

## ORIGINAL ARTICLE

# Derivation of the children's head injury algorithm for the prediction of important clinical events decision rule for head injury in children

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**Background:** A quarter of all patients presenting to emergency departments are children. Although there are several large, well-conducted studies on adults enabling accurate selection of patients with head injury at high risk for computed tomography scanning, no such study has derived a rule for children.

**Aim:** To conduct a prospective multicentre diagnostic cohort study to provide a rule for selection of high-risk children with head injury for computed tomography scanning.

**Design:** All children presenting to the emergency departments of 10 hospitals in the northwest of England with any severity of head injury were recruited. A tailor-made proforma was used to collect data on around 40 clinical variables for each child. These variables were defined from a literature review, and a pilot study was conducted before the children's head injury algorithm for the prediction of important clinical events (CHALICE) study. All children who had a clinically significant head injury (death, need for neurosurgical intervention or abnormality on a computed tomography scan) were identified. Recursive partitioning was used to create a highly sensitive rule for the prediction of significant intracranial pathology.

**Results:** 22 772 children were recruited over 2½ years. 65% of these were boys and 56% were <5 years old. 281 children showed an abnormality on the computed tomography scan, 137 had a neurosurgical operation and 15 died. The CHALICE rule was derived with a sensitivity of 98% (95% confidence interval (CI) 96% to 100%) and a specificity of 87% (95% CI 86% to 87%) for the prediction of clinically significant head injury, and requires a computed tomography scan rate of 14%.

**Conclusion:** A highly sensitive clinical decision rule is derived for the identification of children who should undergo computed tomography scanning after head injury. This rule has the potential to improve and standardise the care of children presenting with head injuries. Validation of this rule in new cohorts of patients should now be undertaken.

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One million patients with head injuries attend emergency departments each year in the UK, of whom as many as 50% are children<sup>1–3</sup>; this proportion is similar in the US, where there are 95 000 hospital admissions from childhood head injuries, at a cost of over US\$ 1 billion per year.<sup>4–6</sup> In contrast with the high incidence of head injury, mortality is comparatively low (6–10 per 100 000), and as few as 1 in 500 of all people attending the emergency department have a fatal outcome.<sup>7–8</sup> Thus, although emergency physicians see a large number of patients with head injury, they rarely see patients who have life-threatening intracranial complications after the injury.

Over the past decade, several decision rules have been derived and validated using high-quality methods to identify adults with a head injury who require computed tomography scanning.<sup>9–14</sup> Although children account for as many as half of all head injuries, no such well-derived multicentre clinical decision rules exist for children. The American Academy of Pediatrics in 1999<sup>14a</sup> concluded that they could not advocate an evidence-based computed tomography scanning strategy because of the poor quality of studies on children.<sup>15</sup> In 2003, The National Institute of Clinical Excellence in the UK found that the quality of studies on childhood head injuries was so poor that they issued a clinical decision rule for children that was derived and validated only in adults.<sup>16</sup>

Our aim was to derive a sensitive clinical decision rule for the management of children presenting with an acute head

injury, which would identify children at high risk so as to undergo computed tomography scanning and allow the remaining patients to be discharged with no investigation.

## METHODS

### Study setting and population

A prospective diagnostic cohort study was undertaken from February 2000 to August 2002, which aimed to recruit all patients <16 years presenting with head injury, who attended the emergency departments of 10 hospitals in the northwest of England. Three of these hospitals were children's hospitals, three were teaching hospitals and four were district general hospitals.

### Inclusion criteria

Clinical symptoms and signs in young children can be unreliable, and therefore there is no universally agreed category of "trivial" head injury for which there is no risk of a major intracranial complication. Our inclusion criteria for this study were therefore as wide as possible. Any patient with a history or signs of injury to the head was eligible for inclusion into the study. In particular, loss of consciousness (LOC) or amnesia was not a requirement for entry. We also

**Abbreviations:** CHALICE, children's head injury algorithm for the prediction of important clinical events; LOC, loss of consciousness; RCS, Royal College of Surgeons; SXR, skull radiograph

wanted to reflect the whole population with head injuries attending emergency departments and thus did not exclude patients with a head injury that may have been defined as "moderate or severe". The only exclusion criterion was refusal to consent to entry into the study.

### Standardised patient assessment

A specifically designed proforma was created for data collection. This proforma collected data on around 40 clinical variables pertaining to head injury, including variables on the mechanism of injury, symptoms, signs and management of the patient. Every doctor who participated in the study was given a 1-h training session on the study and the use of this proforma for data collection. Primary assessment of all patients who were eligible for our study was conducted using this proforma. This proforma also functioned as the patient's clinical record on admission.

Response rates and quality of completion were monitored in all centres on a monthly basis to ensure high compliance. All doctors were asked to follow the 1999 Royal College of Surgeons (RCS) guidelines for the management of head injuries,<sup>17</sup> and the guidelines were printed clearly on the front of every proforma.

### Outcome measures

The primary outcome measure was a composite comprising death as a result of head injury, requirement for neurosurgical intervention or marked abnormalities on the computed tomography scan (together referred to as "clinically significant intracranial injury"). In contrast with studies on adults where consensus has been reached as to the nature of what constitutes a clinically important brain injury, no consensus has been reached regarding children in studies either in the

US or in the UK.<sup>9, 16</sup> We defined the computed tomography outcome measure as any new, acute, traumatic intracranial pathology as reported by the consultant radiologist, including intracranial haematomas of any size, cerebral contusion, diffuse cerebral oedema and depressed skull fractures. Simple or non-depressed skull fractures alone were not considered to be significant. Secondary outcome measures were the presence of a skull fracture or admission to hospital.

All patients who were documented as having had a skull radiograph, admission to hospital, computed tomography scanning or neurosurgery were followed up. Radiology departments across the 10 hospitals in the study and also from two further tertiary neurosurgical referral centres in the northwest of England (The Walton Centre, Liverpool, and Pendlebury Hospital, Manchester) collated data separately on every child who had a skull radiograph or computed tomography scan of the brain. In addition, hospitals prospectively collated data on patients who were admitted, underwent neurosurgery, stay in the intensive care unit or neurorehabilitation from these 12 centres. These data were then cross-checked with those in the database of the children's head injury algorithm for the prediction of important clinical events (CHALICE). The Office of National Statistics provided us with the details of children in the UK who died, in whom head injury was any part of the cause of death.

### Ethical approval

Multicentre ethical approval was obtained for this study. Verbal consent to participate in this study was obtained from all patients or guardians before entry into the study. The doctor who obtained consent indicated acceptance on the proforma.

### Statistical analysis

Sample size that would allow us to derive, with an 80% power, a clinical decision rule with 100% sensitivity and a lower confidence limit >95% was initially calculated. This required 75 patients with a positive outcome; thus, at an incidence of 1% for clinically significant brain injury, we required 7500 patients and a 1-year study. At interim

**Table 1** Demographics of the children's head injury algorithm for the prediction of important clinical events study (n = 22 772)

Clinical variable	Patients n (%)
Age*	
0-6 months	852 (3.7)
6 months-1 year	1600 (7.0)
1-2 years	3777 (16.6)
2-5 years	6492 (28.5)
5-11 years	6577 (28.9)
11-16 years	3340 (14.7)
Sex†	
Male:female	14767 (64.8):7941 (34.9)
LOC	
Any LOC	1185 (5.2)
LOC >1 min	524 (2.3)
LOC >5 min	213 (0.9)
Amnesia	
Any amnesia	720 (3.2)
Amnesia 1 min	488 (2.1)
Amnesia >5 min	288 (1.3)
Vomiting	
≥1	2498 (11)
≥2	1418 (6.2)
≥3	857 (3.8)
Headache	
Any headache	4783 (21)
Severe headache	95 (0.4)
GCS	
15	21996 (96.6)
14	229 (1.0)
13	73 (0.3)
<13	193 (0.9)
Doctor unable to determine GCS	281 (1.2)

GCS, Glasgow Coma Score; LOC, loss of consciousness.

\*134 (0.6%) patients had undocumented category.

†64 (0.3%) patients had undocumented category.

**Table 2** Patient management and outcomes (n = 22 772)

	Patients
SXR taken	5318 (23.4)
Skull fracture on SXR	259 (1.1)
Skull fracture on SXR or CT	421 (1.9)
Linear fracture	233 (1.0)
Complex fracture	36 (0.2)
Depressed fracture	80 (0.4)
Basilar fracture	67 (0.3)
Intracranial air	57 (0.3)
CT scanning carried out	766 (3.3)
Abnormality on CT scan	281 (1.2)
Epidural haematoma	91 (0.4)
Subdural haematoma	54 (0.2)
Cerebral contusion	83 (0.4)
Subarachnoid haemorrhage	28 (0.1)
Cerebral oedema	58 (0.3)
Admission	1461 (6.4)
Length of stay*	3.5, 1 (1-95) days
Length of stay with normal CT*	1.8, 1 (1-33) days
Length of stay with abnormal CT*	10.7, 6 (1-95) days
Neurosurgical operation	137 (0.6)
Intubation or ICP monitoring	157 (0.7)
Mortality	15 (0.1)

Values are n (%) unless otherwise mentioned.

CT, computed tomography; ICP, intracranial pressure; SXR, skull radiograph.

\*Values are mean, median (range).

analysis, patients who were difficult to predict were identified and thus the study was extended to keep the lower confidence interval >95%.

Univariate analysis was carried out using Fisher’s exact test for binomial categorical data or the  $\chi^2$  test for unranked categorical data. Non-parametric rank data or continuous data were analysed using the Mann–Whitney U test, and unpaired Student’s t test was used for continuous data with a normal distribution. Interobserver agreement for each variable was calculated using the  $\kappa$  coefficient—that is, the proportion of potential agreement beyond chance—along with its 95% confidence interval (CI) in a subset of patients. In this subset from two centres, patients were seen twice by clinicians in the study and their results were compared. A weighted  $\kappa$  was calculated for rank variables.<sup>18 19</sup>

Variables that were both reproducible ( $\kappa > 0.6$ ) and associated with the outcome measure ( $p < 0.1$ ) were assessed by multivariate analysis using recursive partitioning. The primary objective of the multivariate analysis was to find the best combinations of predictor variables that were highly sensitive for detecting the presence of a clinically significant intracranial injury, while achieving the maximum possible specificity.

Our experience and that of other groups<sup>9 20</sup> suggest that recursive partitioning may be more suitable than logistic regression when the objective is to correctly classify one outcome at the expense of the other—that is, when high sensitivity is more important than specificity.

Univariate analysis was carried out using SPSS V.11.5 and recursive partitioning using CART V.4.0 (Salford Systems, San Diego, California, USA), using the GINI splitting rule with a 3 to 1 weighting against misclassification of positive intracranial pathology.

**RESULTS**

In all, 22 772 patients were enrolled into the study, of whom 12 471 were from children’s hospitals, 3241 from teaching hospitals and 7060 from district general hospitals. In all, 65% of these were boys and 56% were <5 years old (table 1). The mean age was 5.7 years. Out of 744 computed tomography

scans, scans of 281 (1.2%) patients showed an abnormality (3.2% of the cohort, of which 37.7% showed abnormality). In all, 1461 (6.4%) children were admitted, 137 (0.6%) had a neurosurgical operation and 15 children died.

In all 5318 skull radiographs (SXR) were taken, from which 259 skull fractures were diagnosed after radiologist reporting (table 2). However, 44 (17%) fractures were missed by emergency physicians and 59 (1% of normal radiographs) fractures diagnosed by emergency physicians were normal, giving a correlation between radiologists and emergency physicians of  $\kappa = 0.80$ . Ninety eight patients with abnormality on computed tomography scan also had an SXR. SXRs reported by emergency physicians had a sensitivity of 77% (95% CI 67% to 85%, 75 fractures in 98 patients) for the prediction of positive pathology on computed tomography scanning.

Doctors were asked to use the 1999 RCS guidelines for the management of head injuries. These guidelines recommend all patients at high risk to be admitted, with computed tomography scanning for those with the highest risk. This protocol resulted in 1461 admissions, but 10 patients were sent home before returning and proving to have an abnormality on the computed tomography scan. Also, another two patients were admitted for a brief time and sent home without being scanned, only to return with intracranial pathology shown on the subsequent computed tomography scan. Of these 12 patients, seven required neurosurgery. Two patients with intracranial pathology who were discharged presented to a different hospital on their second attendance. Of patients who were admitted for observation without immediate computed tomography scanning, 27 patients deteriorated on the ward and 24 of these patients required neurosurgery. Table 2 gives the full details of radiographic and admission demographics.

Univariate analysis was carried out using the primary outcome measure. Table 3 gives the univariate analysis of those variables selected in the final model. The full analysis of the association between all clinical variables and primary outcome is available online at <http://www.archdischild.com/supplemental>. All variables that showed a univariate relationship with  $p < 0.1$  were entered into multivariate analysis.

**Table 3** Association between significant clinical variables and primary outcome

Finding	Total (%) (n = 22 772)	Negative for clinically significant intracranial pathology (n = 22 491)	Positive for clinically significant intracranial pathology (n = 281)	p Value	Positive predictive value
<b>History</b>					
LOC > 5 min	213 (0.9)	118 (0.5)	95 (34)	<0.001	0.45
Amnesia > 5 min	288 (1.3)	226 (1.0)	62 (22)	<0.001	0.22
Drowsiness	949 (4.2)	889 (4.0)	60 (21)	<0.001	0.063
Vomiting $\geq 3$ times	857 (3.8)	801 (3.6)	56 (20)	<0.001	0.065
Suspicion of NAI	61 (0.3)	41 (0.2)	20 (7.1)	<0.001	0.33
Seizure after head injury (in patients without epilepsy)	96 (0.4)	68 (0.3)	28 (10)	<0.001	0.29
<b>Examination</b>					
GCS < 14	266 (1.2)	137 (0.6)	129 (46)	<0.001	0.48
GCS < 15 if age < 1 year	79 (0.3)	71 (0.3)	8 (2.8)	<0.001	0.10
Penetrating or depressed skull injury suspected or tense fontanelle	104 (0.5)	58 (0.3)	46 (16)	<0.001	0.44
Base of skull fracture suspected	536 (2.4)	451 (2.0)	85 (30)	<0.001	0.16
Positive focal neurology	150 (0.7)	96 (0.4)	54 (19)	<0.001	0.36
Presence of bruise/swelling or laceration > 5 cm in children aged < 1 year	52 (0.2)	46 (0.2)	6 (2.1)	<0.001	0.12
<b>Mechanism</b>					
High-speed RTA	204 (0.9)	117 (0.5)	87 (31)	<0.001	0.43
Fall > 3 m	129 (0.6)	103 (0.5)	26 (9.3)	<0.001	0.20
High-speed injury from projectile or object	456 (2.0)	438 (1.9)	18 (6.4)	<0.001	0.039

GCS, Glasgow Coma Score; LOC, loss of consciousness; NAI, non-accidental injury; RTA, road traffic accident.

The common clinical variables with unknown reproducibility were analysed in a subset of the CHALICE study. In all, 412 patients had their clinical condition assessed in this way. Good agreement was found for LOC ( $\kappa = 1$ , 95% CI 0.84 to 1), amnesia ( $\kappa = 0.93$ , 95% CI 0.79 to 1) and vomiting ( $\kappa = 0.94$ , 95% CI 0.81 to 1), but headache showed poor correlation ( $\kappa = 0.39$ , 95% CI 0.25 to 0.54) and was rejected from multivariate modelling owing to its poor predictive ability.

Recursive partitioning analysis produced a highly sensitive model, (see box). As shown in the clinical utility analysis (table 4), this model has an overall sensitivity of 98% (95% CI 96% to 100%) and an overall specificity of 87% (95% CI 86% to 87%). Our model misses only four patients, of whom two had depressed skull fractures that the physician did not suspect on examination, but on reattendance subsequent physicians documented that the depressions were easily palpable. The third patient had an unwitnessed fall against a wall. Initial examination found no high-risk variables and the patient was discharged, but the patient returned 2 h later, vomiting. He was admitted overnight, and the scan the next morning showed an epidural haematoma that required neurosurgery. The fourth patient had a fall into a stream from a swing, and had brief amnesia and a moderate headache. He was discharged but returned 11 days later with a persisting headache. A linear skull fracture and a small subdural and epidural haematoma were found that required no treatment.

## DISCUSSION

We have successfully derived a highly sensitive clinical decision rule for the prediction of clinically significant intracranial pathology in children according to strict methodological standards, in the world's largest prospective cohort of children with head injuries. This rule, if validated, will enable clinicians to request computed tomography scans for their patients on the basis of strong evidence in children.

If our rule is subsequently validated, we believe that patients regarded as high risk should undergo computed tomography scanning to look for intracranial pathology, whereas those with a normal scan might be regarded as low risk. Children who are regarded as low risk by a validated rule should be carefully counselled so that they understand the high-risk symptoms for which they should return. Although the CHALICE rule will increase the rate of computed tomography scanning, we envisage that the admission rate could be markedly reduced and thus the cost implications of our rule could be neutral. This remains to be shown in further studies.

Any decision rule that is to be of value to clinicians seeing undifferentiated children with head injury must be applicable to all such children. At study design stage it was important to take a pragmatic approach to this requirement, as it was clear that the rate of significant events was low and that it would be unethical to expose large numbers of children to unnecessary major radiation exposure. A balance needed to be struck between inclusion bias (selecting only children who already fulfilled some existing rule, which indicated that they should undergo computed tomography scanning) and the ethical limits that would be placed on the study. Thus, a composite end point was agreed and ethically approved. This involved the identification of all children who died, had neurosurgical intervention or had abnormalities on a computed tomography scan. This composite end point was reinforced with a prospective, thorough follow-up strategy, which was designed to ensure that no children who died as a result of their head injury or who had late neurosurgical intervention were missed. Although this approach can be criticised because some children with abnormalities on the computed tomography scan may not have been identified as

## The children's head injury algorithm for the prediction of important clinical events rule

A computed tomography scan is required if any of the following criteria are present.

### ● History

- Witnessed loss of consciousness of >5 min duration
- History of amnesia (either antegrade or retrograde) of >5 min duration
- Abnormal drowsiness (defined as drowsiness in excess of that expected by the examining doctor)
- $\geq 3$  vomits after head injury (a vomit is defined as a single discrete episode of vomiting)
- Suspicion of non-accidental injury (NAI, defined as any suspicion of NAI by the examining doctor)
- Seizure after head injury in a patient who has no history of epilepsy

### ● Examination

- Glasgow Coma Score (GCS) <14, or GCS <15 if <1 year old
- Suspicion of penetrating or depressed skull injury or tense fontanelle
- Signs of a basal skull fracture (defined as evidence of blood or cerebrospinal fluid from ear or nose, panda eyes, Battles sign, haemotympanum, facial crepitus or serious facial injury)
- Positive focal neurology (defined as any focal neurology, including motor, sensory, coordination or reflex abnormality)
- Presence of bruise, swelling or laceration >5 cm if <1 year old

### ● Mechanism

- High-speed road traffic accident either as pedestrian, cyclist or occupant (defined as accident with speed >40 m/h)
- Fall of >3 m in height
- High-speed injury from a projectile or an object

If none of the above variables are present, the patient is at low risk of intracranial pathology.

they did not undergo such scanning, it has considerable strength in that children with both immediate or late significant events are included. Thus, it can be assumed that any undiagnosed abnormalities on the computed tomography scan were clinically non-significant. We believe that this method is superior to the alternative one of telephoning each patient 2 weeks after admission, and previous studies have been criticised for their inability to contact all patients for follow-up.<sup>9 21</sup>

We do not believe that there is considerable circularity between the clinical care drivers during the study and the findings as stated in the CHALICE rule. In particular, the recommendations of the RCS<sup>17</sup> differ from those of the CHALICE in that a major indication for computed tomography in a district general hospital as per the RCS guidance is fracture on the SXR. CHALICE has looked critically at both the indications for SXR and the computed tomography scan in detail, and distilled from a long list (table A available at <http://www.archdischild.com/supplemental>) those that truly

**Table 4** Clinical utility of the children’s head injury algorithm for the prediction of important clinical events rule

	No clinically significant head injury	Clinically significant head injury	Total
CHALICE negative	19 558	4	19 562
CHALICE positive	2 933	277	3 210
Total	22 491	281	22 772
Sensitivity	98.6%	(96.4% to 99.6%)	
Specificity	86.9%	(86.5% to 87.4%)	
Positive predictive value	8.63%	(7.68% to 9.65%)	
Negative predictive value	99.9%	(99.9% to 100%)	
CT ordering rate	14.1%	(13.6% to 14.6%)	

Performance of CHALICE rule for patients with GCS 13–15

	No significant intracranial pathology	Significant intracranial pathology	Total
CHALICE negative	19 558	4	19 562
CHALICE positive	2 853	164	3 017
Total	22 411	168	22 579
Sensitivity	97.6%	(94.0% to 99.4%)	
Specificity	87.3%	(86.8% to 87.7%)	
Positive predictive value	5.44%	(4.65% to 6.31%)	
Negative predictive value	99.9%	(99.9% to 100%)	
CT ordering rate	13.3%	(12.9% to 13.8%)	

Performance of CHALICE rule for prediction of neurosurgical intervention

	No neurosurgical intervention	Neurosurgical intervention	Total
CHALICE negative	19 559	3	19 562
CHALICE positive	3 076	134	3 210
Total	22 635	137	22 772
Sensitivity	97.8%	(93.7% to 99.6%)	
Specificity	86.4%	(86.0% to 86.9%)	

CHALICE, children’s head injury algorithm for the prediction of important clinical events; CT, computed tomography; GCS, Glasgow Coma Score. Values in parentheses are 95% CI.

indicate the likelihood of clinically significant intracranial injury (the composite outcome). It is not surprising that some of the CHALICE rules support previous expert opinion. Perhaps it would be more surprising if it did not.

Our study has other limitations. Clinicians were not always blinded to the outcome of the computed tomography scan before completing the proforma. Although clinicians completed most proformas on the first clinical examination, they were reminded at a later date if they did not do this. Our proforma was also the clinical record sheet and, thus, compliance was generally high. However, we do not have data on the number of missed patients that could have been eligible. Finally, our study is only a derivation study and it should now be prospectively validated, with its reproducibility, acceptability, usability and economic effect evaluated across multiple sites.

Few studies have successfully derived a clinical decision rule applicable to all children from a large cohort of patients. Palchak *et al*<sup>23</sup> in 2003 derived a rule on examining 2043 patients from a single hospital, aged <18 years, who had had head trauma and showed positive findings on history or clinical examination such as LOC, amnesia, vomiting or headache. Of nine predictive variables assessed, abnormal mental status, clinical signs of skull fracture, history of vomiting, scalp haematoma (in children aged ≤2 years) or headache identified 96 of 98 patients with positive intracranial pathology on computed tomography scanning (98% sensitivity, 95% CI 93% to 100%).

Greenes and Schutzman<sup>23</sup> conducted a prospective study on 608 patients aged <2 years in a single hospital.<sup>23</sup> Their results support our finding that children with suspected non-accidental injury, history of lethargy or a major scalp

haematoma had an increased risk of significant intracranial injury. In addition, they found that LOC, seizures or vomiting alone was not adequate to predict intracranial injury, and that the absence of clinical symptoms or signs did not fully exclude the possibility of uncovering positive pathology. Together with a systematic review by the American Academy of Pediatrics and expert consensus, these authors formalised this study by producing guidelines for head injuries in children <2 years old.<sup>24</sup> They allocated patients into four risk groups, with computed tomography scanning recommended in the highest risk group of children who vomited >3 times or had an LOC, a history of lethargy, a high-risk mechanism or considerable bruising. Although these guidelines agree with many of our recommendations, including the suggestion that patients are safe for discharge after a negative finding on a computed tomography scan, like ours, their guidelines have not yet been validated in other hospitals.

Haydel and Shembekar<sup>25</sup> in 2003 assessed the New Orleans criteria<sup>13</sup> in children aged >5 years. They assessed 175 children with GCS 15 from a single institution and concluded that the 14 positive computed tomography scans that they found could be identified by their rule, which was derived from and validated in scans of adults.

The National Institute of Clinical Excellence, UK, systematically reviewed all studies on head injury up to 2002. They concluded that no studies on childhood head injury could be used to construct a robust rule, and advocated extrapolating the Canadian CT head rule for children. We assessed the performance of this rule in children,<sup>26</sup> extending our previous work to the full database. We found that the sensitivity was 94% (95% CI 91% to 97%) and the specificity was 89% (95% CI 89% to 90%), with a computed tomography ordering rate

of 12%. Sixteen patients would have been missed if this rule had been strictly applied to our database. Thus, we conclude that the CHALICE rule is safer than extrapolating an adult head injury guideline to children without a considerably increased computed tomography ordering rate. We also found that the RCS guidelines were being poorly applied to children, with half the radiographs, admissions and computed tomography scans recommended by the RCS guidelines not being carried out.<sup>26</sup>

Many of the variables identified as significant in our study have also been identified in a meta-analysis of clinical variables identified from 16 papers in the paediatric literature.<sup>27</sup> Focal neurology, seizures, LOC and abnormal GCS were all major predictors, but headache was found not to considerably predict significant intracranial pathology.

Although computed tomography scanning is a safe procedure for those who are able to comply with the investigation, young children may require sedation, which is not without complications.<sup>28</sup> Occasionally, the risk of the investigation should be balanced with the possibility of delayed diagnosis with observation alone in children who have been identified as high risk by our rule.

Finally, we do not support the continued use of SXR for children with acute head injury, except for highly selected patients who may have had non-accidental injury. Although many studies have found that the evidence of a fracture on SXR markedly increases the incidence of intracranial pathology,<sup>29–31</sup> we agree with other studies that the SXR has a poor sensitivity for identifying patients with intracranial pathology, that fractures are identified on only a small number of radiographs and that fractures are easily missed by those interpreting the radiographs.<sup>32</sup> We thus advocate that a clear decision rule (such as the CHALICE rule) that uses clinical variables alone and that identifies children at high risk of significant intracranial injury for computed tomography scanning is the optimal rule for the management of head injuries in children.

## CONCLUSION

The CHALICE rule, derived from 22 772 children attending the emergency departments of 10 hospitals in the UK, may provide a comprehensive clinical decision rule for the management of head injuries in children that identifies patients at risk of significant intracranial pathology. Validation studies are now needed.

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**Competing interests:** None.

## What is already known on this topic

- 1 in 500 children with a minor head injury will have serious intracranial complications.
- Clinical guidelines extrapolated from adult guidelines and expert consensus are currently available to identify these patients in the emergency department.

## What this study adds

- The CHALICE rule identifies children at high risk of serious intracranial complications following a head injury.
- The CHALICE rule is the first head injury decision rule derived entirely from prospective multicentre data from head injuries in children. The CHALICE database is the world's largest prospective cohort study in childhood head injuries with 22 772 children studied from 10 centres.

This paper conforms to the STARD guidelines for reporting of diagnostic cohort studies.

**Contributors:** JD was the lead researcher, and led the study and prepared the manuscript. KM-J conceived the project, obtained funding, supervised the research, and oversaw and supervised its conduct. JPD created the proforma and supervised data collation. J-PL carried out the analysis for interobserver agreement. FL and JB organised the multi-centre participation and supervised its conduct. All authors had access to all study data and participated in manuscript preparation and checking.

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**Table 6 for E-journal inclusion :****Association between all clinical correlates and CT results.**

<b>Finding</b>	<b>Total (%)</b>	<b>Negative CT scan (%)</b>	<b>Positive CT scan (%)</b>	<b>P-value</b>
	<b>(N=22,772)</b>	<b>(N=22,491)</b>	<b>(N=281)</b>	
<b>Age</b>				
0-6mths	852 (3.8)	841 (3.8)	11 (3.9)	
6mths – 1 year	1600 (7.1)	1589 (7.1)	11 (3.9)	
1 year – 2 years	3777 (17)	3758 (17)	19 (6.8)	
2 years – 5 years	6492 (29)	6468 (29)	24 (9)	
5 years–11 years	6577 (29)	6473 (29)	104 (37)	
11 years-16years	3340 (15)	3228 (14)	112 (40)	P<0.001
Missing	134 (0.6)			
<b>Sex</b>				
Male	14767 (65)	14568 (65)	199 (71)	
Female	7941 (35)	7859 (35)	82 (29)	P=0.024
Missing	64 (0.3)			
<b>Hours since incident</b>				
0-3hrs	14937 (76)	14705 (76)	232 (86)	
3-6hrs	2984 (15)	2977 (15)	7 (2.6)	
6-12hrs	591 (3)	582 (3)	9 (3.3)	
12-24hrs	511 (2.6)	501 (2.6)	10 (3.7)	
24-48hrs	307 (1.6)	305 (1.6)	2 (0.7)	
>48hrs	290 (1.5)	280 (1.4)	10 (3.7)	P<0.001
Missing	3152 (14)			
<b>Type of accident</b>				
RTA occupant	189 (0.8)	175 (0.8)	14 (5.0)	P<0.001
RTA cyclist	786 (3.5)	743 (3.3)	43 (15)	P<0.001
RTA pedestrian	372 (1.6)	293 (1.3)	79 (28)	P<0.001
Any type of RTA	1347 (5.9)	1211(5.4)	136 (48)	P<0.001
Fall from a height	4506 (20)	4451 (20)	55 (20)	P=0.994
0-1m	2230 (9.8)	2226 (9.9)	4 (1.4)	P<0.001
1-2m	1809 (7.9)	1797 (8.0)	12 (4.3)	P=0.024
2-3m	330 (1.4)	317 (1.4)	13 (4.6)	P<0.001
>3m	124 (0.5)	98 (0.4)	26 (9.3)	P<0.001
Slip/Trip/Fall	12058 (53)	12025 (54)	33 (12)	P<0.001
Hit by projectile/object	2361 (10)	2328 (10)	33 (12)	P=0.435
Assault	933 (4)	923 (4)	10 (3.6)	P=0.763
Other mechanism	1525 (6.7)	1512 (6.7)	13 (4.6)	P=0.191
Fall down stairs	1202 (5.3)	1194 (5.3)	8 (2.8)	P=0.079
Child dropped	398 (1.7)	390 (1.7)	8 (2.8)	P=0.163
<b>Speed of injury</b>				
Slow	14345 (63)	14306 (64)	39 (14)	
Medium	6815 (30)	6729 (30)	86 (32)	

Fast	1455 (6.4)	1307 (5.8)	148 (54)	P<0.001
Missing	157 (0.7)			
Other death at incident	10 (0.1)	5 (0.1)	5 (1.8)	P<0.001
Unwitnessed injury	936 (4.1)	886 (3.9)	50 (18)	P<0.001
<b>Agent</b>				
Broad/Hard	11652 (52)	11451 (51)	201 (74)	
Broad/Soft	2478 (11)	2463 (11)	15 (5.5)	
Localised/Hard	8124 (36)	8067 (36)	57 (21)	
Localised/Soft	391 (1.7)	391 (1.7)	0 (0)	P<0.001
Missing	127 (0.6)			
<b>Loss of Consciousness</b>				
Any LOC	1185 (5.2)	1041 (4.6)	144 (51)	P<0.001
LOC >1min	524 (2.3)	400 (1.8)	124 (44)	P<0.001
LOC>5mins	213 (0.9)	118 (0.5)	95 (34)	P<0.001
Any amnesia	720 (3.2)	651 (2.9)	69 (25)	P<0.001
<b>Amnesia</b>				
Amnesia>1min	488 (2.1)	419 (1.9)	69 (25)	P<0.001
Amnesia >5mins	288 (1.3)	226 (1.0)	62 (22)	P<0.001
Any LOC or amnesia	1502 (6.6)	1340 (6.0)	162 (58)	P<0.001
LOC or Amnesia >5mins	418 (1.8)	291 (1.3)	125 (45)	P<0.001
<b>Vomiting</b>				
Any vomiting	2498 (11)	2383 (10)	115 (41)	P<0.001
Vomiting 2 or more times	1418 (6.2)	1336 (5.9)	82 (29)	P<0.001
Vomiting 3 or more times	857 (3.8)	801 (3.6)	56 (20)	P<0.001
<b>Headache</b>				
Headache Mild	3972 (19)	3960 (19)	12 (5.0)	
Headache Moderate	716 (3.4)	688 (3.3)	28 (12)	
Headache Severe	95 (0.4)	78 (0.4)	17 (7.1)	P<0.001
<b>Symptoms</b>				
Vertigo/Dizziness	644 (2.8)	630 (2.8)	14 (5.0)	P=0.043
Drowsiness	949 (4.2)	889 (4.0)	60 (21)	P<0.001
Nausea/not feeding	615 (2.7)	601 (2.7)	14 (5.0)	P=0.025
Hearing loss	23 (0.1)	22 (0.1)	1 (0.4)	P=0.249
Visual symptoms	242 (1.1)	238 (1.1)	4 (1.4)	P=0.547
Disorientation/Abnormal Behaviour	234 (1.0)	193 (0.9)	41 (15)	P<0.001
Alcohol or drug intoxication	48 (0.2)	35 (0.2)	13 (4.6)	P<0.001
Seizure	109 (0.5)	81 (0.4)	28 (10)	P<0.001
Difficulty taking history	255 (1.1)	248 (1.1)	7 (2.5)	P=0.040
<b>Examination</b>				
Bruising mean (SD)	1.3 (1.3)	1.3 (1.3)	3.5 (1.8)	P<0.001
Swelling mean (SD)	1.3(1.4)	1.3 (1.4)	4.0 (1.7)	P<0.001
Laceration mean (SD)	0.9 (1.0)	0.9 (1.0)	2.7 (1.7)	P<0.001

Bruise/Swelling/Laceration >5cm in under 1 year old	52 (0.2)	46 (0.2)	6 (2.1)	P<0.001
<b>Depth of Injury</b>				
Superficial	13189 (90)	13155 (91)	34 (23)	P<0.001
Deep injury	991 (6.8)	964 (6.7)	27 (18)	P<0.001
Injury down to bone	430 (2.9)	344 (2.4)	86 (59)	P<0.001
<b>Type of Injury</b>				
Facial injury	5212 (23)	5167 (23)	45 (16)	P=0.006
Frontal injury	8291 (36)	8200 (37)	91 (32)	P=0.171
Parietal injury	2216 (9.7)	2158 (9.6)	58 (22)	P<0.001
Temporal injury	1100 (4.8)	1048 (4.7)	52 (19)	P<0.001
Occipital injury	3429 (15)	3390 (15)	39 (14)	P=0.610
Vertex injury	600 (2.6)	590 (2.6)	10 (3.6)	P=0.343
Suspected penetrating injury	49 (0.2)	38 (0.2)	11 (3.9)	P<0.001
Depressed skull fracture	57 (0.3)	18 (0.1)	39 (14)	P<0.001
Tense fontanelle	4 (0.1)	2 (0.1)	2 (0.7)	P=0.001
Suspect major head injury (penetrating injury, depressed skull fracture, fontanelle)	104 (0.5)	58 (0.3)	46 (16)	P<0.001
Blood from ear or nose	464 (2)	402 (1.8)	62 (22)	P<0.001
CSF from ear or nose	36 (0.2)	20 (0.1)	16 (5.7)	P<0.001
Serious facial injury	33 (0.1)	22 (0.1)	11 (3.9)	P<0.001
Facial crepitus	3 (0.1)	0	3 (1.1)	P<0.001
Panda eyes	38 (0.2)	20 (0.1)	18 (6.4)	P<0.001
Haemotympanum	20 (0.1)	11 (0.1)	9 (3.2)	P<0.001
Battle's sign	12 (0.1)	10 (0.1)	2 (0.7)	P=0.009
Suspect basal skull fracture(blood or CSF/nose/ear, serious facial injury or crepitus, panda eyes or haemotympanum)	536 (2.4)	451 (2.0)	85(30)	P<0.001
Other major trauma	126 (0.6)	73 (0.3)	53 (19)	P<0.001
Suspect Non-accidental injury	61 (0.3)	41 (0.2)	20 (7.1)	P<0.001
No responsible adult available to supervise pt at home	8 (0.1)	8 (0.1)	0	P=0.905
Child on protection register	16 (0.1)	13 (0.1)	3 (1.1)	P=0.001
Learning disability	102 (0.4)	98 (0.4)	4 (1.4)	P=0.038
History of neurosurgery	29 (0.1)	27 (0.1)	2 (0.7)	P=0.050
Coagulopathy	14 (0.1)	14 (0.1)	0	P=0.840
History of Epilepsy	50 (0.2)	48 (0.2)	2 (0.7)	P=0.127
Other relevant past medical History	142 (0.6)	135 (0.6)	7 (2.5)	P=0.002
<b>Glasgow Coma Score</b>				
GCS<15	495 (2.2)	339 (1.5)	156 (56)	P<0.001
GCS<14	266 (1.2)	137 (0.6)	129 (46)	P<0.001
GCS<13	193 (0.8)	80 (0.4)	113 (40)	P<0.001
GCS<15 if age <1 year	79(0.3)	71 (0.3)	8(2.8)	P<0.001

Mean GCS score (S.D.)	15 (0.68)	15 (0.38)	12 (3.9)	P<0.001
Mean Eyes GCS (S.D.)	4.0 (0.21)	4.0 (0.13)	3.1 (1.2)	P<0.001
Mean Motor GCS (S.D.)	6.0 (0.24)	6.0 (0.14)	5.0 (1.5)	P<0.001
Mean Voice GCS (S.D.)	5.0 (0.29)	5.0 (0.18)	3.7 (1.6)	P<0.001
Number of pts under 1 with GCS unobtainable	189 (7.7)			
Number of pts age 1-2 with GCS unobtainable	53 (1.4)			
Number of pts over 2 years of Age with GCS unobtainable	39 (0.2)			
<b>Focal Neurology</b>				
Pupils not equal and reactive	81 (0.4)	48 (0.2)	33 (12)	P<0.001
Papilloedema	12 (0.1)	5 (0.1)	7 (2.5)	P<0.001
Nystagmus	12 (0.1)	8 (0.1)	4 (1.4)	P<0.001
Motor weakness	35 (0.2)	20 (0.1)	15 (5.3)	P<0.001
Sensory weakness	8 (0.1)	6 (0.1)	2 (0.7)	P=0.004
Abnormal reflexes	3 (0.1)	3 (0.1)	0	P=1
Abnormal co-ordination	7 (0.1)	6 (0.1)	1 (0.4)	P=0.083
Any focal neurology (Pupils, papilloedema, nystagmus, motor, sensory, reflex, coordination weakness )	150 (0.7)	96 (0.4)	54 (19)	P<0.001

Appendix 1

STARD Checklist

Section and topic	Item	Describe	Reported on page #
TITLE/ABSTRACT/ KEYWORDS	1	The article as a study on diagnostic accuracy (recommend MeSH heading 'sensitivity and specificity')	Page 33
INTRODUCTION	2	The research question(s), such as estimating diagnostic accuracy or comparing accuracy between tests or across participant groups	Aim stated on page 5
<b>METHODS</b>			
<i>Participants</i>	3	The study population: the inclusion and exclusion criteria, setting(s) and location(s) where the data were collected	Page 5
	4	Participant recruitment: was this based on presenting symptoms, results from previous tests, or the fact that the participants had received the index test(s) or the reference standard?	Inclusion criteria stated in Methods page 5
	5	Participant sampling: was this a consecutive series of patients defined by selection criteria in (3) and (4)? If not specify how patients were further selected.	Consecutive series stated in Methods 5 ( all patients in the North-west recruited
	6	Data collection: were the participants identified and data collected before the index test(s) and reference standards were performed (prospective study) or after (retrospective study)?	Proforma details in Methods section page 6
<i>Reference standard</i>	7	The reference standard and its rationale	Gold standard for positive and hegative outcome for significant intracranial pathology stated in detail page 6-7
<i>Test methods</i>	8	Technical specification of material and methods involved including how and when measurements were taken, and/or cite references for index test(s) and reference standard	Stated pages 5-7
	9	Definition and rationale for the units, cutoffs and/or categories of the results of the index test(s) and the reference standard	Definition of Significant intracranial pathology given in methods from page 5
	10	The number, training and expertise of the persons (a) executing and (b) reading the index test(s) and the reference standard	Positive CT scan as reported by consultant radiologist stated in

			page 5 , additional clinican details given in methods
	11	Whether or not the reader(s) of the index test(s) and reference standard were blind (masked) to the results of the other test(s) and describe any information available to them	Readers were not blind to the clinical status of the patient but this is clear in the context of the study.
<i>Statistical methods</i>	12	Methods for calculating measures of diagnostic accuracy or making comparisons, and the statistical methods used to quantify uncertainty (e.g. 95% confidence intervals)	All statistical tests given in Methods , page 7
	13	Methods for calculating test reproducibility, if done	Methods for Kappa coefficient given from page 7
<b>RESULTS</b>			
<i>Participants</i>	14	When study was done, including beginning and ending dates of recruitment	Given in methods page 5
	15	Clinical and demographic characteristics (e.g. age, sex, spectrum of presenting symptom(s), comorbidity, current treatment(s), recruitment center)	Given in Table 1
	16	How many participants satisfying the criteria for inclusion did or did not undergo the index test and/or the reference standard; describe why participants failed to receive either test (a flow diagram is strongly recommended)	Our negative outcome measure is a composite measure after multimodal prospective monitoring. And thus all our patients underwent this rigorous process.
<i>Reference standard</i>	17	Time interval and any treatment administered between index and reference standard	Not applicable
	18	Distribution of severity of disease (define criteria) in those with the target condition; describe other diagnoses in participants without the target condition	Table 2
<i>Test results</i>	19	A cross tabulation of the results of the index test(s) by the results of the reference standard; for continuous results, the distribution of the test results by the results of the reference standard	Given in table 3
	20	Indeterminate results, missing responses and outliers of index test(s) stratified by reference standard result and how they were handled	N/A
	21	Adverse events of index test(s) and reference standard	False negatives discussed page 10-11

<i>Estimation</i>	22	Estimates of diagnostic accuracy and measures of statistical uncertainty (e.g. 95% confidence intervals)	Table 3
	23	Estimates of variability of diagnostic accuracy between subgroups of participants, readers or centers, if done	Given table 3
	24	Measures of test reproducibility, if done	Kappa coefficients given in results page 10
DISCUSSION	25	The clinical applicability of the study findings	Discussed fully