1	Short term neurocognitive and symptomatic outcomes following
2	mild traumatic brain injury: a prospective multicentre
3	observational cohort study
4	Dr Benjamin M Bloom, MB ChB BSc FRCEM, Consultant in Emergency Medicine (1)(2); Ms Kathryn
5	Kinsella, Specialist Research Nurse (3); Mr Jason Pott, BHSc, Specialist Research Nurse (2); Mr
6	Hiren C Patel MB ChB PhD FRCS, Consultant Neurosurgeon (4); Professor Tim Harris, BM BS
7	FRCEM, Professor & Consultant in Emergency Medicine (1)(2); Professor Fiona Lecky, MB ChB PhD
8	FRCEM FRCS(Ed), Clinical Professor & Honorary Consultant in Emergency Medicine (3)(5)(6);
9	Rupert Pearse, MB BS MD FRCA FFICM, NIHR Research Professor & Consultant in Intensive Care
10	Medicine (1)
11 12	Corresponding author: Dr Ben Bloom
13	Postal address: Emergency Department Research Office, Royal London Hospital, Whitechapel,
14	London, E1 1BB, UK
15	Email: ben.bloom@nhs.net
16	Tel: +44 20 3594 0043
17 18	Affiliations (1) William Harvey Institute, Queen Mary University of London, London, UK;
19	(2) Department of Emergency Medicine, Royal London Hospital, London, UK;
20	(3) Department of Emergency Medicine, Salford Healthcare Directorate, Salford Royal Foundation
21	Trust, Salford, UK;
22	(4) Department of Neurosurgery, Salford Royal NHS Foundation Trust, Salford, UK;
23	(5) School of Health and Related Research University of Sheffield, UK;
24	(6) Trauma Audit and Research Network, Institute of Population Health, University of Manchester,
25	Manchester, UK.

- 1
- 2 Keywords
- 3 Mild traumatic brain injury, closed head injury, concussion, neurocognitive outcome,
- 4 neuropsychological outcome
- 5
- 6 Word Count
- 7 (Excluding title page, abstract, references, figures or tables)
- 8 3737
- 9

1 ABSTRACT

2 Objective

- 3 To determine the short term cognitive and symptomatic outcome following mild traumatic brain
- 4 injury.

5 Setting

6 Emergency Departments of two UK tertiary referral hospitals.

7 Participants

- 8 Adult patients presenting to the Emergency Departments of the Royal London Hospital and Salford
- 9 Royal Hospital with suspected traumatic brain injury within 24 hours, and Glasgow Coma Score >8. A
- 10 non-TBI comparison group included adult patients with no head or neck injury.

11 Design

12 Prospective multi-centre cohort study.

13 Main Measures

- 14 The Standardised Assessment of Concussion (SAC), the Concussion Symptom Inventory (CSI), and
- 15 total number of symptoms, measured at baseline and 72 hours.

16 *Results*

- 17 We enrolled 189 patients with and 51 patients without TBI. Patients with TBI had marked cognitive
- impairment which persisted at 72 hours (SAC score baseline 25 [23-27] vs 72 hours 25 [22-27];
- 19 p=0.1). Patients with TBI had persistent high symptom severity although this had decreased at 72
- 20 hours (CSI score baseline 9 [4-22] vs 72 hours 5 [1-19], p=0.002). A similar pattern was observed with
- 21 the total number of symptoms (baseline 4 [2-8] vs 72 hours 0 [0-4]; p<0.001). Patients with TBI had
- 22 worse neurocognitive function, higher overall symptom severity, and higher total number of
- 23 symptoms compared with patients without TBI. Patients without TBI' neurocognitive function and

- 1 symptom severity remained constant, but number symptoms reduced between baseline and 72
- 2 hours.

3 **Conclusion**

- 4 There is a cognitive deficit and symptom burden in patients with mild TBI presenting to the
- 5 Emergency Department which persists at 72 hours.

1 INTRODUCTION

2 Around 1.7 million patients attend emergency departments in the US and 1.4 million in the UK 3 annually with a traumatic brain injury (TBI) [1, 2]. A further 500,000 to 800,000 patients a year are 4 estimated to seek clinic and out-patient based care for TBI [3]. Approximately 90% of all TBIs are 5 mild [4]. Mild TBI can result in persistent symptoms and have impact on return to work times 6 following injury [5]. The cardinal features of mild TBI are acute and include alteration in level of 7 consciousness and memory dysfunction, with resolution within 30 minutes. However, decreased 8 cognitive function and symptoms such as headache and dizziness may persist for hours, days or 9 sometimes weeks following the injury. This has been incompletely reported in Emergency 10 Department populations [6]. We have limited understanding of the impact of mild TBI in Emergency 11 Department patients on enduring cognitive deficits. 12 Mild TBI is an acute condition characterised by transient altered mental status and disorders of 13 memory [7]. There is therefore a cognitive dysfunction associated with mild TBI. The evolution of 14 neurocognitive dysfunction in the early phase of mild TBI is poorly understood. Several small studies 15 report an immediate neurocognitive deficit, however most of these enrolled fewer than fifty 16 patients with TBI and all were single centre studies [8-11]. In a population of more than a million patients in the US alone, many of whom are of working age, the consequences of failure to 17 18 understand how neurocognitive dysfunction develops are enormous. Mild TBI has been called the 19 silent epidemic because neurocognitive deficits that are not immediately apparent may persist [12]. 20 There remains a need to understand how neurocognitive function deficits develop over the early 21 period following injury. How neurocognitive function is affected in patients that attend the 22 Emergency Department for non-neurological or non-neurotraumatic reasons is completely

23 unknown. There may be a cognitive deficit associated with Emergency Department attendance for

24 any reason.

The objective of this study was to study the cognitive function, symptom severity and number of symptoms in patients with mild to moderate TBI at baseline in the Emergency Department, and to re-evaluate them at 72 hours. The secondary objective of this study was to compare cognitive function, symptom severity and number of symptoms at both time points between patients with mild TBI and without TBI. We hypothesised that there would be an improvement in cognition, symptom severity and number of symptoms between baseline and 72 hours, and a difference between patients with and without mild TBI.

1 METHODS

2 Study design & Setting

3 This was a prospective observational cohort study conducted between September 2011 and March 4 2012 in the Emergency Departments of the Royal London Hospital and Salford Royal Hospital. Both 5 hospitals are large university hospitals and designated Major Trauma Centres, which is equivalent to 6 level one trauma centres. The annual Emergency Department patient attendance rates are 130,000 7 and 85,000 respectively. Data were collected as part of a study of a hand-held quantitative 8 electroencephalogram designed for use in mild to moderate TBI. The study was approved by the 9 National Research Ethics Service, North West 6 Research Ethics Committee, Greater Manchester 10 South (reference 11/H1003/6).

11

12 Participants

13 Patients aged 18 to 80 years that attended the Emergency Department and were suspected of an 14 acute traumatically induced structural brain injury and/or clinical manifestations of functional brain 15 injury, as a result of insult to the head from an external force, including acceleration or deceleration 16 movements without direct external trauma to the head, with a Coma Score of >8, within the last 24 hours, were included. Mild TBI was defined as GCS 13-15, and moderate TBI as GCS 9-12. Patients 17 18 that had chronic neurological, psychiatric or cognitive conditions; temperature \geq 37.7°C; critical 19 illness; open head injury; received procedural sedation; were mechanically ventilated; receiving 20 dialysis; in stage four chronic kidney disease; or pregnant were excluded. Patients without TBI were 21 eligible if they were aged 18 to 80 and attended the Emergency Department with any condition 22 excluding: an injury with any trauma above the clavicle; a history of road traffic collision requiring an 23 Emergency Department visit; TBI within the past year; an primary acute neurological complaint or 24 complaint of syncope. Those patients that had a CT scan of the head performed, had one done so in

line with national guidance [2]. Written informed consent was obtained from the patient, and in
 instances where the patient was unable to provide consent, consultee declaration to participate was
 obtained from a family member or the primary treating physician.

Screening and enrolment procedures occurred during Monday to Friday, between 0800hrs and
2000hrs due to availability of research staff. Sources of bias were minimised by measures taken to
obtain a complete dataset, including data abstraction from medical and pre-hospital emergency
services records; and discussion with medical and emergency medical service personnel.

8 Variables

9 Neurocognitive function was measured using the Standardised Assessment of Concussion (SAC). The 10 SAC provides an objective reproducible and standardised report of the consequences of concussion 11 [13]. The SAC is a paper-and-pencil assessment consisting of four domains (orientation, immediate 12 memory, concentration, and delayed recall). It has a maximum score of 30, with higher scores 13 indicating better neurocognitive function. It takes between five and ten minutes to complete. The 14 SAC has been extensively validated for use in sport related concussion and has been reported as 15 sensitive to sports concussion if administered within the first 48 hours [14-17].

16 Symptom severity and quantity was measured using the Concussion Symptom Inventory (CSI). The 17 CSI is a list of 12 symptoms that are graded in severity by the patient on a seven point Likert scale 18 [18]. The symptoms recorded are: headache; nausea; balance problems/dizziness; fatigue; drowsiness; feeling like "in a fog"; difficulty concentrating; difficulty remembering; sensitivity to 19 20 light; sensitivity to noise; blurred vision; feeling slowed down. It has a maximum severity score of 72 21 with lower scores indicating lower severity, and a maximum symptom number score of 12. The total 22 number of symptoms reported on the CSI, i.e. any symptom that did not have a score of 0, was 23 calculated. Within group (baseline vs follow up) and between group (TBI vs non-TBI) comparisons 24 were calculated. The comparison of numbers of concussion symptoms between groups was 25 calculated because the sensitivity of the diagnosis of post-concussion syndrome is not limited to

patients that have sustained a concussion, and consequently it is possible that symptoms of acute
 concussion are not limited to head injured ED patients [19].

Clinical variables collected were assessed by the treating physician or research personnel, and
utilised information from the patient, the prehospital medical record, and witness reports. Loss of
consciousness and amnesia were dependent on collateral reports. Altered mental state was
assessed by the treating physician. Previous TBI was determined as remembered by the patient and
defined as 'head injury' with or without loss of consciousness.

8 The primary outcome measures were overall SAC scores, representing cognitive function, overall CSI 9 scores, representing symptom severity, and total number of symptoms registered on CSI, 10 representing symptom number. These were collected at baseline in the Emergency Department and 11 at 72 hours, either face to face if the participant was an in-patient, or via telephone. Seventy-two 12 hours was chosen as an appropriate follow-up time because it is a suitable time point to determine 13 resolution of signs, duration of symptoms, and repeat CT scans, and also because there is little 14 evidence on short term neurocognitive follow up in ED patients with mild TBI [10, 11, 20]. Demographic and clinical variables, mechanisms of injury and details of the TBI (loss of 15 16 consciousness, amnesia) were obtained. Symptom presence was assessed using a list of 22 17 symptoms with binary yes/no answers to indicate presence or absence. A predefined subgroup of 18 participants with acute intracranial haemorrhage on CT head scan was analysed. This was done to 19 assess the cognitive changes in complex mild TBI, in which patients have a GCS of 13 or more but an 20 acute intra-cranial haemorrhage on CT scan [21].

21 Statistical methods

Continuous data was compared using the paired or unpaired t-test, the related samples Wilcoxon
 Signed Rank test, or the independent sample Mann-Whitney U test as appropriate. 95% confidence
 intervals (CI) were calculated for differences between means. Categorical data was compared using
 the chi-squared test. Normally distributed data is represented as mean (standard deviation, SD). Non-

normally distributed data is represented as median [interquartile range, IQR]. Categorical data is
represented as number (percentage). Normality was checked using the Shapiro-Wilk test and by
visually assessing the frequency distribution. Analyses were performed using the R Project for
Statistical Computing (https://www.r-project.org/). Significance was set at p<0.05. There was no
imputation of missing data. Loss to follow up was managed with a whole group and longitudinal
analysis.

1 **RESULTS**

2 A total of 240 patients were enrolled between September 2011 and April 2012. Of these, 189 3 patients presented with TBI and 51 patients were included as non-TBIs (figure 1). The mean age was 4 43 (16) years and 169 (70%) of participants were male. Demographic and clinical details of the TBI 5 and non-TBI groups are given in tables 1, 2 and 3, and in supplementary material table 1. At Royal 6 London 414 patients were screened of which 153 (37%) were recruited, and at Salford Royal 253 7 patients were screened of which 87 (34%) were recruited. Further detail is given in supplementary 8 material table 2. It was not possible to complete the 72 hours assessment in 110 cases (46%), which 9 comprised 88 (46%) in the TBI group and 22 (43%) in the non-TBI group. Of the 189 patients with TBI, 10 174 (92%) provided consent themselves on initial recruitment, 15 (8%) were recruited via consultee 11 declaration and 7 (4%) of those were able to provide retrospective consent. No patients withdrew. 12 Neurocognitive and symptom data are presented in Table 4. Patients with TBI presented with 13 marked neurocognitive impairment which did not improve between baseline and 72 hours. Patients 14 with TBI had poorer neurocognitive function than non-TBIs at baseline (difference in SAC score 1, 15 p=0.02, 95% CI -1.4 to -2.4), and at 72 hours (difference in SAC score 2, p=0.04, 95% CI -3.0 to 0.0) 16 (figure 2). Patients with TBI also reported notably higher symptom scores than non-TBIs. Patients 17 with TBI' symptom scores reduced significantly between baseline and 72 hours but were greater 18 than those reported by non-TBIs at both time points (difference between TBI and non-TBIs in CSI 19 score at baseline 9, p<0.001, 95% CI 8.4 to 13.7; and at 72 hours 5, p<0.001, 95% CI 5.7 to 11.6) 20 (figure 3). Patients with TBI also had high total numbers of symptoms than non-TBIs at both time 21 points (difference in total number of symptoms between TBI and non-TBIs at baseline 4, p<0.001, 22 95% Cl 2.6 to 4.4; and 72 hours 4, p=0.001, 95% Cl 1.9 to 4.1) (figure 4). The most frequently 23 occurring symptoms were pain, headache and fatigue, which were experienced by more than 50% of 24 TBI participants (figure 5).

1	Table 5 contains neurocognitive and symptom data for the subgroups with (CT+) and without (CT-)
2	acute intracranial haemorrhage. Of the 189 TBI participants, there were 25 (13%) CT+ and 154 (87%)
3	CT Mean age and gender was similar to the TBI and non-TBI group (43 [15] years, 18 [72%] males).
4	Neurocognitive function was considerably worse in the CT+ compared to CT- subgroup at both time
5	points (difference in SAC score between CT+ and CT- at baseline 3, p=0.009, 95% CI -1.0 to -3.0, and
6	at 72 hours 3, p=0.009, 95% CI -1.0 to -5.0). CT+ patients also had higher symptom scores than CT-
7	patients at baseline (difference in CSI 11, p = 0.01, 95% CI -15.0 to -2.0) and at 72 hours (difference in
8	CSI 10, p = 0.06, 95% CI -13.0 to 0.0). CT+ patients also had greater numbers of symptoms compared
9	with CT- patients at both time points (difference in total number of symptoms 4, p=0.027, 95% CI -
10	4.0 to 0.0; and 3, p=0.038, 95% CI -5.0 to 0.0 at baseline and follow up respectively).
11 12	Sensitivity analyses Sensitivity analyses using mild TBI definitions of GCS 13-15 (n=186) and 14-15 (n=183) were
13	performed. There was no material difference in results when compared with the primary analysis
14	(supplementary material tables 3 and 4). Further sensitivity analyses designed to apply the outcome
15	measure in the lowest acuity patients were performed. In patients with GCS 14-15 that had a
16	negative CT scan or no CT scan performed (n=162), there was no improvement in cognitive function
17	or symptom burden between baseline and follow up (supplementary material table 5). This suggests
18	that patients that qualify for a CT, even if their scan is normal, may have neurocognitive dysfunction
19	and a symptom burden that persists for three days. In patients with GCS 14-15 that had a scan which
20	was negative (n=71), not only cognitive function but also symptom scores and total number of
21	symptoms remained unchanged between baseline and follow up (supplementary material table 6).
22	An analysis of the patients with TBI that completed the outcome assessments at both baseline and
23	follow up (i.e. excluding the patients that were lost to follow up or were unable to complete an
24	assessment) (n=99) showed no material difference compared to the primary analysis
25	(supplementary material table 7). In a subgroup of patients with TBI that had sustained one or more
26	previous head injuries (n=63) there was no change in cognitive function or symptom burden

between baseline and follow up (supplementary material table 8). This is in contrast to a subgroup
of patients with TBI that had never had a previous head injury (n=111), where neurocognitive
dysfunction persisted to follow up but symptom burden improved (supplementary material table 8).
Three TBI subgroups consisting of CT not done, CT with no intracranial haemorrhage and CT with
intracranial haemorrhage were analysed. There is a trend towards improved cognitive function and
lighter symptom burden from intracranial haemorrhage to no CT performed (supplementary table
9).

1 **DISCUSSION**

2 The principal finding of this study was that patients with mild TBI have a clinically relevant 3 neurocognitive deficit immediately after the injury that persists to at least 72 hours. A difference in 4 SAC of two or more points is thought to be clinically relevant, although the SAC is not sensitive 5 enough to pick up subtle changes in neurocognitive function, and there is a ceiling effect associated 6 with its application [22, 23]. Patients with mild TBI also have persistently greater severity of 7 symptoms and more concussive symptoms than patients without TBI, both of which also persist to 8 72 hours. Patients with TBI with acute haemorrhage on their CT scan had poorer neurocognitive 9 function than those without.

10 To our knowledge, our study is the largest that enrolled patients with mild TBI and followed them 11 over the short term. It is also the only multi-centre study that focuses on the neurocognitive effects 12 of mild TBI in patients presenting to the Emergency Department. Neurocognitive function is usually 13 measured either by psychological test that requires administration by a trained psychologist; by 14 standardised paper and pencil tests such as the SAC; or by computer administered tests such as 15 ImPACT. Our findings of a neurocognitive deficit immediately following mild TBI are similar to 16 previously published studies, however a deficit persisting at 72 hours has not been reported before 17 in this patient group.

18 When measured using paper and pencil tests, in studies enrolling 100 and 246 patients with TBI, 19 there was a significant difference in neurocognitive function at baseline, but no follow up was 20 performed [8]. In further studies of 29 and 49 patients with TBI, neurocognitive function had 21 significantly improved by one month [10]. In a study of 62 patients presenting to the Emergency 22 Department with concussion, cognitive function measured on the SAC improved between baseline 23 and six hours later (from 21 to 24) [24]. The results reported in this latter study represent poorer 24 baseline neurocognitive function than we report. This may be because the composition of the 25 patients included in that study's population comprised a greater proportion of patients that

1 reported loss of consciousness and post traumatic amnesia compared with our sample, both of 2 which have been associated with poorer SAC scores [25]. A study of 29 patients with TBI found a 3 significant deficit compared with non-TBIs at around 31 hours post injury [11]. The same authors 4 measured SAC at baseline post injury and a month later and reported significant improvement [10]. 5 We report no improvement by 72 hours, however the authors' studies measured cognitive function 6 at different time points to ours: a single observation at 31 hours; and follow up at one month. The 7 results of our study taken with previous work implies a continuum of recovery, during which there is 8 a neurocognitive deficit present up to and beyond 72 hours but which may resolve at some point 9 before one month. This theory is backed up by the results of neurocognitive function testing by the 10 computerised ImPACT programme, which showed gradual improvement in function measured at 24 11 hours, one week and three months post injury [26].

12 Normal values for SAC scores are primarily derived from athletes that completed the SAC prior to a 13 sports season and therefore prior to any injury. A normal SAC varies from 27 to 28 [14-16]. Patients 14 with TBI in our study had baseline and 72 hours SAC scores 2-3 points lower than this, and although 15 the two populations are different, this represents a clinically relevant deficit. Our non-TBI group also 16 had lower than normal SAC scores at baseline. However, they increased by one point, which was not 17 a statistically significant increase, to 27, which seems to be the lower end of normal. We also report 18 that there were significant differences in overall symptom severity as measured on the CSI, and total 19 numbers of symptoms, between baseline and 72 hours, and between patients with and without TBI. These findings are in line with previously published work on symptom pattern post mild TBI, which 20 21 suggests that both overall symptom severity and total number of symptoms may discriminate 22 between patients with and without mild TBI [27]. However, our findings are important because we 23 have reported the persistence of neurocognitive deficit in the largest group of hospital Emergency 24 Department patients thus far described. In addition we reported several subgroup analyses which 25 suggest that cognitive deficit persists regardless of whether the patient has a GCS of 13, 14, or 15; or 26 whether the patient is in a presumed low acuity group (i.e. did not require or did not have a CT

scan); or whether they had a history of previous head injuries or not. Finally, we report that patients
with mild TBI and intracranial haemorrhage have poorer neurocognitive function than those without
intracranial haemorrhage.. This adds weight to the concept of complex mild TBI, i.e. mild TBI with
positive findings on CT, and emphasises the importance of this group of patients [21].

5 Our study has strengths and weaknesses. To our knowledge it is one of the largest studies and the 6 only multicentre study examining short term change in neurocognitive function following mild TBI. 7 Although convenience sampling was necessitated based on resources, selection bias was minimised 8 by approaching potential participants that had been admitted to hospital but were still within 24 9 hours of their TBI as well as by approaching all potential participants in real time. It was not possible 10 to eliminate bias in the form of drop-outs or lost-to-follow-up, and consequently bias was quantified 11 and is reported in figure 1. The lost-to-follow-up rate is high; 46% in the TBI group and 43% in the 12 non-TBI group. This was because, for the purposes of the EEG study, follow up was to be at three days, i.e. 72 to 96 hours. This narrow window presented significant difficulties in contacting 13 14 participants. The exclusion criteria could be said to be unnecessarily narrow. They are, however, in 15 line with other similar studies [10]. For many participants, 72 hour follow-up was by telephone. 16 Telephone based cognitive assessments are employed in cognitive research, particularly in screening 17 for cognitive defects and dementia, however the SAC is not validated for use over the telephone. 18 The proportion of follow ups completed by telephone was not recorded and so any difference 19 between telephone and face-to-face follow groups is not known. There may be an element of 20 learning that is dependent in part on visual stimulus, which clearly is missing during a telephone 21 follow up. That learning for the SAC memory recall is partly dependent on visual stimulus is enforced 22 by the observation that the domain that represented the greatest decrease in SAC between initial 23 attendance and 72 hours in the non-TBI group was the delayed recall domain. This may explain the 24 results seen that the non-TBI group had a wider SD between baseline and 72 hours. There were 25 many more patients enrolled with than without TBI, which may introduce bias in comparisons 26 between TBI and non-TBIs. This was partly because the primary outcome was the difference

between baseline and follow up within the head injured group, partly because the protocol for the
EEG study required a lower number of patients without TBI, and partly because of the nature of
convenience sampling. Whilst recognising this as a limitation, we do not believe that this is an
insurmountable flaw in the methodology. Finally, because this was an analysis of data from a
separate study, there was no specific sample size calculation associated with either TBI or non-TBI
based endpoints.

7 Methods for assessing and managing acute mild TBI in the Emergency Department are varied. This 8 reflects the uncertainty surrounding optimal management strategies. Decision making tools that 9 help determine whether or not a patient should have a computed tomography (CT) scan of the head 10 are based on studies that were designed to assess whether a patient has an intracranial 11 haemorrhage, not whether or not they have concussion [2]. We report that neurocognitive 12 dysfunction is associated with mild TBI but the speed of recovery and the repercussions on patients' 13 work and home lives is still unknown. The clinical follow up for these patients is important. Leaflets 14 explaining the likely clinical course and provision of access to TBI clinics may well contribute to an 15 improvement in clinical variables [28].

16 **CONCLUSION**

Emergency Department patients with mild TBI experience cognitive deficit and concussive symptoms that persist to at least 72 hours. This has significant implications on the management of mild TBI, including the potential for early treatment, and explicit explanations to patients on what they can expect following 'normal' scan results. Further work evaluating the pattern of neurocognitive recovery, repercussions on home and work life, and management strategies is warranted.

1 REFERENCES

Faul M, Xu L, Wald MM, Coronado VG. 2010. Traumatic brain injury in the united states:
 Emergency department visits, hospitalizations and deaths 2002–2006. Atlanta (GA): Atlanta (GA):
 Centers for Disease Control and Prevention, National Center for Injury Prevention and Control.

Triage, assessment, investigation and early management of head injury in children, young
 people and adults. Cg176. 2014. London: National Institute for Health and Care Excellence.

Mannix R, O'Brien MJ, Meehan WP. The epidemiology of outpatient visits for minor head
injury: 2005 to 2009. Neurosurgery 2013;73:129-134; discussion 134.

Rickels E, von Wild K, Wenzlaff P. Head injury in germany: A population-based prospective
 study on epidemiology, causes, treatment and outcome of all degrees of head-injury severity in two
 distinct areas. Brain injury : [BI] 2010;24:1491-1504.

Temkin NR, Corrigan JD, Dikmen SS, Machamer J. Social functioning after traumatic brain
 injury. J Head Trauma Rehabil 2009;24:460-467.

McCrea M. Standardized mental status testing on the sideline after sport-related concussion.
 Journal of athletic training 2001;36:274-279.

Holm L, Cassidy JD, Carroll LJ, Borg J. Summary of the who collaborating centre for
 neurotrauma task force on mild traumatic brain injury. Journal of rehabilitation medicine
 2005;37:137-141.

Sheedy J, Harvey E, Faux S, Geffen G, Shores EA. Emergency department assessment of mild
 traumatic brain injury and the prediction of postconcussive symptoms: A 3-month prospective study.
 J Head Trauma Rehabil 2009;24:333-343.

Peterson SE, Stull MJ, Collins MW, Wang HE. Neurocognitive function of emergency
 department patients with mild traumatic brain injury. Annals of emergency medicine 2009;53:796 803.e791.

Luoto TM, Silverberg ND, Kataja A, Brander A, Tenovuo O, Ohman J, Iverson GL. Sport
 concussion assessment tool 2 in a civilian trauma sample with mild traumatic brain injury. J
 Neurotrauma 2014;31:728-738.

Silverberg ND, Luoto TM, Ohman J, Iverson GL. Assessment of mild traumatic brain injury
 with the king-devick test(r) in an emergency department sample. Brain Inj 2014;1-4.

Langlois JA, Marr A, Mitchko J, Johnson RL. Tracking the silent epidemic and educating the
public: Cdc's traumatic brain injury-associated activities under the tbi act of 1996 and the children's
health act of 2000. The Journal of head trauma rehabilitation 2005;20:196-204.

McCrea M, Kelly JP, Kluge J, Ackley B, Randolph C. Standardized assessment of concussion in
football players. Neurology 1997;48:586-588.

8 14. McCrea M, Kelly JP, Randolph C, Kluge J, Bartolic E, Finn G, Baxter B. Standardized
9 assessment of concussion (sac): On-site mental status evaluation of the athlete. J Head Trauma
10 Rehabil 1998;13:27-35.

Barr WB, McCrea M. Sensitivity and specificity of standardized neurocognitive testing
 immediately following sports concussion. Journal of the International Neuropsychological Society :
 JINS 2001;7:693-702.

McCrea M, Guskiewicz KM, Marshall SW, Barr W, Randolph C, Cantu RC, Onate JA, Yang J,
 Kelly JP. Acute effects and recovery time following concussion in collegiate football players: The ncaa
 concussion study. JAMA 2003;290:2556-2563.

McCrea M, Barr WB, Guskiewicz K, Randolph C, Marshall SW, Cantu R, Onate Ja, Kelly JP.
 Standard regression-based methods for measuring recovery after sport-related concussion. Journal
 of the International Neuropsychological Society : JINS 2005;11:58-69.

Randolph C, Millis S, Barr WB, McCrea M, Guskiewicz KM, Hammeke Ta, Kelly JP. Concussion
 symptom inventory: An empirically derived scale for monitoring resolution of symptoms following
 sport-related concussion. Archives of clinical neuropsychology : the official journal of the National
 Academy of Neuropsychologists 2009;24:219-229.

24 19. Dean PJA, O'Neill D, Sterr A. Post-concussion syndrome: Prevalence after mild traumatic
25 brain injury in comparison with a sample without head injury. Brain injury : [BI] 2012;26:14-26.

26 20. Naunheim RS, Matero D, Fucetola R. Assessment of patients with mild concussion in the
27 emergency department. The Journal of head trauma rehabilitation 2008;23:116-122.

Mounce LT, Williams WH, Jones JM, Harris A, Haslam SA, Jetten J. Neurogenic and
 psychogenic acute postconcussion symptoms can be identified after mild traumatic brain injury. J
 Head Trauma Rehabil 2013;28:397-405.

Guskiewicz KM, Register-Mihalik J, McCrory P, McCrea M, Johnston K, Makdissi M, Dvorák J,
Davis G, Meeuwisse W. Evidence-based approach to revising the scat2: Introducing the scat3. British
journal of sports medicine 2013;47:289-293.

Randolph C, McCrea M, Barr WB. Is neuropsychological testing useful in the management of
sport-related concussion? J Athl Train 2005;40:139-152.

9 24. Naunheim RS, Matero D, Fucetola R. Assessment of patients with mild concussion in the
10 emergency department. J Head Trauma Rehabil 2008;23:116-122.

McCrea M, Kelly JP, Randolph C, Cisler R, Berger L. Immediate neurocognitive effects of
 concussion. Neurosurgery 2002;50:1032-1040; discussion 1040-1032.

Ponsford J, Cameron P, Fitzgerald M, Grant M, Mikocka-Walus A, Schonberger M. Predictors
 of postconcussive symptoms 3 months after mild traumatic brain injury. Neuropsychology
 2012;26:304-313.

27. Roe C, Sveen U, Alvsaker K, Bautz-Holter E. Post-concussion symptoms after mild traumatic
brain injury: Influence of demographic factors and injury severity in a 1-year cohort study. Disabil
Rehabil 2009;31:1235-1243.

19 28. Haboubi NH, Long J, Koshy M, Ward AB. Short-term sequelae of minor head injury (6 years
20 experience of minor head injury clinic). Disability and rehabilitation 2001;23:635-638.

21

22

1 TABLES

	ТВІ	Non-TBI	<i>p</i> - value (95% CI)
Demographics			
Number	189 (79)	51 (21)	
Age	43 (16)	40 (15)	0.20 (-1.6 to 7.7)
Male Sex	133 (70)	36 (71	0.98 (-0.1 to 0.1)
Years in education	16 (4)	17 (5)	0.12 (-2.5 to 0.3)
Disposition			
Discharge home from ED	95 (50)	23 (45)	0.97 (-0.1 to 0.1)
Admission to CDU	37 (20)	15 (29)	0.13 (-0.04 to 0.2)
Admission to hospital	57 (30)	13 (26)	0.52 (-0.1 to 0.07)
Neurosurgery performed	1 (0.5)	N/A	
Previous head injury			
Total	62 (33)	10 (20)	0.016 (0.014 to
	02 (33)		0.018)
One	39 (21)	6 (12)	0.13 (-0.2 to 0.13)
Greater than one	23 (12)	4 (8)	0.4 (-0.2 to 0.07)

2 Table 1

3 Demographics, and characteristics specific to TBI and non-TBI groups. Data are reported as number (%), or

4 mean (standard deviation). TBI, traumatic brain injury; CI, confidence interval; ED, Emergency Department;

5 CDU, clinical decision unit.

Mechanism of TBI		
Motor vehicle collision	20 (11)	
Pedestrian struck by vehicle	20 (11)	
Bicyclist	15 (8)	
Fall	62 (33)	
Other	41 (22)	
TBI characteristics		
GCS 14-15	183 (97)	
GCS 13	3 (1.5)	
GCS 9-12	3 (1.5)	
LOC	72 (38)	
Seizure	3 (1)	
РТА	64 (34)	
RGA	34 (18)	
AMS	90 (48)	
Radiological characteristics		
CT performed	102 (54)	
Of TBI group, CT+	25 (13)	
Diagnosis within CT+ group		
EDH	5 (21)	
SDH	6 (25)	
SAH	3 (13)	
Contusion and IPH	9 (38)	
IVH	0 (0)	
Mixed	1 (4)	

1 Table 2

2 Characteristics of TBI group. Data are reported as number (%). TBI, traumatic brain injury; GCS, Glasgow coma

3 score; LOC, loss of consciousness; PTA, post traumatic amnesia; RGA, retrograde amnesia; AMS, altered mental

4 status; CT, computed tomography; CT+, acute haemorrhage seen on CT; EDH, extradural haemorrhage; SDH,

5 subdural haemorrhage; SAH, subarachnoid haemorrhage; IPH, intra-parenchymal haemorrhage; IVH, intra-

6 ventricular haemorrhage.

Presenting complaint (non-TBI group)						
Abdominal pain	12 (24)					
Fracture/sprain/dislocation	11 (22)					
Back/limb pain	10 (20)					
Other	10 (20)					
Chest pain	6 (10)					
Laceration	3 (6)					

1 Table 3

2 Presenting complaints of non-TBI patients

		TBI (n		Non-TBI (n=52)					
	Baseline	72 hours	Difference P (95% CI)		Baseline	72 hours	Diffe	Difference P (95% CI)	
SAC	25 (23-27)	25 (22-27)	0	0.1 (-0.4 to 1.2)	26 (24-28)	27 (24-29)	1	0.5 (-0.6 to 1.7)	
CSI	9 (4-21)	5 (1-18)	4	0.002 (1.2 to 6.3)	0 (0-2)	0 (0-2)	0	0.3 (-0.5 to 3.4)	
Total no. symptom	4 (2-8)	4 (1-6)	0	0.051 (-1.5 to 0)	0 (0-2)	0 (0-1)	0	0.15 (-0.1 to 0.9)	

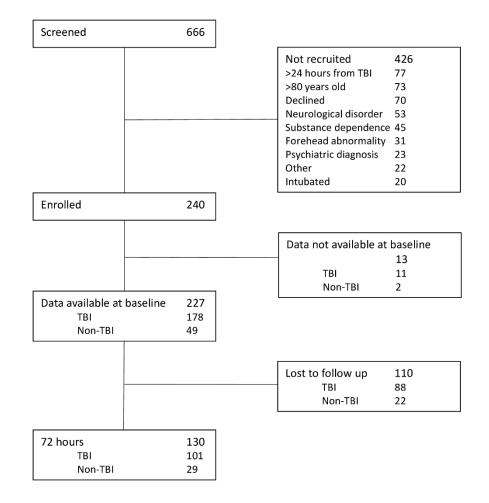
- 1 Table 4
- 2 Neurocognitive outcomes; symptom severity; and total number of concussive symptoms as
- 3 measured in the concussion symptom inventory, in TBI and non-TBI groups at baseline and 72 hours.
- 4 TBI, traumatic brain injury; SAC, standardised assessment of concussion; CSI, concussion symptom
- 5 inventory; IQR, interquartile range. Maximum SAC score possible is 30, indicating best
- 6 neurocognitive function; maximum CSI score is 72, indicating maximum symptom severity, and
- 7 maximum number of symptoms possible is 12. Data are reported as median (interquartile range).

		CT+ (r		CT- (n=164)				
	Baseline	72 hours	Difference P (95% CI)		Baseline	72 hours	Difference <i>P</i> (95% Cl)	
SAC	23 (22-26)	22 (19-24)	1	0.5 (-0.6 to 1.7)	26 (23-28)	25 (22-27)	1	0.2 (-0.6 to 1.2)
CSI	20 (11-30)	15 (6-21)	5	0.3 (-0.5 to 3.4)	9 (4-19)	5 (1-15)	4	0.006 (0.7 to 6.2)
Total no. symptom	8 (4-9)	6 (5-9)	2	0.14 (-0.1 to 0.9)	4 (2-7)	3 (1-6)	1	0.01 (0.2 to 1.7)

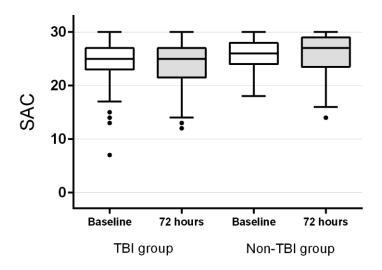
1 Table 5

- 2 Neurocognitive outcomes; symptom severity; and total number of concussive symptoms as
- 3 measured in the concussion symptom inventory, in TBI patients with and without intracranial
- 4 haemorrhage, at baseline and at 72 hours. CT+, acute intracranial haemorrhage; CT-, no acute
- 5 intracranial haemorrhage; TBI, traumatic brain injury; SAC, standardised assessment of concussion;
- 6 CSI, concussion symptom inventory; SD, standard deviation; IQR, interquartile range. Maximum SAC
- 7 score possible is 30, indicating best neurocognitive function; maximum CSI score is 72, indicating
- 8 maximum symptom severity, and maximum number of symptoms possible is 12.

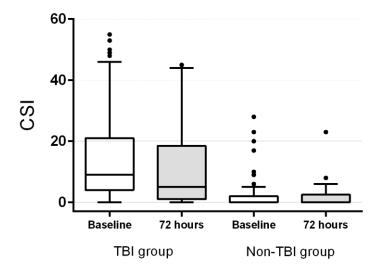
1 FIGURES



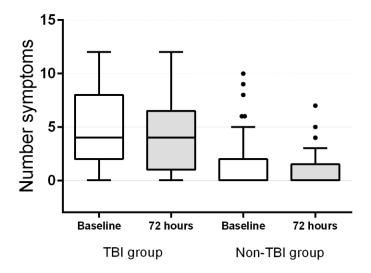
- 3 Figure 1.
- 4 Patient enrolment flow diagram.



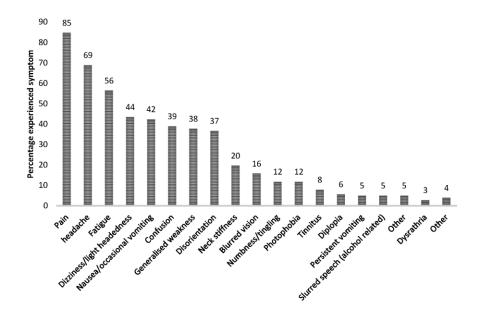
- 1
- 2 Figure 2.
- 3 Neurocognitive function. Box and whisker plot of standardised assessment of concussion (SAC)
- 4 scores. The SAC is a neurocognitive test comprised of four domains (orientation, immediate
- 5 memory, concentration, and delayed recall). Maximum SAC score possible is 30, indicating best
- 6 neurocognitive function. Baseline is initial assessment within 24 hours. TBI, traumatic brain injury.



- 1
- 2 Figure 3.
- 3 Symptom scores. Box and whisker plot of Concussion Symptom Inventory (CSI). The CSI is a list of 12
- 4 symptoms, the severity of which patients self-report on a seven point Likert scale. Maximum CSI
- 5 score is 72, indicating maximum overall symptom severity. Baseline is initial assessment within 24
- 6 hours. TBI, traumatic brain injury.



- 1
- 2 Figure 4.
- 3 Total number of symptoms. Box and whisker plot of number of symptoms. The maximum number of
- 4 symptoms possible is 12. Baseline is initial assessment within 24 hours. TBI, traumatic brain injury.



- 3 Figure 5.
- 4 Symptom frequency. The percentage of patients in the TBI group that experienced each symptom.

1 CONFLICT OF INTEREST STATEMENT:

2 No author states any conflict of interest

3 FUNDING DISCLOSURE:

- 4 Funding was received from BrainScope Co, Inc. (Bethesda, Maryland, USA) for conducting the study.
- 5 The funder had no role in the collection or analysis of the data, or of the drafting of the manuscript.

6 ACKNOWLEDGMENTS, CREDITS, OR DISCLAIMERS

- 7 Nil
- 8