PEDIATRIC EMERGENCY MEDICINE CRITICAL ARTICLE REVIEW (PEMCAR)	
QUESTION	In children less than 18 years old presenting to the ED more than 24 hours after head injury, do history and physical exam factors predict those with traumatic brain injury on CT scan (TBI CT) and clinically important TBI (ciTBI) when compared to patients presenting within 24 hours of head injury?
TYPE	Diagnosis: Clinical Decision Rule: Derivation
TOPIC	Trauma: Head Trauma: Decision Rule
DATE	October 2019
REVIEWER	Mariju Baluyot, MD, Michael Mojica, M.D.
CITATION	Borland ML, Dalziel SR, Phillips N, Lyttle MD, Bressan S, Oakley E, Hearps SJC, Kochar A, Furyk J, Cheek JA, Neutze J, Gilhotra Y, Dalton S, Babl FE; Paediatric Research in Emergency Department International Collaborative (PREDICT) Group. Delayed Presentations to Emergency Departments of Children with Head Injury: A PREDICT Study. Ann Emerg Med. 2019 Jul;74(1):1-10., PubMed ID: 30655017

STUDY DEFINITIONS	
POPULATION	Inclusion: Children < 18 years with head injury of any severity Exclusion: GCS <14, re-presentations to the ED for the same injury (could have presented < 24 hours to a non-ED setting) Setting: 10 pediatric EDs (Australia, New Zealand) in the PREDICT research network (Paediatric Research in Emergency Department International CollaboraTive, 4/2011-11/2014.
RULE PARAMETERS	Rule parameters from the PECARN, CATCH and CHALICE pediatric head trauma decision rules were included. These included: Age, sex, vomiting, LOC, headache, amnesia, seizure, nonaccidental injury concern, altered mental state (such as drowsiness or abnormal GCS score), exam suggestive of depressed skull fracture, abnormal neuro exam, presence of nonfrontal scalp hematoma. It is unclear if the parameter “acting normally as per parents” was assessed and suspected nonaccidental trauma was not included in PECARN
REFERENCE STANDARD	1. CT at MD discretion 2. Clinical follow-up of discharged patients. 3. Hospital course for admitted patients Traumatic Brain Injury on CT (TBI CT)* Intracranial hemorrhage or contusion, cerebral edema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, signs of brain herniation, midline shift, diastasis of the skull, pneumocephalus, and depressed skull fracture. Clinically Important Traumatic Brain Injury (ciTBI)* 1. Death 2. Intubation for TBI >24 hours 3. TBI-related hospital admission for ≥ 2 nights 4. Neurosurgery: ICP monitoring, craniotomy, hematoma evacuation, elevation of depressed skull fracture, dura repair, tissue debridement, and lobectomy) *Definitions of TBI CT and ciTBI are identicle to PECARN head trauma rule with the exception of the fall height required to be a high risk injury mechanism PREDICT: < 1 meter, 1-1.5 meters, 1.5-3 meters, > 3 meters PECARN: > 0.9 meters (< 2 years), > 1.5 meters (> 2 years)

OUTCOME	1. Comparison: Prevalance of TBI CT and ciTBI (< 24 hrs vs > 24 hrs) 2. Predictors of TBI CT and ciTBI > 24 hrs 3. Test characteristics of statistically significant predictors
DESIGN	Observational: Prospective cohort (a secondary analysis of the Australasian Paediatric Head Injury Rule Study cohort)

CRITICAL REVIEW FORM: CLINICAL DECISION RULE: DERIVATION

HOW SERIOUS WAS THE RISK OF BIAS?	
Were all important predictors included in the derivation process?	Yes (Table 1). Predictors identified by the PECARN, CATCH and CHALICE head trauma rule were included: age, sex, vomiting, mechanism of injury, loss of consciousness, any amnesia, altered mental status, non-frontal scalp hematoma, exam suggestive of a depressed skull fracture and abnormal neurologic exam. The parameter "not acting normally as per parent" in the < 2 year old PECARN cohort was not included. The parameter of suspected non-accidental trauma was not included in PECARN
Were all important predictors present in significant proportion of the study population?	No. Logistical regression analyses were undertaken but could not be completed because predictors and outcomes had rare frequency (cell sizes were violated). Suspected non-accidental trauma 0.4% (<24hr) and 1.4% (>24 hr), altered mental status: 2.7 % (<24 hr) and 2.3% (>24 hr) were infrequent making it difficult to draw conclusions about these predictors
Were the outcome event and predictors clearly defined?	Yes. Outcomes were clinically important traumatic brain injury and CT evidence of brain injury with definition listed above as defined by the PECARN study with the exception of height of fall required to be a high risk mechanism of injury
Were those assessing the outcome event blinded to the presence of the predictors and were those assessing the presence of predictors blinded to the outcome event?	Yes. ED physicians were blinded to outcome event as they completed a case report form to collect predictive clinical data prior to imaging. Research assistants were presumably not blinded as they recorded ED and hospital management data after the visit and conducted telephone follow-up for patients who did not undergo imaging. No blinding to the predictors by outcome assessors would likely not affect the intretation of TBI CT and ciTBI.
Was the sample size adequate (including an adequate number of outcome events)?	No. Using the criteria for logistic regression, an adequate sample size is generally considered to be 10 outcomes for every predictor. The l ow sample size precluded the use of logistic regression. TBI CT: 1 significant predictor, 37 with TBI CT ciTBI: 2 significant predictors, 8 with ciTBI

WHAT ARE THE RESULTS?
HOW WELL DID THE RULE CORRECTLY IDENTIFY PATIENTS WITH THE PRIMARY OUTCOME? HOW PRECISE WAS THIS MEASUREMENT? (SENSITIVITY AND PREDICTIVE VALUE OF A NEGATIVE RULE WITH 95% CONFIDENCE INTERVALS)

HOW WELL DID THE RULE CORRECTLY IDENTIFY PATIENTS WITHOUT THE PRIMARY OUTCOME? HOW PRECISE WAS THIS MEASUREMENT? (SPECIFICITY AND PREDICTIVE VALUE OF A POSITIVE RULE WITH 95% CONFIDENCE INTERVALS)

N=918 (> 24 hours), Female: 39.6%, < 2 years: 28.3%
CT Rate:
> 24 hours: 21.7%, 95% CI (19.1, 24.3%)
< 24 hours: 8.6%, 95% CI (8.2, 9.0%)

SIGNIFICANT DIFFERENCES BETWEEN EARLY AND LATE PRESENTERS (TABLE 1)

Parameter	> 24 hours	< 24 hours	Risk Difference (95%CI)
Non-frontal scalp hematoma	20.8%	18.1%	2.7 % (0.1, 5.3%)
Headache	31.6%	19.9%	11.7% (8.8, 14.7%)
Any vomiting	30.0%	16.3%	13.7% (10.8, 16.6%)
Non-accidental injury concern	1.4%	0.4%	1.0% (0.3, 1.7%)
Loss of consciousness*	11.4%	13.5%	-2.1% (-4.2, 0.0%)
Amnesia	6.3%	8.2%	-1.9% (-3.5, -0.3%)

GREEN = Statistically Significant, RED = Not Statistically Significant
*Discrepancy: Text indicates 13.5% vs 14.3%

COMPARISON: OUTCOME PREVALENCE (TABLE 2)

	TBI CT	ciTBI
> 24 hours	3.8% (37/981), (2.6, 5.0%)[1]	0.8% (8/981) (0.3, 1.4%)[2]
< 24 hours	1.2% (233/18,784), (1.1, 1.4%)	0.8% (151/18,784) (0.7, 0.9%)
Risk Difference (95%CI)	2.53% (1.33, 3.73%)	0.1%, (-0.57, 2.02%)
Odds Ratio (95%CI)	3.1 (2.2, 4.4)	1.0,(0.5, 2.0)

GREEN = Statistically Significant, RED = Not Statistically Significant
1. Most common: Intracranial hemorrhage/contusion (31), depressed skull fracture (8),
2. Hospital stay > 48 hrs for TBI (8), Neurosurgery (2), Intubation > 24 hrs for TBI (0), Death (0)

SIGNIFICANT PREDICTORS: PRESENTING AFTER 24 HOURS OF INJURY (TABLE 5)

	TBI CT	ciTBI	ciTBI
Predictor	Non-frontal Scalp Hematoma	Non-frontal Scalp Hematoma	Concern Depressed Skull Fracture
Prevalence	3.8% (2.6, 5.0%)	0.8% (0.3, 1.4%)	0.8% (0.3, 1.4%)
Sensitivity	81.1% (65.8, 90.5%)	75.0% (40.9, 92.9%)	12.5% (2.2, 47.1%)
Specificity	81.6% (79.0, 89.3%)	79.7% (77.0, 82.1%)	99.3% (98.5, 99.7%)
Predictive Value (+)	14.7% (10.5, 20.2%)	2.9% (1.4, 6.3%)	12.5% (2.2, 47.1%)
Predictive Value (-)	99.1% (98.2, 99.6%)	99.7% (99.1, 99.9%)	99.3% (98.5, 99.7%)
Likelihood Ratio (+)	4.41 (3.58, 5.40)	3.69 (2.42, 5.60)	17.9 (2.5, 125.39)
Likelihood Ratio (-)	0.23 (0.12, 0.45)	0.31 (0.09, 1.04)	0.88 (0.68, 1.15)
Odds Ratio	19.0 (8.2, 43.9)	11.7 (2.4, 58.6)	19.7 (2.1, 182.1)

GREEN = Statistically Significant, RED = Not Statistically Significant
Test characteristics calculated from Table 5 data: CEBM DIAGNOSTIC TEST CALCULATOR

HOW WOULD USE OF THE RULE IMPACT RESOURCE UTILIZATION?

The authors did not create a rule from their predictor values. The absence of the predictors for TBI CT and ciTBI had high predictive values of a negative test indication and low post test probability of the outcomes. However, the lower limits of the confidence intervals allow for a small percentage of patients to be missed.

WAS THERE AN INTERNAL STATISTICAL VALIDATION OF THE RESULTS? HOW DID IT COMPARE TO THE PRIMARY RESULTS?

There was not an internal statistical validation of the results.

HOW CAN I APPLY THE RESULTS TO PATIENT CARE?	
At what level of development is this rule? How can it be applied? (See Appendix)	○ I ○ II ○ III ○ IV Not applicable. The authors identified predictor variables but did not create a decision rule.
Does the rule make clinical sense?	The identified predictor variables make clinical sense. A concern for a depressed skull fracture has been associated with TBI CT and ciTBI. A non-frontal scalp hematoma is associated with TBI CT and ciTBI in the less than 2 year old PECARN cohort but not the greater than 2 years old. Of the 8 patients with ciTBI (Table 4) 1 of the 5 patients over two years of age had an isolated non-frontal scalp hematoma.
Will the reproducibility of the rule and its interpretation be satisfactory in my clinical setting?	Reproducibility of non-frontal scalp hematoma and suspected depressed skull fracture was not assessed. However, PECARN predictors were only included if they had a kappa of greater than 0.6.
Is the rule applicable to the patients in my practice?	The neuroimaging rate is lower in Australian/New Zealand studies than in US. In the PECARN study, 35% of children presenting < 24 hours with head trauma were scanned compared to 8.5% of children presenting <24 hours with head trauma and 21.7% of children presenting >24 hours in this study. The lower CT rate in the PREDICT cohort likely resulted in a lower rate of TBI CT (1.2%, 95% CI (1.1, 1.4%)) compared to PECARN (5.2%, 95% CI (4.9, 5.6%) in those presenting within 24 hours of injury. This also likely explains the higher rate of TBI CT in those presenting after 24 hours of injury (3.8%) 95% CI. (2.6, 5.0%). Interestingly, the overall PRECICT TBI CT rate of 5% (1.2% < 24hours + 3.8% after 24 hours) is similar to the PECARN TBI CT rate (5.2%). The PREDICT ciTBI rate in those presenting within 24 hours of injury of 0.8% (0.3, 1.4%) and those presenting after 24 hours of injury of 0.8%, 95% CI (0.7, 0.9%) is comparable to the PECARN ciTBI rate of 0.9%, 95% CI (0.8, 1.0%).
Will the rule results change my management strategy?	A patient with a suspected depressed skull fracture would have gotten a CT regardless of the study results. The PECARN rule did not indentify a non-frontal hematoma as a predictor of ciTBI in the older than 2 year cohort.
What are the benefits of applying the rule to my patients?	The absence of the identified predictors suggests a lower risk of ciTBI. The post test probability of ciTBI was 0.3% 95% CI (0.1, 0,3%) for non-frontal scalp hematoma and 0.7%% (0.3, 1.5%) for suspected depressed skull fracture. There is a potential to forego CT and radiation exposure in patients without these risk factors. Since a regression analysis was not performed it is difficult to

	assess the the interaction of these factors with other predictors.
What are the risks of applying the rule to my patients?	The probability of ciTBI in the absence of the identified predictors is not zero. What is an acceptable miss rate is debatable.

CLINICAL BOTTOM LINE

BACKGROUND: Blunt head trauma in the pediatric patient is a common presentation to emergency department. Clinical decision rules such as the PECARN rule (Lancet. 2009, PubMed ID: 19758692), CATCH rule (CMAJ 2010, PubMed ID: 20142371) and CHALICE rule (Arch Dis Child 2006, PubMed ID: 17056862) identified predictor variables for traumatic brain injury on CT (TBI CT) and clinically important traumatic brain injury (ciTBI). These rules have been validated and are used to guide the decision for CT scanning in the pediatric patient, weighing the risks and benefits of radiation exposure in this sensitive population. However The PECARN and CATCH decision rules and were derived in patients presenting within 24 hours of injury. The CHALICE rule (did not exclude patient presenting after 24 hours from injury but did not analyze them separately. This study aims to determine the prevalence of TBI and clinically important TBI in pediatric patients with delayed ED presentations compared to early representation for head trauma and determine which predictor variables from previously published clinical decision rules may identify those at increased risk of TBI CT and ciTBI inorder to guide imaging decisions.

CLINICAL QUESTION: In children less than 18 years old presenting to the ED more than 24 hours after head injury, do history and physical exam factors predict those with traumatic brain injury on CT scan and clinically important TBI when compared to patients presenting within 24 hours of head injury?

DESIGN/RISK OF BIAS: This was a prospective, observational cohort study, a secondary analysis of the Australasian Paediatric Head Injury Rule Study cohort. Predictor variables that were analyzed included those from the PECARN, CATCH and CHALICE pediatric head trauma decision rules. There included: age, sex, vomiting, loss of consciousness, headache, amnesia, seizure, nonaccidental injury concern, altered mental state (such as drowsiness or abnormal GCS score), exam suggestive of depressed skull fracture, abnormal neurologic exam, and presence of nonfrontal scalp hematoma. The reference standard was CT (at the clinicians discretion), hospital course for admitted patients and phone follow-up for discharged patients. TBI CT and ciTBI were as defined previously in the PECARN head trauma study.

PRIMARY RESULTS: 981 pediatric patients presented 24 hours after head injury. 37 patients (3.8%, 95% CI 2.6-5.0%) had TBI CT and 8 (0.8%, 95% CI 0.4-1.6%) had clinically important TBI with 2 patients (0.2%, 95% CI 0.0-0.5%) requiring neurosurgical intervention. Those presenting within 24 hours were statistically less likely to have TBI CT (1.2%, 95% CI(1.1, 1.4%) but there was no difference in the rate of ciTBI 0.8%, 95% CI (0.7, 0.9%)). The small number of patients with TBI CT and ciTBI precluded the use of regression anaylysis and did not allow for the cohort to be divided into less than two years and greater than 2 years as are the PECARN decision rules.

Patients presenting after 24 hours were statistically more likely to have a non-frontal scap hematoma, vomiting, headache and a suspicion of nonaccidental trauma when compared to those

presenting within 24 hours of injury. Patients presenting after 24 hours were statistically less likely to have a loss of consciousness and amnesia when compared to those presenting within 24 hours of injury.

In the bivariable analysis, TBI CT was statistically more likely in those with a non-frontal scalp hematoma presenting after 24 hours (Odds Ratio 19.0, 95% CI (8.2, 43.9). ciTBI was statistically more likely in those with a non-frontal scalp hematoma (Odds Ratio: 11.7, 95% CI (2.4, 58.6) and in those with a suspected depressed skull fracture (Odds Ratio: 19.7, 95% CI(2.1, 182.1) presenting after 24 hours. There was no statistically significant association in any other of the predictors analyzed. The lower limits of the 95% confidence intervals for the negative predictive values allows for a small percentage of those with TBI CT and ciTBI to be missed. Whether this miss rate is acceptable is a matter of judgement.

The impact of these predictors on neuroimaging decisions is unclear. It is likely that anyone with a suspected depressed skull fracture would have a head CT scan regardless of this study's results. In addition, a non-frontal scalp hematoma was a predictor of ciTBI in the PECARN cohort less than 2 years but not the cohort greater than twp years. One of the five patients with ciTBI over 2 years of age had an isolated non-frontal scalp hematoma.

SIGNIFICANT PREDICTORS: PRESENTING AFTER 24 HOURS OF INJURY (TABLE 5)

	TBI CT	ciTBI	ciTBI
Predictor	Non-frontal Scalp Hematoma	Non-frontal Scalp Hematoma	Concern Depressed Skull Fracture
Prevalence	3.8% (2.6, 5.0%)	0.8% (0.3, 1.4%)	0.8% (0.3, 1.4%)
Sensitivity	81.1% (65.8, 90.5%)	75.0% (40.9, 92.9%)	12.5% (2.2, 47.1%)
Specificity	81.6% (79.0, 89.3%)	79.7% (77.0, 82.1%)	99.3% (98.5, 99.7%)
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Odds Ratio	19.0 (8.2, 43.9)	11.7 (2.4, 58.6)	19.7 (2.1, 182.1)

GREEN = Statistically Significant, RED = Not Statistically Significant
Test characteristics calculated from Table 5 data: CEBM DIAGNOSTIC TEST CALCULATOR

APPLICABILITY: It may be difficult to apply these results to our practice because the neuroimaging rate is lower in Australian/New Zealand studies than in United States. In the PECARN study, 35% of children presenting less than 24 hours with head trauma were scanned compared to 8.5% of children presenting within 24 hours with head trauma and 21.7% of children presenting after 24 hours in this study.

The lower CT rate in the PREDICT cohort likely resulted in a lower rate of TBI CT (1.2%, 95% CI (1.1, 1.4%)) compared to PECARN (5.2%, 95% CI (4.9, 5.6%) in those presenting within 24 hours of injury. This also likely explains the higher rate of TBI CT in those presenting after 24 hours of injury (3.8%) 95% CI. (2.6, 5.0%). Interestingly, the overall PRECICT TBI CT rate of 5% (1.2% < 24hours + 3.8% after 24 hours) is similar to the PECARN TBI CT rate (5.2%).

The PREDICT ciTBI rate in those presenting within 24 hours of injury of 0.8% (0.3, 1.4%) and those presenting after 24 hours of injury of 0.8%, 95% CI (0.7, 0.9%) is comparable to the PECARN ciTBI

rate of 0.9%, 95% CI (0.8, 1.0%).

Reproducibility of non-frontal scalp hematoma and suspected depressed skull fracture was not assessed. However, PECARN predictors were only included if they had a kappa of greater than 0.6.

AUTHOR'S CONCLUSION: "Delayed presentation greater than 24 hours after head injury in children, although infrequent, may be significantly associated with traumatic brain injury. Factors associated with traumatic brain injury include suspicion for depressed skull fracture and nonfrontal scalp hematoma. Treating clinicians should evaluate and manage delayed presentations outside of the current head injury clinical decision rule parameters because these rules have not been validated for this subset of patients."

POTENTIAL IMPACT: This is the first prospective study to attempt to characterize pediatric patients with delayed presentations to the emergency department following head trauma. Its generalizability is limited by the small number of patients with TBI CT and ciTBI which precluded the use of regression anaylysis and did not allow for the cohort to be divided into less than two years and greater than 2 years are PECARN decision rules.

The impact of the identified predictors of TBI CT and ciTBI on neuroimaging decisions is unclear. Those patients with a suspected depressed skull fracture would very likely have a head CT regardless of the study's results. The predictive ability of a non-frontal scalp hematoma in patients older than 2 years is unclear. Only 1 of the 5 patients over 2 years of age with ciTBI had an isolated non-frontal scalp hematoma.