (2018) Safety and efficacy of brain injury guidelines at a Level III trauma center. The Journal of Trauma and Acute Care Surgery 84(3): 483-489	- No useable diagnostic data
Masood, S., Woolner, V., Yoon, J. H. et al. (2020) Checklist for Head Injury Management Evaluation Study (CHIMES): a quality improvement initiative to reduce imaging utilisation for head injuries in the emergency department. BMJ Open Quality 9(1): 02	- No useable diagnostic data
McGraw, M. and Way, T. (2019) Comparison of PECARN, CATCH, and CHALICE clinical decision rules for pediatric head injury in the emergency department. Canadian Journal of Emergency Medicine 21(1): 120-124	- Secondary publication of an included study that does not provide any additional relevant information
Melnick, E. R.; Keegan, J.; Taylor, R. A. (2015) Redefining Overuse to Include Costs: A Decision Analysis for Computed Tomography in Minor Head Injury. Joint Commission Journal on Quality & Patient Safety 41(7): 313-22	- No useable diagnostic data
Minkkinen, M., Iverson, G. L., Kotilainen, A. K. et al. (2019) Prospective Validation of the Scandinavian Guidelines for Initial Management of Minimal, Mild, and Moderate Head Injuries in Adults. Journal of Neurotrauma 36(20): 2904-2912	- Diagnostic test/factor not relevant to review protocol
Mishra, R. K., Munivenkatappa, A., Prathyusha, V. et al. (2017) Clinical predictors of abnormal head computed tomography scan in patients who are conscious after head injury. Journal of Neurosciences in Rural Practice 8(1): 64-67	- Diagnostic test/factor not relevant to review protocol

Study	Code [Reason]
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	- Study design not relevant to this review protocol
Mojica, C.; Ganan-Vesga, J. G.; Arenas Correa, H. C. (2016) Use of the PECARN clinical decision guidelines as a predictor of an intracranial lesion in mild traumatic brain injury in the paediatric population of Tunja, Boyaca. Pediatria 49(3): 78-83	- Study not reported in English
Mondello, S., Sorinola, A., Czeiter, E. et al. (2021) Blood-Based Protein Biomarkers for the Management of Traumatic Brain Injuries in Adults Presenting to Emergency Departments with Mild Brain Injury: A Living Systematic Review and Meta-Analysis. Journal of Neurotrauma 38(8): 1086-1106	- Diagnostic test/factor not relevant to review protocol
Mori, K., Abe, T., Matsumoto, J. et al. (2021) Indications for Computed Tomography in Older Adult Patients With Minor Head Injury in the Emergency Department. Academic Emergency Medicine 28(4): 435-443	- Diagnostic test/factor not relevant to review protocol
Mortimer, D., Bosch, M., McKenzie, J. E. et al. (2018) Economic evaluation of the NET intervention versus guideline dissemination for management of mild head injury in hospital emergency departments. Implementation Science 13(1): 147	- Study design not relevant to this review protocol
Mozafari, J., Fahimi, M. A., Mohammadi, K. et al. (2019) The diagnostic accuracy of serum and urinary S100B protein in children and adolescents with mild traumatic brain injury. New Zealand Journal of Medical Laboratory Science 73(3): 88-91	- Diagnostic test/factor not relevant to review protocol
Muther, M., Sporns, P. B., Hanning, U. et al. (2020) Diagnostic accuracy of different clinical screening criteria for blunt cerebrovascular injuries compared with liberal state of the art computed tomography angiography in major trauma. The Journal of Trauma and Acute Care Surgery 88(6): 789-795	- Reference standard not relevant to review protocol
Nayak, R., Jagdhane, N., Attry, S. et al. (2020) Serum Albumin Levels in Severe Traumatic	- Diagnostic test/factor not relevant to review protocol

Study	Code [Reason]
Brain Injury: Role as a Predictor of Outcome. Indian Journal of Neurotrauma 17(1): 24-27	
Niele, N., van Houten, M., Tromp, E. et al. (2020) Application of PECARN rules would significantly decrease CT rates in a Dutch cohort of children with minor traumatic head injuries. European Journal of Pediatrics 179(10): 1597-1602	- No outcomes relevant to protocol reported
Nishijima, D. K., Yang, Z., Urbich, M. et al. (2015) Cost-effectiveness of the PECARN rules in children with minor head trauma. Annals of Emergency Medicine 65(1): 72-80.e6	- No useable diagnostic data
Okonkwo, D. O., Puffer, R. C., Puccio, A. M. et al. (2020) Point-of-Care Platform Blood Biomarker Testing of Glial Fibrillary Acidic Protein versus S100 Calcium-Binding Protein B for Prediction of Traumatic Brain Injuries: A Transforming Research and Clinical Knowledge in Traumatic Brain Injury Study. Journal of Neurotrauma 37(23): 2460-2467	- Diagnostic test/factor not relevant to review protocol
Posti, J. P., Takala, R. S. K., Lagerstedt, L. et al. (2019) Correlation of Blood Biomarkers and Biomarker Panels with Traumatic Findings on Computed Tomography after Traumatic Brain Injury. Journal of Neurotrauma 36(14): 2178-2189	- Diagnostic test/factor not relevant to review protocol
Puffenbarger, M. S., Ahmad, F. A., Argent, M. et al. (2019) Reduction of Computed Tomography Use for Pediatric Closed Head Injury Evaluation at a Nonpediatric Community Emergency Department. Academic Emergency Medicine 26(7): 784-795	- Study design not relevant to this review protocol
Ravindra, V. M., Bollo, R. J., Sivakumar, W. et al. (2017) Predicting Blunt Cerebrovascular Injury in Pediatric Trauma: Validation of the "Utah Score". Journal of Neurotrauma 34(2): 391-399	- Reference standard not relevant to review protocol
Ravindra, V. M., Riva-Cambrin, J., Sivakumar, W. et al. (2015) Risk factors for traumatic blunt cerebrovascular injury diagnosed by computed tomography angiography in the pediatric population: a retrospective cohort study. Journal of Neurosurgery. Pediatrics. 15(6): 599-606	- Diagnostic test/factor not relevant to review protocol

Study	Code [Reason]
Runde, D. (2017) Calculated decisions: Canadian CT Head Injury/Trauma Rule. Emergency Medicine Practice: 1-2	- Full text paper not available
Runde, D. (2020) Calculated decisions: Canadian CT head injury/trauma rule. Emergency Medicine Practice 22(suppl8): CD5-CD6	- Study design not relevant to this review protocol
Runde, D. and Beiner, J. (2017) Calculated decisions: PECARN pediatric head injury/trauma algorithm. Emergency Medicine Practice: 9-11	- Full text paper not available
Runde, D. and Beiner, J. (2018) Calculated Decisions: PECARN Pediatric Head Injury/Trauma Algorithm. Pediatric Emergency Medicine Practice 15(suppl6): CD3-CD4	- Study design not relevant to this review protocol
Sawaya, R. D., Wakil, C., Wazir, A. et al. (2020) Does implementation of the PECARN rules for minor head trauma improve patient-centered outcomes in a lower resource emergency department: a retrospective cohort study. BMC Pediatrics 20(1): 439	- Study design not relevant to this review protocol
Schonfeld, D., Bressan, S., Da Dalt, L. et al. (2015) Pediatric Emergency Care Applied Research Network head injury clinical prediction rules are reliable in practice. Postgraduate Medical Journal 91(1081): 634-8	- Secondary publication of an included study that does not provide any additional relevant information
Sharp, A. L., Huang, B. Z., Tang, T. et al. (2018) Implementation of the Canadian CT Head Rule and Its Association With Use of Computed Tomography Among Patients With Head Injury. Annals of Emergency Medicine 71(1): 54-63.e2	- No outcomes relevant to protocol reported
Thelin, E. P., Zibung, E., Riddez, L. et al. (2016) Assessing bicycle-related trauma using the biomarker S100B reveals a correlation with total injury severity. European Journal of Trauma & Emergency Surgery 42(5): 617-625	- Diagnostic test/factor not relevant to review protocol
Tran, J., Jeanmonod, D., Agresti, D. et al. (2016) Prospective Validation of Modified NEXUS Cervical Spine Injury Criteria in Low-risk Elderly Fall Patients. The Western Journal of Emergency Medicine 17(3): 252-7	- Population not relevant to this review protocol

Study	Code [Reason]
Tunthanathip, T. and Oearsakul, T. (2021) Application of machine learning to predict the outcome of pediatric traumatic brain injury. Chinese Journal of Traumatology 24(6): 350-355	- Study does not contain an diagnostic test/factor relevant to this review protocol
Turcato, G., Zaboli, A., Pfeifer, N. et al. (2021) Decision tree analysis to predict the risk of intracranial haemorrhage after mild traumatic brain injury in patients taking DOACs. American Journal of Emergency Medicine 50: 388-393	- Study design not relevant to this review protocol
Unden, L., Calcagnile, O., Unden, J. et al. (2015) Validation of the Scandinavian guidelines for initial management of minimal, mild and moderate traumatic brain injury in adults. BMC Medicine 13: 292	- Diagnostic test/factor not relevant to review protocol
Utsumi, S., Ohnishi, S., Amagasa, S. et al. (2022) Role of Routine Repeat Head CT for Pediatric Patients under 2 Years Old with Mild-to-moderate Traumatic Brain Injury. Neurologia Medico-Chirurgica 62(3): 133-139	- Study does not contain an diagnostic test/factor relevant to this review protocol - Study design not relevant to this review protocol
Valle Alonso, J., Fonseca Del Pozo, F. J., Vaquero Alvarez, M. et al. (2016) Comparison of the Canadian CT head rule and the New Orleans criteria in patients with minor head injury in a Spanish hospital. Medicina Clinica 147(12): 523-530	- Study not reported in English
Valiuddin, H., Calice, M., Alam, A. et al. (2021) Incidence of Traumatic Delayed Intracranial Hemorrhage Among Patients Using Direct Oral Anticoagulants. Journal of Emergency Medicine 61(5): 489-498	- Study does not contain an intervention relevant to this review protocol - Study design not relevant to this review protocol
Wolf, H., Machold, W., Frantal, S. et al. (2014) Risk factors indicating the need for cranial CT scans in elderly patients with head trauma: an Austrian trial and comparison with the Canadian CT Head Rule. Journal of Neurosurgery 120(2): 447-52	- Diagnostic test/factor not relevant to review protocol
Yang, K., Zhao, M., Sun, J. et al. (2021) Accuracy of PECARN decision rule in minor blunt head trauma in pediatric emergency	- Meta-analysis of PECARN but not enough details on quality of study

Study	Code [Reason]
department: A meta-analysis. International Journal of Clinical Practice 75(11): e14586	
Yue, J. K., Upadhyayula, P. S., Avalos, L. N. et al. (2020) The Role of Blood Biomarkers for Magnetic Resonance Imaging Diagnosis of Traumatic Brain Injury. Medicina 56(2): 22	- Diagnostic test/factor not relevant to review protocol
Zyluk, A. (2015) Indications for CT scanning in minor head injuries: a review. Neurologia i Neurochirurgia Polska 49(1): 52-7	- Systematic review used as source of primary studies

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.

Table 60: Studies excluded from the health economic review

Reference	Reason for exclusion
Studies identified in the 2014 update and excluded in the 2014 and current updates.	
Norlund 2006[65]	Cost analysis of immediate computed tomography during triage for admission versus observation in hospital. Study set in Sweden. Excluded due to the availability of directly applicable economic evidence based on a cost-utility analysis.
Smits 2010[85]	CUA set in the Netherland. Societal perspective adopted. The study was excluded due to its partial applicability and to its very serious limitations, as the findings of the probabilistic sensitivity analysis contradicted those of the deterministic analysis (the CCHR was found cost-effective in the former case, and the CHIP rule in the latter).
Studies included in 2007 Head injury update, but selectively excluded in the 2014 and current updates.	
Hassan 2005[37]	A UK costing of the implementation of the 2003 guideline that compared the X-ray and admission based practice with the Canadian CT head rule and directly applicable to the UK. This study was selectively excluded in the 2014 update due to the availability methodologically sounder cost-utility evidence comparing a wider range of clinical decision rules (Pandor et al, 2011).

Reference	Reason for exclusion
Shravat 2006[82]	A UK cohort study with costing examining the implementation of the 2003 guideline costs were found to increase by £77 per patient with the Canadian CT head rule. This study was selectively excluded in the 2014 update due to the availability of methodologically sounder cost-utility evidence comparing a wider range of clinical decision rules (Pandor et al, 2011).
Stein 2006[86]	A decision analysis that compared the Canadian CT head rule with several strategies including 'CT all', 'admit all', 'discharge all' and 'X-ray all' in a US context. Quality-adjusted life-years (QALYs) and costs were estimated for both prompt and delayed surgery by comparing the mortality and recovery rates in different case series. This study was selectively excluded in the 2014 update due to the availability of directly applicable and methodologically sounder cost-utility evidence comparing a wider range of clinical decision rules (Pandor et al, 2011).

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