TITLE: Accuracy of PECARN, CATCH and CHALICE head injury decision rules in children. A prospective cohort study.

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ABSTRACT

Background:

Clinical decision rules (CDRs) can assist in determining the need for computed tomography (CT) in children with head injuries (HIs). Three high quality CDRs (PECARN, CATCH and CHALICE) have not been externally validated and compared in a large sample.

Methods:

Prospective observational study of children <18 years with HIs of any severity at 10 Australian/New Zealand centres. We assessed the diagnostic accuracy of the CDRs a) strictly as derived (validation cohort), and b) in a comparison cohort of mild HIs (GCS 13-15) which used CDR-specific predictor variables and the standardised outcome of clinically important traumatic brain injury (ciTBI).

Findings:

We analysed 20,137 children, of whom 5,374 (26·7%) were <2 years and 217 (1.1%) had GCS <13. CTs were obtained in 2,106 (10·5%) and 83 (0·4%) underwent neurosurgery. PECARN <2 years, PECARN ≥2 years, CATCH and CHALICE were applicable in 4,011 (74·6%), 11,152 (75·7%), 4,957 (24·6%) and 20,029 (99·5%) patients respectively.

Validation sensitivities (95% CI) were ranked as follows: PECARN <2 years 38/38 (100·0%; 90·7% to 100·0%), PECARN ≥2 years 97/98 (99·0%; 94·4% to 100·0%), CATCH (high risk) 20/21 (95·2%; 76·2% to 99·9%) and CHALICE 370/401 (92·3%; 89·2% to 94·7%). Comparison cohort (n=18,913) sensitivities for ciTBI were PECARN <2 years 42/42 (100·0%, 91·6% to 100·0%), PECARN ≥2 years 117/118 (99·2%; 95·4% to 100·0%), CATCH (high/medium risk) 147/160 (91·9%; 86·5% to 95·6%) and CHALICE 148/160 (92·5%; 87·3% to 96·1%). Negative predictive values for all rules were 99% to 100%.

Interpretation:

The sensitivities of the PECARN, CATCH and CHALICE CDRs were high when used as designed. PECARN appeared to miss the fewest patients when the CDRs were used in a cohort of children with mild HIs.

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INTRODUCTION

Children with head injuries (HIs) frequently present to acute care settings. The major management uncertainty is which children should undergo cranial computed tomography (CT). Most HIs are mild and do not require neurosurgical management. However, a small portion may present as mild but have clinically significant intracranial injuries. While CT provides definitive and rapid diagnosis to confirm or exclude intracranial injuries there is concern about radiation induced cancer, particularly in younger patients.[1-3] Furthermore, CT scanners are resource intense and sedation may be required to facilitate a CT scan.[4,5] Reports of large increases in CT rates and wide variability in its use for paediatric HI are also of concern.[6-9]

Clinical decision rules (CDRs) have been developed to identify children at higher risk of intracranial injuries, assisting clinicians to minimise CT scans while still identifying all relevant injuries.[10,11] Three CDRs derived in large multicentre studies with high methodological quality are (i) the prediction rule for the identification of children at very low risk of clinically important traumatic brain injury (ciTBI) developed by the Pediatric Emergency Care Applied Research Network (PECARN, USA)[9], (ii) the Canadian Assessment of Tomography for Childhood Head Injury (CATCH) rule[8] and (iii) the Children's Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE, UK).[12] Unfortunately, a direct comparison of the three rules is not possible as they addressed different questions (who to CT vs. who not to CT), targeted different age groups and injury severities, and used different outcomes (**Table 1**).[10] Despite having undergone only limited external validation,[13-16] these rules are widely used or recommended: the American Academy of Pediatrics suggests that PECARN criteria should be used to determine whether imaging is indicated[17], elements of CATCH are in the Canadian Pediatric Society position statement[18] and CHALICE has been incorporated into UK guidance.[19] In some countries, such as in Australia and New Zealand, none predominate.[20]

For clinicians, hospitals or national bodies contemplating implementation of one of these rules it is essential to confirm and compare the accuracy of the rules in an appropriately powered external validation. Two single centre comparative validation studies have been performed, though their results are difficult to translate to practice; one had very wide confidence intervals affecting the interpretation of CDR sensitivities,[14] while the other had a very low underlying CT rate.[16]

We therefore set out to conduct a sufficiently powered multicentre external validation study of these three CDRs for childhood HI (PECARN, CATCH, CHALICE) to: 1. determine their diagnostic

accuracy outside their derivation setting and 2. investigate the CDR performance in a clinically homogenous cohort of children with mild HI, the population which creates the greatest dilemma for clinicians. Given the potentially catastrophic consequences of missing an intracranial lesion requiring neurosurgery clinicians and the public are likely to desire near perfect sensitivity, which is also the focus of our study.[8,9,12]

METHODS

Study design, setting and patients

We performed a prospective multi-centre observational study which enrolled children presenting with HI of any severity to 10 paediatric emergency departments (EDs) in Australia and New Zealand between April 2011 and November 2014. All emergency departments (EDs) are members of the Paediatric Research in Emergency Departments International Collaborative (PREDICT) research network.[21]

We collected all rule-specific predictor and outcome variables for PECARN, CATCH and CHALICE CDRs for all head injured children aged <18 years. The following patients were excluded: trivial facial injury only,[22] patient/ family refusal to participate, referral from ED triage to an external provider (i.e. not seen in the ED), did not wait to be seen, or neuroimaging done prior to the transfer to a study site.

The study was approved by the institutional ethics committees at each participating site. We obtained informed verbal consent from parents/ guardians apart from instances of significant life-threatening or fatal injuries where participating ethics committees granted a waiver of consent.

The trial protocol (described in detail elsewhere[22]) was developed by the study investigators. The study was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12614000463673 and followed the STandards for Reporting Diagnostic accuracy studies (STARD) guidelines.[23]

Study procedures

Patients were enrolled by the treating ED clinician who collected predictive clinical data prior to any neuroimaging. The research assistant (RA) recorded ED and hospital management data after the visit and conducted a telephone follow-up for patients who had not undergone neuroimaging. Up to 6 follow up call attempts were made up to 90 days after injury. In addition, data of any patients who

had representations to the study hospitals leading to a CT scan within the follow up period prior to the phone call were used to assess outcomes. Any patients who had a representations to other hospitals based on the telephone follow up had neuroimaging and neurosurgery reports requested for review.

The RAs were not blinded to the purpose of the study. Data were collected on the inclusion and exclusion criteria of the three CDRs, their predictor variables and outcome measures (**Table 1**) as well as demographic and epidemiological information.[8-10,12] Site investigators, RAs and participating ED clinicians received formal training prior to and during the study.

Primary outcome was the diagnostic accuracy (sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV)) of each CDR using their own variables and outcomes (**Table 1**).

To overcome difficulties in comparing CDRs due to differences in inclusion and exclusion criteria, particularly age and Glasgow Coma Score (GCS) parameters, and differences in rule-specific outcomes, a homogenous comparison cohort was created. This included all mildly head injured children <18 years of age who presented within 24 hours of injury with GCS 13-15. The PECARN-specific outcome of ciTBI was selected as the clinically meaningful outcome measure in this cohort (**Table 1**).[9]

We used the GCS as assigned by the ED clinician in the analysis, or if not available, GCS at triage. We used senior radiologist reports to determine the results of CT scans and operative reports for patients who underwent neurosurgery. RAs and site investigators abstracted the information from CT and operative reports in terms of outcome measures and locally consulted with site radiologists in terms of the interpretation of individual scans. Copies of CT reports were provided to the central site. If there was a question as to the classification of the CT or operative reports a central site investigator would review the reports and if needed use a third site investigator to resolve disagreements.

Statistical analysis

Data were entered into Epidata (The Epidata Association, Odense, Denmark), and later REDCap,[24] and analysed using Stata 13 (Statacorp, College Station, Texas, USA). Descriptive statistics were calculated for key variables with 95% confidence intervals (CI) where relevant.

We calculated the primary diagnostic accuracy of the rules using rule-specific predictor variables and outcome measures, applied within cohorts that satisfied rule-specific inclusion and exclusion criteria (**Table 1**). We used percentages with 95% CIs to describe measures of diagnostic accuracy. The CATCH rule presented four high risk and three medium risk predictors (**Table 1**, high risk marked with*) which identify children who need neurological intervention and who have brain injury on CT scan respectively. For CATCH we calculated the validation accuracy based on the presence of the four high risk predictors as well as the presence of any high or medium risk predictors indicating the need for a CT of the head.

In the secondary analysis using the comparison cohort we calculated the diagnostic accuracy of each CDR based on the presence of any rule-specific predictor variables and the presence of the same outcome variable, ciTBI. In addition, we undertook this analysis for the secondary outcomes of presence of traumatic brain injury on CT, neurosurgery and skull fractures. For CATCH we calculated the comparison cohort accuracy based on the presence of any high or medium risk predictor variables.

Missing predictor variables were treated as missing presumed negative. A sensitivity analysis was carried out as well, comparing negatively imputed results to those where missing data was excluded (with the exception of any predictor positive variables).

We had calculated the sample size based on the assumed smallest subgroup, the PECARN rule for children <2 years. In order to achieve a point sensitivity of 94% and above we conducted a precision based calculation which required the enrolment of 50 patients with ciTBI in those <2 years. If the rule predicted 50 out of 50 head injured patients with PECARN specific outcome, the rule would be 100% sensitive with a 95% CI of 93% to 100%, if 47 of 50 were predicted the rule would be 94% sensitive with a 95% CI of 83% to 99%.[22] This precision was comparable to the original report for the PECARN rule for children <2 years, sensitivity 100% (95% CI 86·3% to 100%).REF

Based on a ciTBI rate of those with GCS 14 or 15 of approximately 1%[9] and equal distribution of children <2 years and ≥2 years of age in our setting[25] we initially estimated a total sample of 10,000 would be required. Analysis of the first 1,000 enrolled patients[26], however, demonstrated that children <2 years comprised only 25% of head injury presentations, thus requiring an increase in sample size to 20,000 to achieve the desired precision.

Role of the funding source

The funders had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication. FEB, CM, KJ, and SDo had access to the raw data. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

RESULTS

During the study 29,433 patients attended study EDs with HIs. Of these 5,203 were missed and 1,706 were excluded (**Figure 1**). Of 22,524 eligible patients, 2,240 (9·9%) were lost to follow up and for 147 records were not evaluable (22 had a missing GCS, 125 represented for the same HI), thus leaving 20,137 patients evaluable for analysis. Missed patients were similar in terms of CT rate (550, 10·6%) and neurosurgery rate (30, 0·6%). Of the evaluable patients, 5,374 (26·7%) were <2 years old; 7,309 (36·3%) were female; 990 (6·5%) presented >24 hours after the HI; 2,106 (10·5%) underwent CT scans; 4,544 (22·6%) were admitted; 83 (0·4%) underwent neurosurgery; and 15 (0·1%) died (**Table 2**). Most patients had a GCS 15 (19,207, 95·4%) or 14 (578, 2·9%). Falls were the main mechanism of injury affecting 14,119 (70·1%). Most frequent CT findings were intracranial haemorrhage or contusions in 321 (1·6%) and depressed skull fractures in 100 (0·5%) (**Table S1** available online). The most frequent neurosurgical procedures were intracranial pressure monitoring in 51 (0·3%) patients and craniotomy in 48 (0·2%) (**Table S1**).

Given most patients had GCS 14 or 15, our study sample was broadly similar to the original derivation cohorts of PECARN, CATCH and CHALICE despite the differences in eligibility criteria (**Table 2**). The distribution of rule-specific predictor variables are shown in **Table 3**.

Using the primary rule-specific outcomes across all evaluable patients, 280 (1·4%) had ciTBI (PECARN), 185 (0·9%) had a need for neurological intervention as defined by CATCH, and 403 (2·0%) had clinically significant intracranial injury as defined by CHALICE (**Table 1, Table 2**). When applying rule-specific inclusion and exclusion criteria, PECARN <2 years, PECARN $\geq$2 years, CATCH and CHALICE were applicable in 4,011 (74·6% of those <2 years), 11,152 (75·7% of those $\geq$2 years), 4,957 (24·6%) and 20,029 (99·5%) patients respectively (**Figure 1, Table 3**). Reasons for non–applicability are listed in **Table S2** (available online).

Validation analysis

Using rule-specific eligibility criteria, predictor variables and outcome measures, all CDRs had high sensitivity (**Table 4**). Sensitivities (95% CI) were as follows: PECARN <2 years 38/38 (100·0%; 90·7% to 100·0%), PECARN ≥2 years 97/98 (99·0%; 94·4% to 100·0%), CATCH (using high risk criteria) 20/21 (95·2%; 76·2% to 99·9%) and CHALICE 370/401 (92·3%; 89·2% to 94·7%). PECARN <2 years did not miss any patients, PECARN ≥2 years missed one patient who did not require neurosurgery. CATCH missed one patient with a bleeding disorder who required neurosurgery. CHALICE missed 31 patients, two of whom required neurosurgery (**Table S4,** available online). The specificity of the two PECARN rules was approximately 50% with CATCH and CHALICE having specificities at 84.2% and 78·1% respectively. All CDRs had high NPVs with the lower boundary of the 95% CI of all CDRs being ≥99·5%. The CATCH rule using both medium and high risk predictors to identify brain injury on CT had a lower point sensitivity and specificity than the CATCH rule using just high risk predictors to identify need for neurological intervention (**Table 4**).

A sensitivity analysis where missing data were excluded showed no change to sensitivity, PPV or NPV, and some reduction in specificity (**Table S3** available online).

Comparison cohort analysis

In the comparison cohort 18,913 patients, 93·8% of the evaluable cohort, had a GCS of 13-15 and presented within 24h of injury. Point sensitivity of identifying ciTBI was higher for PECARN than CHALICE and CATCH (using medium and high risk predictor variables) although the 95% CIs overlapped for all examined CDRs (**Table 5**). PECARN <2 years did not miss any ciTBI, PECARN ≥2 years missed one patient who did not require neurosurgery. This patient was positive for basal skull fracture criteria for CHALICE (defined to include serious facial injury) but not PECARN which includes signs of basilar skull fracture as a predictor variable but not signs of serious facial injury. The patient was not positive for any CATCH predictors. CATCH missed 13 ciTBI, including one who required neurosurgery. CHALICE missed 12 ciTBI, two of whom required neurosurgery (**Table S5**, available online). The specificity of CATCH and CHALICE was higher than the two PECARN CDRs. All rules had similar PPVs and NPVs. For the secondary outcomes of TBI on CT and need for neurosurgery, the sensitivity and specificity patterns were similar to that for ciTBI (**Table 5**).

DISCUSSION

In this large, appropriately powered multicentre validation study external to the original derivation settings, we have demonstrated that the PECARN, CATCH and CHALICE CDRs[8,9,12] have good performance accuracy in identifying children with significant HIs. HI decision rules need to have very

high sensitivities in identifying injuries, and very high negative predictive values indicating that patients designated as low risk do not include patients with significant intracranial injuries. In the validation analysis PECARN had high point sensitivities in both age cohorts (<2 years and ≥2 years) at 100% and 99% respectively, similar to the original derivation study. [9] In total the PECARN CDRs missed one ciTBI, and this patient did not require neurosurgery. CATCH sensitivity (95%) was similar to the derivation study[8] (100%), with wide confidence intervals (76% to 100%, 86% to 100% in derivation study[8]), at least in part because it could only be applied to a relatively small proportion of the total population (24·6%). CHALICE point sensitivity was lower than in the derivation study[12] (92% vs 99%), though with overlapping confidence intervals, and it missed 31 patients of whom two required neurosurgery. All CDRs had negative predictive values of 99% to 100%. Results were similar when patients with missing predictor variables were excluded from analysis.

Based on differing rule-specific composite outcome measures, and the different inclusion and exclusion criteria (**Table 1**),[10] the three rules are impossible to directly compare in terms of their diagnostic accuracy. Thus, in a secondary analysis we assessed all three CDRs without their rule-specific inclusion and exclusion criteria for a common outcome of ciTBI as defined by PECARN in a homogenous cohort of 93·9% of patients with mild HI (GCS 13 to 15) presenting within 24 hours of their injury. ciTBI was chosen as the outcome of interest by consensus in the research team as this was felt to most closely reflect the issues which would be of greatest importance to families, clinicians and the health care system. The CATCH primary outcome (death or neurosurgical intervention) was deemed too restrictive and at risk of missing possible considerable morbidity associated with HI. While also encompassing death and neurosurgery, CHALICE outcome includes CT abnormality alone which was deemed to lack a correlation between clinical impact and radiological findings. Although not using the rules as designed, this cohort reflects real world practice; clinicians may not recall the detailed inclusion and exclusion criteria for the individual CDRs; further, if clinicians utilise PECARN they may apply the PECARN CDRs to the 25% of head injured patients in which they do not strictly apply; similarly, if CATCH is used clinicians may apply CATCH to the 75% of head injured patients in which this CDR does not strictly apply.

While this study was not designed or powered to compare the rules statistically, we found that all three rules had high sensitivities (PECARN 100% and 99%; CHALICE 93%; CATCH 92%) and overlapping confidence intervals in detecting ciTBI in a homogenous cohort. Sensitivities in detecting traumatic brain injury on CT and identifying patients requiring neurosurgery were similar to the

detection of ciTBIs. Our results, indicating the fewest missed patients with PECARN are similar to the results of a single centre comparison of the rules by Easter et al using the same outcome measure.[14]

Compared with the other rules, CATCH missed patients mainly because they were vomiting or had a change in mental status, both of which are inclusion criteria of the CATCH rule. The features present in patients with missed injuries according to CHALICE were falls < 3 meters, fewer than three vomits, and change in mental status besides abnormal drowsiness.

When the CDRs were analysed as derived and published using our patient cohort (validation analysis) the specificities of the two PECARN CDRs ranged between 45% and 55%. In both validation and comparison cohorts, CATCH and CHALICE had higher specificities. While there is a balance to be struck, it is difficult to accept an increased specificity at the cost of reduced sensitivity in our healthcare setting given the mortality and morbidity associated with missing an intracranial lesion requiring neurosurgery. Both patients and clinicians therefore prioritise a very high sensitivity.[8,9,12]

These findings will provide a useful starting point for individual clinicians as well as hospitals or regional bodies contemplating the introduction or modification of one of the CDRs. However, it will be important to relate the findings to a number of other factors prior to implementation. These include the baseline CT rate in a particular setting, the impact of the rules on the projected CT rate, the baseline clinician diagnostic accuracy and experience, parental expectations, the medicolegal climate and economic considerations. Our CT rate across any severity HI was 10·5% overall. In the comparison cohort analysis it was 8·9% and 8·3% when the initial presentation only was considered. Applying CHALICE or CATCH to this latter cohort would increase the CT rates to 22·0% and 30·2%, respectively a 150% to 250% rise. The projected CT rate for PECARN is more difficult to determine and as patients who are not low risk (46·6%) may either undergo CT scanning or be observed.[9] Studies assessing the effect of implementing PECARN in clinical practice showed an effective reduction in CT rate in a setting with a high CT rate[27] and no increase in a setting with a low CT rate.[28]

This study has a number of limitations. CT scans were obtained on a minority of patients; it would have been unethical to obtain CT scans on patients the clinicians did not think required them. When we developed the data report forms we recreated the rule-specific information based on the derivation publications,[8,9,12] not the original data report forms used in the derivation studies. While this should more accurately reflect the real world use of the CDRs in an external validation, this may

have introduced an element of imprecision. Due to the pronounced heterogeneity of the eligibility criteria and outcome measures in the derivation studies, the only way to realistically compare performance accuracy between the CDRs was to create a homogenous cohort. Furthermore, we believe this pragmatic approach reflects how the CDRs are used by clinicians. We included GCS 13 to 15 in the comparison group similar to other studies.[8,14,29,30] Patients with GCS 13 may be regarded as routinely requiring CT and be excluded from an analysis of mild HIs·[9] In our sample none of the 135 patients with GCS 13 were missed by any of the rules. The use of ciTBI, the PECARN primary outcome variable, may have biased the results in favour of the PECARN CDRs. However, given that the secondary outcomes of neurosurgery and traumatic brain injury on CT also favoured PECARN, comparable to the primary outcomes of CATCH and CHALICE respectively, this effect is unlikely. We lost 9·9% of patients to telephone follow-up, who were excluded from analysis (if they did not have neuroimaging during the follow-up period) as we could not 100% determine the presence or absence of the outcome of interest in the various analyses undertaken. However it remains unlikely that these patients had subsequent abnormal neuroimaging; four sites are isolated regional paediatric neurosurgical centers, with a fifth site being a feeder hospital to one; four sites are the only regional paediatric neurosurgical centers within two cities; and one site was located in a city with another non-participating paediatric neurosurgical center, although both hospitals are part of the same network. While a survey preceding the study did not indicate preferential or widespread use of any of the studied CDRs at the study sites, we do not know if individual clinicians followed any of the published rules.[20] Finally, the patients reflect an Australian and New Zealand cohort with a bias towards tertiary children's hospitals and the neuroimaging rate in our setting is much lower than reported from the US and Canada who also mainly included tertiary children's hospitals.[8,9]

Summary

Our study provides a multicentre external validation of the PECARN, CATCH and CHALICE CDRs. We found that the sensitivities of all three rules studied were high when they were used as derived, as well as in a comparison cohort of children with mild HIs. PECARN appeared to miss the fewest patients when the CDRs were used in a homogenous cohort of children with mild HIs.

Research in Context

Evidence before this study

We searched Medline, Embase, and the Cochrane Library for reports published from 2006 (the publication year of the CHALICE rule) until 1 June 2016 with the following search terms (with acronyms, synonyms and closely related words): “craniocerebral trauma”, “tomograph, xray computed”, “decision support techniques”, “newborn, infant, child, adolescent, paediatric” , “Pediatric Emergency Care Applied Research Network, PECARN, clinically-important brain injury, Canadian Assessment of Tomography for Childhood Head Injury, CATCH, Children’s Head Injury Algorithm for the Prediction of Important Clinical Events, CHALICE”. We did not apply any study design or language restrictions. We identified further studies by examining the reference lists of all included articles and searching relevant websites. We reviewed titles or abstracts for relevance, and assessed original reports and reviews related to PECARN, CATCH and CHALICE head injury rules. We did not find any external validation studies (not including derivation sites or derivation authors) of the PECARN, CATCH and CHALICE rules or comparative analysis of the rules in large multicentre samples.

Added value of this study

To our knowledge, this study is the first large, appropriately powered multicentre study to externally validate the PECARN, CATCH and CHALICE clinical decision rules. While all rules had high performance accuracy, the PECARN rules did not miss a single patient requiring neurosurgery.

Implications of all the available evidence

The externally validated performance accuracies of the head injury rules in this study are an important starting point for clinicians considering the introduction of one of the rules. While a number of factors outside rule accuracy need to be considered as well, PECARN appears to miss the fewest patients.

Declaration of conflicts of interests

None of the authors have conflicts of interests.

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Author Contributions

Franz E Babl: Conceived the study, obtained grant funding, designed the study, provided overall supervision, interpreted the data, wrote the initial draft of the paper, gave final approval to be published, and agreed to be accountable for all aspects of the work.

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Stuart R Dalziel: Designed the study, obtained the data, provided supervision, interpreted the data, drafted or revised it critically, gave final approval to be published, and agreed to be accountable for all aspects of the work.

Susan Donath: Designed the study, supervised the analysis of the data, contributed to the interpretation of the data, revised the paper critically, gave final approval to be published, and agreed to be accountable for all aspects of the work.

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Table 1: Inclusion and exclusion criteria, predictor variables and outcome measures of PECARN, CATCH and CHALICE clinical decision rules[8,9,12]

	PECARN <2	PECARN ≥ 2	CATCH	CHALICE
Inclusion Criteria	Under 18y Present within 24h of HI		Under 17y All of the following: ▪ Blunt trauma to the head resulting in witnessed LOC, definite amnesia, witnessed disorientation, persistent vomiting (2 or more distinct episodes of vomiting 15 min apart), persistent irritability in the ED (in children <2y) ▪ Initial GCS in ED ≥13 as determined by treating physician ▪ Injury within the past 24h	Under 16y Any history or signs of injury to the head
Exclusion Criteria	Any of: ▪ Trivial mechanism defined by ground-level fall or walking or running into stationary objects and no signs or symptoms of head trauma other than scalp abrasions and lacerations· ▪ Penetrating trauma ▪ Known brain tumours ▪ Pre-existing neurological disorder complicating assessment ▪ Neuroimaging at an outside hospital before transfer ▪ Patient with ventricular shunt ▪ Patient with bleeding disorder ▪ GCS <14		Any of: ▪ Obvious penetrating skull injury ▪ Obviously depressed fracture ▪ Acute focal neurological deficit ▪ Chronic generalised developmental delay ▪ HI secondary to suspected child abuse ▪ Returning for reassessment of previously treated HI ▪ Patients who were pregnant	Refusal to consent
Predictor	**Mechanism of injury**			

Variables ≠	Severe mechanism of injury (MVC with patient ejection, death of another passenger, or rollover; pedestrian/bicyclist without helmet struck by motorised vehicle; falls>0·9 m; head struck by high impact object)	Severe mechanism of injury (MVC with patient ejection, death of another passenger, or rollover; pedestrian/bicyclist without helmet struck by motorised vehicle; falls >1·5 m; head struck by high impact object)	Dangerous mechanism of injury (e·g. MVC; fall from elevation ≥3 ft (≥ 91cm) or 5 stairs; fall from bicycle with no helmet)·	High speed RTA as pedestrian, cyclist, occupant (defined as accident with speed >40 miles/h or 64 km/h) Fall >3m in height High speed injury from projectile or object
	History			
	LOC ≥5 s	Any or suspected LOC		Witnessed LOC >5 min
		History of vomiting		≥3 vomits after head injury (discrete episodes)
	Not acting normally per parent			Amnesia (antegrade/retrograde >5 min) Suspicion of NAI (NAI defined as any suspicion of NAI by the examining doctor) Seizure in patient with no history of epilepsy
		Severe headache	History of worsening headache*	
	Examination			
	GCS <15	GCS <15	GCS <15 at 2h after injury*	GCS <14, or <15 if <1 y old
	Other signs of altered mental status (agitation, somnolence, repetitive questioning, slow response to verbal communication)	Other signs of altered mental status (agitation, somnolence, repetitive questioning, slow response to verbal communication)	Irritability on examination*	Abnormal drowsiness (in excess of that expected by examining doctor)
				Positive focal neurology
		Clinical signs of basilar skull fracture	Any sign of basal skull fracture (e·g. haemotympanum, “racoon” eyes, otorrhoea or rhinorrhoea of the cerebrospinal fluid, Battle’s sign)	Signs of basal skull fracture (haemotympanum, racoon eyes, otorhea or rhinorrhea of cerebrospinal fluid, Battle’s sign)
	Palpable or unclear skull fracture		Suspected open or depressed	Suspicion of penetrating or

	Occipital, parietal or temporal scalp haematoma		skull fracture* Large, boggy scalp haematoma	depressed skull injury, or tense fontanelle· Presence of bruise/swelling/laceration >5cm if <1 y old
Primary Outcome	Clinically-important traumatic brain injury (ciTBI); defined as death from TBI, neurosurgical intervention for traumatic brain injury (intracranial pressure monitoring, elevation of depressed skull fracture, ventriculostomy, haematoma evacuation, lobectomy, tissue debridement, dura repair, other), intubation of more than 24 h for traumatic brain injury or hospital admission of 2 nights or more for traumatic brain injury** in association with traumatic brain injury on CTţ		Need for neurological intervention; defined as either death within 7 days secondary to the head injury or need for any of the following procedures within 7 days: craniotomy, elevation of skull fracture, monitoring of intracranial pressure, insertion of endotracheal tube for the management of head injury	Clinically significant intracranial injury; defined as death as a result of head injury, requirement for neurosurgical intervention or marked abnormality on CT (defined as any new, acute, traumatic intracranial pathology as reported by consultant radiologist, including intracranial haematomas of any size, cerebral contusion, diffuse cerebral oedema and depressed skull fractures)
Secondary Outcome	None		Brain injury on CT; defined as any acute intracranial finding revealed on CT that was attributable to acute injury, including closed depressed skull fracture (i·e depressed past the inner table) and pneumocephalus but excluding non-depressed skull fractures and basilar skull fractures	Presence of skull fracture Admission to hospital

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;
CT=Computed tomography; ED=Emergency department; GCS=Glasgow coma score; HI=Head injury; LOC=loss of consciousness; MVC=motor vehicle crash; NAI=non-accidental injury; RTA=road traffic accident
h=hours; d=day; m=month; y=year; min=minute; m=metre; cm=centimetre; ft=feet.

* High risk predictors for CATCH (need for neurological intervention)

**Hospital admission for traumatic brain injury defined by admission for persistent neurological symptoms or signs such as persistent alteration in mental status, recurrent emesis due to head injury, persistent severe headache or ongoing seizure management.
ţ Traumatic brain injury on CT is defined by any of the following descriptions: 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 by at least the width of the table of the skull.
≠ In each of the three clinical decision rules, the absence of all of the above predictor variables indicates that cranial CT scan is unnecessary.
Note: while the predictor variables are reproduced verbatim, the order in which the variables from each clinical decision rule are presented has been altered to facilitate comparison.

Table 2. Patient characteristics in current study compared with PECARN, CATCH and CHALICE studies[8,9,12]

Criteria	Current study n=20,137		PECARN n=42,412	CATCH n=3,866	CHALICE n=22,772
	n	%	%	%	%
Demographics					
Mean age (years, (standard deviation))	5·7 (4·7)		7·1 (5·5)	9·2 (NR)	5·7 (NR)
Patients < 2 years	5,374	26·7	25	7·2	16·6
Patients ≥ 2 years	14,763	73·3	75	92·8	83·4
Female	7,309	36·3	NR	35	35
Clinician assigned GCS					
3-8	121	0·6	-	-	0·9 total, not
9-12	96	0·5	-	-	differentiated
13	135	0·7	-	2·5	0·3
14	578	2·9	3	7·3	1·0
15	19,207	95·4	97	90·2	96·6
Example symptoms and signs					
Known or suspected LOC	2,707	13·5	15	32·8 *	5·2 *
History of amnesia	1,688	8·4 ^	NR	58·5	3·2
History of vomiting	3,452	17·1	13	40·9 #	21
Headache	4,127	20·5 ^	30 ^	NR	21
Witnessed disorientation	2,943	14·6	NR	53·8	NR
Mechanism of Injury					
Fall related	14,119	70·1	44	44·9	NR
Motor vehicle incident	849	4·2	9	3·0	NR
Head hit by high impact object/projectile	1,320	6·6	NR	NR	2·0
Suspected NAI	112	0·6	7	2·6	0·3
Cranial CT performed	2,106	10·5	35·3	52·8	3·3
Neurosurgery performed	83	0·4	0·3	0·6	0·6
*Hospital admissions **	4,544	22·6	14·0	NR	NR
*Mortality****	15	0·1			
ciTBI (PECARN)	280	1·4	1·0	NR	NR
Need for neurological intervention (CATCH)	185	0·9	NR	0·6	NR
CSII (CHALICE)	403	2·0	NR	NR	1·2

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;
GCS=Glasgow Coma Scale; NR=Not reported; CT=computed tomography; NAI=non accidental injury; ciTBI=clinically important traumatic brain injury; CSII=clinically significant intracranial injury;
* known LOC only
^ does not include preverbal children
# ≥2 episodes
**Admission rates variably calculated. In this study defined it as admitted to inpatient ward, short stay ward or intensive care unit
***Mortality due to head injury alone (n=13), due to multitrauma with head injury (n=2)

Table 3: Presence of PECARN, CATCH and CHALICE[8,9,12] predictor variables in the validation and the comparison cohort analysis

	Validation cohort		Comparison cohort	
	N	**%**	**n**	**%**
PECARN	***n= 15,163***		***n= 18,913***	
PECARN Age < 2	*n= 4,011*		*n= 5,046*	
GCS < 15 [1]	94	2·3	134	2·7
Other signs of altered mental status [2]	267	6·7	318	6·3
Palpable skull fracture [3]	131	3·3	146	2·9
Skull haematoma [4]	552	13·8	622	12·3
History of LOC ≥ 5 seconds	144	3·6	153	3·0
Severe mechanism of injury [5]	991	24·7	1,034	20·5
Acting abnormally per parent	525	13·1	611	12·1
PECARN Age ≥ 2	*n= 11,152*		*n= 13,867*	
GCS < 15 [1]	413	3·7	554	4·0
Other signs of altered mental status [2]	921	8·3	1,080	7·8
Signs of basilar skull fracture [6]	64	0·6	71	0·5
History of LOC	1,665	14·9	1,783	12·9
History of vomiting	1,976	17·7	2,244	16·2
Severe mechanism of injury [5]	3,852	34·5	4,154	30·0
Severe headache	109	1·0	122	0·9
CATCH	***n= 4,957***		***n= 18,913***	
GCS < 15 at 2h after injury	316	6·4	477	2·5
Suspected skull fracture [7]	52	1·1	173	0·9
History of worsening headache	92	1·9	160	0·9
Irritability on examination	441	8·9	618	3·3
Any sign of basal skull fracture [6]	38	0·8	92	0·5
Large, boggy haematoma of the scalp	155	3·1	460	2·4
Dangerous mechanism of injury [8]	1,763	35·6	4,733	25·0
CHALICE	***n= 20,029***		***n= 18,913***	
Witnessed LOC > 5 minutes	98	0·5	64	0·3
History of amnesia > 5 minutes [9]	706	3·5	694	3·7
Abnormal drowsiness [10]	651	3·3	545	2·9
≥ 3 vomits after head injury [11]	1,252	6·3	1,106	5·9
Suspicion of non-accidental injury [12]	107	0·5	81	0·4
Seizure after head injury [13]	331	1·7	281	1·5
GCS < 14, or GCS < 15 if < 1 year old [14]	402	2·0	182	1·0
Suspicion of penetrating or depressed skull fracture or tense fontanelle [15]	261	1·3	177	0·9
Signs of basal skull fracture [16]	328	1·6	276	1·5
Positive focal neurology [17]	289	1·4	232	1·2
Bruise, swelling, or laceration > 5cm if < 1 year old	85	0·4	58	0·3
High-speed MVA as pedestrian, cyclist or	202	1·0	168	0·9

	Validation cohort		Comparison cohort	
	N	%	n	%
vehicle occupant [18]				
Fall > 3 m	156	0·8	138	0·7
High-speed injury from a projectile or an object	1,302	6·5	1,228	6·5

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;
CI = confidence interval; LOC = loss of consciousness; GCS= Glasgow Coma Scale; m= meters; cm = centimetres; MVA = motor vehicle accident
PECARN definitions as published: [1] GCS at clinician assessment; [2] other signs of altered mental status: agitation, drowsiness, repetitive questioning, slow response to verbal communication; [3] palpable skull fracture: on digital inspection or unclear on the basis swelling or distortion of the scalp; [4] scalp haematoma: occipital, parietal, or temporal; [5] severe mechanism of injury: motor vehicle accident with patient ejection or rollover, death of another passenger, pedestrian or cyclist without helmet struck by motor vehicle, falls of ≥1m (<2 y), fall ≥1.5m (≥2y), head struck by high impact object; [6] signs of basilar skull fracture: haemotympanum, 'raccoon' eyes, otorrhoea or rhinorrhoea of the cerebrospinal fluid, Battle's signs.

CATCH definitions as published: [6] any sign of basal skull fracture: haemotympanum, racoon eyes, otorhea or rhinorrhea of cerebrospinal fluid, Battle's sign; [7] suspected open or depressed skull fracture; [8] dangerous mechanism of injury: motor vehicle accident, fall from ≥1m or ≥5 stairs, fall from bicycle with no helmet

CHALICE definitions as published: [9] antegrade or retrograde amnesia; [10] abnormal drowsiness drowsiness in excess of that expected by examining clinician: [11] ≥3 discrete episodes of vomiting; [12] any suspicion of non-accidental injury by examining clinician; [13] seizure in patients with no history of epilepsy; [14] GCS at clinician assessment; [15] suspicion of penetrating or depressed skull injury or tense fontanelle; [16] signs of basal skull fracture: blood or CSF from ear or nose, 'panda' eyes, Battle's signs, haemotypmanum, facial crepitus or serious facial injury; [17] positive focal neurology: motor, sensory, coordination or reflex abnormality; [18] high speed MVA: >64kph or 40mph

Table 4: Diagnostic accuracy of the PECARN, CATCH and CHALICE[8,9,12] clinical decision rules when analysed using rule-specific inclusion criteria, exclusion criteria, predictor variables and outcome measures

PECARN

Clinically important traumatic brain injury §
all predictors

	< 2y n=4,011		≥2y n=11,152	
	Positive	Negative	Positive	Negative
Yes	38	0	97	1
No	1834	2139	5987	5067
Sens (95% CI)	38/38	100·0% (90·7–100·0)	97/98	99·0% (94·4– 100·0)
Spec (95% CI)	2139/3973	53·8% (52·3– 55·4)	5067/11054	45·8% (44·9 – 46·8)
PPV (95% CI)	38/1872	2·0% (1·4 – 2·8)	97/6084	1·6% (1·3 – 1·9)
NPV (95% CI)	2139/2139	100·0% (99·8 –100·0)	5067/5068	100·0% (99·9 – 100·0)

CATCH
n=4,957

Need for neurologic intervention*
4 high risk predictors only

	Positive	Negative
Yes	20	1
No	779	4157
Sens (95% CI)	20/21	95·2% (76·2 –99·9)
Spec (95% CI)	4157/4936	84·2% (83·2– 85·2)
PPV (95% CI)	20/799	2·5% (1·5 – 3·8)
NPV (95% CI)	4157/4158	100·0% (99·9–100·0)

Brain Injury on CT ¥
7 high/med risk predictors

	Positive	Negative
Yes	125	16
No	2100	2716
Sens (95% CI)	125/141	88·7% (82·2 –93·4)
Spec (95% CI)	2716/4816	56·4% (55·0– 57·8)
PPV (95% CI)	125/2225	5·6% (4·7 – 6·7)
NPV (95% CI)	2716/2732	99·4% (99·1–99·7)

CHALICE
n=20,029

Clinically significant intracranial injury #
all predictors

	Positive	Negative
Yes	370	31
No	4303	15325
Sens (95% CI)	370/401	92·3% (89·2 – 94·7)
Spec (95% CI)	15325/19628	78·1% (77·5 – 78·7)
PPV (95% CI)	370/4673	7·9% (7·2 – 8·7)
NPV (95% CI)	15325/15356	99·8% (99·7 – 99·9)

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;
Sens=sensitivity; Spec=specificity; PPV=positive predictive value; NPV=negative predictive value; CI=confidence interval
Shaded cells represent diagnostic accuracy results for the original outcome used by each rule
§ clinically important traumatic brain injury (ciTBI) defined as per PECARN CDR as death from traumatic brain injury, need for neurosurgery, intubation >24 hours for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT
* need for neurologic intervention defined as per CATCH clinical decision rule (CDR) as death within 7 days due to the head injury or need for the following within 7 days: craniotomy, elevation of skull fracture, monitoring of intracranial pressure, insertion of endotracheal tube for treatment of head injury
¥ brain injury on CT defined as per CATCH CDR as any acute intracranial findings, including closed depressed skull fracture and pneumocephalus, excluding non-depressed or basilar skull fractures
clinically significant intracranial injury defined as per CHALICE CDR as death as a results of head injury, need for neurosurgical intervention, marked abnormality on CT scan

Table 5: Diagnostic accuracy of the PECARN, CATCH and CHALICE clinical decision rules[8,9,12] in the comparative analysis of all patients with GCS 13-15 presenting within 24 hours of injury when analysed using rule-specific predictor variables and clinically important traumatic brain injuries as outcome measure (see methods section) (n=18,913)

	PECARN		CATCH	CHALICE
	< 2y n=5,046	≥2y n=13,867		
Primary outcome				
	Positive Negative	Positive Negative	Positive Negative	Positive Negative
Clinically important traumatic brain injury *	Yes 42 0 No 2047 2957	Yes 117 1 No 6606 7143	Yes 147 13 No 5560 13193	Yes 148 12 No 4018 14735
Sens (95% CI)	42/42 100·0% (91·6 –100·0)	117/118 99·2% (95·4 – 100·0)	147/160 91·9% (86·5– 95·6)	148/160 92·5% (87·3– 96·1)
Spec (95% CI)	2957/5004 59·1% (57·7 – 60·5)	7143/13749 52·0% (51·1 – 52·8)	13193/18753 70·4% (69·7 – 71·0)	14735/18753 78·6% (78·0– 79·2)
PPV (95% CI)	42/2089 2·0% (1·5 -2·7)	117/6723 1·7% (1·4 – 2·1)	147/5707 2·6% (2·2 – 3·0)	148/4166 3·6% (3·0 – 4·2)
NPV (95% CI)	2957/2957 100·0% (99·9 –100·0)	7143/7144 100·0% (99·9 – 100·0)	13193/13206 99·9% (99·8 – 99·9)	14735/14747 99·9% (99·9 – 100·0)
Secondary outcomes				
	Positive Negative	Positive Negative	Positive Negative	Positive Negative
Traumatic brain injury on CT**	Yes 70 0 No 2019 2957	Yes 180 1 No 6543 7143	Yes 220 31 No 5487 13175	Yes 227 24 No 3939 14723
Sens (95% CI)	70/70 100·0% (94·9 – 100·0)	180/181 99·4% (97·0 – 100·0)	220/251 87·6% (82·9 – 91·5)	227/251 90·4% (86·1 – 93·8)
Spec (95% CI)	2957/4976 59·4% (58·0 – 60·8)	7143/13686 52·2% (51·4 – 53·0)	13175/18662 70·6% (69·9 – 71·3)	14723/18662 78·9% (78·3 – 79·5)
PPV (95% CI)	70/2089 3·4% (2·6 – 4·2)	180/6723 2·7% (2·3 – 3·1)	220/5707 3·9% (3·4 – 4·4)	227/4166 5·4% (4·8 – 6·2)
NPV (95% CI)	2957/2957 100·0% (99·9 – 100·0)	7143/7144 100·0% (99·9 – 100·0)	13175/13206 99·8% (99·7 –99·8)	14723/14747 99·8% (99·8– 99·9)
	Positive Negative	Positive Negative	Positive Negative	Positive Negative
Neurosurgery***	Yes 6 0 No 2083 2957	Yes 18 0 No 6705 7144	Yes 23 1 No 5684 13205	Yes 22 2 No 4144 14745
Sens (95% CI)	6/6 100·0% (54·1 – 100·0)	18/18 100·0% (81·5 – 100·0)	23/24 95·8% (78·9 – 99·9)	22/24 91·7% (73·0 – 99·0)
Spec (95% CI)	2957/5040 58·7% (57·3 – 60·0)	7144/13849 51·6% (50·7 – 52·4)	13205/18889 69·9% (69·2 – 70·6)	14745/18889 78·1% (77·5 – 78·6)
PPV (95% CI)	6/2089 0·3% (0·1 – 0·6)	18/6723 0·3% (0·2 – 0·4)	23/5707 0·4% (0·3 – 0·6)	22/4166 0·5% (0·3 – 0·8)
NPV (95% CI)	2957/2957 100·0 (99·9 – 100·0)	7144/7144 100·0% (99·9 – 100·0)	13205/13206 100·0% (100·0 – 100·0)	14745/14747 100·0% (100·0 – 100·0)

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CHALICE Children's Head Injury Algorithm for the Prediction of Important Clinical Events;
Sens=sensitivity; Spec=specificity; PPV=positive predictive value; NPV=negative predictive value; CI=confidence interval;
* clinically important traumatic brain injury (ciTBI) defined as per PECARN CDR as death from traumatic brain injury, need for neurosurgery, intubation >24 hours for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT
** traumatic brain injury defined as per PECARN CDR 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
*** neurosurgical intervention for traumatic brain injury defined as per PECARN CDR as intracranial pressure monitoring, elevation of depressed skull fracture, ventriculostomy, haematoma evacuation, lobectomy, tissue debridement, dura repair, other

Supplementary Table 1: Traumatic brain injuries seen on computed tomography and neurosurgical procedures performed (n=20,137)

Outcome	n	%^
CT finding (any traumatic brain injury n=402*)		
Intracranial haemorrhage or contusion	321	1·6
Depressed skull fracture	100	0·5
Cerebral oedema	76	0·4
Pneumocephalus	64	0·3
Midline shift of intracranial contents or signs of brain herniation	43	0·2
Diastasis of the skull	38	0·2
Diffuse axonal injury	26	0·1
Traumatic infarction	5	0·02
Sigmoid sinus thrombosis	5	0·02
Shearing injury	3	0·01
Neurosurgical procedure (any neurosurgical procedure n=83*)		
Intracranial pressure monitoring	51	0·3
Craniotomy	48	0·2
Haematoma evacuation	34	0·2
Elevation of depressed skull fracture	20	0·1
Dura repair	13	0·06
Tissue debridement	4	0·01
Lobectomy	2	0·01

CT computed tomography

* As defined by PECARN.[9] Patients may have more than one CT finding or neurosurgical procedure

^ Percentage of total patient cohort

Supplementary Table 2: Reasons for exclusion from primary analysis using rule-specific eligibility criteria

PECARN – criteria for non-applicability

Criterion	**<2 yrs old (*n=1,363)***		**≥2 yrs old (*n=3,611*)**	
	n	**%***	**n**	**%***
Trivial injury	1,005	73·7	2,381	65·9
Presented more than 24 hours post injury	280	20·5	710	19·7
GCS <14	70	5·1	282	7·8
Pre-existing neurological disorders	31	2·3	271	7·5
Bleeding disorder	25	1·8	89	2·5
Ventricular shunt	5	0·4	30	0·8
Known brain tumours	0	0	26	0·7
Penetrating trauma	5	0·4	23	0·6

CATCH –criteria for non-applicability (n=15,180)

Criterion	**n**	**%***
Inclusion criteria		
None of: witnessed LOC, definite amnesia, persistent vomiting, witnessed disorientation, or persistent irritability	14,370	94·7
Injury not within the last 24 hours	990	6·5
Initial GCS <13	217	1·4
Age outside range 0-16 years	108	0·7
Exclusion criteria		
Acute focal neurologic deficit	295	1·9
Chronic generalised developmental delay	273	1·8
Head injury secondary to suspected child abuse	112	0·7
Obvious depressed skull fracture	66	0·4
Returning for reassessment of previously treated head injury	63	0·4
Obvious penetrating skull injury	28	0·2
Pregnant	0	0·0

CHALICE –criteria for non-applicability (n=108)

Criterion	**n**	**%***
Age 16 years and older	108	100

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GCS=Glasgow coma score;
*Expressed as a percentage of all patients to whom the CDR was not applicable· Total greater than 100% as some patients fulfilled more than one criterion for non-applicability

Supplementary Table 3: Sensitivity analysis of validation cohort comparing missing negatively imputed vs missing excluded (if not positive)

	Missing Negatively Imputed		Missing Excluded	
PECARN <2 years §				
	Positive	Negative	Positive	Negative
Yes	38	0	38	0
No	1834	2139	1800	1897
Sens (95% CI)	38/38	100·0 (90·7-100·0)	38/38	100·0 (90·7-100·0)
Spec (95% CI)	2139/3973	53·8 (52·3-55·4)	1897/3697	51·3 (49·7-52·9)
PPV (95% CI)	38/1872	2·0 (1·4-2·8)	38/1838	2·1 (1·5-2·8)
NPV (95% CI)	2139/2139	100·0 (99·8-100·0)	1897/1897	100·0 (99·8-100·0)
PECARN 2-18 years §				
Yes	97	1	97	1
No	5987	5067	5904	3990
Sens (95% CI)	97/98	99·0 (94·4-100·0)	97/98	99·0 (94·4-100·0)
Spec (95% CI)	5067/11054	45·8 (44·9-46·8)	3990/9894	40·3 (39·4-41·3)
PPV (95% CI)	97/6084	1·6 (1·3-1·9)	97/6001	1·6 (1·3-2·0)
NPV (95% CI)	5067/5068	100·0 (99·9-100·0)	3990/3991	100·0 (99·9-100·0)
CATCH: High risk predictors *				
Yes	20	1	20	1
No	779	4157	778	3065
Sens (95% CI)	20/21	95·2 (76·2-99·9)	20/21	95·2 (76·2-99·9)
Spec (95% CI)	4157/4936	84·2 (83·2-85·2)	3065/3843	79·8 (78·4-81·0)
PPV (95% CI)	20/799	2·5 (1·5-3·8)	20/798	2·5 (1·5-3·8)
NPV (95% CI)	4157/4158	100·0 (99·9-100·0)	3065/3066	100·0 (99·8-100·0)
CHALICE #				
Yes	370	31	370	16
No	4303	15325	4292	9270
Sens (95% CI)	370/401	92·3 (89·2-94·7)	370/386	95·9 (93·4-97·6)
Spec (95% CI)	15325/19628	78·1 (77·5-78·7)	9270/13562	68·4 (67·6-69·1)
PPV (95% CI)	370/4673	7·9 (7·2-8·7)	370/4662	7·9 (7·2-8·7)
NPV (95% CI)	15325/15356	99·8 (99·7-99·9)	9270/9286	99·8 (99·7-99·9)

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Sens=sensitivity; Spec=specificity; PPV=positive predictive value; NPV=negative predictive value; CI=confidence interval
Shaded cells represent diagnostic accuracy results for the original outcome used by each rule
§ clinically important traumatic brain injury (ciTBI) defined as per PECARN CDR as death from traumatic brain injury, need for neurosurgery, intubation >24 hours for traumatic brain injury, hospital admission >2 nights for traumatic brain injury in association with traumatic brain injury on CT

* need for neurologic intervention defined as per CATCH clinical decision rule (CDR) as death within 7 days due to the head injury or need for the following within 7 days: craniotomy, elevation of skull fracture, monitoring of intracranial pressure, insertion of endotracheal tube for treatment of head injury
# clinically significant intracranial injury defined as per CHALICE CDR as death as a results of head injury, need for neurosurgical intervention, marked abnormality on CT scan

Supplementary Table 4: Characteristics of patients not identified by PECARN, CATCH and CHALICE clinical decision rules[8,9,12] when analysed using rule-specific eligibility criteria, predictor variables and outcome measures

Rule	Age	Gender	GCS	Mechanism of injury	Injury recorded	Treatment
<2 PECARN	No Missed					
>2 PECARN	15y*	M	15	Punched in head - assault	Intracranial haemorrhage/contusion-parenchyma	N.Surg: No; Admission >2d
CATCH	6y*	M	15	Hit by falling object; PMHx: Bleeding disorder	Intracranial haemorrhage/contusion-extra-axial; midline shift or brain herniation; skull fracture- non-depressed	N.Surg: Craniotomy and haematoma evacuation; Admission >2d
CHALICE	4m*	F	15	Fall >1m (unclear mechanism)	Intracranial haemorrhage/contusion-extra-axial; skull fracture-non-depressed	N.Surg: No; Admission >2d
	1y 3m	M	15	Fall 0·6m (unclear mechanism)	Intracranial haemorrhage/contusion-extra-axial (extradural); skull fracture- non-depressed	N.Surg: No; Admission <2d
	1y 3m*	M	15	Fall ≤1m from standing height	Intracranial haemorrhage/contusion-extra-axial & parenchyma; skull fracture- depressed	N.Surg: Elevation of depressed skull fracture, craniotomy and haematoma evacuation; Admission >2d
	1y 5m	F	15	Fall backwards from 2 steps, head strike on concrete	Intracranial haemorrhage/contusion-extra-axial; skull fracture-non-depressed	N.Surg: No; No admission
	1y 7m	M	15	Fall ≤1m (unclear mechanism)	Cerebral oedema; skull fracture- non-depressed	N.Surg: No; No admission
	1y 8 m	F	15	Fall >1m from car seat onto the ground	Skull fracture- depressed	N.Surg: No; Admission <2d
	1y 9m	M	15	Fall 1m, landing on wooden toy	Skull fracture- depressed	N.Surg: No; Admission <2d

	1y 11m	F	15	Fall >1·5m (unclear mechanism)	Intracranial haemorrhage/contusion - extra-axial & parenchyma. Skull fracture - non depressed.	N.Surg: No; Admission <2d
	2y	M	15	Fall 2m onto concrete	Intracranial haemorrhage/contusion- extra-axial; skull fracture- depressed	N.Surg: No; Admission <2d
	3y*	M	15	Fall 1·5m onto tiled surface	Cerebral oedema; diastasis of skull; skull fracture- non-depressed	N.Surg: No; Admission >2d
	3y	M	14	Fall > 1·5m from top bunk bed	Skull fracture- depressed	N.Surg: No; Admission <2d
	3y	F	15	Fall 1m from sofa	Intracranial haemorrhage/contusion- extra-axial; skull fracture- non-depressed	N.Surg: No; Admission >2d
	3y	M	15	Fall >1m from trampoline	Intracranial haemorrhage/contusion- extra-axial; skull fracture- non-depressed	N.Surg: No; No admission
	3y	F	15	Fall >1m from shopping trolley	Intracranial haemorrhage/contusion- extra-axial; midline shift or brain herniation; skull fracture- non-depressed	N. Surg: No; Admission <2d
	3y*	M	15	Pedestrian struck by cyclist <10km/hr	Intracranial haemorrhage/contusion- extra-axial; skull fracture- non-depressed, basal	N.Surg: No; Admission >2d
	4y	M	15	Fall from >1m (unclear mechanism)	Pneumocephalus, skull fracture - non-depressed	N.Surg: No; Admission <2d
	4y	F	15	Fall backwards 1m, head strike to tiles	Intracranial haemorrhage/contusion- extra-axial; skull fracture- non-depressed	N.Surg: No; Admission <2d
	4y*	F	15	Fall backwards from 1·5 m, head strike to tiles	Intracranial haemorrhage/contusion- extra-axial.; skull fracture- non-depressed	N.Surg: No; Admission >2d
	4y	M	15	Fall from push-scooter on to road	Pneumocephalus; basal skull fracture	N.Surg: No; Admission <2d

	6y*	F	15	Fall 1·8 m through railing	Intracranial haemorrhage/contusion-extra-axial; pneumocephalus; skull fracture- non-depressed	N.Surg: No; Admission >2d
	6y	F	15	Climbing on dressing table, table tipped mirror + table landed on child	Intracranial haemorrhage/contusion-extra-axial; skull fracture-non-depressed	N.Surg: No; Admission >2d
	6y*	F	15	Fall from slide 2m	Intracranial haemorrhage/contusion; pneumocephalus; skull fracture- non-depressed	N.Surg: No; Admission >2d
	7y	M	15	Fall from shopping trolley	Intracranial haemorrhage/contusion-extra-axial; diastasis of skull	N.Surg: No; Admission <2d
	7y*	F	15	Fall backwards >1·5m, head strike to concrete	Intracranial haemorrhage/contusion-extra-axial & subarachnoid; midline shift or brain herniation; skull fracture-non-depressed	N.Surg: No; Admission >2d
	7y*	M	14	Fall <1m from push-scooter when crashed into bike	Intracranial haemorrhage/contusion-extra-axial; pneumocephalus; skull fracture- non-depressed, basal	N.Surg: No; Admission >2d
	9y*	M	14	Fall >1·5m from tree	Intracranial haemorrhage/contusion-extra-axial; skull fracture-non-depressed	N.Surg: Craniotomy & haematoma evacuation; Admission >2d
	10y	M	15	Sitting on fence: fall backwards from >1·5m, head strike to concrete	Intracranial haemorrhage/contusion-parenchyma	N.Surg: No; No admission
	12y*	M	14	Fall from push-scooter	Intracranial haemorrhage/contusion-extra-axial & parenchyma; midline shift or brain herniation; skull fracture-non-depressed	N.Surg: No; Admission >2d
	12y*	M	15	Pedestrian struck by motorised vehicle	Cerebral oedema	N.Surg: No; Admission >2d

				<60km/hr		
	13y	M	15	Climbing fence; fall 2m from fence onto concrete	Pneumocephalus; skull fracture- non-depressed	N.Surg: No; Admission <2d
	14y	F	14	Fall backwards from standing ≤1m	Intracranial haemorrhage/contusion	N.Surg: No; Admission <2d

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PMHx=past medical history; GCS=Glasgow coma score; LOC=loss of consciousness; NAI=non-accidental injury;
N.Surg=Neurosurgical intervention; d=days, y=years, m=months

*These patients were also missed within the comparison cohort so are also presented in **Table 5**

Supplementary Table 5: Characteristics of patients with GCS 13-15 presenting within 24 h after injury in comparison cohort not identified by PECARN, CATCH and CHALICE clinical decision rules[8,9,12] when analysed using rule-specific predictor variables and clinically important traumatic brain injury as outcome measure (see methods section)

Rule	Age	Gender	GCS	Mechanism of injury	Injury recorded	Treatment	Presence of PECARN predictors	Presence of CATCH predictors	Presence of CHALICE predictors
<2 PECARN	No Missed								
>2 PECARN	15y*^	M	15	Punched in head - assault	Intracranial haemorrhage/contusion-parenchyma	N.Surg: No; Admission >2d	≥2yrs: None	None	Serious facial injury (='sign of basal skull fracture' in CHALICE only)
CATCH	2m	M	15	Fall <50cm from father's arms	Intracranial haemorrhage/contusion- extra-axial & parenchyma	N.Surg: No; Admission >2d	<2yrs: other signs of altered mental status (drowsy, difficult to wake); not acting normally per parent	None	Abnormal drowsiness (in excess of that expected by examining doctor)
	5m	M	15	Struck by fan on forehead	Intracranial haemorrhage/contusion- extra-axial & sub-arachnoid; pneumocephalus; skull fracture-depressed	N.Surg: No; Admission >2d	<2yrs: palpable or unclear skull fracture; not acting normally per parent	None	Presence of bruise/swelling/laceration > 5cm if < 1 year old (6cm temporal laceration)
	1y 6 m	F	15	Unknown mechanism, suspected NAI	Intracranial haemorrhage/contusion- extra-axial; midline shift or brain herniation	N.Surg: No; Admission >2d	<2yrs: temporal scalp haematoma	None	Suspicion of NAI
	3y	M	15	Kicked in head by horse	Intracranial haemorrhage/contusion-parenchyma; skull fracture-depressed	N.Surg: No; Admission >2d	≥2yrs: severe mechanism of injury (head struck by high impact object)	None	High speed injury from projectile or object

	4y	M	15	Fall ≤1m from bed, head strike on tiled floor	Intracranial haemorrhage/contusion- extra-axial	N.Surg: No; Admission >2d	≥2yrs: other signs of altered mental status (drowsy/difficult to wake, slow to response to verbal communication); history of vomiting	None	Suspicion of NAI; abnormal drowsiness (in excess of that expected by examining doctor)
	4y	F	15	Kicked to the head and shoulder by horse	Intracranial haemorrhage- parenchyma; pueumocephalus	N.Surg: No; Admission >2d	≥2yrs: any or suspected LOC	None	Amnesia (antegrade/retrograde > 5min); serious facial injury (sign of basal skull fracture in Chalice only)
	5y	F	15	Fall ≤1m (unclear mechanism)	Intracranial haemorrhage/contusion- extra-axial; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: history of vomiting	None	≥ 3 vomits after head injury
	6y*	M	15	Hit by falling object; PMHx: bleeding disorder	Intracranial haemorrhage/contusion- extra-axial; midline shift or brain herniation; skull fracture- non-depressed	N.Surg: Craniotomy and haematoma evacuation; Admission >2d	≥2yrs: other signs of altered mental status (drowsy/difficult to wake); history of vomiting	None	≥ 3 vomits after head injury; abnormal drowsiness (in excess of that expected by examining doctor)
	10y	M	15	Hit head on large metal door	Intracranial haemorrhage/contusion- extra-axial; pnuemocephalus; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: severe mechanism of injury (head struck by high impact object)	None	High speed injury from projectile or object
	12y^	M	14	Fall from push-scooter	Intracranial haemorrhage/contusion- extra-axial & parenchyma; midline shift or brain herniation; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: GCS 14; any or suspected LOC; history of vomiting	None	None

	13y	M	15	Struck by high impact object	Intracranial haemorrhage/contusion- extra axial; skull fracture- non-depressed	N.Surg: No; No admission	≥2yrs: history of vomiting; severe mechanism of injury (head struck by a high impact object)	None	≥ 3 vomits after head injury; high speed injury from projectile or object
	15y^	M	15	Punched in head - assault	Intracranial haemorrhage/contusion- parenchyma	N.Surg: No; Admission >2d	≥2yrs: None	None	Serious facial injury ('sign of basal skull fracture' in CHALICE only)
	16y	M	15	Impact injury from football	Intracranial Haemorrhage/contusion- extra axial; pnuemocephalus; skull fracture- non-depressed	N.Surg: No; No admission	≥2yrs: history of vomiting	None	≥ 3 vomits after head injury; amnesia (antegrade/retrograde> 5 mins)
CHALICE	4m*	F	15	Fall >1m (unclear mechanism)	Intracranial haemorrhage/contusion extra-axial. Skull fracture-non depressed.	N.Surg: No; Admission >2d	<2yrs: other signs of altered mental status (agitation/irritability) ; occipital & parietal scalp haematoma; fall >1m; palpable or unclear skull fracture	Irritability on examination	None
	1y 3m*	M	15	Fall ≤1m from standing height	Intracranial haemorrhage/contusion- extra-axial & parenchyma; skull fracture- depressed	N.Surg: Elevation of depressed skull fracture, craniotomy and haematoma evacuation; Admission >2d	<2yrs: palpable or unclear skull fracture; parietal scalp haematoma	Large boggy scalp haematoma	None
	3y*	M	15	Pedestrian struck by cyclist <10km/hr	Intracranial haemorrhage/contusion- extra-axial; skull fracture- non-depressed, basal	N.Surg: No; Admission >2d	≥2yrs: other signs of altered mental status (agitation/irritability) ; history of vomiting	Irritability on examination	None

	3y*	M	15	Fall 1·5m onto tiled surface	Cerebral oedema; diastasis of skull; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: any or suspected LOC; history of vomiting	Dangerous mechanism of injury (fall >1m); large boggy scalp haematoma	None
	4y*	F	15	Fall backwards from 1·5m, head strike to tiles	Intracranial haemorrhage/contusion- extra-axial·; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: severe mechanism of injury (fall > 1·5m); any or suspected LOC; history of vomiting	Dangerous mechanism of injury (fall > 1m)	None
	6y*	F	15	Fall 1·8m through railing	Intracranial haemorrhage/contusion- extra-axial; pnuemocephalus; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: severe mechanism of injury (fall >1·5m)	Dangerous mechanism of injury (fall > 1m)	None
	6y*	F	15	Fall from slide 2m	Intracranial haemorrhage/contusion; pneumocephalus; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: severe mechanism of injury (fall >1·5m); history of vomiting	Dangerous mechanism of injury (fall > 1m); large boggy scalp haematoma	None
	7y*	M	14	Fall <1m from push-scooter when crashed into bike	Intracranial haemorrhage/contusion- extra-axial; pneumocephalus; skull fracture- non-depressed, basal	N.Surg: No; Admission >2d	≥2yrs: GCS 14	GCS 14 2hrs after injury	None

	7y*	F	15	Fall backwards >1·5m, head strike to concrete	Intracranial haemorrhage/contusion- extra-axial & subarachnoid; midline shift or brain herniation; skull fracture- non-depressed	N.Surg: No; Admission >2d	≥2yrs: severe mechanism of injury (fall >1·5m); any or suspected LOC; other signs of altered mental status (slow to response to verbal communication)	Dangerous mechanism of injury (fall >1m)	None
	9y*	M	14	Fall >1·5m from tree	Intracranial haemorrhage/contusion- extra-axial; skull fracture- non-depressed	N.Surg: Craniotomy & haematoma evacuation; Admission >2d	≥2yrs: GCS 14; other signs of altered mental status (agitation/irritability) ; any or suspected LOC; severe mechanism of injury (fall >1·5m); severe headache	GCS 14 2hrs after injury; dangerous mechanism of injury (fall > 1m); irritability on examination	None
	12y*^	M	14	Fall from push-scooter	Intracranial haemorrhage/contusion -extra-axial & parenchyma. Midline shift or brain herniation. Skull fracture - Non depressed.	N.Surg: No; Admission >2d	≥2yrs: GCS 14; any or suspected LOC; history of vomiting	None	None
	12y*	M	15	Pedestrian struck by motorised vehicle <60km/hr	Cerebral oedema	N.Surg: No; Admission >2d	≥2yrs: severe mechanism of Injury (pedestrian stuck by motorised vehicle); other signs of altered mental status (agitation/irritability) ; history of vomiting;	Dangerous mechanism of injury (motor vehicle accident); irritability on examination	None

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PMHx=past medical history; GCS=Glasgow coma score; LOC=loss of consciousness; NAI=non-accidental injury; N.Surg=Neurosurgical intervention; d=days, y=years, m=months
* These patients were also missed within the validation cohort so are also presented in **Table 4**.

^These patients were missed by two rules within the comparison cohort so shown twice within **Table 5**.