Title Page

Risk of traumatic intracranial haemorrhage in children with bleeding disorders

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Short Title: Paediatric minor head injury in bleeding disorders

~~**Acknowledgements**~~

~~We thank participating families, clinicians and research staff from the study sites.~~

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Funding Source: The study was funded by grants from the National Health and Medical Research Council (project grant GNT1046727, Centre of Research Excellence for Paediatric Emergency Medicine GNT1058560), Canberra, Australia; the Murdoch Children's Research Institute, Melbourne, Australia; the Emergency Medicine Foundation (EMPJ-11162), Brisbane, Australia; Perpetual Philanthropic Services (2012/1140), Australia; Auckland Medical Research Foundation (No. 3112011) and the A + Trust (Auckland District Health Board), Auckland, New Zealand; WA Health Targeted Research Funds 2013, Perth, Australia; the Townsville Hospital and Health Service Private Practice Research and Education Trust Fund,

Townsville, Australia; and supported by the Victorian Government's Infrastructure Support Program, Melbourne, Australia. FEB's time was part funded by a grant from the Royal Children's Hospital Foundation and the Melbourne Campus Clinician Scientist Fellowship, Melbourne, Australia and an NHMRC Practitioner Fellowship, Canberra, Australia. SRD's time was part funded by the Health Research Council of New Zealand (HRC13/556).

Financial Disclosure: No authors have a financial relationship to this article to disclose

Conflict of Interest: No authors have conflicts of interest to disclose

Clinical Trial Registration: Registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12614000463673 http://www.anzctr.org.au/TrialSearch.aspx?searchTxt=ACTRN12614000463673&isBasic=True

~~The study was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12614000463673.~~

Acknowledgements: We thank participating families, clinicians and research staff from the study sites.

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- **Word count** (excluding title page, abstract, references, figures and tables): 2477~~2457~~

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ABSTRACT

Objective: To assess computerized tomography (CT) use and the risk of intracranial haemorrhage (ICH) in children with bleeding disorders following a head trauma

Design: Multicentre prospective observational study

Setting: 10 paediatric emergency departments (ED) in Australia and New Zealand

Patients: Children < 18 years with and without bleeding disorders assessed in ED following head trauma between April 2011 and November 2014

Interventions: Data collection of patient characteristics, management and outcomes

Main outcome measures: Rate of CT use and frequency of ICH on CT

Results: Of 20,137 patients overall, 103 (0.5%) had a congenital or acquired bleeding disorder. CT use was higher in these patients compared with children without bleeding disorders (30.1% vs 10.4%; rate ratio 2.91 95%CI 2.16- 3.91). Only one of 31 (3.2%) children who underwent CT in the ED had an ICH. This patient rapidly deteriorated in the ED on arrival and required neurosurgery. None of the patients with bleeding disorders who did not have a CT obtained in the ED or had an initial negative CT had evidence of ICH on follow up.

Conclusions: Although children with a bleeding disorder and a head trauma more often receive a CT scan in the ED, their risk of ICH seems low and appears associated with post-traumatic clinical findings. Selective CT use combined with observation may be cautiously considered in these children based on clinical presentation and severity of bleeding disorder.

Keywords: children, head trauma, bleeding disorders, intracranial haemorrhage.

INTRODUCTION

Minor head trauma is a frequent injury in paediatrics and is a common reason of Emergency Department (ED) visits.[1 2] Children with bleeding disorders seem to be at increased risk of intracranial haemorrhage (ICH) even after sustaining a minor HI.[3-5] Single or repeat minor head injury episodes may thus lead to long-term disability and potentially fatal outcome.[6 7] These children may be exposed more frequently to head computed tomography (CT) to detect haemorrhagic complications and the cumulative risk of repeated radiation exposures should be considered.[4 8 9]

Although children with bleeding disorders are at higher risk of ICH, it is unclear whether this risk warrants routine head CT following any minor head injury, irrespective of mechanism or clinical presentation. In addition, acquired or congenital bleeding disorders are a heterogeneous group of diseases, with different associated risks of post-traumatic ICH. Children with severe haemophilia (factor level <1%) are reported to be at highest risk of spontaneous and traumatic ICH.[3-5 10 11] Children with von Willebrand disease seem to have a lower risk, while ICH is rare in the presence of thrombocytopenia and it correlates with its severity.[5 6 12-14]

High-quality clinical decision rules have been derived and validated to support ED clinicians decide whether CT scans are necessary for paediatric head injury.[15] However, these rules provide no guidance on the management of children with bleeding disorders. The only large prospective study, a secondary analysis of the Pediatric Emergency Care Applied Research Network (PECARN) head injury rule study, analyzed 230 children with different bleeding disorders (all with Glasgow Coma Scale (GCS) 14 and 15).[9 16] In this cohort the CT rate was high at 80.9% in a setting with a baseline CT rate of 36.6% without bleeding disorders. The prevalence of ICH in patients with bleeding disorders was 1.1% (95% CI 0.1-3.8) compared with 4.4% (95% CI 4.1-4.7) in children without bleeding disorders, who more often sustained a severe mechanism of injury.

Given the limited evidence to guide acute neuroimaging decision-making in head injured children with bleeding disorders we assessed the CT rate and ICH prevalence in these children in an Australian and New Zealand setting, with a much lower baseline CT rate.[15]

METHODS

Study Design, Setting and Population

This was a planned secondary analysis of a prospective multi-centre observational study involving 20,137 children 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.[17] The parent study was conducted to assess the accuracy of three head injury clinical decision rules with details described elsewhere.[15 18] The study sites had a census between 19,000 to 78,000 children treated annually. Seven of the 10 EDs were regional trauma centres.

Selection of participants

Children were enrolled in the parent study if they were <18 years with head injuries of any severity irrespective of length of time from injury to presentation. Exclusion criteria were trivial facial injury only (i.e. ground level fall, walking or running into an object with no signs or symptoms of injury other than abrasions or lacerations), patients referred directly from ED triage to an external general practice, those who underwent neuroimaging before transfer to a study site, those who did not wait to be seen, or whose families refused to participate. The analysis for the present study was performed on children with any GCS and a bleeding disorder.

Definitions of main variables analysed are reported in *Table 1*.

Study procedures

Patients were enrolled by the treating ED clinician who collected clinical data, including positive, negative or unknown history of any bleeding disorder prior to any neuroimaging. The case report form included check boxes for bleeding disorder categorization. Head CTs were obtained at the discretion of the treating clinician. Research assistants recorded additional details on past medical history, including bleeding disorder details, ED and hospital management data after the visit and conducted a structured telephone follow-up, between 7 and 90 days following initial ED assessment, for patients who had not undergone neuroimaging. All patients who did not undergo CT in the ED, received telephone follow up. A detailed chart review of cases with bleeding disorders was performed.

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

Outcomes

Primary outcomes were the rate of CT use and the presence of an ICH on CT, as reported by an attending radiologist.

The secondary outcome was the prevalence of initially missed ICH on CT.

Data analysis

We performed basic descriptive statistics and calculated rate differences with 95% confidence intervals (CIs) of the prevalence of signs and symptoms of head trauma, CT scan performance and presence of ICH in children with and without bleeding disorders. We used rate ratios (RRs) with 95% CIs to compare rates of CT imaging and ICH for patients with bleeding disorders versus patients without bleeding disorders.

Data were entered into Epidata (The Epidata Association, Odense, Denmark), and later REDCap, and analysed using Stata 13 (Statacorp, College Station, Texas, USA).[19]

RESULTS

Of 20,137 patients, 103 (0.5%) had a congenital or acquired bleeding disorder. The most common was haemophilia, followed by thrombocytopaenia and von Willebrand disease (*Table 2*). Ninety-eight patients with bleeding disorders (95%) presented within 24 hours of injury. No patients with bleeding disorders had a concurrent suspicion for child abuse. When comparing the demographic and clinical characteristics of patients with and without bleeding disorders presenting with head injury (Supplementary *Table 1*), patients with bleeding disorders were more likely to present following moderate, rather than severe, mechanisms (more detailed information on injury mechanism is reported in *Supplementary Table 2*); less likely to report loss of consciousness, or headache; and on examination have fewer signs of basilar skull fracture, but more frequent scalp hematomas, particularly frontal.

Head CT scan rate was higher in children with bleeding disorders, 31/103 (30.1%) compared with 2,075/20,034 (10.4%) children without bleeding disorders presenting with a head injury (RR 2.91; 95% CI 2.16 - 3.91).

Children with bleeding disorders who received a CT scan in the ED, when compared to those not scanned, were more often affected by haemophilia and more commonly presented the following clinical signs: a history of vomiting or acting abnormally according to parent, an altered mental status and a palpable skull fracture (*Table 3*).

Tables 4 and 5 describe the characteristics of patients with and without bleeding disorders by CT performance, divided by age group (< 2 years and ≥ 2 years respectively). Although the numbers are low, children with bleeding disorders

more frequently received a CT scan for a milder mechanism of injury, for presenting a history of vomiting and for acting abnormally according to parents in both age groups. “Vomiting” is a PECARN head injury rule predictor for the older age group only, while “acting abnormally to parent” is a PECARN predictor for the younger group only. In addition, children with bleeding disorders who underwent a CT scan had overall less post-traumatic signs and symptoms compared to children without bleeding disorders.

One of 31 (3.2%) children with bleeding disorders who underwent CT had an ICH. This was a 6-year-old boy with von Willebrand disease who presented two hours after falling from less than one meter height with GCS of 15 on arrival; he underwent a CT due to rapid deterioration in consciousness with bradycardia. He needed neurosurgery for an extradural haematoma associated with midline shift and an undisplaced skull fracture.

Of the 74 patients with bleeding disorders who did not initially undergo a CT at the time of initial assessment, 13 (17.6%) were observed in the ED for 6 or more hours and 7 (9.5 %) were admitted to the ward, of whom two underwent CT after admission without evidence of ICH or need for neurosurgery. None of the 30 children with a bleeding disorder who had a normal CT scan in the ED, deteriorated and none had a subsequently positive CT scan, based on follow up data.

DISCUSSION

Our large prospective multicentre study of over 20.000 children presenting to Australian and New Zealand EDs following a head injury shows that post-traumatic ICH seems uncommon in children with congenital or acquired bleeding disorders. These patients represent only 0.5% of all children seen in the ED for head trauma. Our findings are consistent with the secondary analysis on the PECARN head injury rule study.[9]

In combined data from both studies only three children with bleeding disorders (3/333, 0.9%; 2 PECARN head injury rule study and 1 current study), had an ICH. While all exhibited signs and symptoms of ICH, either on arrival or soon after arrival to the ED, they had different underlying bleeding disorders (one case each of von Willebrand disease, severe haemophilia and warfarin therapy).[9] All three children met the PECARN ciTBI definition, two for staying in hospital ≥2 nights because of their head injury and one for needing neurosurgery. While the PECARN head injury rules explicitly excluded children with bleeding disorders, the other two highest quality paediatric head injury rules, the Children's Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE) and the Canadian Assessment of Tomography for Childhood Head Injury (CATCH) rule did not mention the presence of an underlying bleeding disorder as an exclusion criterion for their rules.[20 21] Of note, two of the three patients with ICH would not have been identified as high risk by either the CHALICE or CATCH rule, while all three displayed high or intermediate-risk PECARN head injury rule predictors.

We found the rate of CT scans in children with bleeding disorders to be significantly higher compared with children without bleeding disorders. In our low CT rate setting children with bleeding disorders received a CT scan in 30% of cases compared to 10% in children without bleeding disorders, despite the latter more frequently presented a severe mechanism of injury. In the Unites States, where CT use is higher than Australia and New Zealand, the PECARN head injury rule study reported a CT rate of 81% and 37% respectively.[9] Importantly, complete follow up of all included patients in both studies showed that none of the patients who did not receive a CT scan in the ED were later diagnosed with a ciTBI (i.e. there were no false negatives in the CT scan decision-making process).[9]

The population of children with bleeding disorders captured in our study was skewed towards a milder group of head injuries (children with a bleeding disorder more often underwent a CT scan when presenting with a mild mechanism of injury

and had an overall lower number of symptoms compared with children without bleeding disorders). Parents of children with bleeding disorders are taught their children have a higher risk of intracranial injury following a minor head trauma and are more likely to present for a minor head trauma than other children.

CT is routinely performed by many practitioners in children with bleeding disorders who sustain a minor head injury, irrespective of the type and severity of the disorder and the presence of post-traumatic signs and symptoms.[4 8 9] Our findings, in addition to the ones from the PECARN head injury rule study, show that a CT scan may not routinely be necessary in children with congenital and acquired bleeding disorders, and a more selective approach based on the severity of mechanism, the severity of the underlying bleeding disorder and the presence of symptoms and signs of ICH may be considered. However, patients without neuroimaging may benefit from a period of observation to ensure early detection of deterioration.

Consistent with the PECARN study, the most common bleeding disorder in our population was haemophilia. In children with severe haemophilia, treatment with factor replacement takes priority over performance of CT scan and the wide availability and implementation of such treatment has significantly improved survival from ICH in these patients.[22 23] Most of the literature on post-traumatic ICH in children with bleeding disorders selectively focused on haemophilia and is largely comprised of retrospective studies.[3-5 7 10 11] All but one study, which reported five patients with a post-traumatic ICH to be asymptomatic at the time of initial assessment, described post-traumatic signs and symptoms in children with ICH.[3-5 7 9-11] It is important to note, however, that symptoms may be delayed, especially in patients who develop subdural-hematomas, supporting observation as an alternative to CT. Case reports and case series on post-traumatic ICH in thrombocytopenic children, show that ICH is rare and mainly occurs when the platelet count is below $20{,}000 \times 10^9$/L.[3 10 24] The few studies on von Willebrand disease included a limited number of head injury episodes and found an ICH in a minority of patients, all symptomatic.[5 25] Many adult

studies have consistently shown that patients on warfarin are at increased risk of ICH irrespective of post-traumatic signs and symptoms, supporting routine CT scan for asymptomatic patients following a minor head injury.[26] Based on these studies, the NICE head injury guidelines recommend head CT also for children on warfarin treatment, independently of other indications for CT.[27] Only one of the 31 children on anticoagulants in our study and the PECARN head injury rules study combined was diagnosed with an ICH. Although the numbers are very limited they represent the best available paediatric evidence and appear to support an individualised approach rather than the 'CT all' strategy.

Our study has limitations. First, the number of patients with bleeding disorders is limited. However, ours is the second largest prospective cohort of children with head injury from which a sub-analysis on patients with bleeding disorders has been performed and it is unlikely that better prospective evidence will be available in the near future. Second, the platelet count was unknown for nearly half of the patients with thrombocytopaenia. Nevertheless, none of these patients was diagnosed with an ICH. Third, CT was performed in a minority of patients in both children with and without bleeding disorders. Although small asymptomatic ICH may have been missed, no clinically relevant ICH was missed based on our follow up data. CT performance in all patients would have been unethical, all patients included in our study had complete follow up to identify initially missed injuries.

Our findings, along with those from the PECARN head injury rule study, will support guidelines development for head injured children with bleeding disorders, for whom the PECARN rules were not designed.

CONCLUSIONS

Although children with a bleeding disorder more often receive a CT scan in the ED following a head trauma, despite their milder presentation compared with children without bleeding disorders, their risk of ICH seems low and appears to be

associated with post-traumatic clinical findings. A more selective CT use combined with a period of observation may be cautiously considered in these children based on clinical presentation and severity of bleeding disorder.

What is already known on this topic

- Patients with bleeding disorders are assumed to be at higher risk of intracranial haemorrhage (ICH).
- Children with bleeding disorders may be exposed to more computed tomographies (CTs) than other children due to a lower CT imaging threshold.
- Data for neuroimaging in these patients in settings with low baseline CT rates are unknown.

What this study adds

- In our low baseline CT rate setting of children with head injuries, only 30% of 103 of patients with bleeding disorders underwent CT imaging.
- Only 1 of 103 patients had ICH on CT which required neurosurgery. Children without CT imaging did well on follow-up.
- A selective imaging strategy for children with bleeding disorders in low CT settings may be considered

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Table 1. Definitions of main variables analysed in the study

Variable	Definition
Congenital or acquired bleeding disorders	Haemophilia, von Willebrand disease, congenital or acquired thrombocytopaenia (defined as platelet count <150 000/m L), functional platelet disorder, other bleeding disorder, or anti-coagulation therapy (warfarin, heparin, low molecular weight heparin/enoxaparin, clopidogrel). Patients with haemophilia were categorized according to type of factor deficiency and severity (mild, moderate, or severe).[9] For children with thrombocytopaenia, platelet counts at the time of the ED evaluation were obtained when available from the medical record.
Intracranial Haemorrhage (ICH)	Any acute intracranial finding revealed on CT that was attributable to acute injury (i.e. epidural or subdural haematomas, intraventricular haemorrhages, cerebral contusions/haemorrhages, subarachnoid haemorrhages, or traumatic infarctions).
Clinically important traumatic brain injury (ciTBI)	Composite outcome encompassing death, need for neurosurgery, intubation for >24 hours due to TBI or admission for ≥2 nights with a TBI on CT.[16]
Traumatic brain injury on computed tomography (TBI on CT)	Intracranial haemorrhage/contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus thrombosis, midline shift of intracranial contents or signs of brain herniation, diastasis of the skull, pneumocephalus, skull fracture depressed by at least the width of the table of the skull.[16]
Altered mental status	GCS score <15, agitation, sleepiness, slow responses, or repetitive questioning.[16]
Severity of mechanism	*Severe* injury mechanism included: patient ejection in a motor vehicle crash; patient was a passenger in a motor vehicle crash rollover; any passenger death in the motor vehicle crash; patient was a pedestrian or un-helmeted bicyclist struck by an automobile; fall>5feet when >=2years old or >3 feet when <2years old; or head struck by a high-impact object (eg, golf club). *Mild* injury mechanisms included falls to the ground from standing height or walking/running into stationary objects associated with signs or symptoms of blunt head trauma. All other mechanisms were considered *moderate*.[9 16]

Table 2. Type of bleeding disorders (n of patients=103)

Disorder	Number (%)	
Haemophilia*	41 (40)	
Severe		17 (42)
Moderate		11 (27)
Mild		12 (29)
Unknown		1 (2)
Thrombocytopaenia (platelets/μL)	29 (28)	
<5000		7 (24)
5001-20000		4 (14)
20001 -50000		2 (7)
50001 – 150000		3 (10)
Unknown		13 (45)
Von Willebrand Disease*	17 (17)	
Anticoagulation therapy**	15 (15)	
Functional platelet disorder**	1 (1)	
Other bleeding disorder	1 (1)	

*One patient had a dual bleeding disorder (haemophilia and Von Willebrand disease)
**One patient had a dual bleeding disorder (anticoagulation therapy and functional platelet disorder)

Table 3. Demographic and clinical characteristics of patients with bleeding disorders presenting to emergency departments who received and did not receive computed tomography (CT) following initial assessment

	CT Performed 31		CT NOT Performed 72		% Rate Difference	
	n	%	n	%	%	(95% CI)
Mean age, years (SD)	7.5	(4.9)	5.1	(3.7)	2.4	(-0.7, -4.2)
Male sex (%)	30	(96.8)	53	(73.6)	23.2	(11.2, 35.1)
Age <2yrs (%)	4	(12.9)	18	(25.0)	-12.1	(-27.6, 3.4)
Bleeding disorder						
Haemophilia	17	(54.8)	24	(33.3)	21.5	(0.9, 42.1)
Mild	4	(23.5)	8	(33.3)	-9.8	(-37.4, 17.8)
Moderate/severe	13	(76.5)	15	(62.5)	14.0	(-14.0, 41.9)
Unknown	0	(0.0)	1	(4.2)	-4.2	(-12.2, 3.8)
von Willebrand disease	4	(12.9)	13	(18.1)	-5.2	(-19.9, 9.6)
Thrombocytopenia	5	(16.1)	24	(33.3)	-17.2	(-34.1, -0.3)
<20 000 plts/μL	0	(0.0)	11	(45.8)	-45.8	(-65.8, -25.9)
≥20 000 plts/μL	2	(40.0)	3	(12.5)	27.5	(-17.4, 72.4)
Unknown	3	(60.0)	10	(41.7)	18.3	(-28.9, 65.6)
Anti-coagulation therapy	5	(16.1)	11	(15.3)	0.9	(-14.5, 16.2)
Other	0	(0.0)	1	(1.4)	-1.4	(-4.1, 1.3)
History of loss of consciousness	2	(7.1)	4	(5.6)	1.5	(-9.4, 12.5)
Headache	0	(0.0)	1	(1.9)	*	
History of vomiting	10	(32.3)	4	(5.6)	26.6	(9.3, 43.9)
Acting abnormally according to parent	10	(33.3)	5	(7.0)	26.3	(8.4, 44.2)
Altered mental status	2	(6.5)	0	(0.0)	6.5	(-2.2, 15.1)
Signs of basilar skull fracture	0	(0.0)	0	(0.0)	0.0	
Palpable skull fracture (or unclear exam)	1	(3.2)	0	(0.0)	3.2	(-3.0, 9.5)

Scalp hematoma	17	(54.8)	39	(54.9)	-0.1	(-21.1,	20.9)
Frontal	8	(47.1)	26	(66.7)	-19.6	(-47.6,	8.4)
Non-frontal	9	(52.9)	13	(33.3)	19.6	(-8.4,	47.6)
Seizure	3	(10.0)	1	(1.4)	8.6	(-2.5,	19.7)

*Preverbal cases were excluded in the analysis of headache frequency

Table 4. Posttraumatic clinical findings of patients with and without bleeding disorders presenting to emergency departments who received and did not receive computed tomography (CT) following initial assessment, aged <2 years.

	Bleeding disorder						No Bleeding disorder					
	CT Performed n=4		CT NOT Performed n=18		% Rate Difference		CT Performed n=371		CT NOT Performed n=4981		% Rate Difference	
	n	%	n	%	%	(95% CI)	n	%	n	%	%	(95% CI)
Mechanism of injury												
Mild	4	(100.0)	16	(88.9)	11.1	(-3.4, 25.6)	166	(45.1)	3549	(72.1)	-26.9	(-32.2, -21.7)
Moderate	0	(0.0)	1	(5.6)	-5.6	(-16.1, 5.0)	62	(16.9)	410	(8.3)	8.5	(4.6, 12.4)
Severe	0	(0.0)	1	(5.6)	-5.6	(-16.1, 5.0)	140	(38.0)	967	(19.6)	18.4	(13.3, 23.5)
History of LOC	0	(0.0)	3	(16.7)	-16.7	(-33.9, 0.6)	57	(17.9)	242	(5.0)	12.9	(8.6, 17.2)
History of vomiting	1	(25.0)	2	(11.1)	13.9	(-31.0, 58.7)	130	(36.1)	819	(16.6)	19.5	(14.4, 24.6)
Child acting abnormally according to parent	2	(50.0)	0	(0.0)	50.0	(1.0, 99.0)	128	(36.8)	551	(11.3)	25.5	(20.4, 30.7)
Altered mental status	0	(0.0)	0	(0.0)			42	(12.5)	13	(0.3)	12.3	(8.7, 15.8)
Signs of basilar skull fracture	0	(0.0)	0	(0.0)			21	(5.8)	3	(0.1)	5.7	(3.3, 8.1)
Palpable skull fracture	0	(0.0)	0	(0.0)			151	(40.7)	48	(1.0)	39.7	(34.7, 44.7)
Scalp haematoma												
None	1	(25.0)	6	(33.3)	-8.3	(-56.0, 39.4)	117	(31.8)	3000	(60.5)	-28.7	(-33.7, -23.8)
Frontal	0	(0.0)	3	(16.7)	-16.7	(-33.9, 0.6)	186	(50.5)	802	(16.2)	34.4	(29.2, 39.6)
Non Frontal	3	(75.0)	9	(50.0)	25.0	(-23.3, 73.3)	65	(17.7)	1156	(23.3)	-5.7	(-9.7, -1.6)

Table 5. Posttraumatic clinical findings of patients with and without bleeding disorders presenting to emergency departments who received and did not receive computed tomography (CT) following initial assessment, aged >=2 years.

	Bleeding disorder						No Bleeding disorder					
	CT Performed n=27		CT NOT Performed n=54		% Rate Difference		CT Performed n=1704		CT NOT Performed n=12978		% Rate Difference	
	n	%	n	%	%	(95% CI)	n	%	n	%	%	(95% CI)
Mechanism of injury												
Mild	13	(48.2)	29	(54.7)	-6.6	(-29.7, 16.6)	402	(23.7)	6646	(52.0)	-28.3	(-30.5, -26.1)
Moderate	12	(44.4)	18	(34.0)	10.5	(-12.2, 33.2)	641	(37.8)	4132	(32.3)	5.5	(3.0, 7.9)
Severe	2	(7.4)	6	(11.3)	-3.9	(-17.0, 9.1)	653	(38.5)	1999	(15.7)	22.9	(20.5, 25.3)
History of LOC	2	(8.3)	1	(1.9)	6.5	(-5.2, 18.1)	681	(45.2)	1721	(13.9)	31.4	(28.8, 34.0)
History of vomiting	9	(33.3)	2	(3.8)	29.6	(11.1, 48.1)	721	(43.6)	1768	(13.7)	29.8	(27.4, 32.3)
Child acting abnormally according to parent	8	(30.8)	5	(9.4)	21.3	(1.9, 40.7)	621	(38.6)	1380	(10.8)	27.8	(25.4, 30.3)
Altered mental status	2	(7.4)	0	(0.0)	7.4	(-2.5, 17.3)	371	(22.3)	117	(0.9)	21.4	(19.4, 23.4)
Signs of basilar skull fracture	0	(0.0)	0	(0.0)			95	(5.6)	6	(0.1)	5.6	(4.5, 6.7)
Palpable skull fracture	1	(3.7)	0	(0.0)	3.7	(-3.4, 10.8)	269	(15.8)	89	(0.7)	15.1	(13.4, 16.9)
Scalp haematoma												
None	13	(48.2)	26	(49.1)	-0.9	(-24.1, 22.3)	923	(54.5)	8991	(69.6)	-15.1	(-17.6, -12.6)
Frontal	9	(33.3)	10	(18.9)	14.5	(-6.2, 35.1)	510	(30.1)	2206	(17.1)	13.0	(10.8, 15.3)
Non Frontal	5	(18.5)	17	(32.1)	-13.6	(-32.9, 5.8)	261	(15.4)	1727	(13.4)	2.0	(0.2, 3.9)

Supplementary Tables

Supplementary Table 1. Demographic and clinical characteristics of patients with and without bleeding disorders presenting with a head injury to emergency departments

	Bleeding disorder N=103		No Bleeding disorder N=20,034		% Rate Difference	
	n	%	n	%	%	(95% CI)
Mean age, years (SD)	5.8	(4.2)	5.7	(4.7)	0.1	(-0.8, -1.0)
Male sex (%)	83	(80.6)	12,740	(63.6)	17.0	(9.3, 24.6)
Age < 2yrs (%)	22	(21.4)	5,352	(26.7)	-5.4	(-13.3, 2.6)
Severity of Mechanism						
Mild	60	(58.3)	11,844	(59.1)	-0.9	(-10.4, 8.7)
Moderate	33	(32.0)	4,203	(21.0)	11.1	(2.0, 20.1)
Severe	9	(8.7)	3,720	(18.6)	-9.8	(-15.3, -4.4)
GCS (%)						
≤ 13	1	(1.0)	351	(1.8)	-0.8	(-2.7, 1.1)
14	2	(1.9)	576	(2.9)	-0.9	(-3.6, 1.7)
15	100	(97.1)	19,107	(95.4)	1.7	(-1.6, 5.0)
History of loss of consciousness	6	(6.1)	2,701	(14.2)	-8.1	(-12.8, -3.4)
Headache	1	(1.5)	835	(5.2)	-3.8	(-6.6, -1.0)
History of vomiting	14	(13.7)	3,438	(17.4)	-3.6	(-10.3, 3.1)
Acting abnormally according to parent	15	(14.9)	2,680	(13.7)	1.2	(-5.8, 8.1)
Altered mental status	2	(1.9)	543	(2.8)	-0.8	(-3.5, 1.9)
Signs of basilar skull fracture	0	(0.0)	125	(0.6)	-0.6	(-0.7, -0.5)
Palpable skull fracture (or unclear exam)	1	(1.0)	557	(2.8)	-1.8	(-3.8, 0.1)
Scalp hematoma	56	(54.9)	6,913	(34.7)	20.2	(10.6, 29.9)

Frontal	34	(60.7)	3,209	(47.2)	13.5	(0.6,	26.3)
Non-frontal	22	(39.3)	3,584	(52.8)	-13.5	(-26.3,	-0.6)
Seizure	4	(4.0)	332	(1.7)	2.3	(-1.5,	6.1)
CT obtained	31	(30.1)	2,075	(10.4)	19.7	(10.9,	28.6)
ICH on CT	1	(1.0)	316	(1.6)	-0.6	(-2.5,	1.3)
Extra axial (subdural/extradural)	1	(1.0)	212	(1.1)	-0.1	(-2.0,	1.8)
Parenchyma	0	(0.0)	107	(0.5)	-0.5	(-0.6,	-0.4)
Sub-arachnoid	0	(0.0)	68	(0.3)	-0.3	(-0.4,	-0.3)
TBI on CT	1	(1.0)	394	(2.0)	-1.0	(-2.9,	0.9)
ciTBI	1	(1.0)	279	(1.4)	-0.4	(-2.3,	1.5)
Neurosurgery	1	(1.0)	82	(0.4)	0.6	(-1.3,	2.5)

ciTBI: clinically important traumatic brain injury; CT computed tomography; GCS: Glasgow Coma Scale; ICH: intracranial haemorrhage; TBI:traumatic brain injury

Supplementary Table 2. Severity of injury mechanism per type of bleeding disorders (n of patients=103)

	Haemophilia*		Thrombocytopaenia		Von Willebrand Disease*		Anticoagulation therapy**		Functional platelet disorder**		Other bleeding disorder	
	n = 41	(39.8)	n = 29	(28.2)	n = 17	(16.5)	n = 16	(15.5)	n = 1	(1.0)	n = 1	(1.0)
	n	%	n	%	n	%	n	%	n	%	n	%
Mechanism of Injury, n (%)												
Severe	5	(12.2)	2	(6.9)	1	(5.9)	1	(6.3)	0	(0.0)	0	(0.0)
Moderate	11	(26.8)	11	(37.9)	6	(35.3)	3	(18.8)	0	(0.0)	0	(0.0)
Mild	25	(61.0)	16	(55.2)	10	(58.8)	11	(68.8)	1	(100.0)	1	(100.0)
CT performed, n (%)	17	(41.5)	5	(17.2)	4	(23.5)	5	(31.3)	0	(0.0)	0	(0.0)
CT findings, n (%)												
Normal	17	(100.0)	5	(100.0)	3	(75.0)	5	(100.0)	na		na	
Intracranial haemorrhage	0	(0.0)	0	(0.0)	1	(25.0)	0	(0.0)	na		na	

*One patient had a dual bleeding disorder (haemophilia and Von Willebrand disease)
**One patient had a dual bleeding disorder (anticoagulation therapy and functional platelet disorder)
na=not applicable

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Title:
Risk of traumatic intracranial haemorrhage in children with bleeding disorders

Date:
2020-12

Citation:
Bressan, S., Monagle, P., Dalziel, S. R., Borland, M. L., Phillips, N., Kochar, A., Lyttle, M. D., Cheek, J. A., Neutze, J., Oakley, E., Dalton, S., Gilhotra, Y., Hearps, S., Furyk, J. & Babl, F. E. (2020). Risk of traumatic intracranial haemorrhage in children with bleeding disorders. JOURNAL OF PAEDIATRICS AND CHILD HEALTH, 56 (12), pp.1891-1897. https://doi.org/10.1111/jpc.15073.

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