

## FACTORS ASSOCIATED WITH PERSISTENT POST-CONCUSSION SYMPTOMS FOLLOWING MILD TRAUMATIC BRAIN INJURY IN ADULTS

Jennie PONSFORD, PhD<sup>1,2</sup>, Sylvia NGUYEN, DPsych<sup>1,2</sup>, Marina DOWNING, PhD<sup>1,2</sup>, Marije BOSCH, PhD<sup>3,4,12</sup>, Joanne E. MCKENZIE, PhD<sup>5</sup>, Simon TURNER, MBIostat<sup>5</sup>, Marisa CHAU, BBNS(Hons)<sup>3,4</sup>, Duncan MORTIMER, PhD<sup>6</sup>, Russell L. GRUEN, PhD<sup>7-9</sup>, Jonathan KNOTT, PhD<sup>10,11</sup> and Sally GREEN, PhD<sup>5</sup>

From the <sup>1</sup>Monash-Epworth Rehabilitation Research Centre, Epworth Healthcare, <sup>2</sup>Monash Institute of Cognitive and Clinical Neuroscience, School of Psychological Sciences, Monash University, <sup>3</sup>Department of Surgery, Central Clinical School, Monash University, <sup>4</sup>National Trauma Research Institute, The Alfred & Monash University, <sup>5</sup>School of Public Health and Preventive Medicine, Monash University, <sup>6</sup>Centre for Health Economics, Monash Business School, Monash University, <sup>7</sup>Department of Neurosurgery and <sup>8</sup>Department of Trauma, The Alfred Hospital, Melbourne, Australia, <sup>9</sup>Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, <sup>10</sup>Melbourne Medical School, The University of Melbourne, <sup>11</sup>Department of Emergency Medicine, Royal Melbourne Hospital, Melbourne, Australia and <sup>12</sup>Faculty of Economics and Business, University of Groningen, the Netherlands

**Objectives:** Debate regarding factors associated with persistent symptoms following mild traumatic brain injury continues. Nested within a trial aiming to change practice in emergency department management of mild traumatic brain injury, this study investigated the nature of persistent symptoms, work/study outcomes, anxiety and quality of life and factors associated with persistent symptoms following injury, including the impact of receiving information about mild traumatic brain injuries in the emergency department.

**Methods:** A total of 343 individuals with mild traumatic brain injury completed the Rivermead Post-Concussion Symptom Questionnaire, Hospital Anxiety Depression Scale – Anxiety Scale, and Quality of Life – Short Form an average 7 months post-injury.

**Results:** Overall, 18.7% of participants reported 3 or more post-concussional symptoms, most commonly fatigue (17.2%) and forgetfulness (14.6%). Clinically significant anxiety was reported by 12.8%, and was significantly associated with symptom reporting, as were mental and physical quality of life scores. Significant predictors of post-concussional symptoms at follow-up were pre-injury psychological issues, experiencing loss of consciousness, and having no recall of receiving information about brain injury in the emergency department.

**Conclusion:** This study confirms that loss of consciousness and pre-injury psychological issues are associated with persistent symptom reporting. Not receiving injury information in the emergency department may also negatively influence symptom reporting.

**Key words:** mild traumatic brain injury; post-concussion symptoms; anxiety; quality of life.

Accepted Sep 4, 2018; Epub ahead of print Nov 14, 2018

J Rehabil Med 2019; 51: 00–00

Correspondence address: Jennie Ponsford, School of Psychological Sciences, Monash University, Clayton, Victoria, 3800, Australia. E-mail: jennie.ponsford@monash.edu

Mild traumatic brain injury (mTBI) continues to present considerable controversy. mTBI com-

### LAY ABSTRACT

Loss of consciousness and pre-injury psychological issues are associated with persistent post-concussional symptom reporting. Not receiving information about mild traumatic brain injuries in the emergency department may also negatively influence symptom reporting.

monly results in post-concussional symptoms (PCS) in the hours, days or weeks after injury. Whilst most patients have fully recovered within 1–3 months of injury, 15–25% of cases still experience symptoms 3 months post-injury, causing stress and disability (1, 2). Frequencies of persistent PCS vary with study recruitment criteria, setting and timing (3).

Most prospective studies have not followed up individuals with mTBI beyond 3 months post-injury. Of studies measuring PCS on the Rivermead Post-Concussion Symptom Checklist (RPQ) 6 or 12 months post-mTBI, rates of PCS have varied from 21% (4) to 49.8% (5) at 6 months, and from 27.3% (6) to 47.9% (5) at 12 months. Overall, there is limited agreement on when symptoms resolve (7).

Regarding predictors of persistent PCS, injury severity measures including GCS and PTA do not generally predict outcome following mTBI (1, 4, 8, 9), although recent studies (10, 11) show that higher GCS is associated with less symptom reporting. Loss of consciousness (LOC) has not reliably predicted outcome following mTBI. Intracranial abnormalities are associated with persistent PCS in some studies (12–15), but not others (10, 16). However, most mTBI patients do not show intracranial abnormalities and/or are not scanned. Of demographic predictors, female sex is associated with greater PCS (2, 5, 8–10, 17–20). Older age has been associated with persistent PCS in only 3 mTBI studies (20–22), whilst Van der Naalt et al. (10) found a non-linear relationship of age with PCS reporting. Of all pre-injury factors, presence of pre-injury mental health issues has been the strongest outcome predictor (2, 8–10, 22–24). Studies have also shown that concurrent anxiety and depression is associated with PCS reporting (4, 8, 10, 16, 25).

Limited evidence supports efficacy of interventions to reduce PCS following mTBI. Some evidence suggests provision of written information regarding expected symptoms and suggested coping strategies results in fewer reported PCS and lower anxiety 3 months post-injury (26–28).

The recently completed NET trial (29) examined the effectiveness of an implementation intervention to increase uptake of 3 recommendations for management of mTBI patients in emergency departments (ED): (i) prospective assessment of PTA using a validated tool; (ii) use of guideline-developed criteria to determine use and timing of computed tomography (CT) imaging; and (iii) provision of written patient information upon discharge from the ED. Control sites received access to an evidence-based clinical practice guideline without further implementation support. The present study utilized a cohort of patients participating in a follow-up component of this study (NET-Plus); first to describe long-term PCS symptoms, work/study outcomes, anxiety levels and quality of life in mTBI patients presenting to ED with GCS 14 or 15; and secondly, to identify factors associated with persistent PCS at follow-up, including the impact of receiving mTBI information in ED. It was hypothesized that persistent PCS would be reported in 20% of cases, and symptom reporting associated with age, sex, pre-injury mental health issues, concurrent anxiety, and recall of receipt of written information regarding the nature of expected symptoms.

## METHODS

The NET trial was a cluster randomised trial (CRT) involving 31 Australian EDs. The NET protocol has previously been published and this study only provides a brief overview of procedures relevant to the NET-Plus component of the trial (29).

### Recruitment

The trial had 2 levels of hospital participation, designated NET and NET-Plus. EDs participating in NET measured clinical practice outcomes only, whereas EDs participating in NET-Plus assessed patient outcomes following discharge in a subgroup of individuals who agreed to be followed up from the larger cohort. This paper examines data from the NET-Plus cohort. Of the 31 EDs in the NET study, 24 agreed to participate in the NET-Plus trial and recruited participants. In this cohort, 10 EDs were allocated to the intervention and 14 to the control group. However, 7 control EDs reported receiving (limited) education regarding the management of mTBI as part of standard clinical education programmes or in-service training during the trial. One control site had an existing validated PTA assessment tool, administered by occupational therapists. For the current paper, the NET-Plus cohort was analysed as a single group. Trained chart auditors identified eligible candidates on the basis of 4 pre-defined inclusion criteria obtained from medical records: (i) aged 18 years or older; (ii) presented to the ED within 24 h of

injury; (iii) sustained an acute blunt head trauma; and, (iv) documented a GCS score of 14 or 15 at presentation. Patients with penetrating injuries or non-traumatic brain injuries (e.g. stroke) were excluded. Eligible candidates were initially contacted by an ED staff member and invited to participate in a follow-up telephone interview. Exclusion criteria at this phase were: (i) non-English speaking background; (ii) limited hearing ability; (iii) cognitive impairment from intellectual disability and/or other neurological syndrome; and, (iv) severe substance use disorder and/or major psychiatric disorder requiring previous hospitalization. Interested candidates were posted an information sheet with a 2-week opt out option. After 2 weeks, consent was presumed and contact details were provided to researchers with clinical training and experience in conducting interviews with a brain trauma population. Researchers further screened for capacity to provide informed consent at interview commencement and calls were terminated if participants were intoxicated, distressed or impaired cognition was suspected. Overall, 343 participants were recruited into the study.

### Procedures

Ethical approval for the study protocol was granted by Alfred Health Human Research Ethics Committee (approval number 398/12). Local ethics was further obtained for each hospital site. Four attempts were made to contact consenting participants. Patient outcomes were collected through a structured telephone interview. The interview took approximately 15 min to complete and included questions on whether patient information was received in the hospital (see the following website for a copy of this information resource, which included information about expected symptoms and suggested coping strategies: <https://www.monash.edu/medicine/psych/research-programs/merrc/resources>), healthcare utilization since discharge (i.e. whether they visited healthcare facilities in the 4 weeks prior to the assessment for the head injury or another reason, and whether they had taken medication for headaches, anxiety, sleep issues or nausea), and return to work/study (i.e. status prior and post-injury). Pre-injury psychiatric history and substance use was documented by asking participants to answer yes or no to the following questions: “Have you ever had psychological/psychiatric problems?”, “Are you currently taking or have previously taken illicit drugs?”, and, “Has drinking alcohol ever disrupted your lifestyle?” The interview also included scales measuring PCS, anxiety and quality of life, discussed below. Participant responses were entered directly into the online database with real-time checks to minimize risk of error and missing data. Researchers conducting interviews received training and supervision in initial interviews to ensure standardized protocol delivery. Information regarding injuries (LOC, GCS, other injuries) and whether information had been given to patients was sought from medical records.

### Measures

**Primary outcome for current study.** The Rivermead Post Concussion Symptom Questionnaire (RPQ) (30) was used to assess symptom experience. Participants rated on a 5-point scale their experience of each of 16 symptoms at time of assessment (over the last 24 h), with 0=symptom not present, 1=symptom no more of a problem than pre-injury, and scores of 2, 3, and 4 reflecting mild, moderate and severe post-injury symptoms, respectively. Higher scores thus indicated greater severity of PCS. The overall score was computed by summing scores for all 16 items (range 0–64). A total score represented the sum of scores *only* if scores

of 2, 3, or 4 were given, reflecting novel mild, moderate or severe post-injury symptoms respectively (range 2–64).

**Secondary outcomes.** The Anxiety scale of the Hospital Anxiety and Depression Scale (HADS) (31) was used to assess anxiety symptoms post-injury, since it has been shown to be sensitive in TBI populations (32, 33). HADS-Anxiety requires participants to rate on a 4-point scale (0–3) their experience of 7 symptoms over the past week, with total possible Anxiety score ranging from 0 to 21. A score >7 indicates clinically significant anxiety, with scores 8–10 indicating mild, 11–14 moderate and ≥15 severe anxiety.

The Quality of Life – Short Form (QoL SF-12) (34) questionnaire was used to assess quality of life post-injury. This includes 12 questions, 10 on a 5-point scale and 2 on a 3-point scale. Higher scores indicate better quality of life than lower scores. Physical functioning composite scores (PFCS) and Mental functioning composite scores (MCS) can be derived, with higher scores indicating greater functioning (mean 50 (standard deviation 10)).

Return to work/study outcomes were also documented. This included questions on whether participants were working/studying pre-injury (and for what hours) and at the time of the interview, and whether their duties or enrolment status had changed.

#### Data analysis

All analyses were conducted with SPSS v22 (SPSS Inc., Chicago, IL, USA) and Stata v12. For the RPQ, a total PCS score was computed for each participant, whereby scores of 0 and 1 were excluded based on the procedure adopted by King et al. (30) as 0=symptom not present and 1=symptom no more of a problem than pre-injury. An overall RPQ score was also computed including all scores. Overall RPQ scores were then dichotomized into no new post-injury symptoms vs. mild, moderate and severe symptoms for the prediction analysis. HADS anxiety scale scores were summed from response scores on HADS anxiety items. For the QoL questionnaire, separate physical functioning and mental functioning composite scores were generated and standardized according to Australian norms (35).

Descriptive statistics, including frequencies, were computed for all measures.  $\chi^2$  analysis was conducted to determine whether there were differences in PCS reporting, based on recall of receipt of information at discharge from ED. Pearson's correlation coefficient was calculated to estimate the linear correlation between PCS, HADS Anxiety and SF-12 QoL. A series of logistic regression models, accounting for the clustered nature of the sample arising from potential correlated responses of individuals within EDs, were conducted to identify factors associated with PCS reporting on the RPQ (i.e. mild, moderate or severe) vs. no new post-injury symptom reporting. Stata logistic regression with clustered/robust variance estimation is equivalent to performing a generalized estimated equations (GEE) analysis assuming an independence correlation structure (36). Predictive variables were selected based on previous research and available data, and included demographic variables (age and sex) in Model 1, premorbid psychological history/substance abuse variables in Model 2, injury-related variables (GCS, presence of LOC, time post-injury and other injury) in Model 3, and whether participants recalled having received information on discharge from ED in Model 4. Statistically significant predictors in each of these models, defined using a cut-point of  $p < 0.05$ , were then entered together into a final model (Model 5). Each of these models also controlled for which intervention the ED was allocated in the NET trial.

## RESULTS

### Sample characteristics and descriptive on outcome measures

Of the 1,943 participants completing the NET trial, 536 consented to be contacted for the NET-Plus arm. Of these, 35 declined to proceed with interview, 16 were deemed not competent, and 119 were lost to follow-up (no response after 4 attempts). Interviews were completed by 366 participants, but data from 23 participants were excluded due to co-morbid neurological conditions. The subsequent NET-Plus sample included 343 participants. Details of this sample are shown in Table I. The demographic profile did not differ from the broader NET trial, where the mean age of participants was 51 years (for control group) and 54 years (for intervention group), and 45% were male. The predominant cause of injury for these 343 participants was incidental falls. In comparison with the rest of the NET trial sample, the NET-Plus sample were more likely to have a GCS of 15/15 (95.6% vs 87.6%;  $p = 0.000$ ), but also more likely to have LOC (19.8% vs 17.1%;  $p = 0.001$ ). Other injuries were do-

**Table I.** Participant characteristics of the NET Plus study.  $n = 343$  unless otherwise specified

Characteristic	
Age, years, mean (SD), [range; IQR]	54 (21) [18–99; 36–71]
Sex (male), %	54.5
Time post-injury, days, mean (SD), [range; IQR]	210 (39) [130–321; 181–239]
Cause of injury, %	
Fall	51.9
Violence/assault	14.9
Sport-related injury	8.2
Road traffic accident	6.1
Miscellaneous*	19
GCS, %	
Score of 14	4.4
Score of 15	95.6
Loss of consciousness, %	
Yes	19.8
Unclear or not recorded on file	7.3
No	72.9
Skull fracture, %	
Present	4.7
Absent	9.6
Not scanned	85.7
Reporting other injuries, %	49
Employed prior to injury ( $n = 207$ ), %	60.3
Employed at follow-up (for those employed prior to injury; $n = 192$ )	92.8
Reported change in duties due to head injury ( $n = 21$ )	10.1
Studying prior to injury ( $n = 31$ ), %	9
Studying at follow-up (for those studying prior to injury; $n = 18$ )	58.1
Reported change in enrolment ( $n = 3$ )	9.7
Pre-injury psychological issues ( $n = 331$ ), %	26.3
Pre-injury illicit substance use issues ( $n = 331$ ), %	13
Pre-injury alcohol issues ( $n = 331$ ), %	6.3

\*Head strike on shelf, kicked by horse.

SD: standard deviation; IQR: interquartile range.



**Table II.** Summary statistics for each outcome measure

	Mean (SD); [range; IQR]	n
Total RPQ PCS Score	11.31 (11.73); [2–52; 2–15]	127 <sup>a</sup>
RPQ Overall Score	4.19 (8.98); [0–52; 0–4]	343
HADS Anxiety Score	3.96 (3.88); [0–20; 1–6]	343
Quality of Life – SF-12		
Physical Health	50.10 (8.57); [22–61; 46–57]	331 <sup>b</sup>
Mental Health	52.99 (5.58); [28–70; 50–57]	331 <sup>b</sup>

<sup>a</sup>216 participants (63% of total sample) reported not experiencing any PCS that were more of a problem than prior to their head injury.

<sup>b</sup>12 participants did not complete SF-12.

SD: standard deviation; IQR: interquartile range; PCS: post-concussional symptoms.

cumented in 49% of NET-Plus participants. The vast majority (92.8%) had returned to employment, with 10.1% indicating a change in duties due to the head injury, and 58.1% of those studying had returned to study, with 9.7% indicating a change in enrolment. Ninety-one percent of participants were discharged home after presentation to the ED, 5.5% were admitted to the ward, 2.9% were transferred to another hospital for treatment, and 0.6% went into police custody. There were 26.28% who reported pre-injury psychological issues, 12.99% illicit drug use and 6.34% alcohol problems pre-injury.

Of the 343 participants, 63.6% were in the NET trial control group and 36.4% in the intervention group. Of the 343, 28% said they could recall receiving information about mTBI at discharge, 12.8% were unsure or could not remember, and 59.2% indicated they did not receive information at discharge. In the CHART (i.e. medical) file, 39.9% of participants were documented as having had information provided at discharge, 1.7% having no information provided, 5.5% where it was deemed not applicable to provide information at discharge from ED (e.g. in case of admission to the ward), and in 52.8% of cases it was not recorded.

Table II shows mean scores on the RPQ, HADS and SF-12. The percentage of participants reporting novel post-injury PCS on the RPQ (mild, moderate or severe) is shown in Fig. 1. Three or more symptoms were reported by 18.7% of participants and 12.8% met International Classification of Diseases 10<sup>th</sup> (ICD-10) symptom criteria for PCS.

Participants reporting novel mild-severe symptoms were compared with those reporting no novel symptoms across 3 age groups. For the symptomatic group, 39.4% were <40, 44.4% 40–64, and 26.7% >65 years.  $\chi^2$  analysis was significant,  $\chi^2$  (2,  $n$  = 343) = 8.6,  $p$  = 0.014, with participants older than 65 years reporting fewer novel PCS.

There were 14.9% of participants who scored >7 on the HADS Anxiety scale, indicating clinically significant anxiety symptoms at follow-up, where 7.2% scored as mild, 5.6% moderate and 2.1% were severe. Anxiety was statistically significantly correlated with PCS after

**Table III.** Percentage of participants reporting symptoms following receipt of information at discharge from emergency departments

	Did not report novel PCS post-injury (%) ( $n$ = 216)	Reported novel PCS post-injury (%) ( $n$ = 127)
Received information	27.8	28.3
Unsure	16.2	7.1
Did not receive information	56	64.6

PCS: post-concussional symptoms.

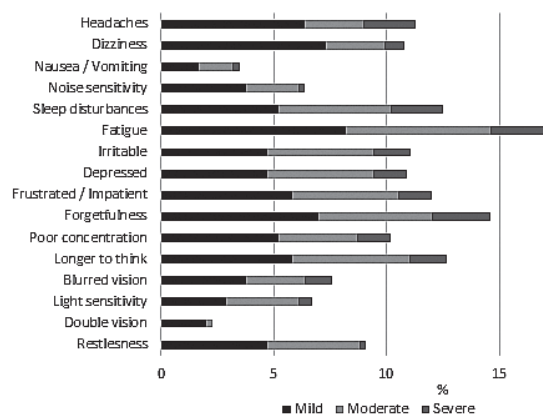
adjusting for cluster, whereby higher anxiety was associated with greater reporting of persistent novel post-injury PCS at follow-up ( $r$  = 0.52,  $p$  < 0.001,  $n$  = 343).

Quality of life on SF-12 was also significantly correlated with PCS, with lower mental health scores and to a lesser extent physical health scores associated with reporting of persistent PCS at follow-up ( $r$  = -0.49,  $p$  < 0.001 and  $r$  = -0.24,  $p$  < 0.001, respectively,  $n$  = 331).

Table III shows the percentages of participants who did and did not report novel mild-severe PCS at follow-up according to whether they did or did not report receiving information about mTBI and PCS at discharge from ED.  $\chi^2$  analysis indicated that there was a significant difference,  $\chi^2$  (2,  $n$  = 343) = 6.18,  $p$  = 0.046, with a higher percentage of participants who reported novel PCS post-injury indicating that they had not received information about mTBI and PCS at discharge from ED. Of participants unsure about whether they received information, a higher proportion did not report novel PCS.

### Predicting symptom reporting at follow-up

Results of each of the models are presented in Table IV. In Model 1 where demographic variables were entered, age was a statistically significant predictor, with younger age being associated with greater symptom reporting at follow-up. In Model 2 where premorbid psychological history/substance abuse variables were entered, the presence of premorbid psychological is-

**Fig. 1.** Percentage of patients reporting novel post-injury symptoms at a mean of 7 months post-injury.

sues was a significant predictor of symptom reporting, whereby the odds of reporting novel PCS at follow-up in participants with these issues pre-morbidly were 2.75 times than those of participants without these issues. In Model 3 where injury-related information was entered, LOC was a statistically significant predictor, whereby the odds of reporting PCS at follow-up in those who had LOC recorded were 1.94 times than those for participants who did not have LOC. Furthermore, those with unclear or not recorded LOC reported novel PCS 2.52 times more than those with no LOC. In Model 4 where recollection of receiving discharge information was entered, it was found to be a statistically significant predictor. Those who did not recall receiving information at discharge reported PCS 2.65 times more than those who were unsure. However, those who recalled receiving information at discharge reported PCS 2.35 times more than those who were unsure of receiving information.

**Table IV.** Results from logistic regression models investigating predictors of novel post-injury symptom reporting, controlling for initial intervention study group and accounting for clustering of responses within emergency departments

	OR	p-value	95% CI	Pseudo R <sup>2</sup>	P for Model
<b>Model 1<sup>a</sup></b>				0.02	0.0106
Study group	1.17	0.625	0.63 to 2.17		
Age	0.98	0.001	0.97 to 0.99		
Sex (males)	1.53	0.081	0.95 to 2.47		
<b>Model 2<sup>b</sup></b>				0.05	<0.000
Study group	1.22	0.475	0.71 to 2.12		
Psychological (absent)	2.75	<0.00	1.68 to 4.50		
Time post injury	1.00	0.179	0.99 to 1.01		
Illicit (absent)	1.26	0.514	0.63 to 2.50		
Alcohol (absent)	1.83	0.131	0.83 to 4.01		
<b>Model 3<sup>a</sup></b>				0.03	<0.000
Study group	1.14	0.658	0.65 to 1.99		
GCS	0.78	0.675	0.25 to 2.45		
LOCc (No)					
Questionable	2.52	0.003	1.35 to 4.67		
Yes	1.94	0.005	1.22 to 3.10		
Other injuryd (Yes)					
No	1.14	0.630	0.66 to 1.97		
Undocumented	0.73	0.135	0.48 to 1.10		
<b>Model 4<sup>a</sup></b>				0.02	0.007
Study group	1.12	0.689	0.64 to 1.98		
Receipt of informatione (Unsure)					
Yes	2.35	0.015	1.18 to 4.68		
No	2.65	0.001	1.52 to 4.63		
<b>Model 5<sup>a</sup></b>				0.09	0.000
Study group	1.31	0.333	0.76 to 2.27		
Age	0.99	0.085	0.98 to 1.00		
Psychological (absent)	2.99	<0.000	1.83 to 4.89		
LOC (No)					
Questionable	2.47	<0.000	1.56 to 3.92		
Yes	2.0	0.029	1.07 to 3.71		
Receipt of information (Unsure)					
Yes	2.01	0.080	0.92 to 4.40		
No	2.34	0.006	1.27 to 4.30		

In all models, the standard error was adjusted for clustering. Intervention group was also included in all models to control for the intervention.

Number of observations: <sup>a</sup>343; <sup>b</sup>331; <sup>c</sup>Comparison group is to those who reported no loss of consciousness (LOC); <sup>d</sup>Comparison group is to those who reported other injury; <sup>e</sup>Comparison group is to those who were unsure of whether they had received information in the emergency department at discharge. OR: odds ratio; CI: confidence interval.

In the final Model (i.e. Model 5), the presence of pre-morbid psychological issues, LOC and receipt of information were statistically significant predictors. Participants reported PCS 2.99 times more if they had pre-morbid psychological issues. If they had experienced a LOC, they reported PCS 2 times more than those who had not experienced a LOC; if LOC was questionable, participants reported PCS 2.47 times more than those who had not experienced a LOC. Participants who reported they did not receive information reported PCS 2.34 times more than those who were unsure. While participants who did recall receiving information at discharge reported PCS 2 times more than those who were unsure, this did not reach statistical significance in the final model.

## DISCUSSION

The aims of this study were to document outcome in terms of reported PCS, return to employment/study, anxiety symptoms and health-related quality of life and identify factors associated with persistent PCS in a series of uncomplicated mTBI cases presenting to the ED and agreeing to follow-up. Whilst 63% of participants reported no persistent PCS at follow-up, 18.7% reported 3 or more symptoms at follow-up, an average of 7 months post-injury, and 12.8% met criteria for an ICD-10 diagnosis of PCS. The most common symptoms were fatigue, forgetfulness, slowed thinking and sleep disturbance, followed by lowered frustration tolerance, irritability, depression, headaches and dizziness. These patterns of persisting symptoms are consistent with those found in previous longitudinal studies (4–6, 22, 37). Overall, however, the rates of PCS were low compared with many previous studies and the severity of reported symptoms was generally in the mild to moderate range. Rates of return to employment or study were high, with 92.8% of those employed pre-injury still working at follow-up, but only 60% of pre-injury students studying at follow-up. This may be partly explained by some students having completed studies. Rates of anxiety symptoms were low. Consistent with previous studies (8, 10), there was a statistically significant association between presence of persisting novel PCS and anxiety symptoms, as well as

with mental and to a lesser extent physical quality of life on the SF-12. That is, individuals who reported lower QoL also reported persisting novel or worsening PCS.

Of the predictive factors examined, 3 were significantly associated with persistent PCS: premorbid psychological issues, LOC, and having no recall of receiving information at discharge from ED. Older age was associated with less PCS reporting than in the middle or younger age-groups, but this was not a significant predictor in the final model. The strongest predictor, namely premorbid mental health issues, has been associated with persistent PCS in numerous studies to date (2, 8–10, 23, 24, 38). It has been speculated previously that individuals with a pre-injury psychiatric history may respond to the experience of mTBI and PCS with greater anxiety, which may, in turn, exacerbate their PCS (37). The association of anxiety with PCS reporting supports this premise and is consistent with recent findings by van der Naalt et al. (10).

Nevertheless, the presence of LOC was also associated with persistent PCS, suggesting that the severity of the injury did also contribute to persistent symptoms in this study. The study sample had relatively mild injuries, with only 19.8% having any reported LOC. Previous studies have shown mixed findings, but many have not examined LOC as a predictor, or not found it to be a significant predictor (9). Some previous studies of mTBI outcomes have only included cases with some LOC (2, 8, 37), whereas others have also included a substantial majority without documented LOC (4, 24). From the results of the present study, it would appear that the occurrence of LOC may be an important injury severity marker. The duration of LOC has possibly proven less useful in previous studies, due to variability in methods of its measurement (7, 9).

Finally, it was apparent that a higher percentage of participants who reported novel PCS post-injury reported not receiving information about mTBI and PCS at discharge from ED than those who were unsure. Of participants unsure about whether they received information, a higher proportion did not report novel PCS than did. This lends some support to the use of such information. Although an inexpensive and relatively simple form of intervention, the results of our recently completed implementation trial suggested that achieving reliable distribution of such information is extremely difficult<sup>1</sup>. However, it also needs to

be pointed out that those who did recall receiving the information did not report significantly fewer symptoms than those who did not recall it at this long time after injury.

This study had limitations and results need to be viewed in light of several factors. All predictive models accounted for only a small proportion of the variance, suggesting that there are other factors accounting for reporting of PCS at follow-up that were not measured in the current study (e.g. maladaptive coping (10), post-injury neuropsychological functioning (9), and presence of neck pain in the ED, PCS and post-traumatic stress at 2 weeks post-injury (39)). The participants in this study had very mild injuries, with more than 80% having no LOC and 95.6% having a GCS of 15/15 on presentation to the ED. In part this reflected the fact that only patients with GCS of 14 or 15 were included in the study. However, 85.7% were not scanned, making it possible that some complicated mTBI participants were included in the study, which could have confounded the results. The mean age of participants of 54 years was older than that seen in most mTBI samples, with a higher than usual proportion of women and of injuries due to falls. This may reflect that the participating EDs in this study were predominantly short stay units rather than trauma centres, where many large mTBI studies have historically been conducted and more complex trauma cases are likely to be included, with more associated injuries other than mTBI and potential for post-traumatic stress. This highlights the importance of considering sampling methods in relation to findings from mTBI studies. Only a small proportion of EDs approached agreed to participate in the NET trial and these were predominantly short-stay units rather than trauma centres. This may have influenced the rates of symptom reporting for the above-mentioned reasons. Furthermore, follow-up took place at a wide-ranging interval of 130–321 days post-injury. Whilst time post-injury was not associated with symptom reporting, this relatively long delay after injury may have influenced reliability of recall of information provided. Although all intervention centres were instructed to use the designated information booklets, we cannot be sure that they provided this information rather than some other form of information. Finally, there are limitations related to data collection via the telephone; namely, the inability to control the participant's environment or see their body language.

Overall, this study has identified that the majority of individuals presenting to EDs with uncomplicated mTBI (GCS 14–15) make a good recovery. A relatively small, but significant, proportion (18.7%) have significant persisting problems. They are more likely to have had a history of psychological disturbance and/or lost

<sup>1</sup>Bosch M, McKenzie JE, Ponsford J, Turner S, Chau M, Tavender EJ, et al. Evaluation of a targeted, theory-informed implementation intervention designed to increase uptake of emergency management recommendations regarding adult patients with mild traumatic brain injury: Results of the NET cluster randomised trial. *PLoS Med* (in submission).



consciousness. Not being able to recall receiving information about expected symptoms and how best to deal with them may result in greater long-term reporting of PCS. The study has implications for clinical practice. Screening for history of psychological disturbance and careful documentation of LOC in the ED are important indicators of risk of potential persistent symptoms that could be implemented. Provision of information about potential PCS with suggested coping strategies is an inexpensive intervention that may minimize PCS.

### ACKNOWLEDGEMENTS

The authors would like to thank all the hospital emergency departments (ED) involved in this study, in particular the ED staff who recruited patients for this study. We would like to also thank all MERRC staff who conducted the follow-up interviews. This study is part of a 5-year grant (the Neurotrauma Evidence Translation (NET) Program), funded by the Victorian Transport Accident Commission (TAC), Australia. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

*The authors have no conflicts of interest to declare.*

### REFERENCES

- Carroll LJ, Cassidy JD, Peloso PM, Borg J, von Holst H, Holm L, et al. Prognosis for mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004; 43: 84–105.
- Ponsford J, Willmott C, Rothwell A, Cameron P, Kelly AM, Nelms R, et al. Factors influencing outcome following mild traumatic brain injury in adults. *J Int Neuropsychol Soc* 2000; 6: 568–579.
- Belanger HG, Curtiss G, Demery JA, Lebowitz BK, Vanderploeg RD. Factors moderating neuropsychological outcomes following mild traumatic brain injury: a meta-analysis. *J Int Neuropsychol Soc* 2005; 11: 215–227.
- Hou R, Moss-Morris R, Peveler R, Mogg K, Bradley BP, Belli A. When a minor head injury results in enduring symptoms: a prospective investigation of risk factors for postconcussional syndrome after mild traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2012; 83: 217–223.
- Theadom A, Parag V, Dowell T, McPherson K, Starkey N, Barker-Collo S, et al. Persistent problems 1 year after mild traumatic brain injury: a longitudinal population study in New Zealand. *Br J Gen Pract* 2016; 66: e16–23.
- Sigurdardottir S, Andelic N, Roe C, Jerstad T, Schanke AK. Post-concussion symptoms after traumatic brain injury at 3 and 12 months post-injury: a prospective study. *Brain Inj* 2009; 23: 489–497.
- Carroll LJ, Cassidy JD, Cancelliere C, Cote P, Hincapie CA, Kristman VL, et al. Systematic review of the prognosis after mild traumatic brain injury in adults: cognitive, psychiatric, and mortality outcomes: results of the International Collaboration on Mild Traumatic Brain Injury Prognosis. *Arch Phys Med Rehabil* 2014; 95: S152–173.
- 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.
- Silverberg ND, Gardner AJ, Brubacher JR, Panenka WJ, Li JJ, Iverson GL. Systematic review of multivariable prognostic models for mild traumatic brain injury. *J Neurotrauma* 2015; 32: 517–526.
- van der Naalt J, Timmerman ME, de Koning ME, van der Horn HJ, Scheenen ME, Jacobs B, et al. Early predictors of outcome after mild traumatic brain injury (UPFRONT): an observational cohort study. *Lancet Neurology* 2017; 16: 532–540.
- Dikmen S, Machamer J, Temkin N. Mild traumatic brain injury: longitudinal study of cognition, functional status, and post-traumatic symptoms. *J Neurotrauma* 2017; 34: 1524–1530.
- Lange RT, Iverson GL, Franzen MD. Neuropsychological functioning following complicated vs. uncomplicated mild traumatic brain injury. *Brain Inj* 2009; 23: 83–91.
- Lo C, Shifteh K, Gold T, Bello JA, Lipton ML. Diffusion tensor imaging abnormalities in patients with mild traumatic brain injury and neurocognitive impairment. *J Comput Assist Tomogr* 2009; 33: 293–297.
- Sadowski-Cron C, Schneider J, Senn P, Radanov BP, Bal-linari P, Zimmermann H. Patients with mild traumatic brain injury: immediate and long-term outcome compared to intra-cranial injuries on CT scan. *Brain Inj* 2006; 20: 1131–1137.
- Williams DH, Levin HS, Eisenberg HM. Mild head injury classification. *Neurosurgery* 1990; 27: 422–428.
- Waljas M, Iverson GL, Lange RT, Hakulinen U, Dastidar P, Huhtala H, et al. A prospective biopsychosocial study of the persistent post-concussion symptoms following mild traumatic brain injury. *J Neurotrauma* 2015; 32: 534–547.
- Meares S, Shores EA, Taylor AJ, Batchelor J, Bryant RA, Baguley IJ, et al. Mild traumatic brain injury does not predict acute postconcussion syndrome. *J Neurol Neurosurg Psychiatry* 2008; 79: 300–306.
- Dischinger PC, Ryb GE, Kufera JA, Auman KM. Early predictors of postconcussive syndrome in a population of trauma patients with mild traumatic brain injury. *J Trauma* 2009; 66: 289–296; discussion 296–287.
- King NS. A systematic review of age and gender factors in prolonged post-concussion symptoms after mild head injury. *Brain Inj* 2014; 28: 1639–1645.
- Rabinowitz AR, Li X, McCauley SR, Wilde EA, Barnes A, Hanten G, et al. Prevalence and Predictors of Poor Recovery from Mild Traumatic Brain Injury. *J Neurotrauma* 2015; 32: 1488–1496.
- Thornhill S, Teasdale GM, Murray GD, McEwen J, Roy CW, Penny KI. Disability in young people and adults one year after head injury: prospective cohort study. *BMJ* 2000; 320: 1631–1635.
- Chiang CC, Guo SE, Huang KC, Lee BO, Fan JY. Trajectories and associated factors of quality of life, global outcome, and post-concussion symptoms in the first year following mild traumatic brain injury. *Qual Life Res* 2016; 25: 2009–2019.
- Kumar RG, Bracken MB, Clark AN, Nick TG, Melguizo MS, Sander AM. Relationship of preinjury depressive symptoms to outcomes 3 mos after complicated and uncomplicated mild traumatic brain injury. *Am J Phys Med Rehabil* 2014; 93: 687–702.
- Waljas M, Lange RT, Hakulinen U, Huhtala H, Dastidar P, Hartikainen K, et al. Biopsychosocial outcome after uncomplicated mild traumatic brain injury. *J Neurotrauma* 2014; 31: 108–124.
- King NS, Kirwilliam S. Permanent post-concussion symptoms after mild head injury. *Brain Inj* 2011; 25: 462–470.
- Ponsford J, Willmott C, Rothwell A, Cameron P, Kelly AM, Nelms R, et al. Impact of early intervention on outcome following mild head injury in adults. *J Neurol Neurosurg Psychiatry* 2002; 73: 330–332.
- Turner-Stokes L, Pick A, Nair A, Disler PB, Wade DT. Multi-disciplinary rehabilitation for acquired brain injury in adults of working age. *Cochrane Database of Systematic Reviews* 2015.
- Hadanny A, Efrati S. Treatment of persistent post-concussion syndrome due to mild traumatic brain injury: current status and future directions. *Expert Rev Neurother* 2016;

- 16: 875–887.
29. Bosch M, McKenzie JE, Mortimer D, Tavender EJ, Francis JJ, Brennan SE, et al. Implementing evidence-based recommended practices for the management of patients with mild traumatic brain injuries in Australian emergency care departments: study protocol for a cluster randomised controlled trial. *Trials* 2014; 15: 281.
30. King NS, Crawford S, Wenden FJ, Moss NE, Wade DT. The Rivermead Post Concussion Symptoms Questionnaire: a measure of symptoms commonly experienced after head injury and its reliability. *J Neurol* 1995; 242: 587–592.
31. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
32. Schonberger M, Ponsford J. The factor structure of the Hospital Anxiety and Depression Scale in individuals with traumatic brain injury. *Psychiatry Res* 2010; 179: 342–349.
33. Dahm J, Wong D, Ponsford J. Validity of the Depression Anxiety Stress Scales in assessing depression and anxiety following traumatic brain injury. *J Affect Disorders* 2013; 151: 392–396.
34. Ware J, Jr, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996; 34: 220–233.
35. Andrews G. A brief integer scorer for the SF-12: validity of the brief scorer in Australian community and clinic settings. *Aust N Z J Public Health* 2002; 26: 508–510.
36. Hardin JW, Hilbe JM. Generalized estimating equations. 2 ed. Boca Raton, Florida: Chapman & Hall/CRC Press; 2012.
37. Ponsford J, Cameron P, Fitzgerald M, Grant M, Mikocka-Walus A. Long-term outcomes after uncomplicated mild traumatic brain injury: a comparison with trauma controls. *J Neurotrauma* 2011; 28: 937–946.
38. Wojcik SM. Predicting mild traumatic brain injury patients at risk of persistent symptoms in the Emergency Department. *Brain Inj* 2014; 28: 422–430.
39. Cnossen MC, van der Naalt J, Spikman JM, Nieboer D, Yue JK, Winkler EA, Manley GT, von Steinbuechel N, Polinder S, Steyerberg EW, Lingsma HF. *J Neurotrauma* 2018; 35: 2691–2698.