Clinical Prediction Rules for Abusive Head Trauma: A Systematic Review

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ABSTRACT

Objective: Misdiagnosis of abusive head trauma (AHT) has serious consequences for children and families. This systematic review identifies and compares clinical prediction rules (CPredRs) assisting clinicians in assessing suspected AHT.

Design: We searched MEDLINE, Embase, PubMed and Cochrane databases (January 1996–August 2016). Externally validated CPredRs focusing on the detection of AHT in the clinical setting were included.

Results: Of 110 potential articles identified, three studies met the inclusion criteria: the Pediatric Brain Injury Research Network (PediBIRN) 4-Variable AHT CPredR, the Predicting Abusive Head Trauma (PredAHT) tool and the Pittsburgh Infant Brain Injury Score (PIBIS). The CPredRs were designed for different populations and purposes; PediBIRN: intensive care unit admissions (<3 years) with head injury, to inform early decisions to launch or forego an evaluation for abuse (sensitivity 0.96), PredAHT: hospital admissions (<3 years) with intracranial injury, to assist clinicians in discussions with child abuse specialists (sensitivity 0.72), and PIBIS: well-appearing children (<1 year) in the emergency department with no history of trauma, temperature <38.3°, and ≥1 symptom associated with high risk of AHT, to determine the need for a head CT scan (sensitivity 0.93). There was little overlap between the predictive variables.

Conclusion: Three CPredRs for AHT were relevant at different stages in the diagnostic process. None of the CPredRs aimed to diagnose AHT but to act as aids/prompts to clinicians to seek further clinical, social or forensic information. None were widely validated in multiple settings. To assess safety and effectiveness in clinical practice, impact analyses are required and recommended.

INTRODUCTION

Abusive head trauma (AHT) is a leading cause of traumatic death in children less than one year of age and the most common cause of fatal child abuse. (1) Children with AHT have an estimated mortality rate of 26% (2) and long-term disability ranging from 44% (3) to 92% (4) among survivors. (5) (6) Patients are at increased risk of further injury and death if AHT is missed. (7) (8) However, deciding which children should undergo a full evaluation for AHT is difficult, as histories provided by the caregiver might be absent or fabricated, and the clinical findings may be similar to those seen in accidental trauma. (9) Clinicians might hesitate to raise suspicion of AHT, as a wrongful accusation means emotional strain for the families, endangers patient-doctor relationships and leads to unnecessary investigation-related costs and risks for the child. (10)

Clinical prediction rules (CPredRs) rules are evidence-based tools, which incorporate three or more variables from clinical findings including history, physical examination and results of investigations, to predict aetiology or outcome. (11) They are especially important for conditions where decision-making is difficult, clinical stakes are high and clinical experience and intuition are limited. (12) There are three main phases in the development of CPredRs; derivation, external validation, and impact analysis. (13) Each requires a different and rigorous methodological approach. In the initial phase, predicted probabilities are derived from the statistical analysis of patients with known outcomes, typically using multivariable regression techniques or classification and regression tree analysis. (13) Predictor variables should be clinically sensible and clearly defined (14), and the dataset used to derive the rule should be representative of the target population. Reilly and Evans (2006) distinguish between assistive prediction rules that simply provide clinicians with predicted probabilities without recommending a specific clinical course of action, and directive decision rules that explicitly suggest additional diagnostic tests or treatment in line with the obtained score. (11)

CPredRs must be validated with a dataset external to the one in which it was derived, preferably in multiple settings, and tested in clinical practice to determine their impact on patient care. (15)

There have been few systematic reviews in this field that explore the quality and effectiveness of CPredRs in child abuse. While Louwers et al (2010) compared several screening techniques for child abuse in emergency departments (ED) (16) we set out to find and critically appraise CPredRs that aim to detect AHT across various medical settings and compare them in terms of their quality and performance.

METHODS

We conducted a systematic review to identify CPredRs for AHT and to compare them in terms of derivation, population, definition of AHT, variables used, external validation, and performance. For this purpose, we followed a protocol based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA statement) (Figure 1; for PRISMA checklist see supplemental table 1). (17) Our review was registered with the PROSPERO international prospective register of systematic reviews (http://www.crd.york.ac.uk/; record number CRD42017058141).

Inclusion/exclusion criteria

We included externally validated CPredRs with a focus on the detection of AHT in children from 0 to 18 years of age in the clinical setting. Papers that reported associations between one or two variables or markers and AHT were excluded, as well as clinical assessment tools trying to detect child abuse in general.

Search strategy

We searched the electronic databases MEDLINE, the Cochrane Database of Systematic Reviews, Cochrane Controlled Trials (1996–August 2016), and Embase (1974–

August 2016) using the Ovid and PubMed platforms. No limitations were applied for languages. The search strategy including search terms is presented in the Appendix.

Study selection

Duplicates were removed and relevant abstracts were reviewed. When eligibility could not be determined from the abstract, a full-text review was performed. When there were uncertainties about inclusion, other lead authors were consulted (LC, FB).

Assessment of quality

Maguire, J. et al (18) proposed 17 quality items for the development and validation of CPredRs for children in their systematic review. We chose this approach to compare the methodological quality of the CPredRs, calculating a score (Table 2) according to the number of quality standards achieved.

Data analysis

It became apparent early on that the included CPredRs were heterogeneous and a meta-analysis was unlikely to be possible, therefore a descriptive analysis is provided.

RESULTS

The search in Medline resulted in 74 articles and in Embase 54 articles were found. The search in PubMed and the Cochrane Database of Systematic Reviews and Cochrane Controlled Trials did not add any additional relevant studies. After removing duplicates, reviewing abstracts and excluding irrelevant articles, three recently published, externally validated clinical prediction rules for AHT met the inclusion criteria: the Pediatric Brain Injury Research Network (PediBIRN) 4-variable AHT CPredR (19), the Predicting Abusive Head Trauma (PredAHT) tool (20) and the Pittsburgh Infant Brain Injury Score (PIBIS) for AHT (21) (see Figure 1 and Table 1).

Insert Figure 1

Insert Table 1

PediBIRN

The PediBIRN CPredR (19) was designed to "inform [pediatric intensivists'] early decisions to launch (or forego) an evaluation for abuse" (10). It was derived in a prospective study including 209 children published in 2013 (95 AHT cases) (10) and validated in a further prospective study comprising 291 children (125 AHT cases), published in 2014. (19) The validation study took place in 14 hospitals within the United States, of which ten sites had been part of the derivation study. The population of interest was that of acutely head-injured children aged <3 years admitted to the paediatric intensive care unit (PICU). Following a bivariate analysis of 45 potential factors for discrimination and reliability the authors applied a classification tree to their data using binary recursive partitioning to derive a 4-variable CPredR with maximum sensitivity to determine the risk of AHT. The four variables were respiratory compromise, bruising involving the ears, neck and torso, bilateral/interhemispheric subdural haemorrhages and skull fractures (other than an isolated, unilateral, nondiastatic, linear, parietal skull fracture). If one or more of the variables were present, the child should be thoroughly evaluated for abuse. In the validation study, the CPredR achieved a sensitivity of 0.96 and a specificity of 0.46 to detect AHT cases.

PredAHT

The PredAHT CPredR provides an estimated probability of AHT to assist clinicians in discussions with child abuse specialists. (19) It was derived from a pooled analysis of individual patient data from six previously published studies, which included prospectively collected data on 133 children (58 AHT cases) and retrospective data on 920 children (290 AHT cases) with head injury. (22) PredAHT identified the positive predictive values and odds ratios for AHT given any combination of six possible variables using multi-level logistic regression. The validation study comprised a retrospective dataset of 60 children (23 AHT cases) in Cardiff, United Kingdom, and prospective data on 138 children (42 AHT

cases) from Lille, France. (23) The Welsh dataset included children <3 years of age with intracranial injuries confirmed on neuroimaging, that were admitted to hospital, whereas the French cases were comprised of patients <2 years old with craniocerebral traumatic lesions diagnosed on CT and referred alive to the ED, PICU or neurosurgical department. Missing data were accounted for using multiple imputation by chained equations. PredAHT gave probabilities of AHT that ranged from 4% if none of the variables were present to close to 100% when all six variables were present. (22) Following validation, the probability of AHT was always greater than 81.5% if any three or more of the predictive variables – head/neck bruising, seizures, apnoea, rib fractures, long-bone fractures or retinal haemorrhages – were present. In the validation study the CPredR performed with a sensitivity of 0.72 and a specificity of 0.86 in detecting AHT, using a cut-off probability of AHT of 50%.

PIBIS

The Pittsburgh Infant Brain Injury Score (PIBIS) for AHT (21) assists in determining which high-risk infants in the ED should undergo head CT to rule out abnormalities including AHT. It was derived based on retrospective data on 187 children (150 without brain injury and 37 with mild AHT), which was not published, and validated using logistic regression in a prospective study carried out in the United States with 1040 infants. Missing data were handled with listwise deletion. The included sample was of well-appearing children between 30 and 364 days of age with a temperature <38.3°, no history of trauma and at least one symptom associated with high risk of AHT (ALTE/apnoea, vomiting without diarrhoea, seizures/seizure-like activity, soft tissue swelling of the scalp, bruising or other non-specific neurologic symptoms such as lethargy, fussiness or poor feeding). If children received a score of 2 points or more when adding: abnormality such as bruises observed on dermatologic examination (2 points), age equal to or greater than 3 months (1 point), head circumference >85th percentile (1 point) and haemoglobin <11.3 g/d (1 point), further neuroimaging should

be performed. In the validation study, the CPredR performed with a sensitivity of 0.93 and a specificity of 0.53 to detect abnormal neuroimaging. It is important to stress that the outcome case definition did not exclusively comprise AHT, but included other clinically significant traumatic and non-traumatic abnormalities.

Comparing the Rules

All three CPredRs defined their outcome and predictive variables clearly, reported their results adequately and used 95% confidence intervals on rule properties. Using a standardised approach (18) the PediBIRN CPredR (19) received the highest score for methodological quality (Table 2). It was the only CPredR that described an independent blinded assessment of predictive and outcome variables and an evaluation of inter-rater reliability in the derivation study, comparing the assessment of blinded duplicate data on 20% of included patients by different investigators. (10) The PIBIS study conducted the only follow up of cases (6 months after enrolment or up to 1 year of age) to identify further abnormal neuroimaging and assess the progress of symptoms at presentation. (10) This approach was an attempt to verify the true negatives as only 61% of controls had neuroimaging. The PediBIRN and the PIBIS CPredRs both proposed a clear course of action (PediBIRN - thorough evaluations for abuse, PIBIS - CT scan), whereas PredAHT provided a probability of AHT in order to "assist (24) clinicians in their discussions with child abuse specialists, in addition to facilitating discussions between child abuse specialists and social welfare, law enforcement, or other professionals involved in the child protection process". (20)

Insert Table 2

DISCUSSION

We identified three validated CPredRs that met inclusion criteria. These prediction rules are aimed at very different populations and different time points within the clinical

assessment (Figure 2): PIBIS (21) is targeted at a specific population of well appearing infants in the ED who might benefit from a head CT scan. PredAHT (20) applies to children <3 years of age admitted to hospital with intracranial injury, where children have been examined and may have had some ophthalmological and radiological investigations, and PediBIRN (19) applies to a narrower population of <3 year olds admitted to PICU with a cranial or intracranial injury excluding head trauma resulting from motor vehicle collisions. It is notable that PredAHT (20) does not apply to children with cranial injury only, as defined within the Centers for Disease Control and Prevention definition of AHT (25).

Insert Figure 2

Just as the populations are different, so are the predictor variables prima facie. As apparent in Table 3, the only overlap among the items used by the different CPredRs are cutaneous injuries and respiratory compromise/apnoea. However, some of the PIBIS high-risk AHT symptoms used for the inclusion of patients (apnoea, seizures, bruising) appeared among the predictor variables of PediBIRN and PredAHT. Beyond that, both of these CPredRs had tested some of the same predictive variables in their derivation studies (e.g. PediBIRN: seizures and PredAHT: skull fractures), yet they had not significantly improved their CPredRs performance. (10, 22)

Insert Table 3

In terms of published accuracy of the rules, the PediBIRN CPredR (19) performed best with a sensitivity of 0.96, closely followed by PIBIS (21) with 0.93, whereas the PredAHT CPredR detected 0.72 of AHT cases applying a 50% cut-off – however the PredAHT tool provides a sliding scale of probability from 4% to nearly 100% depending upon the presence or absence of each of the six features. (20) The pre-test prevalence in the PediBIRN population (19), was 0.43, which raises the question whether all children in this high-risk group should be

screened. (26) In the PredAHT and PIBIS studies the pre-test probabilities were lower at 0.33 and 0.26 respectively. (20, 21)

The PIBIS (21) variables are all available from physical examination, simple blood test, and history, whereas neuroimaging is required for PediBIRN (19) and further investigations such as ophthalmologic examination and rib and long bone X-rays are required for PredAHT (20) (Table 3). These tests would usually only be performed if physical abuse or serious trauma had already been suspected placing PredAHT as a potentially useful tool for assessing the significance of the results of these investigations at a specific stage in the diagnostic process.

Due to the lack of gold standard diagnostic criteria for AHT, different approaches were chosen to minimize circular reasoning whereby AHT may have been decided based upon the presence of the predictor variables within the CPredRs. The PediBIRN CPredR aimed to avoid definitional criteria that involved intracranial injuries, injury severity, any of the predictor variables, and child protection team assessment. (19) When challenged on the issue that bruising was included in their definitional criteria and as a predictor variable (27), the authors stated that of 73 patients with bruising, 61 met other definitional criteria based on the history and the 12 remaining patients were subsequently diagnosed with definite/probable AHT by the treating physicians. (28) The PredAHT group applied the outcome of the child protection process including only cases where multidisciplinary or court proceedings had confirmed AHT. (20) Arguably this decision will include a consideration of clinical features, as is the case in any clinical diagnosis. However within the child protection social care and legal process, there are multiple additional forensic, clinical, social and historical factors that are included in decisions about the balance of probability of abuse and future risks for the child. Similar reasoning applies to PIBIS where the child protection team assessment decision was also used. (21) Regarding PIBIS the true negatives could not be identified as only 61%

of controls had neuroimaging. Case follow up was undertaken for 6-12 months to determine if any neurological imaging was performed at a later stage and cases potentially missed. None of the CPredRs have yet been widely validated in multiple settings or undergone an impact analysis to determine their safety and effectiveness in clinical practice. Hymel et al have undertaken a theoretical impact analysis of PediBIRN in the combined population of the derivation and validation study. (29) Of note, because the PIBIS rule as originally derived was updated in the validation study, ideally this CPredR should be validated in another external dataset before it can be applied to new patients. (30)

As the three CPredRs apply at different time points in the diagnostic process, in different populations and with a different degree of investigations completed, this explains and allows for differences in sensitivity and specificity. At the outset, it is paramount to ensure that cases are not missed and undergo sufficient investigation, therefore high sensitivity is the focus, with specificity of lower importance. When more investigations have been undertaken, a higher specificity would be desirable to ensure that a diagnosis of AHT is not made incorrectly. This suggests that the three CPredRs might complement each other in clinical practice. For instance, if a well-appearing infant between 30 and 364 days of age met the inclusion criteria and predictive values of PIBIS, underwent neuroimaging and had an intracranial injury, further investigations should include skeletal survey and ophthalmological exam, providing more of the items required for PredAHT. In the critically ill children admitted to PICU, the PediBIRN rule would apply and would be useful to inform decision-making at a time when the child may be too sick to undergo a skeletal survey.

Limitations

The number of included studies was small and a meta-analysis was not possible. A further CPredR by Wells et al on the radiological differentiation of intentional and non-

intentional intracranial haemorrhage was excluded, as it had not been externally validated. (31)

CONCLUSION

The three CPredRs for AHT focus on different populations with different inclusion criteria. They use different predictive variables available at different stages in the diagnostic process, and different outcome variables. PediBIRN aims to rule out AHT in the PICU. PredAHT calculates the probability of AHT for hospitalised children. PIBIS aims to detect abnormal neuroimaging in the ED. None of the CPredRs aimed to diagnose AHT but to act as aids or prompts to clinicians to seek further clinical, social or forensic information and move towards a multidisciplinary child protection assessment should more information in support of AHT arise. Wider validation in multiple settings is recommended for each CPredR, in addition to impact analyses to assess their safety and effectiveness in clinical practice.

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Conflict of Interest: AMK and LEC were involved with the development of one of the clinical prediction rules described in this paper

Abbreviations: abusive head trauma (AHT); clinical prediction rule (CPredR); computed tomography (CT); emergency department (ED); magnetic resonance imaging (MRI); Pediatric Brain Injury Research Network (PediBIRN); Pittsburgh infant brain injury score (PIBIS); paediatric intensive care unit (PICU); Predicting Abusive Head Trauma tool (PredAHT tool)

What is already known on this subject

- Abusive head trauma (AHT) has high morbidity and mortality; if AHT is missed, patients are at increased risk of further injury and death.
- Clinical prediction rules (CPredRs) may assist in deciding which head injured children might have sustained injury as a result of AHT.

What this study adds

- Three recently validated CPredRs for AHT investigate very different populations, focus on different stages of the diagnostic process and use differing predictive and outcome variables.
- The aim of the CPredRs was not to diagnose AHT but to act as aids or prompts to seek further information, investigation and assessment.

Contributors' Statement

Helena Pfeiffer: Ms Pfeiffer contributed to the design of the study, conducted the systematic review, and drafted and revised the article.

Louise Crowe, Alison M. Kemp and Laura E. Cowley: Dr. Crowe, Prof Kemp and Ms Cowley contributed to the design of the study, reviewed the search, made substantial contributions to the interpretation and discussion of findings and critically revised the manuscript for important intellectual content.

Anne Smith: Dr. Smith contributed to the design of the study and critically revised the manuscript for important intellectual content.

Franz E. Babl: Prof Babl had the initial study idea, contributed to the design of the study, and critically revised the manuscript for important intellectual content. He takes responsibility for the paper as a whole.

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Table 1. Comparison of 3 Clinical Prediction Rules for Abusive Head Trauma

Name	**PediBIRN 4-Variable AHT CPredR**	**PredAHT tool**	**Pittsburgh Infant Brain Injury Score (PIBIS) for Abusive Head Trauma**
Country	USA	UK	USA
Derivation paper	Hymel, Derivation of a Clinical Prediction Rule for Pediatric Abusive Head Trauma, Pedr Crit Care Med, 2013 (10)	Maguire, Estimating the Probability of NAHI, Pediatrics, 2011 (22)	Unpublished data
	Prospective: N = 209	Prospective: N = 133 Retrospective: N = 920	Retrospective: N = 187
Validation paper	Hymel, Validation for a Clinical Prediction Rule for Pediatric Abusive Head Trauma, Pediatrics, 2014 (19)	Cowley, Validation of a Prediction Tool for Abusive Head Trauma, Pediatrics, 2015 (20)	Berger, Validation of the Pittsburgh Infant Brain Injury Score for Abusive Head Trauma, Pediatrics, 2016 (21)
	Prospective: N = 291	Prospective: N = 138 Retrospective: N = 60	Prospective: N = 1040
CPredR	Every acutely head-injured infant/child meeting the inclusions criteria and presenting with **≥ 1 of these 4** predictor variables should be thoroughly evaluated for abuse • Any clinically significant **respiratory compromise** (infrequent/laboured respirations, apnoea or any need for intubation or assisted ventilation) at the scene of injury, during transport, in the ED or before admission • Any **bruising** involving the child's **ears, neck and torso** (including chest, abdomen, genitourinary region, back or buttocks) • Any **subdural haemorrhages** or fluid collections that are bilateral or involve the interhemispheric space • Any **skull fractures** other than an isolated, unilateral, nondiastatic, linear parietal skull fracture	Estimated probability of AHT varies from 4% when none of the features are present to close to 100% when all six features are present and >81.5% (63.3% - 91.8%) when **≥ 3 of these 6** features are present • **Head or neck bruising** • **Seizures** • **Apnoea** (documented in initial history or during inpatient stay) • **Rib fracture** (documented after appropriate radiologic imaging) • **Long-bone Fracture** (") • **Retinal Haemorrhage** (documented after indirect ophthalmologic examination by a paediatric ophthalmologist)	Children with a score of **≥ 2** should undergo neuroimaging to check for abnormal findings • **Abnormality on dermatologic examination** (2 points) • **Age ≥ 3.0 months** (1 point) • **Head circumference >85th percentile** (1 point) • **Haemoglobin <11.2 g/dL** (1 point)
Objective	Detection of AHT among acutely head-injured children admitted to PICU	Prediction of the likelihood of AHT in head-injured children	Detection of abnormal neuroimaging in well-appearing children with non-specific symptoms
Inclusion	• Children < 3 years of age • Admission to PICU • Symptomatic, acute, closed, traumatic, cranial or intracranial injuries confirmed by CT or MRI	Dataset 1 (Cardiff, UK): • Children < 3 years of age • Hospital admission • ICI (combination of extraaxial haemorrhage, diffuse or focal parenchymal injury, cerebral oedema, cerebral contusion, hypoxic ischemic injury or diffuse axonal injury) confirmed on neuroimaging Dataset 2 (Lille, France): • Children < 2 years of age • Craniocerebral traumatic lesions diagnosed based on at least 1 CT [20] • Referred alive to the neurosurgical department, the PICU or the ED	• 30 – 364 d of age • Well-appearing • Temperature <38,3°C • No history of trauma • Seeking medical evaluation for 1 of the following symptoms o ALTE/apnoea o Vomiting without diarrhoea o Seizures or seizure-like activity o Soft tissue swelling of the scalp o Bruising o Other non-specific neurologic symptom not described above, such as lethargy, fussiness or poor feeding
Exclusion	• Children ≥ 3 years of age • HI resulting from a collision involving a motor vehicle • Initial neuroimaging revealed clear evidence of pre-existing brain malformation, disease, infection or hypoxia-ischemia	• Children ≥ 3 years of age (Dataset 2: ≥ 2 years of age) • Normal neuroimaging • Underlying structural abnormality or pre-existing disease (hydrocephalus, cystic lesion/tumour, metabolic cause, malformation, abnormal brain development) • Injuries caused by neglect • Birth injuries	• Previous abnormal CT scan of the head

Definition of AHT	• The primary caregiver [25] admitted abusive acts • Abusive acts by the PC were witnessed by an unbiased, independent observer • The PC specifically denied that the preambulatory child in his/her care had experienced any head trauma • The PC provided an account of the child's HI event that was clearly historically inconsistent with repetition over time • The PC provided an account of the child's HI event that was clearly developmentally inconsistent with the child's known (or expected) gross motor skills • Further workup confirmed the presence of two or more categories of extracranial injuries considered moderately or highly suspicious for abuse > classic metaphyseal lesion fracture or epiphyseal separation > rib fracture, fracture of the scapula or sternum > fractures of the digits > vertebral body fractures > dislocation/fracture of spinous process > skin bruising/abrasion/ laceration in two or more distinct locations other than knee, shins or elbows > patterned bruising or dry contact burns > scalding burns with uniform depth, clear lines of demarcation, and paucity of splash marks > confirmed intra-abdominal injuries > retinoschisis confirmed by an ophthalmologist > retinal haemorrhages described by an ophthalmologist as dense, extensive, covering a large surface area and/or extending to the ora serrata	Confirmed cases on AHT (ranked 1 or 2 for abuse) • Rank 1: > Abuse confirmed at case conference or civil, family, or criminal court proceedings > admitted by perpetrator > independently witnessed • Rank 2 > Abuse confirmed by stated criteria including multidisciplinary assessment	Brain injury due to definite/probable, but not possible, abuse as assessed by the hospital-based Child Protection Team at each enrolled site (Cases = abnormal neuroimaging)
Definition of nAHT	• All remaining patients	• Witnessed accidental mechanisms • Confirmed organic causes • Abuse excluded after child protection investigations	• N.s.
Validation study Sensitivity* Specificity Prevalence PPV NPV LR+ LR- Area under the curve	N = 291 **0.96** (0.90 – 0.99) 0.43 (0.35 – 0.50) **0.43** (0.37 – 0.49) 0.55 (0.48 – 0.62) 0.93 (0.85 – 0.98) 1.67 (1.46 – 1.91) 0.09 (0.04 – 0.23) 0.78 * Accuracy of detecting AHT cases among children with HI admitted to PICU	N = 198 **0.72** (0.60 – 0.82) 0.86 (0.79 – 0.91) **0.33** (0.27-0.40) 0.71 (0.59 – 0.81) 0.86 (0.80 – 0.91) 5.06 (3.25-7.88) 0.32 (0.22-0.48) 0.88 (0.82-0.93) * Accuracy of detecting AHT cases among admitted children with HI	N = 862 **0.93** (0.89-96.0) 0.53 (0.49-0.57) **0.26** 0.39 (0.35-0.44) 0.96 (0.94-0.98) 1.98 0.13 0.82 * Accuracy of detecting cases with abnormal neuroimaging in well-appearing children with at least 1 non-specific symptom, that is common in AHT

Abbreviations: AHT, abusive head trauma; ALTE, apparent life-threatening event; CT, computed tomography; CPredR, clinical prediction rule; ED, emergency department; HI, head injury; ICI, intracranial injury; PC, primary caregiver; PICU, paediatric intensive care unit; PPV, positive predictive value; nAHT, accidental head trauma (non-inflicted); NPV, negative predictive value; LR +, positive likelihood ratio; LR -, negative likelihood ratio.

Table 2. Assessment of Methodological Quality as proposed by Maguire et al(18)
Present = score of 1, not specified/no = score of 0

Quality Item	PediBIRN tool (19)	PredAHT (20)	PIBIS (21)
Prospective Validation	Yes	Only DS 2	Yes
Study site well described	Yes	Yes	Yes
Population well described	Yes	Yes	Yes
Rule applied to all patients at risk	>90%	N.s.	No
Predictive variables			
Clear definition	Yes	Yes	Yes
Blind assessment	Yes	N.s.	N.s.
Reproducible	Yes	N.s.	N.s.
Outcome variable			
Definition	Yes	Yes	Yes
Blind assessment	Yes	N.s.	N.s.
Adequate follow-up	N.s.	N.s.	Yes
Sensibility			
Clinically sensible	Yes	Yes	Yes
Easy to use	Yes	Yes	Yes
Course of action	Yes	No	Yes
Statistical analysis			
Mathematical technique reported	Yes	Yes	Yes
Adequate calculated power reported	No	No	No
Adequate reporting of results	Yes	Yes	Yes
95% CIs reported on rule properties	Yes	Yes	Yes
Score	15	9	12

Abbreviations: CI, Confidence interval; DS, Dataset; N.s., Not specified; PediBIRN, Brain Injury Research Network; PIBIS, Pittsburgh infant bran injury score; PredAHT tool, Predicting Abusive Head Injury tool.

Table 3. Variables used in the clinical prediction rules

Variable	Hymel	Cowley	Berger	Availability of item
Abnormality on dermatologic examination/bruising	X	X	X	Physical examination
Respiratory compromise/apnoea	X	X		Physical examination/history
Subdural haemorrhages (bilateral, interhemispheric)	X			MRI/CT
Skull fractures (other then isolated unilateral, nondiastatic, linear parietal skull fracture)	X			MRI/CT/Skull X-ray
Rib fractures		X		Chest X-ray
Long-bone fracture		X		Long bone X-rays
Retinal haemorrhage		X		Ophthalmologic fundoscopy
Seizures		X		Physical examination/history
Age ≥ 3.0 months			X	History
Head circumference >85th percentile			X	Physical examination
Haemoglobin <11.2 g/dL			X	FBE

Abbreviations: CT, computed tomography; FBE, full blood examination; MRI, magnetic resonance imaging

Figure 1. Flow diagram of literature search based on PRISMA

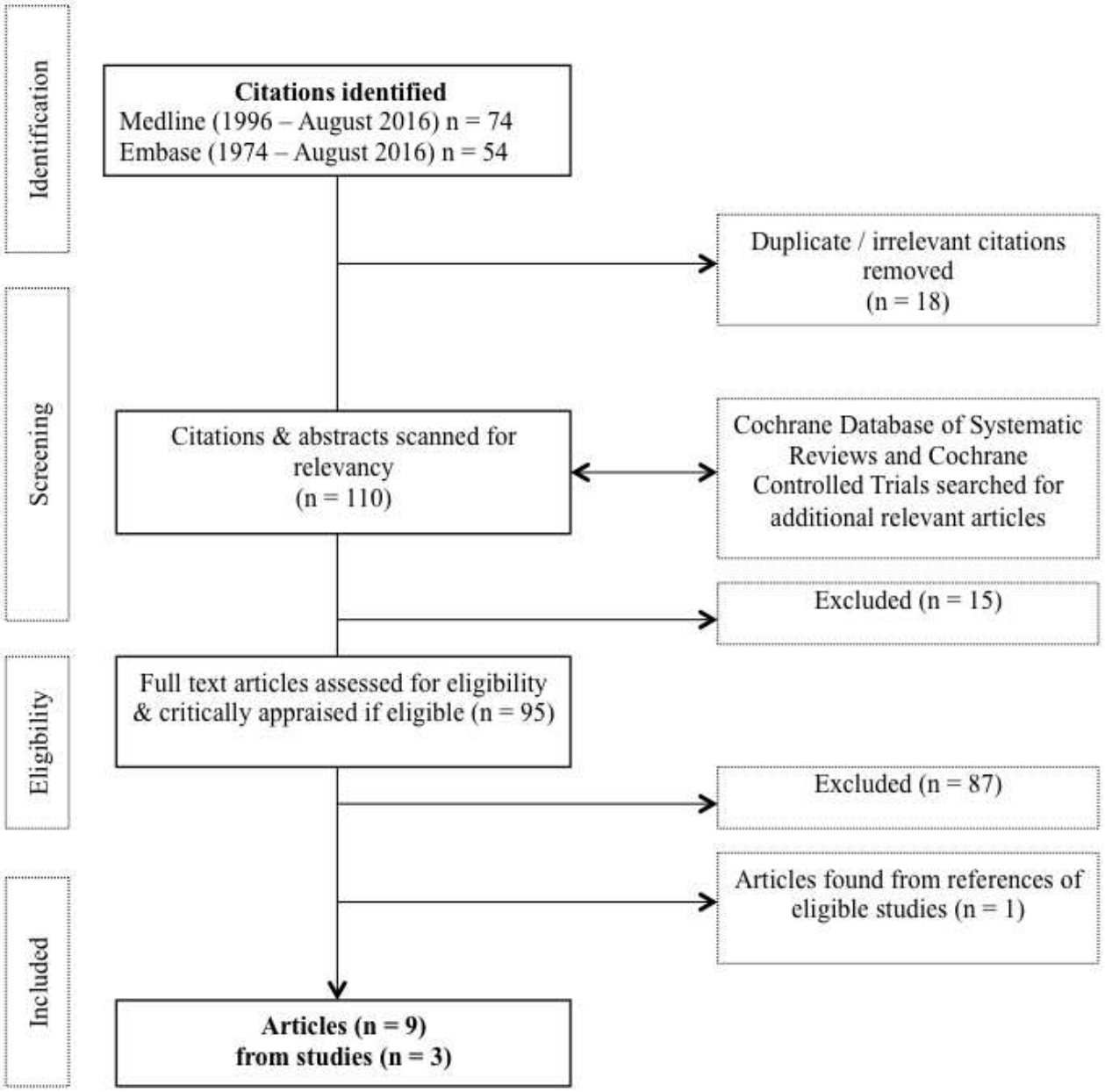
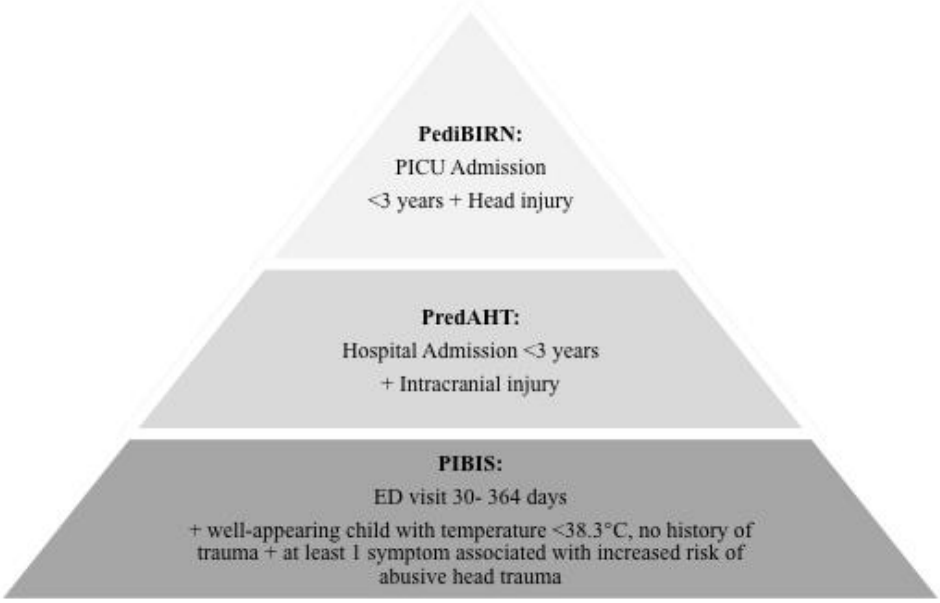


Figure 2: Focus of the clinical prediction rules: the pyramid represents the time point and population size where each CPredR is relevant



Abbreviations: ED emergency department, PediBIRN Pediatric Brain Injury Research Network, PIBIS Pittsburgh infant bran injury score, PICU Pediatric Intensive Care Unit, PredAHT tool Predicting Abusive Head Injury tool.

APPENDIX

Search Strategy: Ovid Medline
January 1996 – August 2016

1. exp Craniocerebral Trauma/di [Diagnosis]

2. exp Child Abuse/di [Diagnosis]

3. (prediction adj3 (tool* or score* or rule*)).tw,kf,hw.

4. exp decision support techniques/

5. mass screening/ or anonymous testing/ or multiphasic screening/

6. "reproducibility of results"/ or "sensitivity and specificity"/ or "predictive value of tests"/ or roc curve/

7. 1 and 2 and (3 or 4 or 5 or 6)

8. (abuse* or abusive or non-accidental).tw,kf,hw.

9. exp Craniocerebral Trauma/

10. (diagnos* or examination).tw,kf,hw.

11. magnetic resonance imaging/ or diffusion magnetic resonance imaging/ or echo-planar imaging/ or fluorine-19 magnetic resonance imaging/ or magnetic resonance angiography/ or magnetic resonance imaging, cine/ or exp tomography, x-ray/

12. (newborn* or neonat* or infan* or pre-schooler* or preschooler* or child* or adolescen* or pediatric* or paediatric* or youth* or teen or teens or teenage*).af.

13. 8 and 9 and (10 or 11) and (3 or 4 or 5 or 6) and 12

14. 1 and 8 and (3 or 4 or 5 or 6) and 12

15. 7 or 13 or 14

Appendix I: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Supplementary file
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5, Figure 1

Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5, Figure 1
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	NA
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	NA
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	NA

Appendix I: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8, Table 2
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	NA
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6-8
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	NA
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	NA

Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	NA
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	NA
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	NA
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	8-11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	11-12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	12
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	12

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097.
doi:10.1371/journal.pmed1000097

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