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# Screening for Post-Traumatic Stress Disorder in a Civilian Emergency Department Population with Traumatic Brain Injury

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#### Abstract

Post-traumatic stress disorder (PTSD) is a condition associated with traumatic brain injury (TBI). While the importance of PTSD and TBI among military personnel is widely recognized, there is less awareness of PTSD associated with civilian TBI. We examined the incidence and factors associated with PTSD 6 months post-injury in a civilian emergency department population using measures from the National Institute of Neurological Disorders and Stroke TBI Common Data Elements Outcome Battery. Participants with mild TBI (mTBI) from the Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot study with complete 6-month outcome batteries (n=280) were analyzed. Screening for PTSD symptoms was conducted using the PTSD Checklist-Civilian Version. Descriptive measures are summarized and predictors for PTSD were examined using logistic regression. Incidence of screening positive for PTSD was 26.8% at 6 months following mTBI. Screening positive for PTSD was significantly associated with concurrent functional disability, post-concussive and psychiatric symptomatology, decreased satisfaction with life, and decreased performance in visual processing and mental flexibility. Multi-variable regression showed injury mechanism of assault (odds ratio [OR] 3.59; 95% confidence interval [CI] 1.69–7.63; p = 0.001) and prior psychiatric history (OR 2.56; 95% CI 1.42-4.61; p=0.002) remained significant predictors of screening positive for PTSD, while education (per year OR 0.88; 95% CI 0.79–0.98; p=0.021) was associated with decreased odds of PTSD. Standardized data collection and review of pre-injury education, psychiatric history, and injury mechanism during initial hospital presentation can aid in identifying patients with mTBI at risk for developing PTSD symptoms who may benefit from closer follow-up after initial injury care.

Keywords: emergency department screening; post-traumatic stress disorder; traumatic brain injury

### Introduction

OST-TRAUMATIC STRESS DISORDER (PTSD) is a condition asresociated with traumatic brain injury (TBI).<sup>1-4</sup> PTSD is considered a stressor-related disorder, characterized by intrusion, avoidance, negative alterations in cognition and mood, and alterations in arousal and reactivity following exposure to a traumatic event.<sup>5</sup> PTSD is found among those who have experienced all levels of TBI severity.<sup>2</sup> However, higher rates occur in individuals with mild TBI (mTBI), compared with those in a general trauma population<sup>3,6–9</sup> or among those with severe head injury.<sup>2</sup> It has been hypothesized that greater cognitive deficits associated with severe TBI protect against development of subsequent PTSD symptoms.<sup>2</sup> Among those with mTBI, younger individuals report more severe PTSD symptoms, compared with older subjects.<sup>10</sup>

PTSD is well-characterized among military personnel with a history of TBI and has been estimated to affect 32-66% of subjects with military-related TBI.<sup>3</sup> However, PTSD is not limited to military populations. Independent reports have estimated that PTSD occurs in 11-40% of civilians following TBI.8,10,11 Prior work has identified that PTSD symptoms tend to emerge between 1-3 months following injury and peak around 6 months post-TBI.<sup>2,6,8,12</sup> Independent reports have begun to identify predictors of PTSD following TBI. These include a spectrum of risk factors present

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prior to TBI (pre-TBI), at the time of TBI, or following TBI (post-TBI). For example, a history of pre-existing psychiatric disease, (e.g., anxiety or depression), lower socioeconomic status, lower levels of education, prior trauma, and single marital status have been shown to confer risk for PTSD.<sup>2,8,11,14</sup> The incidence of PTSD varies with injury severity and mechanism of injury. For example, patients with mTBI and those who are assaulted have a greater risk of developing subsequent PTSD symptoms, compared with individuals with more severe TBI or those whose TBI results from motor vehicle accidents or falls. Duration of post-traumatic amnesia (PTA) and a positive toxicology study also appear to confer added risk.<sup>2,3,8</sup> Following brain injury, a lack of social support, increased life stress, poor health satisfaction ratings, and presence of disability are associated with risk of PTSD.<sup>2,7,8,15–17</sup> However, the relative contributions of each risk factor and consensus as to the most salient factors for the development of PTSD symptoms in a civilian population following TBI has yet to be established.

A relationship between development of PTSD and functional disability following TBI has been suggested. In military populations, self-reported concussive and PTSD symptoms after TBI was associated with disability at time of military discharge.<sup>16</sup> Similarly, soldiers evacuated following a blast injury resulting in TBI had greater disability, as measured by the Glasgow Outcome Scale-Extended (GOS-E), than those evacuated for other medical reasons.<sup>17</sup> There have been multiple reports of associations between lower GOS-E, depression, post-concussive symptoms, and PTSD in civilian<sup>16</sup> and military populations.<sup>17,18</sup> Specifically, up to 87% of service members with TBI meeting PTSD symptom screening criteria demonstrate concurrent moderate disability on the GOS-E  $(\leq 6)$ .<sup>17</sup> While reports of moderate disability range from 13–23% after mTBI,<sup>19,20</sup> in civilian populations, the proportion of patients who develop PTSD symptoms and thus may benefit from symptom alleviation through PTSD-based therapy has yet to be characterized and/or validated.

Several limitations exist in current literature examining PTSD in the civilian population.<sup>21,22</sup> Studies frequently target the examination of the more accessible, more "injured" hospitalized patients, while excluding the evaluation of the concussed and "walking wounded" and their associated demographic and socioeconomic risk factors. Further, follow-up and comprehensive assessment of mTBI patients in the post-acute setting remains challenging and measures of PTSD symptomatology typically have not been included in standardized civilian outcomes batteries. In the current study, mTBI (Glasgow Coma Scale [GCS] score 13-15) patients were assessed with a broad range of outcome measures selected from the National Institute of Neurological Disorders and Stroke (NINDS) TBI Common Data Elements (TBI-CDE) Outcome Battery that included the PTSD Checklist-Civilian Version (PCL-C).23-26 We report the incidence of PTSD symptoms at 6 months-a time when PTSD symptoms are reported to peak<sup>3,27</sup>—examine pre- and peri-injury risk factors, and describe associations with functional disability distinctive from other post-injury outcomes.

#### Methods

#### Participants

Participants were recruited from three Level I trauma centers as part of the multi-center, prospective Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) Pilot study.<sup>28</sup> These trauma centers included San Francisco General Hospital (SFGH), San Francisco, California, University of Pittsburgh Medical Center (UPMC), Pittsburgh, Pennsylvania, and University Medical Center at Brackenridge (UMCB), Austin, Texas. Study protocols were approved by the institutional review boards at each participating center. Eligible patients for the TRACK-TBI Pilot study presented to the emergency department (ED) within 24 h of sustaining head trauma of sufficient severity to triage to a non-contrast head computed tomography (CT) scan using the American College of Emergency Physicians/Centers for Disease Control and Prevention evidence-based joint practice guidelines.<sup>29</sup> Informed consent was obtained from the patient or through proxy. Individuals who were non-English speakers, pregnant, in legal custody, or under a medically-evaluated psychiatric hold at the time of enrollment were excluded from the study.

Of 586 patients age  $\geq$ 16 years enrolled in the TRACK-TBI Pilot study, a total of 338 completed the full 6-month TBI-CDE Outcome Battery, which included the PCL-C measure. Of these, 280 patients were classified as mTBI by ED admission GCS (13–15) and were included in the analysis. A higher number of study participants were enrolled at the SFGH site (*n*=196), compared with at the UPMC (*n*=65) and UMCB (*n*=19) sites, and several differences in sample composition are noted. Specifically, SFGH had a higher proportion of participants with positive pre-injury psychiatric history (*p*<0.001) and injury mechanism of assault (*p*<0.001) and fewer Caucasian participants (*p*<0.001; data not presented).

#### Measures

Demographic and injury characteristics were collected at the time of enrollment. The TRACK-TBI Pilot study outcome assessment battery listed below consisted of the core measures recommended by the NINDS consensus-based TBI-CDEs (Version 1).<sup>23–26</sup> Administered and self-reported neurocognitive and neuropsychological measures and global outcome ratings also were collected via in-person interview at 6 months post-injury.

**Demographics.** Data collected included age, race, gender, ethnicity, years of education, marital status, and employment status.

Baseline health status. Participants were queried according to TBI-CDE (Version 1) standard checklist of prior medical and psychiatric history.<sup>23,24</sup> This self-reported information was supplemented with data gathered through medical record abstraction.

Injury characterization. A variety of indices were collected to characterize TBI etiology and severity. These included GCS score<sup>30</sup> assessed by a neurosurgeon at hospital admission, duration of loss of consciousness (LOC), PTA, injury severity score (ISS),<sup>31</sup> hospital length of stay, discharge disposition, and location of discharge from the ED. Finally, CT scans were categorized as being positive or negative for acute intracranial lesions.

PCL-C. The PCL- $C^{25,32}$  is a standardized self-report rating scale of 17 PTSD symptoms that correspond to *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision* (DSM-IV-TR) criteria for PTSD across three component subcategories ("Re-experiencing," "Avoidance," and "Hypervigilance"), causing clinically significant distress or impairment for more than one month.<sup>33</sup> Respondents are asked to rate on a 5-point scale (1 = not at all to 5 = extremely) how much they have been bothered by each symptom in the past month. A higher score indicates more symptomatology of PTSD. Subjects simultaneously endorsing a score of  $\geq$ 3 in one or more symptoms under "Re-experiencing," three or more symptoms under "Avoidance," and two or more symptoms under "Hypervigilance" subcategories on the PCL-C were coded as positive for PTSD.

**GOS-E**. The  $\text{GOS-E}^{34}$  provides an overall measure of disability based on scales of cognition, independence, employability,

and social/community participation collected via structured interview. Individuals are described by one of the eight outcome categories: 1 = dead, 2 = vegetative state, 3 = lower severe disability, 4 = upper severe disability, 5 = lower moderate disability, 6 = upper moderate disability, 7 = lower good recovery, and 8 = upper good recovery. Good recovery is defined as a score of 7–8, moderate disability is defined by a score of 5–6, and severe disability is defined as a score of 3–4. A GOS-E score of 8 reflects full recovery to baseline status with no disability.

Brief Symptom Inventory 18. The Brief Symptom Inventory 18 (BSI18)<sup>35</sup> is used to assess psychological distress, with each item rated on a 5-point scale from 0 (not at all distressed) to 4 (extremely distressed). The Global Severity Index is represented by a T-score composed of the sum of three subscales—depression, somatization, and anxiety—containing six items each. Higher scores reflect greater psychological distress. An overall score of  $\geq$ 63 meets the cutoff for clinical screening indicating a need for further assessment.

Rivermead Post-Concussion Symptom Questionnaire-13 Item. The Rivermead Post-Concussion Symptom Questionnaire-13 Item (RPQ-13)<sup>36</sup> queries the presence and severity of somatic, cognitive, and emotional symptoms that are commonly reported following TBI. Participants are asked to compare current (past 24 h) versus pre-injury symptom severity on a scale of 0 to 4 (0=not experienced; 1=no more of a problem; 2=mild problem; 3=moderate problem; 4=severe problem). A score of ≥20 meets the cutoff for clinical screening for symptoms of post-concussion syndrome, a clinical state of persistent symptoms of a TBI.<sup>37</sup>

Satisfaction With Life Scale. The Satisfactions With Life Scale (SWLS)<sup>38</sup> is a global measure of life satisfaction consisting of five statements that the respondent is asked to endorse on a 7-point Likert scale (1 = strongly disagree to 7 = strongly agree). A higher score indicates greater life satisfaction. A score of >20 indicates some degree of satisfaction, and a score of <20 indicates some degree of dissatisfaction.

Trail Making Test. The Trail Making Test (TMT)<sup>39</sup> is a cognitive assessment consisting of two timed parts (TMT-A and TMT-B) that measure executive function and mental flexibility. Specifically, TMT-A assesses visual processing and TMT-B assesses mental flexibility and processing speed.

California Verbal Learning Test-Second Edition. The California Verbal Learning Test-Second Edition (CVLT-II)<sup>40</sup> is a verbal learning and memory task in which there are five learning trials, an interference trial, immediate (short-delay) recall trials, and post-20 min (long-delay) recall trials. The standard score (normalized for age, years of education, and handedness) for long-delay free recall was used in this analysis as a measure of encoded verbal memory.

Wechsler Adult Intelligence Scale-Fourth Edition, Processing Speed Index. The Wechsler Adult Intelligence Scale-Fourth Edition, Processing Speed Index (WAIS-PSI)<sup>41</sup> subscale is composed of the Symbol Search and Coding tasks, which require visual attention and motor speed. The scaled composite PSI score (normalized for age), which ranges from 50 to 150 to correspond to the 0.1 to 99.9 percentile of performance across age groups, was used in this analysis. Scores of ~90, 100, and ~110 correspond to the 25th, 50th, and 75th percentiles, respectively.

#### Statistical analysis

Patients who completed the 6-month PCL-C data were selected for this study (n=280). PTSD status was determined by dichotomous classification on the PCL-C according to DSM-IV criteria based on the number and categories of symptoms reported.<sup>33</sup> Statistical analysis first examined differences in baseline variables, comparing participants who were positive for PTSD symptoms and those who were not. Differences in means and frequencies for continuous and categorical variables, respectively, were compared between those who screened positive for PTSD symptoms and those who did not screen positive at 6-month follow-up. Continuous variables identified as having a skewed distribution (Shapiro-Wilk W statistic <0.05) were compared using the Wilcoxon Mann-Whitney test. Categorical variables were compared using Pearson's chi-square test and Fisher's exact test for comparisons with group counts <5.

To further explore the association between potential relevant baseline predictors and positive screening for PTSD at 6 months, we selected possible predictors as identified from the literature<sup>2,8,11,14</sup> and from clinical knowledge, including demographics (age, gender, race, education, marital status), medical history, mechanism of injury, acute toxicology, head injury severity (CT, GCS), and overall injury severity (ISS). Baseline variables identified as having a significant association with PTSD in univariate analysis (p < 0.05) were selected to be included in a multi-variable logistic regression model predicting the probability of being diagnosed with PTSD based on the PCL-C scale. These variables included demographic, pre-injury, and injury-related variables, including race, years of education, marital status, prior psychiatric history, and injury mechanism (assault vs. all other causes). Caucasian race and married marital status were included as binary variables.

Other 6-month outcome measures were not included as independent variables in the model as the aim of the study was to examine baseline factors associated with PTSD. These measures were analyzed by comparing mean scores between those with and without a positive screen for PTSD to understand symptoms and conditions associated with PTSD at the time of follow-up.

A variable selection procedure was then applied to improve the performance of the initial non-parsimonious prediction model using a step-wise forward procedure (*p*-entry  $\leq 0.25$ ; *p*-remain  $\leq 0.15$ ) based on the Hosmer and Lemeshow goodness-of-fit statistic. The association between each potential predictor and the outcome is reported on the odds ratio scale, together with its 95% confidence intervals. The parsimonious model's goodness-of-fit is expressed using the c-statistic. All statistical analyses were run on SPSS v.21 (Chicago, IL).

### Results

Of 280 patients included in the analysis, mean age was 42.9 years (standard deviation [SD] = 17.8) and 69.3% of patients were male. Mean years of education was 14.4 (SD=2.9) and patients were predominantly Caucasian (81.8%).

#### Comparison to demographic variables at time of injury

Overall, 75 (26.8%) screened positive for PTSD symptom criteria at 6 months post-injury (PTSD-positive). The PTSD-positive group was less likely to be of Caucasian race (73.3% vs. 84.9%; p=0.027), reported fewer years of education (13.5 vs. 14.7 years; p=0.002), were less likely to be married (20.0% vs. 35.1%; p=0.015), and had a higher incidence of self-reported pre-injury psychiatric disturbance (53.3% vs. 26.8%; p<0.001) than the PTSD-negative group (Table 1). With regard to the index injury of enrollment, the PTSD-positive group included more victims of assault (33.3% vs. 8.8%; p<0.001). A nonsignificant statistical trend of lower ISS was observed in the PTSD-positive group (7.3±8.5 vs. 9.8±10.4; p=0.062). The PTSD-positive group

### SCREENING FOR POST-TRAUMATIC STRESS DISORDER IN TBI

	Sample size	No PTSD	Yes PTSD	
Characteristic	(n=280)	(n = 205)	(n = 75)	р
Age, years (mean ± SD)	280	$43.3 \pm 18.8$	$42.0 \pm 14.9$	0.602
Gender $n$ (%)	280			0.551
Male		140 (68.3)	54 (72.0)	
Female		65 (31.7)	21 (28.0)	
Race, Caucasian n (%)	280	174 (84.9)	55 (73.3)	0.027
Education, years (mean $\pm$ SD)	255	$14.7 \pm 2.8$	$13.5 \pm 2.9$	0.002
Marital status $n$ (%)	280			0.017
Single		104 (50.7)	44 (58.7)	
Married		72 (35.1) [a]	15 (20.0) [b]	
Separated/divorced		13 (6.3) [a]	12 (16.0) [b]	
Widowed		7 (3.4)	3 (4.0)	
Other/unknown		9 (4.4)	1 (1.3)	
Married marital status	280		- ()	0.015
Married	200	72 (35.1)	15 (20.0)	01010
Not married		133 (64.9)	60 (80.0)	
Study $n$ (%)	280	100 (01.9)	00 (00.0)	0.300
San Francisco General Hospital	200	138 (67.3)	58 (77.3)	0.500
University of Pittsburgh Medical Center		52 (25.4)	13 (17.3)	
University Medical Center at Brackenridge		15 (7.3)	4 (5.3)	
Prior psychiatric history $n$ (%)	280	55 (26.8)	40 (53.3)	< 0.001
Military service history $n$ (%)	280	31 (15.1)	4 (5.3)	0.039
Mechanism of injury $n$ (%)	280	51 (15.1)	+ (3.3)	< 0.001
MV (driver/passenger)	200	35 (17.1)	8 (10.7)	<0.001
MV (univer/passenger) MV (motorcyclist)		11 (5.4)	3 (4.0)	
MV (hotorcyclist) MV (pedestrian/cyclist)		70 (34.1) [a]	14 (18.7) [b]	
Fall		. ,	. ,	
		60 (29.3)	25 (33.3)	
Assault Other		18 (8.8) [a]	23 (30.7) [b]	
	290	11 (5.4)	2 (2.7)	-0.001
Injury mechanism of assault	280	18 (8.8)	05 (22.2)	< 0.001
Yes, mechanism of assault		18 (8.8)	25 (33.3)	
No, other mechanisms		187 (91.2)	50 (66.7)	
ED toxicology screen	280		<b>T</b> (0, 0)	0.044
Positive screen		7 (3.4)	7 (9.3)	
Negative screen		198 (96.6)	68 (90.7)	
Intracranial lesion on CT $n$ (%)	280	95 (46.3)	30 (40.0)	0.345
ED admission Glasgow Coma Scale $n$ (%)	280			0.254
13		6 (2.9)	2 (2.7)	
14		36 (17.6)	20 (26.7)	
15		163 (79.5)	53 (70.7)	
ED disposition $n$ (%)	280			0.247
ED discharge		72 (35.1)	33 (44.0)	
Hospital admission		87 (42.4)	31 (41.3)	
Intensive care unit admission		46 (22.4)	11 (14.7)	
ISS (mean $\pm$ SD)	280	$9.8 \pm 10.4$	$7.3 \pm 8.5$	0.062
Injury severity n (%)	280			0.211
Minor/moderate injury (ISS <16)		140 (68.3)	57 (76.0)	
Moderate/severe/critical injury (ISS ≥16)		65 (31.7)	18 (24.0)	

TABLE 1. DEMOGRAPHIC AND INJURY CHARACTERISTICS BY 6	6-Month PTSD Status after Mild TBI
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[a] and [b] denote statistically significant subgroup differences. Number qualifying and proportions are shown for categorical variables. Means and standard deviations (SD) are shown for continuous variables.

PTSD, post-traumatic stress disorder; TBI, traumatic brain injury; SD, standard deviation; MV, motor vehicle; ED, emergency department; CT, computed tomography; ISS, injury severity score.

contained a lower proportion of persons reporting military service history for those with complete data (5.3% vs. 15.1%; p = 0.039).

# Comparison to outcome measures at 6 months post-injury

At 6 months post-injury, the PTSD-positive group experienced higher levels of less than favorable outcome (GOS-E  $\leq$  6, 65.3% vs. 21.5%; *p* < 0.001), higher scores indicating psychological distress

(BSI18,  $66.8\pm7.5$  vs.  $50.9\pm9.7$ ; p<0.001), a higher rate of persistent post-concussive symptoms (RPQ-13,  $26.8\pm10.3$  vs.  $9.1\pm9.3$ ; p<0.001), lower executive functioning and flexibility (TMT Part A time,  $40.2\pm21.3$  vs.  $33.2\pm14.8$  sec, p=0.004; TMT Part B time,  $104.4\pm70.8$  vs.  $81.0\pm50.7$  sec, p=0.008), lower verbal learning and memory (CVLT-II,  $-0.3\pm1.3$  vs.  $0.1\pm1.1$ ; p=0.006), lower nonverbal processing speed (WAIS-PSI,  $96.5\pm15.9$  vs.  $102.2\pm14.9$ ; p=0.009) and lower satisfaction with life (SWLS,  $15.2\pm6.3$  vs.  $23.4\pm7.4$ ; p<0.001; Table 2).

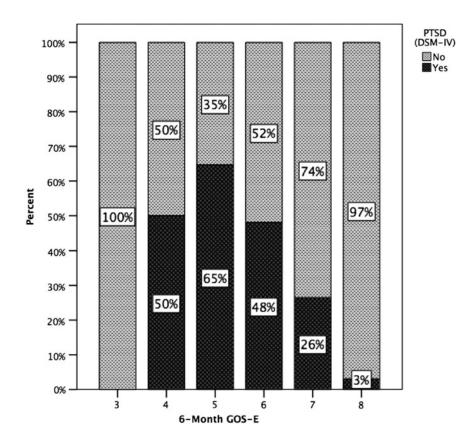
Outcome measure	Sample size (n=280)	<i>No PTSD</i> ( <i>n</i> = 205)	Yes PTSD $(n=75)$	р
Glasgow Outcome Scale-Extended (GOS-E): less than favorable outcome (GOS-E $\leq$ 6 vs. GOS-E $\geq$ 7) <i>n</i> (%)	280	34 (21.5)	49 (65.3)	< 0.001
Brief Symptom Inventory 18 Global Severity Index T Score (mean±SD)	278	$50.9 \pm 9.7$	$66.8 \pm 7.5$	< 0.001
Rivermead Post-Concussion Questionnaire-13 (mean ± SD)	279	$9.1 \pm 9.3$	$26.8 \pm 10.3$	< 0.001
Trail Making Test, Part A time, in sec (mean ± SD)	248	$33.2 \pm 14.8$	$40.2 \pm 21.3$	0.004
Trail Making Test, Part B time, in sec (mean $\pm$ SD)	247	$81.0 \pm 57.9$	$104.4 \pm 70.8$	0.008
California Verbal Learning Test-Second Edition, Long Delay Free Recall Standard Score (mean ± SD)	240	$0.1 \pm 1.1$	$-0.3 \pm 1.3$	0.006
Wechsler Adult Intelligence Scale-Fourth Edition Processing Speed Index, composite score (mean ± SD)	247	$102.2 \pm 14.9$	$96.5 \pm 15.9$	0.009
Satisfaction With Life Scale (mean ± SD)	276	$23.4 \pm 7.4$	$15.2 \pm 6.3$	< 0.001

TABLE 2. PERFORMANCE ON CONCURRENT OUTCOME MEASURES BY 6-MONTH PTSD STATUS AFTER MILD TBI

Number qualifying and proportions are shown for the GOS-E. Means and standard deviations (SDs) are shown for all other outcome measures. PTSD, post-traumatic stress disorder; TBI, traumatic brain injury.

The frequency of PTSD symptoms reported at 6 months post-TBI was highest in patients with a GOS-E score of 5 (22 of 34; 64.7%), followed by GOS-E scores of 6 (25 of 52; 48.1%) and 7 (23 of 87; 26.4%). Patients identified as having a moderate disability (GOS-E scores of 5 and 6) on global outcome at 6 months accounted for 62.7% of all PTSD-positive patients in the study (Fig. 1). rized to a domain of mental health (BSI18), post-concussive symptoms (RPQ-13), and cognitive deficit (CVLT-II, WAIS-PSI). Clinical screening cutoffs were established by test administration guidelines for each measure: BSI18  $\geq$  63, RPQ-13  $\geq$  20, CVLT-II  $\leq$  -2 SD, and WAIS-PSI  $\leq$ 5th percentile. Patients meeting the clinical cutoff for each domain were classified as positive for that domain. In 62 PTSD-positive patients with a full outcome battery, only four (6.5%) had isolated PTSD. Participants were likely to have

To examine the co-occurrence of PTSD symptom reporting and other conditions at the time of follow-up, measures were catego-



**FIG. 1.** Incidence of 6-month post-traumatic stress disorder (PTSD) after traumatic brain injury (TBI) within functional disability score categories. The proportion of subjects meeting screening criteria for PTSD by *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV) criteria within each functional disability score category (Glasgow Outcome Scale-Extended [GOS-E]) is shown.

Predictor	В	OR	95% CI	р
Caucasian race	-0.71	0.49	0.26-0.93	0.029
Education (per-year)	-0.16	0.85	0.77-0.94	0.002
Married marital status	-0.79	0.45	0.25-0.82	0.015
Prior psychiatric history	1.14	3.12	1.80-5.40	<.001
Mechanism of assault	1.53	4.60	2.31-9.15	< 0.001

Univariate predictors with  $p \le 0.05$  for 6-month post-traumatic stress disorder by *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* criteria on binary logistic regression are shown.

PTSD, post-traumatic stress disorder; TBI, traumatic brain injury; OR, odds ratio; CI, confidence interval.

indicators of other conditions, including the presence of postconcussive and psychiatric disturbance, which accounted for the largest proportion (30 of 62; 48.4%), followed by psychiatric disturbance only (15 of 62; 24.2%), and then by all three coincident domains (8 of 62; 12.9%); three patients (4.8%) had cognitive impairment with PTSD, and two patients (3.2%) had only postconcussive symptoms with PTSD.

Logistic regression analysis confirmed the univariate predictive value of five baseline and clinical presentation variables: Caucasian race, years of education, marital status (married vs. all other), prior psychiatric history, and mechanism of assault. Reduced odds of screening positive for PTSD were associated with Caucasian race (OR, 0.49; 95% CI 0.26–0.93; p = 0.029), more years of education (per year OR, 0.85; 95% CI 0.77–0.94; p=0.002), married marital status (OR, 0.45; 95% CI 0.25–0.82; p = 0.015). Increased odds of screening positive for PTSD were associated with prior psychiatric history (OR, 3.12; 95% CI 1.84–5.40; p < 0.001) and mechanism of assault (OR, 4.60; 95% CI 2.31–9.15; p < 0.001; Table 3) These five univariate predictors were selected for possible inclusion into the step-wise multi-variable logistic regression model. We did not assess the effect of CT pathology on PTSD as the focus of this analysis was the relationship between 6-month positive PTSD screen and baseline presentation.

Multi-variable analysis demonstrated that mechanism of assault (OR, 3.59; 95% CI 1.69–7.63; p=0.001) and prior psychiatric history (OR, 2.56; 95% CI 1.42–4.61; p=0.002) remained statistically significant predictors with increased odds of screening positive for PTSD at 6-months post-TBI. Education (per year OR, 0.88; 95% CI 0.79–0.98; p=0.021) remained a statistically significant predictor, with decreased odds of screening positive for PTSD. The multi-variable model performed fairly (c-statistic, 0.713; 95% CI 0.642–0.785; p<0.001) and conformed to goodness-of-fit (Hosmer and Lemeshow chi-square statistic 11.081; p=0.135). Caucasian race and marital status did not persist as predictors after step-wise multi-variable analysis (Table 4).

#### Discussion

The frequency of participants screening positive for PTSD criteria among patients returning for follow-up in our study of mTBI was 26.8%, a prevalence that is consistent with prior reports of PTSD symptoms in civilian populations.<sup>8,13</sup> PTSD symptoms at 6 months post-injury rarely occurred in isolation. Rather, 94% of subjects with PTSD reported additional somatic, cognitive, and/or emotional symptoms. Analysis of the TRACK-TBI Pilot study data allowed the inclusion of patients traditionally excluded from previous hypothesis-driven research in the field, as pre-existing mental health conditions are common exclusion criteria. Incorporating educational history into the analysis led to the discovery that patients reporting PTSD symptoms at 6 months post-injury were more likely to have fewer years of education. Higher educational attainment previously has been shown to mitigate effects of moderate to severe TBI on cognitive status.<sup>42</sup> Although educational attainment was seen as a protective factor for reporting of PTSD symptoms, it is unclear if this finding was mediated by a relationship between educational status and cognitive outcomes.

This investigation revealed a high percent of individuals screening positive for PTSD (62.7%) in the moderate functional disability category by the GOS-E (score of 5 or 6). Studies assessing outcomes from individuals recruited in EDs typically do not use systematic approaches for ascertaining pre- and peri-injury mental health status.<sup>43,44</sup> Findings from Haagsma and colleagues identified an association with PTSD and functional disability measured by the GOS-E at 6 months follow-up,<sup>18</sup> consistent with the high proportions of patients screening positive for PTSD in the GOS-E 5 (64.7%) and GOSE 6 (48.1%) groups. Screening for PTSD, in conjunction with standardized examinations of pre-injury history at the time of initial medical care for TBI, could identify individuals who can benefit from more comprehensive follow-up.

Understanding the mechanism of injury is particularly important when considering the relationship between mTBI and PTSD. Previous studies suggest that individuals who sustain a TBI from intentional injuries are more likely to report PTSD symptoms and have poorer functional outcomes than other mechanisms of injury,<sup>10,11,45</sup> findings that are in agreement with the present study. However, the majority of our sample was enrolled from a single urban site which may not be representative of all patients with mTBI. Further examination of the relationship between pre-injury history, injury mechanism, and outcomes in individuals seeking care in urban emergency settings is warranted.

Estimating outcomes from TBI is complex. As recent reports indicate, behavioral variables may be more accurate in estimating functional outcomes of mTBI than injury severity ratings.<sup>8,19,42</sup> The relationship between PTSD symptom reporting and disability status following mTBI merits development of better PTSD clinical screening practices aimed at identifying patients and ameliorating

TABLE 4. MULTIVARIABLE PREDICTORS OF 6-MONTH PTSD AFTER MILD TBI

Predictor	В	OR	95% CI	р	Model significance (p)
Education (per year)	-0.13	0.88	0.79-0.98	0.021	< 0.001
Prior psychiatric history	0.94	2.56	1.42-4.61	0.002	
Mechanism of assault	1.28	3.59	1.69-7.63	0.001	

For each iterative step, variables that did not achieve the pre-determined level of significance (*p*-entry  $\leq 0.25$ ) were not added to the model. Variables entered, but which did not remain significant within each iterative step (*p*-remain  $\leq 0.15$ ) were eliminated from the model (Caucasian race, married marital status). Three variables were ultimately included in the final model: education years, prior psychiatric history, and mechanism of assault. PTSD, post-traumatic stress disorder; TBI, traumatic brain injury; OR, odds ratio; CI, confidence interval.

55

the impact of TBI and PTSD on long-term outcomes for individuals. Notably, in the current study, injury mechanism, psychiatric history, and education level persisted as independent risk factors after adjustment and thus underscores the importance of considering each demographic, socioeconomic, and event-of-injury characteristic during acute clinical evaluation of TBI. Conducting a more detailed patient history at the time of the initial injury and providing coordinated, multi-disciplinary care (e.g., social work, neuropsychology/psychiatry, rehabilitation) as recovery commences are practices reported to reduce PTSD symptoms and show promise for reducing long-term disability following TBI.<sup>46</sup>

Individuals who sustain a TBI and seek care in the ED are heterogeneous in clinical presentation, treatment, resources, and culture-all of which support the adoption of specific, relevant, and standardized data collection (TBI-CDEs) in order to: 1) accurately detect, characterize, and predict the incidence and/or development of PTSD after mTBI, and 2) converge data from multiple clinical sites with potentially distinct demographics and management practices for robust, reproducible, high-quality research to elucidate strategies to prevent or reduce PTSD symptoms after mTBI. In the TRACK-TBI Pilot study, education level, and incidence of baseline psychiatric history emerged as specific differences between those who reported PTSD symptoms throughout the 6-month recovery period among well-established urban Level I trauma centers. Hence, by implementation of the TBI-CDE Core Outcome Battery, we not only validate its utility, but also provide increased granularity of PTSD characterization and prediction, as well as provide support for previous findings that PTSD-like symptoms are indeed present following civilian mTBI. Given the approximately 27% incidence rate observed in this study, PTSD in civilian populations should be a topic of confirmatory and longitudinal analyses in the near future.

#### Study limitations

This study has several limitations. First, baseline medical history was collected primarily through self-report. Higher levels of granularity related to the patient's medical and psychiatric history at baseline, as well as the professional level of assessment (clinical cutoff points, self-report of symptoms) and the frequency of symptoms experienced, will yield more precision in identifying predictors for PTSD.

Second, a high frequency of participants who screened positive for PTSD were in a less than favorable outcome category even though they suffered mTBI based on GCS at admission. For the current study, we did not analyze comorbidities at the time of index TBI, such as polytrauma, which may contribute to or confound this finding. Future studies should explore the relationship of polytrauma and comorbidities at the time of injury to symptom reporting of post-injury outcomes.

Third, as this sample was not taken from a military population, military service history data were only applicable for a small proportion of the total sample (35 of 280), and the baseline assessment protocol did not include a detailed interview related to military service (e.g., number of years served, combat experience, and exposure to trauma during service). To better characterize the landscape of post-TBI PTSD in veterans within the civilian population, military service history data should be included in data standards for both TBI research and clinical care.

Fourth, injury mechanism of assault was a significant variable in the model. Although the subset of these individuals with intentional injury is small, TBI due to assault is associated with specific demographic factors. Individuals with intentional injuries are more likely to be male, non-Caucasian, single, and unemployed, and have lower levels of educational attainment, higher rates of intoxication, and a history of criminal behavior.<sup>47–50</sup> The connection between common factors of assault-related TBI and PTSD warrants further investigation, and in larger populations with more diverse demographic characteristics, location of medical care, and racial subgroups for validation.

Fifth, only 6.5% of patients screening positive for PTSD experienced it in isolation with respect to other psychiatric conditions. The high degree of coincidence of PTSD as defined by the stringent DSM-IV clinical criteria with multiple psychiatric, post-concussive symptom reporting, and neurocognitive outcome measures above their respective cutoffs for clinical screening suggests a multidimensional association of TBI and PTSD. Symptoms of PTSD and depression can overlap; indeed, in one study, subjects with major depressive disease reported comparable responses to as many classical PTSD items as patients who were diagnosed with PTSD.<sup>51</sup> In recent literature,<sup>52</sup> measures of cognitive effort were administered to validate cognitive and psychiatric symptoms. The current study utilizes measures arising from the TBI-CDEs, which currently do not include effort measures. As additive neurological dysfunction tends to overwhelm individual symptoms, current treatments for other domains of mental health may proportionally alleviate the behavioral burden of PTSD. As part of future research, collection and analysis of multi-dimensional psychiatric and cognitive measures, along with effort measures, may serve to alert the clinician to risks of developing PTSD during recovery and lead to earlier interventions during the subacute and chronic phases after TBI. Further study on larger populations will also likely reveal the contribution of pre-index injury factors, such as previous TBIs.

The sixth limitation is the use of DSM-IV<sup>33</sup> criteria in scoring the primary outcome measure of the study. The TRACK-TBI Pilot was completed prior to publication of the DSM-5, and the PCL-C was designed according to DSM-IV criteria for PTSD. Results from the current study await the augmentation and validation in future research using the PTSD Checklist for DSM-5 (PCL-5),<sup>53</sup> which corroborates the criteria of the DSM-5.

#### Conclusion

Expanding evidence supports the concept of TBI as a chronic disease characterized by delayed onset and possible progressive symptoms. In this study, positive screen for PTSD was identified in a large proportion of civilian patients 6 months following acute mTBI. Pre-injury demographic and socioeconomic status, prior psychiatric history, and assault mechanism emerged as risk factors for positive 6-month PTSD screen, and should be evaluated at time of injury to better identify those who may benefit from post-injury follow-up. In the civilian ED setting of predominantly mTBI, standardized data collection of these injury characteristics and preexisting risk factors at the time of injury care may assist in identifying significant morbidity attributable to PTSD and development of therapeutic strategies that may reduce the psychiatric burden associated with TBI. Our findings support the necessity of increasing awareness of PTSD in the civilian TBI population and promoting more routine PTSD screening of mTBI patients who are still symptomatic 6 months after their injury.

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#### Author Disclosure Statement

No competing financial interests exist.

#### Appendix

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