TITLE: Accuracy of NEXUS II head injury decision rule in children. A prospective cohort study.

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ASTRACT

Objective The National Emergency X-Radiography Utilisation Study II (NEXUS II) clinical decision rule (CDR) can be used to optimise the use of CT in children with head trauma. We set out to externally validate this CDR in a large cohort.

Methods We performed a prospective observational study of patients aged <18 years presenting with head trauma of any severity to 10 Australian/New Zealand EDs. In a planned secondary analysis, we assessed the accuracy of the NEXUS II CDR (with 95% CI) to detect clinically important intracranial injury (ICI). We also assessed clinician accuracy without the rule.

Results Of 20 137 total patients, we excluded 28 with suspected penetrating injury. Median age was 4.2 years. CTs were obtained in ED for 1962 (9.8%), of whom 377 (19.2%) had ICI as defined by NEXUS II. 74 (19.6% of ICI) patients underwent neurosurgery. Sensitivity for ICI based on the NEXUS II CDR was 379/383 (99.0 (95% CI 97.3% to 99.7%)) and specificity was 9320/19 726 (47.2% (95% CI 46.5% to 47.9%)) for the total cohort. Sensitivity in the CT-only cohort was similar. Of the 18 022 children without CT in ED, 49.4% had at least one NEXUS II risk criterion. Sensitivity for ICI by the clinicians without the rule was 377/377 (100.0% (95% CI 99.0% to 100.0%)) and specificity was 18 147/19 732 (92.0% (95% CI 91.6% to 92.3%)).

Conclusions NEXUS II had high sensitivity, similar to the derivation study. However, approximately half of unimaged patients were positive for NEXUS II risk criteria; this may result in an increased CT rate in a setting with high clinician accuracy.

INTRODUCTION

Over the last 20 years, a number of head injury clinical decision rules (CDRs) have been developed. They are generally designed to determine which patients should or should not undergo CT of the head by stratifying patients into those at increased or decreased risk of intracranial injury (ICI). In children with head injuries, concerns about diagnostic speed, accuracy, resource use and variation in practice are amplified by concerns about radiation exposure and subsequent iatrogenic cancer risk[1 2] and the need for sedation in young and uncooperative patients.[3]

Several child-specific head injury CDRs have been developed using large data sets.[4–8] This necessitates that clinicians use a CDR for paediatric patients and a separate CDR for adult patients. In contrast, the National Emergency X-Radiography Utilisation Study II (NEXUS II) collaboration aimed to provide a low-risk decision instrument for head injured patients of all ages.[9 10] This CDR, prospectively derived in a multicentre data set of 13 728 patients who underwent CT for their blunt head injury includes eight predictor variables (age over 65 years, evidence of skull fracture, scalp haematoma, neurological deficit, abnormal alertness, abnormal behaviour, coagulopathy or persistent vomiting). A 7-criteria NEXUS II instrument, excluding the age predictor variable, was then tested in the paediatric subgroup of 1666 children included in the original derivation data set, showing a very high sensitivity (98.6%, 95% CI 94.9% to 99.8%) and negative predictive value (NPV) (99.1%, 95% CI 96.9% to 99.9%). However, the NEXUS II CDR has not been externally validated in a child-specific cohort of undifferentiated head injuries.

Only CDRs that have been derived according to rigorous methodological standards and are externally validated should be implemented in routine clinical practice.[4] As >80% of paediatric emergencies are managed in EDs that care for both adult and paediatric patients CDRs developed to be used for patients of all ages have the potential to be ideal decision instruments for emergency physicians in mixed departments.

We undertook an external validation of the NEXUS II CDR in head injured children using prospectively collected multicentre data outside the derivation setting.[11 12] We used the NEXUS II predictor variables and the rule-specific outcome of clinically important ICI to determine the diagnostic accuracy of the rule in an undifferentiated cohort of children with head injuries of any severity. We also analysed the accuracy in the cohort that underwent head CT, consistent with the original derivation cohort inclusion criteria.

METHODS

Study design and setting

This was a planned secondary analysis of a prospective multicentre observational study, which enrolled children aged <18 years presenting with head injury of any severity to 10 paediatric EDs in Australia and New Zealand between April 2011 and November 2014. All EDs are members of the Paediatric Research in Emergency Departments International Collaborative research network.

While the focus of the parent study[11] was on the validation of three other paediatric-specific neuroimaging rules ((i) the prediction rule for the identification of children at very low risk of clinically important traumatic

brain injury developed by the Paediatric Emergency Care Applied Research Network (PECARN),6 (ii) the Canadian Assessment of Tomography for Childhood Head Injury (CATCH) rule7 and (iii) the Children's Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE))8 published elsewhere,11 we also collected the predictor and outcome variables of the NEXUS II rule.9 10 Using the published predictor variables and ICI as outcome variable as defined by NEXUS, we assessed the accuracy (sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV)) of NEXUS II in patients in the whole cohort of patients, using systematic telephone follow-up data as a surrogate for negative primary outcome of no ICI if no CT scan had been performed. In a secondary analysis, we assessed the accuracy of NEXUS II only in the cohort who underwent a CT scan, similar to the original derivation papers.9 10 As predictor and outcome variables were not collected verbatim as published,9 10 we adapted them based on available data (see online supplementary tables 1 and 2). We also assessed clinician accuracy for predicting the outcome of ICI by whether they conducted a CT in the ED and compared the results with the accuracy of NEXUS II.

We obtained informed verbal consent from parents/guardian apart from instances of significant life-threatening or fatal injuries where participating ethics committees granted a waiver of consent. The trial protocol was published in detail elsewhere.12 The study was registered with the Australian New Zealand Clinical Trials Registry ACTRN12614000463673 and followed the Standards for Reporting Diagnostic accuracy studies guidelines.13

Selection of participants

Patients were enrolled by the treating ED clinician who collected demographic, epidemiological and clinical data on a standardised case report form prior to any neuroimaging. ED clinicians decided to obtain head CTs at the initial presentation in ED based on their clinical judgement and their own criteria, the study exerted no influence on this process. A research assistant (RA) recorded ED and hospital management data after the visit and conducted a telephone follow-up for patients who had not undergone neuroimaging. Up to six follow-up call attempts were made up to 90 days after injury. In addition, data of any patients who had representations to the study hospitals leading to a CT scan within the follow-up period prior to the phone call were used to assess outcomes. Any patients who had representations to other hospitals based on the telephone follow-up had neuroimaging and neurosurgery reports requested where applicable.

Patients were excluded if they had trivial facial injuries, refused participation, had neuroimaging prior to arrival in ED, did not wait to be seen or were referred for care outside the ED and if there were social issues preventing an approach of the patient or family. RAs were not blinded to the purpose of the study. Site investigators, RAs and participating ED clinicians received formal training prior to and during the study.

Methods and measurements

The NEXUS II decision instrument9 10 was used for this study. It includes eight risk criteria: evidence of significant skull fracture, altered level of alertness, neurological deficit, persistent vomiting, presence of scalp haematoma, abnormal behaviour and coagulopathy and age >65 years. Patients fulfilling one or more of these

criteria are considered at high risk for ICI and are recommended to undergo a head CT. Similar to Oman *et al*,10 we removed the age criterion as not relevant; online supplementary table 1 presents the definition of the seven risk criteria used10 and how closely they matched the predictor variables available from PEACRN, CATCH and CHALICE.

Outcomes

The definition of ICI applied in this study was based on the original definition proposed by Mower *et al*,9 according to the presence of one or more of a number of CT findings shown in online supplementary table 2. These were derived from previous clinical work,14 which showed that patients with these CT findings may require neurosurgical intervention (craniotomy, intracranial pressure monitoring or mechanical ventilation), or are likely to suffer significant long-term neurological impairment. 10 14

In this study, we used senior radiologist reports to determine the results of CT scans. RAs and site investigators abstracted these data from CT reports for agreement with the outcome measures and consulted local site radiologists if there was uncertainty in the interpretation of individual scans. De-identified copies of CT findings were provided to the central site. If there was a question as to the classification of the CT, a central site investigator would review the reports and if needed use a third site investigator to resolve disagreements.

A comparison between the NEXUS II CT criteria and the corresponding information used in our study is provided in online supplementary table 2. For the descriptive analyses of neurosurgical interventions, we used operative reports. RAs and site investigators abstracted the information from operative reports. If there was a question as to the classification of the operative reports, a central site investigator would review the reports and if needed use a third site investigator to resolve disagreements.

Analysis

Data were entered into Epidata (The Epidata Association, Odense, Denmark), and later REDCap,15 and analysed using Stata 13 (StataCorp, College Station, Texas, USA). Descriptive statistics were calculated for key variables with 95% CIs where relevant. Primary analysis was the diagnostic accuracy (sensitivity, specificity, NPV and PPV) of NEXUS II for ICI in patients in the cohort of all presenting patients. In this analysis, patients who did not undergo a CT scan, but were followed up by telephone up to 90 days after the injury were coded as not having ICI. In a secondary analysis, the diagnostic accuracy (sensitivity, specificity, NPV and PPV) of NEXUS II for ICI was tested in the cohort who underwent a CT scan. Finally, we assessed the diagnostic accuracy of clinician practice to detect ICI if a CT scan had been conducted. Missing predictor variables were treated as missing presumed negative. A sample size calculation had been conducted for the parent study11 12; no additional sample size calculation was conducted for this substudy and all available patients who fulfilled inclusion criteria were used.

We conducted a secondary analysis where patients with missing predictor variables were excluded. As in the study by Oman *et al*,10 we also performed a subgroup analysis in children aged ≤3 years. This subgroup analysis was performed in consideration of the fact that assessment of criteria pertaining to behavioural and

neurological functioning domains, as well as to other domains, may be more challenging in children of this very young age10 and thus may affect the diagnostic accuracy of the CDR instrument.

RESULTS

Characteristics of study subjects

A total of 29,433 patients presented to the ED with injury of any severity, of which 5,203 were missed. Of the remaining 24,230 patients assessed for eligibility, 1,706 were excluded. Of the 22,524 eligible patients, 2,240 were lost to follow-up, 147 had records that were not evaluable and 28 were suspected by the ED clinician to have sustained a penetrating head injury; this led to a total number of 20,109 patients evaluable for analyses. Patient flow is described in figure 1. Of 1,962 (9.6%) patients who received a CT scan in the ED, 377/1,962 (19.2%) had ICI as defined by NEXUS II (table 1). Mean age of patients was 6.6 (SD 5.2) years for patients with ICI and 8.8 (SD 5.2) years for those without ICI on CT. Overall, 26.3% of patients with a CT scan were <3 years of age. Main signs and symptoms were loss of consciousness and vomiting, main mechanism of injury was fall related. Ten children died from their head injuries. The most frequent types of ICI identified on CT were skull fractures, and subdural/extradural haemorrhages and contusions, with the most frequent neurosurgical interventions (74, 19.6%) being monitoring of intracranial pressure and craniotomy (table 2).

Main results

The most frequent positive NEXUS II risk criteria in children with ICI (table 3) were scalp haematomas (217/377; 57.6%) and altered level of alertness (235/377; 62.3%). Four patients with CT confirmed ICI had no NEXUS II risk criteria. These four children were aged between 4 and 15 years, presented with a GCS of 15 and fell from height, fell off scooter or were struck by another person at school. All were admitted and none required neurosurgery (see online supplementary table 3). Most children with ICI had two or three positive risk criteria (table 3). When analysing risk criteria among 18 022 children who had no initial or subsequent CT scan, 8909 (49.4%) had at least one risk criterion and 2476 (13.7%) had at least two risk criteria (see online supplementary table 4).

When analysing the diagnostic accuracy of the rule based on all presenting patients, with the assumption that patients not undergoing a CT scan were negative for ICI based on telephone follow-up, it showed a sensitivity of 379/383 (99.0% (95% CI 97.3% to 99.7%)) and specificity of 9320/19 726 (47.2% (95% CI 46.5% to 47.9%)) (table 4). When assessing the accuracy of NEXUS II based on initial CT scan in ED, the sensitivity for ICI based on the NEXUS II CDR was 373/377 (98.9%; 95% CI 97.3% to 99.7%) and specificity 156/1585 (9.8%; 95% CI 8.4% to 11.4%) (table 4). Results were similar when all CTs performed at any time point were included and in children aged <3 and ≥3 years (table 5). The sensitivity of NEXUS II increased with the number of risk criteria (table 6). We also conducted a sensitivity analysis where patients who had a CT scan with missing risk criteria were excluded. Accuracy results were unchanged (see online supplementary table 5). Clinician accuracy in detecting ICI without the rule was 377/377 (100.0 (95% CI 99.0% to 100.0%)) and specificity was 18 147/19 732 (92.0% (95% CI 91.6% to 92.3%)) (table 4).

DISCUSSION

In this multicentre validation study, we found NEXUS II to have high sensitivity in detecting the NEXUS-specific outcome of ICI in the overall cohort and in the cohort who underwent CT scanning. Four patients were missed by the rule, that is, had no NEXUS II risk criteria but were positive for ICI; none of them required neurosurgery. Overall accuracy results did not change when patients were excluded who had missing information for NEXUS criteria. Both high sensitivity (98.9%; 95% CI 97.3% to 99.7%) and low specificity (9.8%; 95% CI 8.4% to 11.4%) in the CT-only cohort were similar to the analysis of the original NEXUS data overall9 and for the paediatric cohort in particular (sensitivity 98.6% (95% CI 94.9 to 99.8); specificity 15.1% (95% CI 13.3 to 16.9)).10 Our data set differed from the NEXUS II cohort in that more young children were enrolled compared with the 'J'-shaped distribution with an increased number of teenagers in NEXUS.

External validation for NEXUS II in children is limited. In three paediatric studies from Finland,16 Italy17 and the USA18 outside the derivation setting, NEXUS II was assessed in terms of accuracy and compared with other head injury rules. All were limited by being conducted in single-centre settings and by the retrospective nature of data extraction16 18 or the use of a prospective data set collected before the NEXUS II derivation data had been published.17 Neither paper lists in detail how the NEXUS definitions were modified to conform with pre-existing data sets. NEXUS sensitivities were reported at 96% (95% CI 90 to 99),16 88.9% (95% CI 63.9 to 95.6)17 and 78.3% (95% CI 69.9 to 86.7),18 respectively. It is not clear if a multicentre prospective study of NEXUS II from Korea includes any children. 19 Recently, the original team which derived the NEXUS II

CDR conducted a validation study in a new data set including 11 750 blunt head injuries20; in an analysis of the paediatric cohort of 1018 children sensitivity was 98.0% (95% CI 89.1% to 99.9%) and specificity of 34.0% (95% CI 31.0% to 37.0%) for the assessment of high-risk status in patients with ICI.21 However, similar to the derivation cohort only patient who had received a CT scan were included in the study. While we also followed the original adult and paediatricpapers for NEXUS II9 10 by analysing rule accuracy (external validation) solely based on patients who actually underwent CT scanning, in particular as CT imaging was required for outcome assessment, this does not reflect how rules such as NEXUS II may actually be used in the clinical setting. Therefore, we primarily analysed the accuracy using all patients, including those without

CT scans; while sensitivity was similar, specificity was higher in the overall cohort compared with the CT-only cohort. Of 18 022 head injured children in our study who did not undergo CT imaging, 49.4% of these patients fulfilled at least one of the NEXUS predictor variables and therefore, based on the rule, were deemed not at very low risk. If this rule was applied and followed in an undifferentiated cohort of paediatric patients, it would have the potential to increase the head CT rate. When adding predictor positive patients who underwent any CT scan (n=1497) and those who did not (n=8909), 51.7% (10 406 of 20 109) of all head injured children would be required to undergo CT imaging as compared with 10.4% (2087 of 20 109) who actually did, an increase of about 400%. This is particularly striking considering the high sensitivity—where clinicians did not miss a single patient with ICI—and specificity of clinician practice at the participating sites without using the NEXUS rule.

NEXUS II used ICI as primary outcome. Although the outcome was consensus based and aimed to capture CT changes that may require neurosurgical intervention, 'or lead to rapid deterioration or significant long-term neurological impairment', the actual criteria used to define ICI were solely based on recorded CT changes.[9 22] Other paediatric CDRs, such as PECARN, use definitions of clinically important traumatic brain injury that explicitly require, in addition to specified CT changes, relevant clinical changes, such as admission >2 days or intubation >1 day (in addition to death or neurosurgery).[6] Such tightening of the outcome definition would likely change sensitivity and specificity calculations of NEXUS II in both the derivation data set and in our data.

This study has a number of limitations. The predictor and outcome variables for the NEXUS II CDR would have ideally been collected verbatim. Any changes in definitions and wording of head injury rules have the potential to alter the final results.[23] The focus of the parent study[11] used for this paper, however, was on the paediatric-specific CATCH, CHALICE and PECARN rules.[6–8] We felt that by collecting the predictor and outcome variables of three rules in detail, the modified definitions could be closely approximated to the actual NEXUS II criteria used for this study. A further limitation of this study was a 10% loss to follow-up in the parent study, which may have affected the analysis including patients who did not undergo CT scanning.

In the NEXUS derivation study as well as in the validations study by the same group, patients who were not imaged were generally not followed up.[9] In our study, participating sites were usually also the only paediatric neurosurgical centres in the local areas. A further limitation is that CT scans were not reviewed centrally; rather CT reports were used to assess ICI. Finally, this study reflects practice at tertiary Australian and New Zealand centres, where imaging rates are generally lower than in North America[6 7 11 24] and no specific rule predominates.[25] The developers of NEXUS presumed that patients in the derivation study perceived by clinicians to be at high risk (independent of the NEXUS criteria per se) would be imaged by treating clinicians anyway. Therefore, no comprehensive follow-up system was put in place and only a small fraction of the original derivation cohort (9.2%) were followed up by interview[9]; it is unclear how many head injured children were included in this cohort.

Although no denominator of patients presenting to participating EDs or the actual imaging rate at NEXUS sites was provided in the NEXUS derivation or validation papers,[9 10 20 21] in settings with a presumably high CT rate this may accurately capture all or most relevant patients. In settings with a much lower scan rate, such as in our setting, this may not be true and patients may be missed unless a comprehensive follow-up system is in place. In this multicentre prospective external validation study, the NEXUS II CDR had high sensitivity and low specificity similar to the derivation study. However, as approximately half of patients who did not receive a CT scan were positive for NEXUS II risk criteria, this CDR has the potential to lead to increased scanning rates in a setting with high clinician accuracy.

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Contributors FEB: conceived the study, obtained grant funding, designed the study, provided overall supervision, interpreted the data, wrote the initial draft of the paper, gave final approval to be published and agreed to be accountable for all aspects of the work. MLB, NP, AK, SD, JAC, YG, JF, JN, MDL, MA, SH, SB, LMC, EO, SRD: designed the study, obtained the data, provided supervision, interpreted the data, drafted or revised it critically, gave final approval to be published and agreed to be accountable for all aspects of the work. SD: designed the study, supervised the analysis of the data, contributed to the interpretation of the data, revised the paper critically, gave final approval to be published and agreed to be accountable for all aspects of the work.

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Provenance and peer review Not commissioned; externally peer reviewed.
Data sharing statement There are no additional data available.

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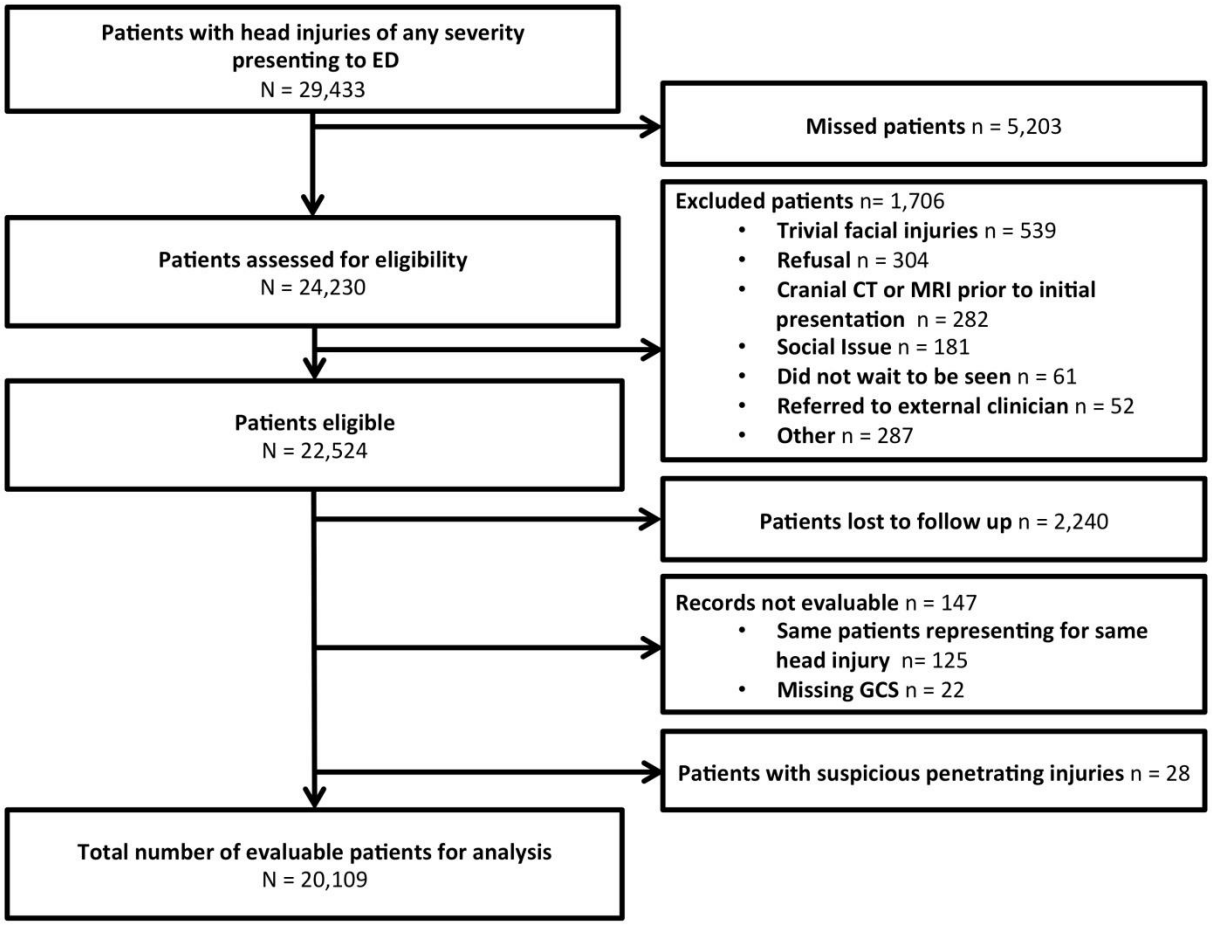
Figure 1: Patients flow



*Head injuries not including trivial facial injuries defined as a ground level fall or walking or running into an object with no signs or symptoms of injury other than facial abrasions or lacerations below the eyebrows. CT=computed tomography; ED = Emergency Department; GCS=Glasgow Coma Score; MRI=magnetic resonance imaging.

Table 1. Definition of the seven risk criteria according to Oman et al., (2006) and adaptations to fit the definitions to our dataset

	DEFINITION (Oman et al., 2006)	ADAPTATION
1	**Evidence of significant skull fracture** Evidence of skull fracture includes but it is not limited to any signs of basilar skull fracture (periorbital or peri-auricular ecchymoses, hemotympanum, and drainage of clear fluid from the ears or nose) or signs of depressed or diastatic skull fracture (a palpable step-off of the skull, a stellate laceration from a point source, or any injury produced by an object striking a localized region of the skull (e.g. a baseball bat, club, pool cue, golf-ball, baseball, pipe).	**Presence of either one of the following was defined as satisfying risk criterion:** A. Obvious palpable skull fracture: *YES/unknown* B. Possible skull fracture on palpation: *YES/unknown* C. Open skull fracture: *YES/unknown* D. Signs of basal skull fracture: *YES/unknown* E. Was the injury caused by high speed projectile? *YES/unknown* F. Was the injury caused by a high impact object? *YES/unknown*
2	**Altered level of alertness** Abnormal level of alertness is evidenced by a variety of findings, including but not limited to a Glasgow coma score of 14 or less; delayed or inappropriate response to external stimuli; excessive somnolence; disorientation to person, place, time or events; inability to remember three objects.	**Presence of either one of the following was defined as a satisfying risk criterion:** A. What is the current GCS? *14 or less* B. Is your patient abnormally drowsy/difficult to wake? *YES/unknown* C. Is your patient slow to respond to speech? *YES/unknown* D. Does your patient have an altered mental status? *YES/unknown*
3	**Neurological deficit** Neurologic deficits may include motor deficit which is a finding of abnormal weakness in any 1 or more of the 4 extremities, as determined by systematic testing of muscle strength in all 4 limbs; gait abnormality which is the inability to walk normally as a result of inadequate strength, loss of balance, or ataxia as determined by systematic testing of gait, including tandem and heel-to-toe walking, and Romberg testing; cerebellar abnormality which is manifested by ataxia, dysmetria, dysdiadokinesis, or other impairment of cerebellar function as determined by systematic testing of cerebellar function, including tests of ataxia, and finger-nose-finger, heel-to-shin, and rapid alternating movement testing; cranial nerve abnormality which is an abnormality of cranial nerve II to XII, determined by systematic testing of each of these cranial nerves.	Is there any focal neurology present? *YES/unknown*
4	**Persistent vomiting** High-risk vomiting is evidenced by recurrent, projectile, or forceful emesis (either observed or by history) after trauma or vomiting associated with altered sensorium.	*Has there been more than one episode of vomiting? YES* ***AND/OR*** *Have there been 3 or more discrete episodes? YES*

5	**Scalp hematoma** A significant scalp hematoma includes any swelling of traumatic origin to the soft tissues overlying the calvarium. Injuries to the face, neck, and jaw are not considered scalp hematomas.	Scalp Hematoma: *YES/unknown; **AND Location MUST BE**: either frontal, or temporal, or occipital or parietal (or more than one of these)*
6	**Abnormal behavior** Abnormal behavior is any inappropriate action displayed by the victim. It includes such things as excessive agitation, inconsolability, refusal to cooperate, lack of affective response to questions or events, and violent activity.	Presence of either one of the following was defined as satisfying risk criterion**:** A. Is your patient irritable or agitated? *YES/unknown* B. Is your patient asking questions repetitively? *YES/unknown* C. According to the parent/guardian, is your patient acting abnormally? *YES/unknown*
7	**Coagulopathy** Coagulopathy is any impairment of normal blood clotting such as occurs in hemophilia, secondary to medications (e.g. Coumadin, heparin, aspirin, etc.), hepatic insufficiency and other conditions.	Is there a bleeding disorder? *YES/unknown*

Table 2. Comparison between CT findings consistent with clinically important intracranial injury (ICI) according to Mower et al., and corresponding CT findings coded in this study

	Clinically important ICI definitions (Mower et al., 2005)	**Clinically important ICI definition as coded in the current study**
1	Substantial epidural or subdural hematoma (>1.0 cm in width or causing mass effect)	Intracranial hemorrhage/contusion – extra-axial (subdural/extradural)
2	Substantial cerebral contusion (>1.0 cm in diameter or >1 site)	Intracranial hemorrhage/contusion – parenchyma
3	Extensive subarachnoid hemorrhage	Intracranial hemorrhage/contusion – sub-arachnoid
4	Mass effect or sulcal effacement	*Not available*
5	Signs of herniation	Midline shift or brain herniation
6	Basal cistern compression or midline shift	Midline shift or brain herniation
7	Hemorrhage in the posterior fossa	Intracranial hemorrhage/contusion
8	Intraventricular hemorrhage	Intracranial hemorrhage/contusion
9	Bilateral hemorrhage of any type	Intracranial hemorrhage/contusion
10	Depressed or diastatic skull fracture	Diastasis of skull OR/AND Skull fracture - depressed
11	Pneumocephalus	Pneumocephalus
12	Diffuse cerebral edema	Cerebral edema
13	Diffuse axonal injury	Diffuse axonal injury

Table 3. Demographics of the evaluable patients

	CT in ED				No CT (in ED)		Entire Sample	
	Clinically Important ICI		No Clinically Important ICI					
N	377		1,585		18,147		20,109	
Demographics								
Age								
Mean, SD	6.6	5.2	8.2	5.2	5.5	4.5	5.7	4.7
<3 years, n %	129	34.2	360	22.7	7,383	40.7	7,872	39.1
Male, n %	242	64.2	1,061	66.9	11,502	63.4	12,805	63.7
Symptoms and signs, n %								
Known or suspected LOC	164	43.5	528	33.3	2,006	11.1	2,698	13.4
History of amnesia*	66	17.5	473	29.8	1,144	6.3	1,683	8.4
History of vomiting	148	39.3	682	43.0	2,618	14.4	3,448	17.1
Headache	122	32.4	762	48.1	3,233	17.8	4,117	20.5
Witnessed disorientation*	132	35.0	604	38.1	1,955	10.8	2,691	13.4
Mechanism of Injury, n %								
Fall related	210	55.7	997	62.9	12,904	71.1	14,111	70.2
Motor vehicle incident	100	26.5	207	13.1	537	3.0	844	4.2
Bicycle-related; wearing no helmet	24	6.4	61	3.9	297	1.6	382	1.9
Head hit by high impact object/projectile,	36	9.6	164	10.4	1,110	6.1	1,310	6.5
Suspected NAI	24	6.4	44	2.8	44	0.2	112	0.6
*Cranial CT rate**, n %*	377	100.0	1,585	100.0	125	0.7	2,087	10.4
Neurosurgery rate, n %	74	19.6	1	0.1	1	0.0	76	0.4
Admission rate, n %	354	93.9	982	62.0	3,192	17.6	4,528	22.5
Mortality, n %	10	2.7	1	0.1	1	0.0	12	0.1

* = Preverbal cases excluded.

***= CT either in ED or subsequently (CT2)*

Table 4. Types of injuries and neurosurgical interventions in patients with clinically important ICI identified on ED CT (n=377)

	Patients With Clinically Important ICI	
Type of Injury	n	%
Skull Fracture		
Depressed	87	23.1
Non-depressed	152	40.3
Basal skull	35	9.3
Diastasis of Skull	34	9.0
Extra-axial bleed		
Subdural/extradural hemorrhage/contusion	203	53.8
Sub-arachnoid hemorrhage/contusion	65	17.2
Parenchymal lesions		
Parenchyma hemorrhage/contusion	102	27.1
Cerebral edema	71	18.8
Diffuse axonal injury	26	6.9
Midline shift or brain herniation	38	10.1
Pneumocephalus	57	15.1
Other (shearing injury, traumatic infarction, sigmoid sinus thrombosis)	12	3.2

Neurosurgical intervention	n	%
Monitoring of intracranial pressure	44	59.5
Elevation of depressed skull fracture	14	18.9
Ventriculostomy	0	0.0
Craniotomy	43	58.1
Hematoma Evacuation	32	43.2
Lobectomy	1	1.4
Tissue debridement	2	2.7
Dura repair	9	12.2

Table 5. Frequency and count of Individual Risk Criteria for all children, and for subsample ≤3 years

Criterion	<18 years				<3 years			
	no ICI		ICI		no ICI		ICI	
	n	%	n	%	n	%	N	%
N	19,732		377		7,743		129	
Risk Criteria Count								
0	9,320	47.2	4	1.1	3,503	45.2	0	0.0
1	6,902	35.0	53	14.1	2,899	37.4	9	7.0
2	2,435	12.3	99	26.3	969	12.5	40	31.0
3	783	4.0	117	31.0	283	3.7	44	34.1
4	240	1.2	74	19.6	73	0.9	25	19.4
5	49	0.3	26	6.9	15	0.2	9	7.0
6	3	0.0	4	1.1	1	0.0	2	1.6
7	0	0.0	0	0.0	0	0.0	0	0.0
Risk Criteria								
1 - Evidence of skull fracture	1,819	9.2	214	56.8	394	5.1	93	72.1
2 - Scalp hematoma	5,570	28.2	237	62.9	2,641	34.1	104	80.6
3 - Neurological deficits	585	3.0	41	10.9	181	2.3	16	12.4
4 - Altered levels of alertness	1,663	8.4	235	62.3	604	7.8	66	51.2
5 - Abnormal behavior	3,382	17.1	216	57.3	1,372	17.7	75	58.1
6 - Persistent vomiting	2,019	10.2	98	26.0	756	9.8	22	17.1
7 – Coagulopathy	306	1.6	11	2.9	111	1.4	2	1.6

le 6. Frequency and count of Individual Risk Criteria by ICI +/- for initial and follow up CT scans.

	ED CT				Either CT					
	ICI+		ICI-		ICI+		ICI-		CT-	
	n	%	n	%	n	%	n	%	n	%
	377		1585		383		1704		18022	
Criteria Count										
	4	1.1	156	9.8	4	1.0	207	12.2	9113	50.6
	53	14.1	429	27.1	56	14.6	466	27.4	6433	35.7
	99	26.3	488	30.8	101	26.4	512	30.1	1921	10.7
	117	31.0	324	20.4	118	30.8	331	19.4	451	2.5
	74	19.6	146	9.2	74	19.3	146	8.6	94	0.5
	26	6.9	39	2.5	26	6.8	39	2.3	10	0.1
	4	1.1	3	0.2	4	1.0	3	0.2	0	0.0
	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Criteria										
vidence of skull fracture	214	56.8	443	28.0	216	56.4	460	27.0	1357	7.5
calp hematoma	237	62.9	631	39.8	239	62.4	654	38.4	4914	27.3
Neurological deficits	41	10.9	147	9.3	41	10.7	152	8.9	433	2.4
ltered levels of alertness	235	62.3	618	39.0	235	61.4	631	37.0	1032	5.7
bnormal behavior	216	57.3	770	48.6	218	56.9	798	46.8	2582	14.3
ersistent vomiting	98	26.0	522	32.9	101	26.4	538	31.6	1478	8.2
oagulopathy	11	2.9	43	2.7	12	3.1	47	2.8	258	1.4

Table 7. Diagnostic testing of NEXUS II clinically important ICI, tested by presence of any risk criteria (of the 7)

Initial CT Scan (ED CT)		
	Risk Criteria	
	Positive	Negative
Positive ICI	373	4
Negative ICI	1429	156
Sensitivity (95% CI)	373/377	98.9 (97.3-99.7)
Specificity (95% CI)	156/1585	9.8 (8.4-11.4)
PPV (95% CI)	373/1802	20.7 (18.8-22.6)
NPV (95% CI)	156/160	97.5 (93.7-99.3)

CT at any time		
	Risk Criteria	
	Positive	Negative
Positive ICI	379	4
Negative ICI	1497	207
Sensitivity (95% CI)	379/383	99.0 (97.3-99.7)
Specificity (95% CI)	207/1704	12.1 (10.6-13.8)
PPV (95% CI)	379/1876	20.2 (18.4-22.1)
NPV (95% CI)	207/211	98.1 (95.2-99.5)

Total Cohort		
	Risk Criteria	
	Positive	Negative
Positive ICI	379	4
Negative ICI	10406	9320
Sensitivity (95% CI)	379/383	99.0 (97.3-99.7)
Specificity (95% CI)	9320/19726	47.2 (46.5-47.9)
PPV (95% CI)	379/10785	3.5 (3.2-3.9)
NPV (95% CI)	9320/9324	100.0 (99.9-100.0)

ID	Age	Sex	GCS	Mechanism of injury	Injury recorded	Treatment
1	4 y	M	15	Fell from scooter without wearing helmet	Pneumocephalus; basal skull fracture.	Neurosurgery: No; Admission: 2 days
2	5 y	M	15	Fall >3 m	Intracranial hemorrhage/contusion - extra-axial; pneumocephalus; basal skull fracture –non depressed	Neurosurgery: No; Admission: 4 days
3	6 y	F	15	Fall 1.8m from home stairs.	Intracranial hemorrhage/contusion - extra-axial; pneumocephalus; skull fracture – non-depressed.	Neurosurgery: No; Admission: 5 days
4	15 y	M	15	Struck by/or collision with person at school.	Intracranial hemorrhage/contusion-parenchyma.	Neurosurgery: No; Admission: 5 days

Supplement Table 2. Diagnostic testing of NEXUS II clinically important ICI, tested by presence of any risk criteria (of the 7) – MISSING EXCLUDED

Initial CT Scan (ED CT)		
	Risk Criteria	
	Positive	Negative
Positive ICI	373	4
Negative ICI	1429	154
Sensitivity (95% CI)	373/377	98.9 (97.3-99.7)
Specificity (95% CI)	154/1583	9.7 (8.3-11.3)
PPV (95% CI)	373/1802	20.7 (18.8-22.6)
NPV (95% CI)	154/158	97.5 (93.6-99.3)

CT at any time		
	Risk Criteria	
	Positive	Negative
Positive ICI	379	4
Negative ICI	1497	204
Sensitivity (95% CI)	379/383	99.0 (97.3-99.7)
Specificity (95% CI)	204/1701	12.0 (10.5-13.6)
PPV (95% CI)	379/1876	20.2 (18.4-22.1)
NPV (95% CI)	204/208	98.1 (95.1-99.5)