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Predictors of six-month inability to return to work in previously employed subjects after mild traumatic brain injury: A TRACK-TBI pilot study

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Abstract

Introduction: Return to work (RTW) is an important milestone of mild traumatic brain injury (mTBI) recovery. The objective of this study was to evaluate whether baseline clinical variables, three-month RTW, and three-month post-concussional symptoms (PCS) were associated with six-month RTW after mTBI.

Methods: Adult subjects from the prospective multicenter Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot study with mTBI (Glasgow Coma Scale 13–15) who were employed at baseline, with completed three- and six-month RTW status, and three-month Acute Concussion Evaluation (ACE), were extracted. Univariate and multivariable analyses were performed for six-month RTW, with focus on baseline employment, three-month RTW, and three-month ACE domains (physical, cognitive, sleep, and/or emotional postconcussional symptoms (PCS)). Odds ratios (OR) and 95% confidence intervals [CI] were reported. Significance was assessed at $p < 0.05$.

Results: In 152 patients aged 40.7 ± 15.0 years, 72% were employed full-time at baseline. Three- and six-month RTW were 77.6% and 78.9%, respectively. At three months, 59.2%, 47.4%, 46.1% and 31.6% scored positive for ACE physical, cognitive, sleep, and emotional PCS domains, respectively. Three-month RTW predicted six-month RTW (OR = 19.80, 95% CI [7.61–51.52]). On univariate analysis, scoring positive in any three-month ACE domain predicted inability for six-month RTW (OR = 0.10–0.11). On multivariable analysis, emotional symptoms predicted inability to six-month RTW

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(OR = 0.19 [0.04–0.85]). Subjects who scored positive in all four ACE domains were more likely to be unable to RTW at six months (4 domains: 58.3%, vs. 0-to-3 domains: 9.5%; multivariable OR = 0.09 [0.02–0.33]).
Conclusions: Three-month post-injury is an important time point at which RTW status and PCS should be assessed, as both are prognostic markers for six-month RTW. Clinicians should be particularly vigilant of patients who present with emotional symptoms, and patients with symptoms across multiple PCS categories, as these patients are at further risk of inability to RTW and may benefit from targeted evaluation and support.

Keywords
Concussion, disability, mild traumatic brain injury, post-concussion syndrome, return to work

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Introduction

Traumatic brain injury (TBI) is a significant public health burden; there are about 2.8 million new cases of TBI in the United States (U.S.) per year,[1] and 2% of the U.S. population currently lives with TBI-related disability.[2] Up to 90% of TBI is mild (mTBI),[3] defined as head injury with a Glasgow Coma Scale (GCS) of 13–15 associated with loss of consciousness under 30 minutes, post-traumatic amnesia less than 24 hours, alteration of consciousness, and/or focal neurologic deficits.[4] Historically, subtle and long-term mTBI sequelae may have been underappreciated given the lack of apparent severity at the time of injury. However, substantial evidence now suggests that this condition can lead to lasting deficits in a significant minority of patients.[5–7] Residual symptoms have important implications for patients' abilities to return to their baseline functional level, and may warrant more proactive and targeted follow-up, screening, and intervention to support long-term recovery after mTBI.

One important recovery milestone for mTBI patients is return to work (RTW), which is a surrogate marker of functional recovery. Resuming work-related activities is recognized by the World Health Organization as a critical outcome measure in the context of injury and disability, and delays have been shown to have significant psychosocial and economic consequences.[8,9] Furthermore, lost income associated with delayed RTW may have a synergistic relationship with injury-related medical expenses, leading to financially devastating impacts on patients and their families, and creating further barriers to optimal follow-up care and rehabilitation. Optimizing RTW is nuanced, and often depends on patient-provider communication, and patient self-efficacy,[10] in addition to clinical recovery. Although recent guidelines have encouraged gradual return to tolerable activity across the course of days after mTBI,[11–13] these guidelines are often eschewed in symptomatic patients by negative patient expectations and concerned clinicians which lead to delayed RTW.[10,13] It is important to note that RTW encompasses not only the ability to resume prior duties, but doing so with equal quality, efficiency, and stamina as pre-injury performance.[14,15]

As effective rehabilitation options begin to emerge,[16,17] it becomes increasingly important to accurately chart recovery trajectories and identify predictors of delayed RTW to proactively intervene. Several candidate risk factors for delayed RTW have been identified, e.g. lower educational level, concurrent extracranial injuries, re-injury, sex, and social/workplace-specific factors.[13,18–21] Certain post-injury symptomas such as dizziness and fatigue have also been shown to predict delayed RTW.[8,22] There is no current consensus on the symptoms most predictive of delayed RTW, nor the interval follow-up time points at which clinicians should be most vigilant for deficits and symptoms.[18–20,23] To address these questions, in the current study we specifically evaluated whether baseline employment, three-month RTW, and three-month postconcussional symptoms (PCS) were associated with six-month RTW in a prospective, multicenter cohort of mTBI patients.

Methods

The prospective, multicenter Transforming Research and Clinical Knowledge in Traumatic Brain Injury Pilot (TRACK-TBI Pilot) study was conducted at three U.S. Level I trauma centers (University of California San Francisco (UCSF) - Zuckerberg San Francisco General Hospital (San Francisco, California), University of Pittsburgh Medical Center (Pittsburgh, Pennsylvania), University Medical Center Brackenridge (Austin, Texas)) using the National Institute of Neurological Disorders and Stroke (NINDS) TBI Common Data Elements (CDEs).[24]

Inclusion criteria for TRACK-TBI Pilot were acute external force trauma to the head and presentation to a participating center, and a clinically-indicated head computed tomography (CT) scan within 24 hours of injury. Exclusion criteria were pregnancy, ongoing life-threatening disease (e.g., end-stage malignancy), police custody, involuntary psychiatric hold, and non-English speakers due to multiple outcome measures administered and/or normed only in English.

Eligible subjects were enrolled by convenience sampling from years 2010–2012. Institutional Review Board (IRB) approval for human studies was obtained at each participating site. The IRB of record for overall study approval was the UCSF Committee on Human Research (CHR), and TRACK-TBI Pilot was approved as CHR # 10–00011. Informed consent was obtained from each subject, or proxy, prior to enrollment. Subjects enrolled by surrogate consent were re-consented, if cognitively able, during the course of clinical care and/or follow-up timepoints for study participation.

The goal of the current analysis was to evaluate associations between baseline factors, three-month RTW and postconcussional symptomatology (PCS), and six-month RTW. TRACK-TBI Pilot subjects $\geq$18 years of age who were employed either full-time or part-time at time of injury, presented with GCS 13–15, completed the three-month Acute Concussion Evaluation (ACE), and had documented three- and six-month RTW status were included in the current analysis. The flowchart of included subjects is shown in Figure 1.

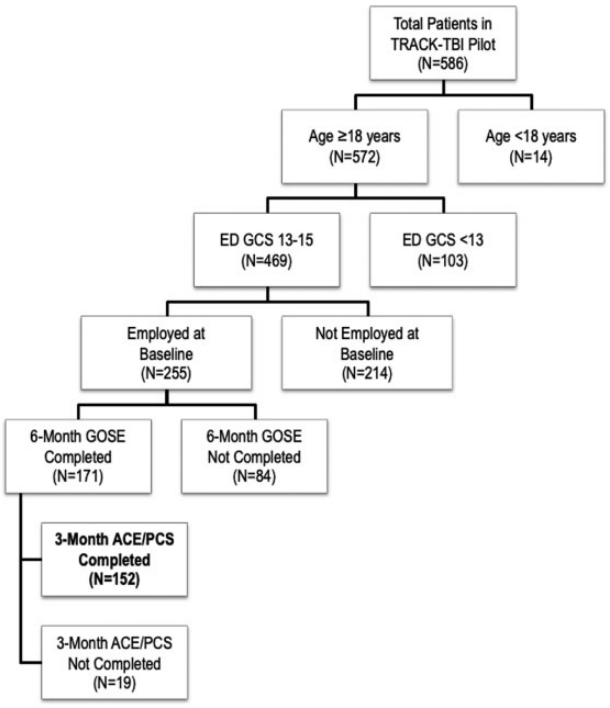

Figure 1. Flowchart of included subjects. Flowchart of included patients in the current study. ACE: acute concussion evaluation; GOSE: Glasgow Outcome Scale–Extended; PCS: postconcussional symptoms; TRACK-TBI: Transforming Research and Clinical Knowledge in Traumatic Brain Injury

Demographic and clinical variables

Subjects were assessed by in-person interview and medical record review for demographic, baseline medical history, as well as clinical and injury history variables upon emergency department (ED) admission in accordance with the NINDS CDE version 1.[25] If admitted to hospital, subjects were followed for the entirety of their hospital course.

Neuroimaging

All subjects received a head CT within 24 hours of injury as part of their clinical evaluation for TBI. Head CTs were read and coded by a central board-certified neuroradiologist blinded to subject characteristics in accordance with the NINDS CDE version 1 for neuroimaging.[26]

Outcomes

In TRACK-TBI Pilot, three-month PCS were evaluated using the Acute Concussion Evaluation (ACE). The ACE was first reported by a consensus sports neuropsychology panel in 1998, and was later adopted by the U. S. Centers for Disease Control and Prevention (CDC) in 2006.[27] It contains 22 specific post-concussive symptoms classified into 4 domains: physical (10 symptoms), cognitive (4 symptoms), sleep (4 symptoms), and emotional (4 symptoms). We decided to use the ACE given its reasonably strong psychometric properties. In particular, it demonstrates good item-total correlation (correlation up to 0.522 for individual items), moderate to high internal consistency (Cronbach $\alpha = 0.82$), non-significant inter-rater variability, and strong validity (including content validity, convergent/discriminant validity, and construct validity as determined by exploratory factor analysis).[28] Subjects were queried regarding the presence/absence of each symptom and the corresponding domain was scored as positive/negative accordingly, where "positive" = "symptom present" and "negative" = "symptom absent". Three- and six-month RTW were assessed using question 5 A of the Glasgow Outcome Scale-Extended (GOSE), which assesses whether subjects were able to return to their baseline work capacity after TBI.[29–31] The GOSE is considered the gold standard for TBI outcomes and widely utilized as an endpoint for clinical trials.[32,33] While the GOSE reliably captures a wide-range of functional

outcomes with good test-retest (kappa 0.92) and inter-rater reliability (kappa 0.84),[34] recent psychometric analyses have shown some evidence of item redundancy and inefficiency.[33] In particular, GOSE question 5B, which asks "how restricted" subjects are with respect to work, has been shown to add relatively low additional information while being subject to interpretation bias.[33] As such, we opted to only use question 5A, which is less prone to interpretation errors and offers greater psychometric reliability and validity.

Statistical analysis

Descriptive statistics were reported using means and standard deviations (SD) for continuous variables and proportions for categorical variables. Variables of interest included baseline employment, three-month PCS by ACE domains (physical, sleep, cognition, emotional), three-month RTW, and six-month RTW. Multivariable regressions were performed for six-month RTW, controlling for known predictors from prior literature[35,36] including age, sex, race, education, psychiatric history, and polytrauma (defined as Abbreviated Injury Score (AIS) of ≥ 3 in any extracranial body system).[33,37–40] A composite score for three-month PCS was developed to reflect whether subjects scored positive in 0, 1, 2, 3, or all 4 domains of the ACE, and this was entered onto a separate regression for six-month RTW. Candidate predictors from univariate analyses with $p < 0.10$ were included in multivariable analyses. Univariate and multivariable odds ratios (OR) and associated 95% confidence intervals [95% CI] were reported for predictors. Statistical significance was assessed at $p < 0.05$. Analyses were performed using Statistical Package for the Social Sciences (SPSS) version 25 (IBM Corporation, Chicago, IL).

Results

Overall, 152 subjects were included in this analysis. Mean age was 40.7 ± 15.0 years, 73% were male, and 80.9% were Caucasian. Average years of education were 14.7 ± 2.6 and 72.4% were employed full-time at baseline. Sixty-three percent had posttraumatic amnesia, of which approximately half were under 30 minutes. Seventy-seven percent had an ED GCS of 15, and 61.2% had no intracranial abnormalities on CT. Measures of injury severity (LOC, PTA, GCS, CT results, and polytrauma) did not differ across six-month RTW status (Table 1). For validity, we compared measures of injury severity in a separate analysis for adult mTBI patients in TRACK-TBI Pilot who were included vs. excluded from the current study, and there were no statistically significant differences (data not shown).

RTW was 77.6% at three months and 78.9% at six months. At three months, the proportion of subjects scoring positive for ACE physical, sleep, cognitive, and emotional symptoms were 59.2%, 47.4%, 46.1% and 31.6%. The distribution of outcomes by six-month RTW status are shown in Table 2.

On univariate analysis, several notable findings were present between subjects who did and did not return to work at six months. Baseline history of illicit drug use showed a nonsignificant statistical trend for inability to RTW (six-month RTW=No: 31.3% with illicit drug use; six-month RTW=Yes: 17.5% with illicit drug use; univariate OR = 0.47 [95% CI 0.19–1.13]). Subjects who returned to work at three months were much more likely to return to work at six months (six-month RTW = No: 31.2% returned to work at three-month; six-month RTW = Yes: 90.0% returned to work at three months; OR = 19.80 [7.61–51.52]. Scoring positive in any three-month PCS domain predicted inability to RTW at six months: ACE–Physical (six-month RTW = No: 90.6% symptomatic; six-month RTW = Yes: 50.8% symptomatic; OR = 0.11 [0.03–0.37]); ACE–Sleep (six-month RTW = No: 84.4% symptomatic; six-month RTW = Yes: 37.5% symptomatic; OR = 0.11 [0.04–0.31]); ACE–Cognitive (six-month RTW = No: 84.4% symptomatic; six-month RTW = Yes: 35.8% symptomatic; OR = 0.10 [0.04–0.29]); ACE–Emotional (six-month RTW = No: 71.9% symptomatic; six-month RTW = Yes: 20.8% symptomatic; OR = 0.10 [0.04–0.25]) (Table 2).

Analysis of the relationship between the number of three-month ACE domains for which a subject scored positive, and six-month RTW, showed a trend between the number of positive ACE domains and inability to RTW (Figure 2). There was a clear dichotomy between scoring positive in all four ACE domains and reduced likelihood of RTW (all four domains: 58.3% unable to RTW at six months versus 0–3 domains: 9.5% unable to RTW at six months, univariate OR = 0.08 [0.03–0.19]).

Two multivariable analyses were performed. When the four individual ACE domains were entered as separate predictors, the ACE-Emotional domain was a significant predictor of inability to six-month RTW (OR = 0.19 [0.04–0.85]) (Table 3). The univariate relationship between scoring positive in all four ACE domains vs. 0–3 domains, and inability to RTW at six months, was conserved (OR = 0.09 [0.02–0.33]) (Table 4). The Nagelkerke R^2 for these analyses were 0.585 and 0.572, respectively.

Discussion

Mild TBI is increasingly understood as a condition with significant long-term sequelae.[5–7] It is crucial to identify those at risk of developing symptoms

Table 1. Descriptive variables by return to work status at six months.

Descriptive variable	Overall ($N = 152$)	No RTW ($N = 32$)	Yes RTW ($N = 120$)	Sig. (p)
Age				0.435
Mean (SD)	40.7 (15.0)	42.5 (14.2)	40.2 (15.2)	
Gender				0.777
Male	111 (73.0%)	24 (75.0%)	87 (72.5%)	
Female	41 (27.0%)	8 (25.0%)	33 (27.5%)	
Race				0.629
Caucasian	123 (80.9%)	24 (75.0%)	99 (82.5%)	
African American/African	7 (4.6%)	2 (6.3%)	5 (4.2%)	
Other races	22 (14.5%)	6 (18.8%)	16 (13.3%)	
Education (years)				0.159
M (*SD*)	14.7 (2.6)	14.1 (2.3)	14.8 (2.7)	
Baseline employment				0.412
Full time	110 (72.4%)	25 (78.1%)	85 (70.8%)	
Part time	42 (27.6%)	7 (21.9%)	35 (29.2%)	
PMH psychiatric				0.794
No	112 (73.7%)	23 (71.9%)	89 (74.2%)	
Yes	40 (26.3%)	9 (28.1%)	31 (25.8%)	
PMH illicit drug use				0.086
No	121 (79.6%)	22 (68.8%)	99 (82.5%)	
Yes	31 (20.4%)	10 (31.3%)	21 (17.5%)	
Mechanism of injury				0.105
MVA/MCC	41 (26.9%)	8 (25.0%)	33 (27.5%)	
PVA	22 (14.5%)	5 (15.6%)	17 (14.2%)	
Fall	67 (44.1%)	11 (24.4%)	56 (46.7%)	
Assault	18 (11.8%)	8 (25.0%)	10 (8.3%)	
Struck by	4 (2.6%)	0 (0.0%)	4 (3.3%)	
LOC				0.543
No	34 (22.4%)	5 (15.6%)	29 (24.2%)	
Yes	107 (70.4%)	25 (78.1%)	82 (68.3%)	
Unknown	11 (7.2%)	2 (6.3%)	9 (7.5%)	
PTA				0.783
No	44 (28.9%)	8 (25.0%)	36 (30.0%)	
Yes	96 (63.2%)	20 (62.5%)	76 (63.3%)	
Unknown	12 (7.9%)	4 (12.5%)	8 (6.7%)	
ED GCS				0.952
13	4 (2.6%)	1 (3.1%)	3 (2.5%)	
14	31 (20.4%)	6 (18.8%)	25 (20.8%)	
15	117 (77.0%)	25 (78.1%)	92 (76.7%)	
CT intracranial lesion				0.519
No	93 (61.2%)	18 (56.2%)	75 (62.5%)	
Yes	59 (38.8%)	14 (43.8%)	45 (37.5%)	
Polytrauma				0.180
No	130 (85.5%)	25 (78.1%)	105 (87.5%)	
Yes	22 (14.5%)	7 (21.9%)	15 (12.5%)	

CT: computed tomography; ED: emergency department; mTBI: mild traumatic brain injury; MCC: motorcycle crash; MVA: motor vehicle accident; PMH: prior medical history; PVA: pedestrian versus auto; RTW: return to work; SD: standard deviation.
Demographic and clinical variables for patients who did and did not return to baseline level of work at six months post-mTBI.

that prevent return to baseline functional and employment status. Failure to RTW within a reasonable timeframe is associated with poor psychosocial outcomes,[41] and can have compounding financial impacts. Lifetime healthcare costs for TBI treatment can reach $1,875,000, and U.S. expenditures on acute medical and rehabilitation services for TBI exceeds $9 billion annually.[42] This financial impact on patients and the healthcare system is exacerbated by an annual $642 million in lost wages.[43] The overall direct and indirect financial impact of TBI in the U.S. is $60 billion.[44]

Table 2. Three-month variables by return to work status at six months.

3-Month variable	Overall ($N = 152$)	No RTW ($N = 32$)	Yes RTW ($N = 120$)	Sig. (p)
Return to work				<0.001
No	34 (22.4%)	22 (68.8%)	12 (10.0%)	
Yes	118 (77.6%)	10 (31.2%)	108 (90.0%)	
ACE physical				<0.001
No	62 (40.8%)	3 (9.4%)	59 (49.2%)	
Yes	90 (59.2%)	29 (90.6%)	61 (50.8%)	
ACE sleep				<0.001
No	80 (52.6%)	5 (15.6%)	75 (62.5%)	
Yes	72 (47.4%)	27 (84.4%)	45 (37.5%)	
ACE cognitive				<0.001
No	82 (53.9%)	5 (15.6%)	77 (64.2%)	
Yes	70 (46.1%)	27 (84.4%)	43 (35.8%)	
ACE emotional				<0.001
No	104 (68.4%)	9 (28.1%)	95 (79.2%)	
Yes	48 (31.6%)	23 (71.9%)	25 (20.8%)	

ACE: acute concussion evaluation; mTBI: mild traumatic brain injury; RTW: return to work.
Comparison of three-month RTW and ACE domains (PCS symptoms) in patients who did and did not return to baseline level of work at six months post-mTBI. ACE domains are dichotomized to "No symptoms" and "Yes symptoms."

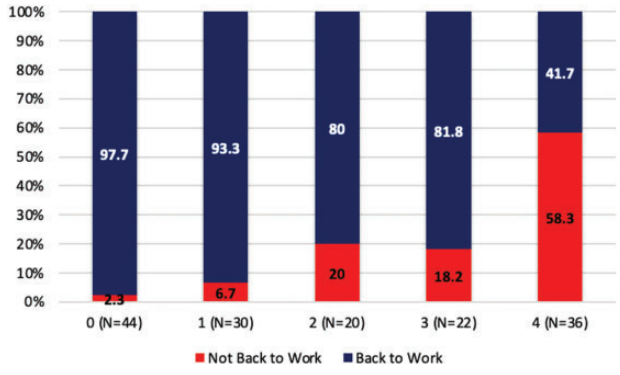

Figure 2. Relationship between symptomatic three-month ACE/PCS domains and six-month RTW. Bar graph showing proportion of patients back to work at three months (dark blue) versus not back to work (red) in accordance to number of concurrent symptomatic ACE domains (physical, cognitive, sleep, emotional). 0: no symptoms, 1: 1 symptomatic ACE domain, 2: 2 symptomatic ACE domains, 3: 3 symptomatic ACE domains, 4: 4 symptomatic ACE domains. Percentages are shown. ACE: acute concussion evaluation; GOSE: Glasgow Outcome Scale–Extended; PCS: postconcussional symptoms; TRACK-TBI: Transforming Research and Clinical Knowledge in Traumatic Brain Injury.

These resources may benefit from targeted application to patients who are most at risk for poorer psychosocial recovery. In fact, one theme that has emerged from qualitative research on RTW in mTBI is that follow-ups remain unfocused on patient priorities.[45] Hence, channeling efforts towards those who require extra support may be more effective than a generalized incentive across all TBI. The development of effective mTBI rehabilitation protocols requires validated risk factors. Prior studies have shown that lower educational level, concurrent extracranial injuries, re-injury, sex, and social and workplace-specific factors may predict delayed RTW.[13,18–21] Subjective symptoms reporting has also demonstrated efficacy in predicting delayed RTW.[8] Multiple rehabilitation models have sought to treat these subjective symptoms with mixed results.[23]

The current study contributes to this discussion. Individually, three-month PCS symptom domains predicted delayed RTW at six months, each with odds ratio of 0.10–0.11 for inability to RTW. Interestingly, on multivariable analysis of individual PCS domains, emotional symptoms (e.g. irritability, sadness, nervousness, or being 'more emotional') were most predictive of delayed RTW. While emotional symptoms were present in a smaller proportion of patients compared to the other 3 domains (32% vs. 46–59%), their status as a multivariable predictor shows that emotional symptoms may constitute a distinct subset from other PCS symptom categories. In reality, emotional complaints are frequently under-assessed and overlooked due to their subjectivity. Patients often feel that their providers doubt their voracity,[45] and this mistrust may lead to delays in appropriate mTBI rehabilitation referrals.[45] Increased awareness and assessment for these symptoms may inform clinicians regarding appropriate follow-up with specialists and targeted referrals for at-risk patients.

Furthermore, we showed that a composite ACE/PCS score is of high importance. While scoring positive in 0–3 ACE symptom domains associated with some reduction in six-month RTW (4–18% unable to RTW), scoring positive in all four domains (physical,

Table 3. Multivariable regression for six-month return to work, with individual three-month postconcussional symptom categories.

Predictor	OR [95% CI]	Sig. (*p*)
Age		
Per-year	0.97 [0.93–1.02]	0.236
Sex		
Male	Reference	–
Female	1.13 [0.24–5.26]	0.876
Race		0.677
Caucasian	Reference	–
African American/African	0.86 [0.07–11.04]	0.908
Other	0.49 [0.10–2.37]	0.377
Education		
Per-year	1.06 [0.84–1.34]	0.645
Baseline employment		
Full time	Reference	–
Part time	5.57 [1.14–27.17]	0.034
PMH psychiatric		
No	Reference	–
Yes	1.45 [0.36–5.85]	0.606
PMH illicit drug use		
No	Reference	–
Yes	0.24 [0.06–0.97]	0.045
CT intracranial lesion		
Negative	Reference	–
Positive	1.45 [0.40–5.34]	0.575
Polytrauma		
No	Reference	–
Yes	0.72 [0.14–3.76]	0.692
RTW at three months		
No	Reference	–
Yes	15.39 [4.21–56.27]	0.000
ACE physical (three months)		
No	Reference	–
Yes	0.86 [0.14–5.17]	0.865
ACE sleep (three months)		
No	Reference	–
Yes	0.31 [0.06–1.52]	0.149
ACE cognitive (three months)		
No	Reference	–
Yes	0.74 [0.13–4.13]	0.729
ACE emotional (three months)		
No	Reference	–
Yes	0.19 [0.04–0.85]	0.030

ACE: acute concussion evaluation; CT: computed tomography; PMH: prior medical history; RTW: return to work.
Multivariable logistic regression of six-month return to work, with odds ratio (OR) and corresponding 95% confidence interval (CI) reported for each predictor. ACE domains are dichotomized to "No symptoms" and "Yes symptoms."

Table 4. Multivariable regression for six-month return to work, with dichotomized three-month postconcussional symptom categories.

Predictor	OR [95% CI]	Sig. (*p*)
Age		
Per-year	0.98 [0.94–1.02]	0.277
Sex		
Male	Reference	–
Female	1.35 [0.28–6.44]	0.705
Race		0.558
Caucasian	Reference	–
African American/African	0.82 [0.06–11.66]	0.885
Other	0.43 [0.10–1.98]	0.281
Education		
Per-year	1.04 [0.82–1.31]	0.736
Baseline employment		
Full time	Reference	–
Part time	4.23 [0.90–19.95]	0.068
PMH psychiatric		
No	Reference	–
Yes	1.65 [0.39–6.97]	0.494
PMH illicit drug use		
No	Reference	–
Yes	0.24 [0.06–0.93]	0.039
CT intracranial lesion		
Negative	Reference	–
Positive	1.43 [0.42–4.93]	0.571
Polytrauma		
No	Reference	–
Yes	0.69 [0.15–3.14]	0.634
RTW at three months		
No	Reference	–
Yes	16.08 [4.63–55.82]	<0.001
ACE concurrent categories at three months		
<4	Reference	–
=4	0.09 [0.02–0.34]	<0.001

ACE: acute concussion evaluation; CT: computed tomography; PMH: prior medical history; RTW: return to work.
Multivariable logistic regression of six-month return to work, with odds ratio (OR) and corresponding 95% confidence interval (CI) reported for each predictor. ACE Concurrent Categories is dichotomized to scoring positive in all four ACE subdomains at three months versus scoring positive in 0–3 categories.

cognitive, emotional, and sleep) associated with a significantly reduced likelihood of six-month RTW (56% unable to RTW). The Nagelkerke R^2 values were comparable across both multivariable analyses for six-month RTW, and were reasonable at explaining over 57% of the variance. Hence, assessing three-month PCS by domain or as a composite score can provide utility in prognosticating six-month RTW. As such, providers should be vigilant in evaluating which patients score positive across multiple symptom categories, and targeted rehabilitation efforts should be invested in these high-risk patients.

We found that part-time versus full-time baseline employment status was associated with increased six-month RTW (OR = 6.12 [1.39–26.94]). This may simply be explained by the relative ease with which patients can return to part-time rather than full-time work. RTW at three months predicted RTW at six

months (OR = 20.40 [6.04–68.86]); conversely, 78% of our cohort returned to work by three months, and of those who had not returned to work by that time, only one-third regained their baseline employment status at six months. Coupled with known poorer outcomes in those who report symptomatic complaints at three months,[46] our data suggests that patients should be screened at or prior to three months for risk of delayed RTW, and at-risk patients should be directed to vocational rehabilitation services as quickly as possible.

Finally, it is worth noting that history of illicit substance use was a predictor for inability to RTW at six months. Substance use has been shown to be a predictor of poorer outcomes after mTBI in prior studies,[47] and the current analysis further underscores the need to identify patients with substance use disorders after mTBI as part of standard assessment, and triage these patients to counseling and treatment after mTBI to decrease the risk for deleterious functional and psychosocial outcomes.

Limitations

This study was limited by the standard NINDS follow-up time frame of six months in TRACK-TBI Pilot. One meta-analysis reports a 12-month RTW rate of 89%,[48] and it is possible that RTW continues to increase over time, which should be the topic of future studies. However, even relatively short-term delays in RTW can have significant financial and psychosocial consequences for patients and families and are thus important to investigate and intervene upon. Our study was also limited by the lack of variables regarding preinjury employment type, rehabilitation interventions and work performance upon return. Certain studies have shown that RTW should not be considered a dichotomous variable, because even those who are able to RTW may continue to have impaired efficiency and/or other deficits compared to their preinjury functional level.[14] These variables were included in the subsequent, recently closed, 18-center Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI study; ClinicalTrials.gov Identifier NCT02119182, recruitment years 2014–2020).

In addition, although the ACE is validated and endorsed by the CDC, alternative measures for PCS have comparable value. For example, despite good agreement between the ACE and Rivermead Post-Concussion Symptoms Questionnaire (RPQ), the RPQ has merits in specifically discriminating between subjective and objective cognitive complaints.[49] However, given the well-categorized structure of the ACE (breakdown into four distinct symptom domains), its higher number of specific questions (22 vs. 16 questions), as well as its superior sensitivity for uncovering complaints in certain categories,[49] we opted to use the ACE in the current study.

It should be noted that due to the complex social, legal, and financial dynamics surrounding many TBI cases, there may be bias in the reporting of subjective PCS complaints either consciously or unconsciously.[50] Although it is well known that litigation can influence both subjective symptom reporting and RTW,[51] determining effort and malingering remain complex endeavors especially given that mTBI can lead to true neuropsychological sequelae affecting motivation, attention, and testing performance.[52,53] We did not attempt to interpret effort in the current study, as appropriate tests for effort detection were not included in the TRACK-TBI Pilot.

Finally, our study was completed through convenience sampling across three Level 1 trauma centers. The urban trauma population may recruit from a population with greater comorbidities and injury severity. As such, our data may have limited generalizability to other mTBI subpopulations.

Future studies should seek to evaluate the details of interval rehabilitation, extended timeframe of follow-up (e.g. 12 months and beyond), measures of work performance in those who RTW after mTBI, as well as reasons for decreased work performance in those who are unable to return to baseline work status. Evaluating emerging vocational rehabilitation programs with successful pilot trials will also be of interest.

Conclusions

Inability to RTW after mTBI is associated with significant psychosocial and financial impacts, which further exacerbate mTBI sequelae and impair recovery. It is important to screen broadly as well as provide focused rehabilitation resources to patients at highest risk of delayed RTW. Three-month post-injury is an important time point at which RTW status and PCS should be assessed, as both are prognostic markers for six-month RTW. Clinicians should be particularly vigilant of patients who present with emotional symptoms, and patients with symptoms crossing multiple PCS categories, as these patients are at further risk of inability to RTW and may benefit from targeted evaluation and support.

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Ethics committee approval

This study received approval from the institutional review board of record at University of California, San Francisco (Committee on Human Research, study #10–00011).

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References

1. Taylor CA, Bell JM, Breiding MJ, et al. Traumatic brain injury-related emergency department visits, hospitalizations, and deaths – United States, 2007 and 2013. *MMWR Surveill Summ* 2017; 66: 1–16.
2. Thurman DJ, Alverson C, Dunn KA, et al. Traumatic brain injury in the United States: a public health perspective. *J Head Trauma Rehabil* 1999; 14: 602–615.
3. World Health Organization. *Neurological disorders: public health challenges*. Geneva: World Health Organization, 2006.
4. King NS, Crawford S, Wenden FJ, et al. Measurement of post-traumatic amnesia: how reliable is it? *J Neurol Neurosurg Psychiatry* 1997; 62: 38–42.
5. Gronwall D and Wrightson P. Delayed recovery of intellectual function after minor head injury. *Lancet* 1974; 2: 605–609.
6. Ruff RM, Camenzuli L and Mueller J. Miserable minority: emotional risk factors that influence the outcome of a mild traumatic brain injury. *Brain Inj* 1996; 10: 551–565.
7. Wood RL. Understanding the 'miserable minority': a diasthesis-stress paradigm for post-concussional syndrome. *Brain Inj* 2004; 18: 1135–1153.
8. Wäljas M, Iverson GL, Lange RT, et al. Return to work following mild traumatic brain injury. *J Head Trauma Rehabil* 2014; 29: 443–450.
9. World Health Organization. International Classification of Functioning, Disability and Health. https://www.who.int/standards/classifications/international-classification-of-functioning-disability-and-health. 2021 (accessed 1 January 2021).
10. Soeker S, Wegner L and Caldwell LL. Returning individuals with mild to moderate brain injury back to work: a systematic client centered approach. *Traumatic Brain Injury* 2014; 373–397.
11. Schneider KJ, Leddy JJ, Guskiewicz KM, et al. Rest and treatment/rehabilitation following sport-related concussion: a systematic review. *Br J Sports Med* 2017; 51: 930–934.
12. Thomas DG, Apps JN, Hoffmann RG, et al. Benefits of strict rest after acute concussion: a randomized controlled trial. *Pediatrics* 2015; 135: 213–223.
13. Silverberg ND and Otamendi T. Advice to rest for more than 2 days after mild traumatic brain injury is associated with delayed return to productivity: a case-control study. *Front Neurol* 2019; 10: 362.
14. Silverberg ND, Panenka WJ and Iverson GL. Work productivity loss after mild traumatic brain injury. *Arch Phys Med Rehabil* 2018; 99: 250–256.
15. Chu S-Y, Tsai Y-H, Xiao S-H, et al. Quality of return to work in patients with mild traumatic brain injury: a prospective investigation of associations among post-concussion symptoms, neuropsychological functions, working status and stability. *Brain Inj* 2017; 31: 1674–1682.
16. Dornonville de la Cour FL, Rasmussen MA, Foged EM, et al. Vocational rehabilitation in mild traumatic brain injury: supporting return to work and daily life functioning. *Front Neurol* 2019; 10: 103.
17. Scheenen ME, Visser-Keizer AC, van der Naalt J, et al. Description of an early cognitive behavioral intervention (UPFRONT-intervention) following mild traumatic brain injury to prevent persistent complaints and facilitate return to work. *Clin Rehabil* 2017; 31: 1019–1029.

18. de Koning ME, Scheenen ME, van der Horn HJ, et al. Prediction of work resumption and sustainability up to 1 year after mild traumatic brain injury. *Neurology* 2017; 89: 1908–1914.
19. Vikane E, Hellstrøm T, Røe C, et al. Predictors for return to work in subjects with mild traumatic brain injury. *Behav Neurol* 2016; 2016: 8026414.
20. Stergiou-Kita M, Mansfield E, Sokoloff S, et al. Gender influences on return to work after mild traumatic brain injury. *Arch Phys Med Rehabil* 2016; 97: S40–5.
21. Cancelliere C, Kristman VL, Cassidy JD, et al. Systematic review of return to work after mild traumatic brain injury: results of the international collaboration on mild traumatic brain injury prognosis. *Arch Phys Med Rehabil* 2014; 95: S201–9.
22. Chamelian L and Feinstein A. Outcome after mild to moderate traumatic brain injury: the role of dizziness. *Arch Phys Med Rehabil* 2004; 85: 1662–1666.
23. Mani K, Cater B and Hudlikar A. Cognition and return to work after mild/moderate traumatic brain injury: a systematic review. *Work* 2017; 58: 51–62.
24. Yue JK, Vassar MJ, Lingsma HF, TRACK-TBI Investigators, et al. Transforming research and clinical knowledge in traumatic brain injury pilot: multicenter implementation of the common data elements for traumatic brain injury. *J Neurotrauma* 2013; 30: 1831–1844.
25. Maas AI, Harrison-Felix CL, Menon D, et al. Common data elements for traumatic brain injury: recommendations from the interagency working group on demographics and clinical assessment. *Arch Phys Med Rehabil* 2010; 91: 1641–1649.
26. Duhaime A-C, Gean AD, Haacke EM, Common Data Elements Neuroimaging Working Group Members, Pediatric Working Group Members, et al. Common data elements in radiologic imaging of traumatic brain injury. *Arch Phys Med Rehabil* 2010; 91: 1661–1666.
27. Lovell MR and Collins MW. Neuropsychological assessment of the college football player. *J Head Trauma Rehabil* 1998; 13: 9–26.
28. Gioia GA, Collins M and Isquith PK. Improving identification and diagnosis of mild traumatic brain injury with evidence: psychometric support for the acute concussion evaluation. *J Head Trauma Rehabil* 2008; 23: 230–242.
29. Wilson JT, Pettigrew LE and Teasdale GM. Structured interviews for the Glasgow outcome scale and the extended Glasgow outcome scale: guidelines for their use. *J Neurotrauma* 1998; 15: 573–585.
30. Zafonte R, Friedewald WT, Lee SM, et al. The citicoline brain injury treatment (COBRIT) trial: design and methods. *J Neurotrauma* 2009; 26: 2207–2216.
31. Wright DW, Yeatts SD, Silbergleit R, NETT Investigators, et al. Very early administration of progesterone for acute traumatic brain injury. *N Engl J Med* 2014; 371: 2457–2466.
32. Weir J, Steyerberg EW, Butcher I, et al. Does the extended Glasgow outcome scale add value to the conventional Glasgow outcome scale? *J Neurotrauma* 2012; 29: 53–58.
33. Ranson J, Magnus BE, Temkin N, TRACK-TBI Investigators, et al. Diagnosing the GOSE: structural and psychometric properties using item response theory, a TRACK-TBI pilot study. *J Neurotrauma* 2019; 36: 2493–2505.
34. Pettigrew LEL, Wilson JTL and Teasdale GM. Reliability of ratings on the Glasgow outcome scales from in-person and telephone structured interviews. *J Head Trauma Rehabil* 2003; 18: 252–258.
35. Jacobs B, Beems T, Stulemeijer M, et al. Outcome prediction in mild traumatic brain injury: age and clinical variables are stronger predictors than CT abnormalities. *J Neurotrauma* 2010; 27: 655–668.
36. Lingsma HF, Yue JK, Maas AIR, TRACK-TBI Investigators, et al. Outcome prediction after mild and complicated mild traumatic brain injury: external validation of existing models and identification of new predictors using the TRACK-TBI pilot study. *J Neurotrauma* 2015; 32: 83–94.
37. Yue JK, Winkler EA, Puffer RC, et al. Temporal lobe contusions on computed tomography are associated with impaired 6-month functional recovery after mild traumatic brain injury: a TRACK-TBI study. *Neurol Res* 2018; 40: 972–981.
38. Winkler EA, Yue JK, McAllister TW, TRACK-TBI Investigators, et al. COMT val 158 met polymorphism is associated with nonverbal cognition following mild traumatic brain injury. *Neurogenetics* 2016; 17: 31–41.
39. Hildebrand F, Giannoudis PV, van Griensven M, et al. Management of polytraumatized patients with associated blunt chest trauma: a comparison of two European countries. *Injury* 2005; 36: 293–302.
40. Chen C-W, Chu C-M, Yu W-Y, et al. Incidence rate and risk factors of missed injuries in major trauma patients. *Accid Anal Prev* 2011; 43: 823–828.
41. O'Neill J, Hibbard MR, Brown M, et al. The effect of employment on quality of life and community integration after traumatic brain injury. *J Head Trauma Rehabil* 1998; 13: 68–79.
42. National Institutes of Health. Rehabilitation of persons with traumatic brain injury. *NIH Consens Statement* 1998; 16: 1–41.
43. Johnstone B, Mount D and Schopp LH. Financial and vocational outcomes 1 year after traumatic brain injury. *Arch Phys Med Rehabil* 2003; 84: 238–241.
44. Coronado VG, Xu L, Basavaraju SV, Centers for Disease Control and Prevention (CDC), et al. Surveillance for traumatic brain injury-related deaths–United States, 1997-2007. *MMWR Surveill Summ* 2011; 60: 1–32.
45. Graff HJ, Deleu NW, Christiansen P, et al. Facilitators of and barriers to return to work after mild traumatic brain injury: a thematic analysis. *Neuropsychol Rehabil* 2020; 1–25.
46. Yue JK, Cnossen MC, Winkler EA, et al. Pre-injury comorbidities are associated with functional impairment and post-concussive symptoms at 3- and 6-months after mild traumatic brain injury: a TRACK-TBI study. *Front Neurol* 2019; 10: 343.
47. Yue JK, Phelps RRL, Winkler EA, et al. Substance use on admission toxicology screen is associated with peri-injury factors and six-month outcome after traumatic

brain injury: a TRACK-TBI pilot study. *J Clin Neurosci* 2020; 75: 149–156.
48. Bloom B, Thomas S, Ahrensberg JM, et al. A systematic review and meta-analysis of return to work after mild traumatic brain injury. *Brain Inj* 2018; 32: 1623–1636.
49. Ngwenya LB, Gardner RC, Yue JK, et al. Concordance of common data elements for assessment of subjective cognitive complaints after mild-traumatic brain injury: a TRACK-TBI pilot study. *Brain Inj* 2018; 32: 1071–1078.
50. Lange RT, Iverson GL and Rose A. Post-concussion symptom reporting and the 'good-old-days' bias following mild traumatic brain injury. *Arch Clin Neuropsychol* 2010; 25: 442–450.
51. Tsanadis J, Montoya E, Hanks RA, et al. Brain injury severity, litigation status, and self-report of postconcussive symptoms. *Clin Neuropsychol* 2008; 22: 1080–1092.
52. Bigler ED. Effort, symptom validity testing, performance validity testing and traumatic brain injury. *Brain Inj* 2014; 28: 1623–1638.
53. Silver JM. Effort, exaggeration and malingering after concussion. *J Neurol Neurosurg Psychiatry* 2012; 83: 836–841.