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Longitudinal Recovery Following Repetitive Traumatic Brain Injury

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Abstract

IMPORTANCE One traumatic brain injury (TBI) increases the risk of subsequent TBIs. Research on longitudinal outcomes of civilian repetitive TBIs is limited.

OBJECTIVE To investigate associations between sustaining 1 or more TBIs (ie, postindex TBIs) after study enrollment (ie, index TBIs) and multidimensional outcomes at 1 year and 3 to 7 years.

DESIGN, SETTING, AND PARTICIPANTS This cohort study included participants presenting to emergency departments enrolled within 24 hours of TBI in the prospective, 18-center Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study (enrollment years, February 2014 to July 2020). Participants who completed outcome assessments at 1 year and 3 to 7 years were included. Data were analyzed from September 2022 to August 2023.

EXPOSURES Postindex TBI(s).

MAIN OUTCOMES AND MEASURES Demographic and clinical factors, prior TBI (ie, preindex TBI), and functional (Glasgow Outcome Scale–Extended [GOSE]), postconcussive (Rivermead Post-Concussion Symptoms Questionnaire [RPQ]), psychological distress (Brief Symptom Inventory-18 [BSI-18]), depressive (Patient Health Questionnaire-9 [PHQ-9]), posttraumatic stress disorder (PTSD; PTSD Checklist for *DSM-5* [PCL-5]), and health-related quality-of-life (Quality of Life After Brain Injury–Overall Scale [QOLIBRI-OS]) outcomes were assessed. Adjusted mean differences (aMDs) and adjusted relative risks are reported with 95% CIs.

RESULTS Of 2417 TRACK-TBI participants, 1572 completed the outcomes assessment at 1 year (1049 [66.7%] male; mean [SD] age, 41.6 [17.5] years) and 1084 completed the outcomes assessment at 3 to 7 years (714 [65.9%] male; mean [SD] age, 40.6 [17.0] years). At 1 year, a total of 60 participants (4%) were Asian, 255 (16%) were Black, 1213 (77%) were White, 39 (2%) were another race, and 5 (0.3%) had unknown race. At 3 to 7 years, 39 (4%) were Asian, 149 (14%) were Black, 868 (80%) were White, 26 (2%) had another race, and 2 (0.2%) had unknown race. A total of 50 (3.2%) and 132 (12.2%) reported 1 or more postindex TBIs at 1 year and 3 to 7 years, respectively. Risk factors for postindex TBI were psychiatric history, preindex TBI, and extracranial injury severity. At 1 year, compared with those without postindex TBI, participants with postindex TBI had worse functional recovery (GOSE score of 8: adjusted relative risk, 0.57; 95% CI, 0.34-0.96) and health-related quality of life (QOLIBRI-OS: aMD, −15.9; 95% CI, −22.6 to −9.1), and greater postconcussive symptoms (RPQ: aMD, 8.1; 95% CI, 4.2-11.9), psychological distress symptoms (BSI-18: aMD, 5.3; 95% CI, 2.1-8.6), depression symptoms (PHQ-9: aMD, 3.0; 95% CI, 1.5-4.4), and PTSD symptoms (PCL-5: aMD, 7.8; 95% CI, 3.2-12.4). At 3 to 7 years, these associations remained statistically significant. Multiple (2 or more) postindex TBIs were associated with poorer outcomes across all domains.

(continued)

Key Points

Question What are the functional, postconcussive, mental health, and health-related quality-of-life outcomes at 1 year and 3 to 7 years postinjury among adults with postindex traumatic brain injuries (TBIs)?

Findings In this cohort study of 2417 patients with TBI, compared with those without postindex TBIs, individuals with postindex TBIs at 1 year and 3 to 7 years were more symptomatic across functional, postconcussive, mental health, and health-related quality of life domains, with greatest symptom burden observed in individuals with multiple postindex TBIs.

Meaning In this study, participants with postindex TBIs were a symptomatic cohort in long-term recovery, and prevention, education, counseling, and follow-up care is needed for these at-risk patients.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Abstract (continued)

CONCLUSIONS AND RELEVANCE In this cohort study of patients with acute TBI, postindex TBI was associated with worse symptomatology across outcome domains at 1 year and 3 to 7 years postinjury, and there was a dose-dependent response with multiple postindex TBIs. These results underscore the critical need to provide TBI prevention, education, counseling, and follow-up care to at-risk patients.

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Introduction

Traumatic brain injury (TBI) is a leading cause of death and disability in the US and worldwide, generating 2.8 million annual TBI-related emergency department (ED) visits, 280 000 hospitalizations, and 64 000 deaths in the US alone.[1-3] Individuals who sustain 1 TBI are at a significantly increased risk of sustaining another.[4-7] Repetitive TBI is frequently studied in contact-sport athletes and military personnel. History of multiple concussions is correlated with depression,[8,9] delayed recovery,[10,11] cognitive impairment,[12,13] and chronic traumatic encephalopathy.[14] However, research on repetitive TBI and its longitudinal association with outcomes in the general population is limited.

TBI may progress from primary injury to chronic disease. Repetitive TBI rates range from 7% to 23% in civillians.[4-6,15-18] Prior TBI increases the risks of psychiatric symptoms[4,5] and decreased satisfaction with life.[19] In a 2013 US multicenter study, participants with prior TBI reported worse 6-month postconcussive symptoms (PCS), psychological distress, verbal memory, and processing speed.[6] A population-based study with matched controls in New Zealand[18] found TBIs sustained after the index TBI of study enrollment within 1 year were associated with worsened PCS.[20] In a large TBI Model Systems study, moderate or severe postindex TBI conferred worse disability rating scores and cognitive dependence at 1, 2, and 5 years after index TBI.[21]

To better characterize the association of repetitive TBI with recovery, we investigated the association between postindex TBI and functional, PCS, psychological distress, posttraumatic stress disorder (PTSD), depressive, and health-related quality-of-life (HRQOL) outcomes at 1 year and 3 to 7 years. We hypothesized that postindex TBI would be associated with poorer outcomes and that multiple postindex TBIs would be associated with more adverse outcomes at 3 to 7 years.

Methods

Participants and Study Design

The prospective, observational Transforming Research and Clinical Knowledge in Traumatic Brain Injury (TRACK-TBI) study enrolled participants with TBI at 18 US level I trauma centers between February 26, 2014, and July 3, 2018.[22-24] Eligible participants met American Congress of Rehabilitation Medicine TBI diagnostic criteria[25] in the ED and received clinically indicated head computed tomography[26] within 24 hours of TBI. Exclusion criteria were incarceration, pregnancy, nonsurvivable physical trauma, psychiatric hold, debilitating mental health disorders, neurologic disease, and non-English or non-Spanish speaking, depending on site. The TRACK-TBI study received institutional review board approval at each local site. Participants or their legally authorized representative provided written informed consent prior to enrollment. In 2019, the TRACK-TBI longitudinal substudy was approved to conduct annual phone calls with TRACK-TBI participants 2 years or more postinjury.

Data from participants 17 years and older who completed outcome assessments at 1 and 3 to 7 years were included in this analysis; deaths were excluded. If more than 1 longitudinal assessment was completed 3 to 7 years after study enrollment, the latest outcome assessment was analyzed.

Study variables were collected in accordance with the National Institutes of Health TBI Common Data Elements.[27-30] Functional, PCS, psychological distress, PTSD, depression, and HRQOL outcomes were selected as primary outcomes for our analysis. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline.

Baseline Measures

Sociodemographic characteristics (age, sex, race and ethnicity, education, insurance), medical history, and injury characteristics were collected at baseline through self-report and medical record review. Race categories included Asian, Black, White, other race (including American Indian and Alaska Native, Inuit, and Native Hawaiian and Other Pacific Islander), and unknown race. Ethnicity categories included Hispanic and non-Hispanic. We adjusted for participants' Neighborhood Disadvantage Index (NDI) score (range, 0-100), a socioeconomic disadvantage score based on 4 US census tract indicators by zone improvement plan code tabulation areas.[31,32] Injury-related characteristics included Glasgow Coma Scale (GCS),[33] loss of consciousness, care level, Injury Severity Score,[34] and computed tomography scans coded as having positive or negative findings for acute traumatic intracranial lesions. To address generalizability, descriptive characteristics of the TRACK-TBI participants included in our study at 1 year and 3 to 7 years were compared with excluded participants (eTable 1 in Supplement 1).

Preindex and Postindex TBI History

At enrollment, lifetime TBI history was assessed using the Ohio State University TBI Identification Method (OSU TBI-ID), a validated structured interview for detection of prior TBI.[35,36] At follow-up time points, postindex TBI information was collected through the OSU TBI-ID Short-Form to ascertain whether the participant sustained another TBI since the index TBI. The interview at 3 to 7 years added a question regarding the number of postindex TBIs.

Primary Outcome Measures

Glasgow Outcome Scale-Extended

The 8-point Glasgow Outcome Scale–Extended (GOSE)[20,37] assesses functional disability after TBI through a structured interview with the participant or caretaker.[38,39] A score of 1 indicates death; 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. A score of 8 reflects complete return to baseline function; a score less than 8 reflects incomplete functional recovery.

Rivermead Post-Concussion Symptoms Questionnaire

The Rivermead Post-Concussion Symptoms Questionnaire (RPQ) measures the severity of 16 PCS across 4 domains (physical, cognitive, mood, and sleep) compared with preinjury levels (ranging from 0 [not experienced] to 4 [severe problem])[40]; 1 was recoded to 0, per accepted protocol.[41] Scores were summed to a maximum of 64; scores of 0 to 12, 13 to 24, 25 to 32, and 33 or greater indicate minimal, mild, moderate, and severe PCS, respectively.[41]

Brief Symptom Inventory-18

The Brief Symptom Inventory-18 (BSI-18)[42] assesses psychological distress using 18 questions across somatization, depression, and anxiety domains, scored from 0 (not at all) to 4 (extremely). The Global Severity Index T score sums responses in each domain normalized by age and sex (maximum score, 72)[42,43]; scores of 63 or more indicate clinically significant distress.

PTSD Checklist for *DSM-5*

The PTSD Checklist for *DSM-5* (PCL-5) measures PTSD symptoms according to *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition) criteria.[44] Twenty items are scored from 0 (not

at all) to 5 (extremely) (maximum score, 80); scores of 33 or higher indicate probable clinically relevant PTSD.[45,46]

Patient Health Questionnaire-9

The Patient Health Questionnaire-9 (PHQ-9)[47] is a self-reported scale measuring depressive symptoms using 9 *Diagnostic and Statistical Manual of Mental Disorders* (Fifth Edition)–focused items scored from 0 (not at all) to 3 (nearly every day).[48] Scores range from 0 to 27; scores of 5 to 9, 10 to 14, 15 to 19, and 20 to 27 represent mild, moderate, moderately severe, and severe depression, respectively.

Quality of Life After Brain Injury–Overall Scale

The Quality of Life After Brain Injury–Overall Scale (QOLIBRI-OS)[49] is a self-reported measure of HRQOL across 6 domains (physical condition, cognition, emotions, daily life function, personal life, and social life) frequently affected by TBI, scored from 1 (not at all) to 5 (very). Scores were converted to QOLIBRI total score (range, 0 to 100); scores less than 52 represent impaired HRQOL.[50,51]

Statistical Analysis

Differences in sociodemographic characteristics, medical history, and injury-related characteristics were assessed using Mann-Whitney *U* tests for continuous variables and Fisher exact tests for categorical variables. Inverse probability weighting was used to account for potential biases due to missing outcomes. A boosted regression algorithm based on all baseline sociodemographic, medical history, and injury-related characteristics was used to model missingness, and statistical weights were derived by inverting and rescaling the resulting propensity estimates (eMethods in Supplement 1). Linear regression was used to model the self-reported outcome measures (RPQ, BSI-18, PCL-5, PHQ-9, and QOLIBRI-OS), and log-binomial regression was used to model probability of complete functional recovery (GOSE score of 8). All regression analyses modeled each time point separately and adjusted for sociodemographic characteristics (age, sex, race, ethnicity, education), GCS, preindex TBI, and psychiatric history. A 2-sided significance threshold of $P < .05$ was used for all analyses, and results were interpreted after Benjamini-Hochberg adjustment for multiple comparisons.[52] We evaluated normality using boxplots and plots of the residuals from the primary models for each outcome measure. All outcome measures were clearly unimodal with a general Gaussian shape. Normality could be assumed for BSI-18, while the RPQ, PCL-5, and PHQ-9 demonstrated mild right skew (1 year: 1.04, 1.07, and 1.20, respectively; 3 to 7 years: 0.95, 0.98, and 1.18), and the QOLIBRI-OS demonstrated mild left skew (1 year: −0.47; 3 to 7 years: −0.61). Boosted regression modeling was performed using the Toolkit for Weighting and Analysis of Nonequivalent Groups software from the Rand Corporation.[53] Other statistical analyses were performed using SAS version 9.4 (SAS Institute) and SPSS version 26 (IBM).

Results

Baseline and Injury-Related Characteristics

Of 2417 TRACK-TBI participants, 1572 completed the outcomes assessment at 1 year (1049 [66.7%] male; mean [SD] age, 41.6 [17.5] years) and 1084 completed the outcomes assessment at 3 to 7 years (714 [65.9%]; mean [SD] age, 40.6 [17.0] years). At 1 year, a total of 60 participants (4%) were Asian, 255 (16%) were Black, 1213 (77%) were White, 39 (2%) were another race, and 5 (0.3%) had unknown race. At 3 to 7 years, 39 (4%) were Asian, 149 (14%) were Black, 868 (80%) were White, 26 (2%) had another race, and 2 (0.2%) had unknown race. Comparison between included and excluded participants (845 at 1 year and 1315 at 3 to 7 years) showed differences in sex, race and ethnicity, education, and socioeconomic disadvantage (eTable 1 in Supplement 1). The flow diagram is shown in **Figure 1**. Site-specific enrollment is shown in eTable 9 in Supplement 1. Participants with postindex TBI (50 of 1572 [3.2%] at 1 year; 132 of 1084 [12.2%] at 3 to 7 years) and without postindex TBI (1522

of 1572 [96.8%] at 1 year; 952 of 1084 [87.8%] at 3 to 7 years) were comparable in sociodemographic and injury characteristics (**Table 1**).

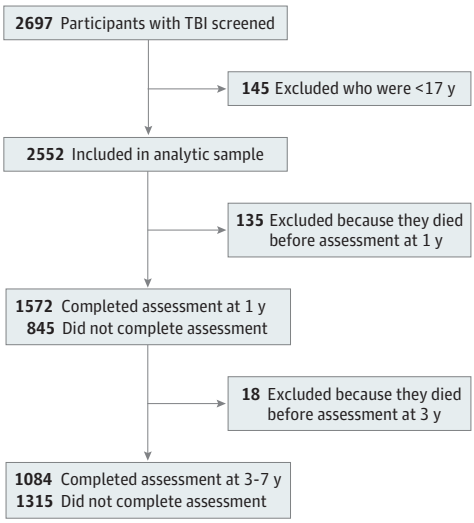
Statistically significant differences between participants with vs without postindex TBIs were observed at 1 year and 3 to 7 years for higher proportion with baseline psychiatric history (1 year: 19 of 50 [38%] vs 344 of 1522 [23%], respectively; $P = .02$; 3 to 7 years: 45 of 132 [34%] vs 214 of 952 [22%]; $P = .009$), higher number of preindex TBIs requiring ED or hospital admission (1 year: ED admission, 12 of 46 [26%] vs 171 of 1416 [12%]; hospital admission, 6 of 46 [13%] vs 101 of 1416 [7%]; $P = .001$; 3 to 7 years: ED admission, 31 of 123 [25%] vs 90 of 888 [10%]; hospital admission, 10 of 123 [8%] vs 59 of 888 [7%]; $P < .001$), and lower mean (SD) Injury Severity Score (1 year: 3.5 [5.9] vs 6.0 [7.3]; $P = .002$; 3 to 7 years: 4.3 [6.0] vs 5.7 [7.3]; $P = .01$).

Postindex TBI and Outcomes

Figure 2 summarizes our main results. At 1 year, the postindex TBI group exhibited poorer outcome across domains (**Table 2**). Compared with those without postindex TBI, participants with postindex TBI were less likely to achieve complete functional recovery (GOSE score of 8; adjusted relative risk [aRR], 0.57; 95% CI, 0.34-0.96), had decreased HRQOL (QOLIBRI-OS: adjusted mean difference [aMD], −15.9; 95% CI, −22.6 to −9.1), and increased symptom severities across other outcomes, including PCS (RPQ: aMD, 8.1; 95% CI, 4.2-11.9), psychological distress (BSI-18: aMD, 5.3; 95% CI, 2.1-8.6), PTSD (PCL-5: aMD, 7.8; 95% CI, 3.2-12.4), and depression (PHQ-9: aMD, 3.0; 95% CI, 1.5-4.4). At 3 to 7 years, participants with postindex TBI remained more symptomatic, at reduced magnitudes (QOLIBRI-OS: aMD, −7.3; 95% CI, −11.4, to −3.2; RPQ: aMD, 4.3; 95% CI, 1.9-6.6; BSI-18: aMD, 3.0; 95% CI, 0.9-5.1; PCL-5: aMD, 6.5; 95% CI, 3.4-9.7; PHQ-9: aMD, 1.8; 95% CI, 0.8-2.8). Likelihood of achieving a GOSE score of 8 was lower in those with postindex TBI (42 of 131 [32%] vs 416 of 917 [45%]), although this finding was not significant at 3 to 7 years (aRR, 0.78; 95% CI, 0.61-1.00). Similar findings were observed for postindex TBI with loss of consciousness vs without (eTables 2 and 3 in Supplement 1). Among participants with preindex TBI, differences between groups with and without postindex TBI in RPQ (aMD, 8.6; 95% CI, 2.1-15.1), BSI-18 (aMD, 6.9; 95% CI, 1.5-12.3), PHQ-9 (aMD, 4.80; 95% CI, 2.26-7.33), and QOLIBRI-OS (aMD, −19.8; 95% CI, −30.9 to −8.8) remained significant at 1 year and in QOLIBRI-OS (aMD, −8.8; 95% CI, −16.1 to −1.6) at 3 to 7 years (eTables 4 and 5 in Supplement 1).

We evaluated the association between multiple postindex TBIs (26 of 1084 [2.4%]) and outcomes at 3 to 7 years. Number of postindex TBIs (0 vs 1, 1 vs 2 or more, and 2 or more vs 0)

Figure 1. CONSORT Flow Diagram



TBI indicates traumatic brain injury.

Table 1. Baseline and Injury Characteristics

Variable	No. (%)					
	Assessment at 1 y			Assessment at 3-7 y		
	Postindex TBI			Postindex TBI		
	No	Yes	*P* value	No	Yes	*P* value
Total	1522 (96.8)	50 (3.2)	NA	952 (87.8)	132 (12.2)	NA
Age, mean (SD), y	41.6 (17.5)	42.7 (17.4)	.84	40.6 (16.9)	40.7 (17.2)	.92
Sex						
Male	1020 (67)	29 (58)	.28	634 (67)	80 (61)	.19
Female	502 (33)	21 (42)		318 (33)	52 (39)	
Race[a]						
Asian	59 (4)	1 (2)	.73	38 (4)	1 (1)	.16
Black	245 (16)	10 (20)		135 (14)	14 (11)	
White	1175 (77)	38 (76)		754 (79)	114 (86)	
Other race[b]	38 (3)	1 (2)		23 (2)	3 (2)	
Unknown, No.	5	0	NA	2	0	NA
Ethnicity[a]						
Hispanic	263 (17)	6 (12)	.16	173 (18)	20 (15)	.19
Non-Hispanic	1253 (83)	44 (88)		776 (82)	111 (85)	
Unknown, No.	6	0		3	1	
Education						
Mean (SD), y	13.7 (2.8)	13.3 (2.2)	.19	13.8 (2.8)	14.0 (2.6)	.46
Unknown, No.	33	0	NA	21	3	NA
Socioeconomic disadvantage[c]						
Mean (SD)	10.7 (6.4)	11.2 (6.0)	.35	10.9 (6.4)	9.7 (5.4)	.04
Unknown, No.	57	0	NA	27	1	NA
Psychiatric history						
No	1178 (77)	31 (62)	.02	738 (78)	87 (66)	.009
Yes	344 (23)	19 (38)		214 (22)	45 (34)	
Preindex TBI						
Any preindex TBI						
No	768 (53)	20 (43)	.09	515 (57)	51 (41)	<.001
Yes, no LOC	392 (27)	13 (28)		230 (25)	37 (30)	
Yes, LOC	281 (20)	14 (30)		163 (18)	35 (28)	
Unknown, No.	81	3	NA	44	9	NA
Preindex TBIs, No.[d]						
Mean (SD)	0.46 (0.92)	0.67 (1.14)	.10	0.41 (0.87)	0.67 (1.03)	<.001
0	1047 (70)	29 (59)	.17	691 (74)	72 (56)	<.001
1	308 (21)	13 (27)		178 (19)	41 (32)	
≥2	137 (9)	7 (14)		71 (8)	16 (12)	
Unknown, No.	30	1	NA	12	3	NA
Age at first preindex TBI						
Mean (SD), y	22.3 (15.1)	28.6 (17.9)	.08	21.6 (14.4)	24.3 (15.3)	.19
<15 y	149 (34)	4 (20)	.32	87 (35)	16 (29)	.43
≥15 y	294 (66)	16 (80)		160 (65)	40 (71)	
Unknown, No.	30	1	NA	14	4	NA
Highest preindex TBI level of care						
None	1144 (81)	28 (61)	.001	739 (83)	82 (67)	<.001
ED only	171 (12)	12 (26)		90 (10)	31 (25)	
Hospital admission	101 (7)	6 (13)		59 (7)	10 (8)	
Unknown, No.	106	4	NA	64	9	NA

(continued)

Table 1. Baseline and Injury Characteristics (continued)

Variable	No. (%)					
	Assessment at 1 y			Assessment at 3-7 y		
	Postindex TBI			Postindex TBI		
	No	Yes	*P* value	No	Yes	*P* value
Index injury factors						
GCS at ED arrival						
Mean (SD)	13.3 (3.5)	13.7 (3.1)	.12	13.1 (3.7)	14.0 (2.6)	.003
Severe (3-8)	184 (12)	5 (10)	.76	131 (14)	8 (6)	.01
Moderate (9-12)	58 (4)	1 (2)		45 (5)	3 (2)	
Mild (13-15)	1251 (84)	42 (88)		754 (81)	117 (91)	
Unknown, No.	29	2	NA	22	4	NA
LOC						
No	179 (12)	4 (8)	.30	109 (12)	15 (12)	.68
Suspected	76 (5)	1 (2)		51 (6)	10 (8)	
Yes	1186 (82)	44 (90)		747 (82)	103 (80)	
Unknown, No.	81	1	NA	45	4	NA
Highest level of care						
ED	350 (23)	7 (14)	.69	209 (22)	31 (23)	.11
Ward	548 (36)	24 (48)		335 (35)	57 (43)	
ICU	624 (41)	19 (38)		408 (43)	44 (33)	
Initial CT findings						
Negative	803 (54)	27 (55)	.88	483 (52)	79 (60)	.25
Positive	682 (46)	22 (45)		438 (48)	53 (40)	
Unknown, No.	37	1	NA	31	0	NA
Major extracranial injury						
No	1233 (81)	44 (88)	.27	779 (82)	111 (84)	.47
Yes	289 (19)	6 (12)		173 (18)	21 (16)	
ISS (all systems)						
Mean (SD)	15.0 (10.1)	10.9 (8.5)	.005	15.1 (10.2)	12.2 (9.1)	.002
Median (IQR)	13 (8-21)	10 (5-14)		14 (9-21)	10 (5-17)	
Unknown/ED only, No.	377	10	NA	231	35	NA
ISS (head/neck)						
Mean (SD)	8.6 (7.8)	6.8 (6.0)	.14	9.0 (8.1)	7.3 (7.1)	.06
Median (IQR)	9 (4-16)	6.5 (3.3-9)		9 (4-16)	4 (1-9)	
Unknown/ED only, No.	377	10	NA	231	35	NA
ISS (nonhead/nonneck)						
Mean (SD)	6.0 (7.3)	3.5 (5.9)	.002	5.7 (7.3)	4.3 (6.0)	.01
Median (IQR)	4 (1-9)	1 (0-4.25)		4 (1-9)	1 (1-6)	
Unknown/ED only, No.	378	10	NA	231	35	NA

Abbreviations: CT, computed tomography; ED, emergency department; GCS, Glasgow Coma Scale; ICU, intensive care unit; ISS, Injury Severity Score; LOC, loss of consciousness; NA, not applicable; TBI, traumatic brain injury.

[a] Race and ethnicity were obtained by participant self-report and medical record review.

[b] The other race category included American Indian and Alaska Native, Inuit, and Native Hawaiian and Other Pacific Islander.

[c] Socioeconomic disadvantage scores ranged from 0 to 100, with higher scores indicating greater disadvantage.

[d] Number of preindex TBIs included only preindex TBIs with ED or hospital admission.

showed a dose-dependent association across all outcomes assessed by rank regression (**Table 3**). Compared with those without postindex TBIs, those with 1 postindex TBI had elevated PCL-5 (aMD, 3.6; 95% CI, 0.2-7.0) and lower QOLIBRI-OS (aMD, −4.8; 95% CI, −9.3 to −0.3). Those with 2 or more vs 1 postindex TBI and those with 2 or more vs 0 postindex TBIs were less likely to attain complete functional recovery (GOSE score of 8; 2 or more vs 1: aRR, 0.31; 95% CI, 0.10-0.96; 2 or more vs 0:

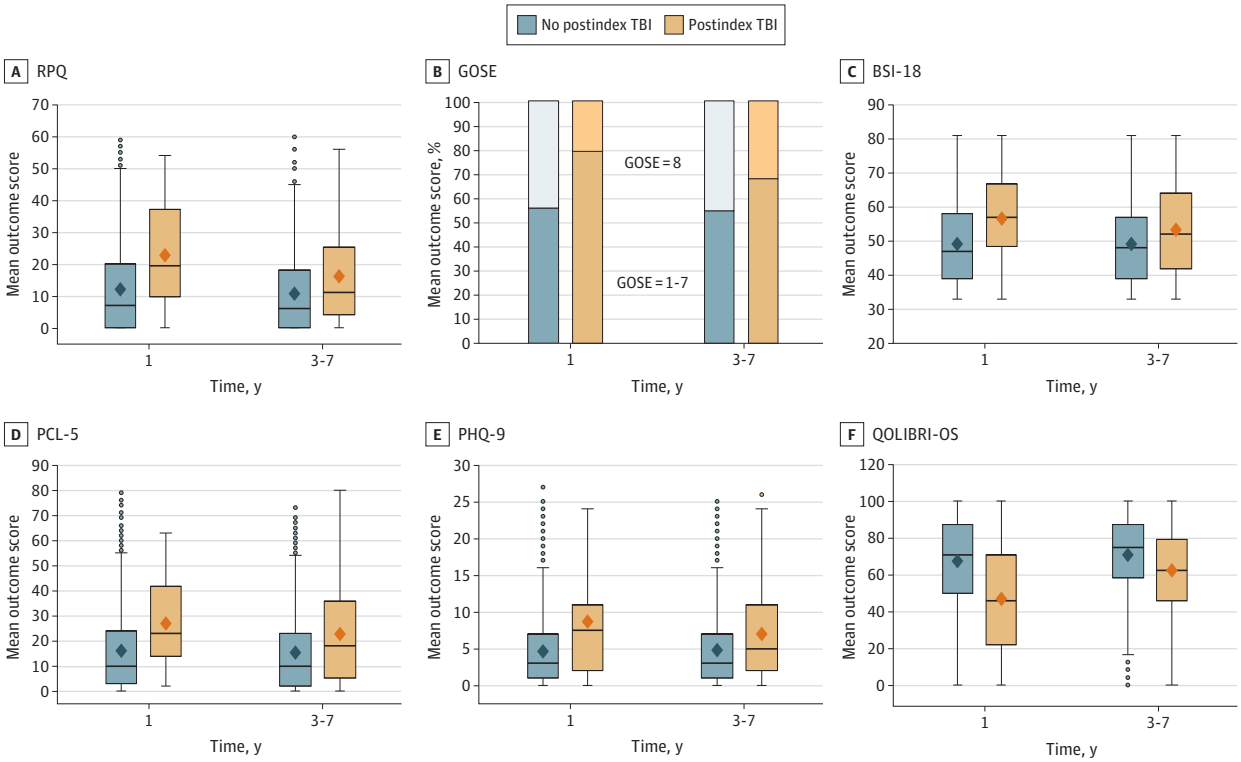
aRR, 0.28; 95% CI, 0.09-0.84) and were more symptomatic across outcome domains, including QOLIBRI-OS (2 or more vs 1: aMD, −12.6; 95% CI, −22.2 to −3.0; 2 or more vs 0: aMD, −17.4; 95% CI, −26.1 to −8.7), RPQ (2 or more vs 1: aMD, 10.1; 95% CI, 4.6-15.6; 2 or more vs 0: aMD, 12.4; 95% CI, 7.4-17.4), BSI-18 (2 or more vs 1: aMD, 6.7; 95% CI, 1.8-11.5; 2 or more vs 0: aMD, 8.4; 95% CI, 4.0-12.8), PCL-5 (2 or more vs 1: aMD, 14.7; 95% CI, 7.4-22.0; 2 or more vs 0: aMD, 18.3; 95% CI, 11.7-25.0), and PHQ-9 (2 or more vs 1: aMD, 4.88; 95% CI, 2.53-7.23; 2 or more vs 0: aMD, 5.71; 95% CI, 3.57-7.85).

We further investigated associations between the timing of postindex TBI and outcomes and observed no difference at 1 year (eTable 6 in Supplement 1). eTable 7 in Supplement 1 summarizes the number of years between postindex TBI and outcomes at 3 to 7 years. An association was observed between the timing of assessment and decreased symptomology (RPQ, BSI-18, PCL-5, PHQ-9, QOLIBRI-OS), and original associations remained significant after adjusting for timing (eTable 8 in Supplement 1).

Discussion

In this multicenter study, participants with postindex TBI were at elevated risk for incomplete functional recovery and greater symptomatology across PCS, mental health, and HRQOL domains at 1 year postinjury. These findings were conserved at 3 to 7 years. Notably, multiple postindex TBIs at 3 to 7 years conferred greater risks of incomplete functional recovery and symptom burden across domains. These results show that participants with postindex TBIs comprise a distinctly symptomatic cohort in long-term recovery, and at-risk patients may benefit from targeted prevention and follow-up care.

Figure 2. Unweighted Mean Outcome Scores by Group Status at 1 Year and 3 to 7 Years



The diamond indicates the mean; midline, the median; box, the IQR; whiskers, the range; and data points, outliers. BSI-18 indicates Brief Symptom Inventory-18; GOSE, Glasgow Outcome Scale–Extended; PCL-5, PTSD Checklist for *DSM-5*; PHQ-9, Patient Health Questionnaire-9; QOLIBRI-OS, Quality of Life After Brain Injury–Overall Scale; RPQ, Rivermead Post-Concussion Symptoms Questionnaire; TBI, traumatic brain injury.

Postindex TBI Risk Factors

Risk factors for postindex TBI at both time points included baseline psychiatric history, preindex TBI frequency and severity, and less severe index peripheral injury. Psychiatric history[54,55] and preindex TBI[4,5] are well-known risk factors for TBI. The finding that peripheral injuries were more severe in individuals without postindex TBI suggests these individuals may be too severely injured to resume high-risk activities that would predispose to TBI. Risk factors specific to 3 to 7 years included less-severe index TBI (higher GCS) and socioeconomic disadvantage. Prior research suggests that civilians with preindex and postindex TBI sustain less-severe index TBI.[5,6,17]

Postindex TBI and Outcomes

At 1 year, multiple regression analyses controlling for major confounders demonstrated that participants with postindex TBI were at risk for reduced complete functional recovery (GOSE score of 8; aRR, 0.57; 95% CI, 0.34-0.96) and were more symptomatic (PCS, psychological distress, PTSD, depression, and HRQOL). Mean outcome scores indicated clinically significant mild PCS, depression, and impaired HRQOL. In participants with preindex TBI, those with postindex TBI remained more symptomatic across PCS, psychological distress, depressive, and HRQOL outcomes with comparable effect sizes, further supporting the association of postindex TBI with outcome. Our results are consistent with literature demonstrating worsened PCS, PTSD, and mental health in civilians with preindex TBI[6] and worsened PCS in civilians with postindex TBI.[18]

At 3 to 7 years, the postindex TBI group remained more symptomatic (PCS, psychological distress, PTSD, depression, and HRQOL) after multiple regressions, at reduced magnitudes. There was no significant association between functional recovery and postindex TBI after multivariable regressions, which may reflect lower composite symptomatology at 3 to 7 years. Among participants with preindex TBIs, those with postindex TBIs reported worse HRQOL but no difference in other outcomes with reduced effect sizes, suggesting that both preindex and postindex TBIs contribute to outcomes at 3 to 7 years.

The number of postindex TBIs (0, 1, or 2 or more) at 3 to 7 years exhibited a dose-dependent association across all domains (functional, PCS, mental health, and HRQOL). A lower proportion of

Table 2. Association Between Postindex Traumatic Brain Injury (TBI) and Outcome[a]

	No postindex TBI		Postindex TBI		Effect size[b]	
Outcome measure	Total, No.	Mean (SD)	Total, No.	Mean (SD)	Measure (95% CI)	*P* value[c]
1 y						
GOSE score of 8, No. (%)	1446	638 (44)	48	10 (21)	aRR, 0.57 (0.34 to 0.96)	.03
RPQ	1456	12.1 (13.9)	48	22.7 (16.0)	aMD, 8.1 (4.2 to 11.9)	<.001
BSI-18	1453	49.1 (11.6)	48	56.6 (12.0)	aMD, 5.3 (2.1 to 8.6)	.001
PCL-5	1433	16.1 (16.6)	48	26.9 (16.7)	aMD, 7.8 (3.2 to 12.4)	.001
PHQ-9	1451	4.6 (5.3)	48	8.7 (7.3)	aMD, 2.96 (1.49 to 4.44)	<.001
QOLIBRI-OS	1452	67.6 (24.5)	48	47.0 (28.4)	aMD, −15.9 (−22.6 to −9.1)	<.001
3-7 y						
GOSE score of 8, No. (%)	917	416 (45)	131	42 (32)	aRR, 0.78 (0.61 to 1.00)	.06
RPQ	917	10.8 (12.7)	130	16.1 (15.1)	aMD, 4.3 (1.9 to 6.6)	<.001
BSI-18	916	49.3 (11.0)	130	53.3 (12.6)	aMD, 3.0 (0.9 to 5.1)	.004
PCL-5	889	15.5 (16.5)	128	22.8 (20.1)	aMD, 6.5 (3.4 to 9.7)	<.001
PHQ-9	918	4.8 (5.3)	130	7.0 (6.3)	aMD, 1.78 (0.77 to 2.78)	.001
QOLIBRI-OS	919	70.8 (21.9)	130	62.2 (24.5)	aMD, −7.3 (−11.4 to −3.2)	<.001

Abbreviations: aMD, adjusted mean difference; aRR, adjusted relative risk; BSI-18, Brief Symptom Inventory-18; GOSE, Glasgow Outcome Scale–Extended; PCL-5, PTSD Checklist for *DSM-5*; PHQ-9, Patient Health Questionnaire-9; QOLIBRI-OS, Quality of Life After Brain Injury–Overall Scale; RPQ, Rivermead Post-Concussion Symptoms Questionnaire.

[a] Multivariable linear regressions were performed for scalar outcome measures (BSI-18, PCL-5, PHQ-9, QOLIBRI-OS, and RPQ), and multivariable logistic regression was performed for complete functional recovery (GOSE score of 8).

[b] All regressions were adjusted for age, sex, race and ethnicity, education, Glasgow Coma Scale, preindex TBI level of care, and psychiatric history and were propensity weighted for missingness.

[c] All significant *P* values ($P < .05$) remained significant after adjustment for multiple comparisons (Benjamini-Hochberg; m = 12).

Table 3. Association of Multiple Postindex Traumatic Brain Injuries (TBIs) with Outcomes at 3 to 7 Years[a]

	No. of postindex TBIs						Effect size[b]						
	0 TBIs		1 TBI		≥2 TBIs		1 vs 0 TBIs		≥2 vs 1 TBI		≥2 vs 0 TBIs		
Outcome measure	Total, No.	Mean (SD)	Total, No.	Mean (SD)	Total, No.	Mean (SD)	Measure (95% CI)	*P* value[c]	Measure (95% CI)	*P* value[c]	Measure (95% CI)	*P* value[c]	Overall *P* value[c,d]
GOSE score of 8, No. (%)	917	416 (45)	105	39 (37)	26	3 (12)	aRR, 0.90 (0.70 to 1.15)	.21	aRR, 0.31 (0.10 to 0.96)	.04	aRR, 0.28 (0.09 to 0.84)	.02	.03
RPQ	917	10.8 (12.7)	104	14.1 (14.1)	26	24.0 (16.9)	aMD, 2.3 (−0.3 to 4.9)	.08	aMD, 10.1 (4.6 to 15.6)	<.001	aMD, 12.4 (7.4 to 17.4)	<.001	<.001
BSI-18	916	49.3 (11.0)	104	52.0 (11.6)	26	58.5 (15.1)	aMD, 1.7 (−0.6 to 4.0)	.14	aMD, 6.7 (1.8 to 11.5)	.007	aMD, 8.4 (4.0 to 12.8)	<.001	.003
PCL-5	889	15.5 (16.5)	102	20.1 (18.2)	26	33.5 (24.0)	aMD, 3.6 (0.2 to 7.0)	.04	aMD, 14.7 (7.4 to 22.0)	<.001	aMD, 18.3 (11.7 to 25.0)	<.001	<.001
PHQ-9	918	4.8 (5.3)	104	6.1 (5.8)	26	10.5 (7.0)	aMD, 0.83 (−0.27 to 1.93)	.14	aMD, 4.88 (2.53 to 7.23)	<.001	aMD, 5.71 (3.57 to 7.85)	<.001	<.001
QOLIBRI-OS	919	70.8 (21.9)	104	64.7 (23.3)	26	52.4 (26.9)	aMD, −4.8 (−9.3 to −0.3)	.04	aMD, −12.6 (−22.2 to −3.0)	.01	aMD, −17.4 (−26.1 to −8.7)	<.001	<.001

Abbreviations: aMD, adjusted mean difference; aRR, adjusted relative risk; BSI-18, Brief Symptom Inventory-18; GOSE, Glasgow Outcome Scale–Extended; PCL-5, PTSD Checklist for *DSM-5*; PHQ-9, Patient Health Questionnaire-9; QOLIBRI-OS, Quality of Life After Brain Injury–Overall Scale; RPQ, Rivermead Post-Concussion Symptoms Questionnaire.

[a] Multivariable linear regressions were performed for scalar outcome measures (BSI-18, PCL-5, PHQ-9, QOLIBRI-OS, and RPQ), and multivariable logistic regression was performed for complete functional recovery (GOSE score of 8).

[b] All regressions were adjusted for age, sex, race and ethnicity, education, Glasgow Coma Scale, preindex TBI level of care, and psychiatric history and were propensity weighted for missingness.

[c] Significance was assessed at $P < .05$. No adjustments were made for multiple comparisons.

[d] Overall significance assumes ordinality of postindex TBI categories and was assessed by rank regression.

participants with 2 or more postindex TBIs reported complete functional recovery (GOSE score of 8; aRR, 0.31; 95% CI, 0.10-0.96) compared with participants with 1 postindex TBI and exhibited mean outcome scores that exceeded the clinical thresholds for PTSD, mild PCS, and moderate depression. Our findings are consistent with the contact-sport literature, which demonstrates that sustaining multiple TBIs contributes to worsened PCS, mental health symptoms, and delayed recovery.[10,11,56,57]

Our analyses of postindex TBI timing further strengthen these results. While no significant associations were observed at 1 year, shorter-interval injuries were associated with poorer recovery in RPQ, BSI-18, PCL-5, PHQ-9, and QOLIBRI-OS at 3 to 7 years. Importantly, all associations between postindex TBI and outcomes remained significant after adjusting for timing via sensitivity analyses at 3 to 7 years. These results impel the need for prevention, education, and follow-up care efforts to decrease the risk of short-interval injuries.

Implications for Clinical Practice

Lack of follow-up care is detrimental to employment and economic outcomes.[58,59] Standardized TBI education, counseling, screening, triage, and referral to care system of patients at risk of repetitive injuries may reduce reinjury and improve likelihood of recovery. Our results show the importance of collecting preindex and postindex TBI histories, as repetitive TBI is a risk factor for poorer multidimensional outcomes.

Utilization of the biopsychosocial-ecological model will inform prevention and follow-up care efforts.[60,61] A combination of biological factors, preinjury and postinjury mental health, social determinants of health (race and ethnicity as well as education), and access to postacute care intersect to influence each patient's recovery. Risk factors for and sequelae of experiencing 1 or more postindex TBIs encompass biological (eg, the TBI), psychological (eg, postinjury psychological symptomatology, preinjury modifiers), and social/socioeconomic factors (eg, neighborhood disadvantage index), in addition to ecological and other factors not evaluated by the current study. Accordingly, postindex TBIs may be part and parcel of an overall phenotype of protracted recovery and/or poor outcome after TBI, and more in-depth understanding of the mediating factors for these repetitive injuries can mitigate these risks and reduce morbidity after a single TBI. Concurrent application of the biopsychosocial-ecological model by clinicians during counseling and in subsequent research may enable more comprehensive evaluation of underlying risk factors and amplify the impact of prevention, education, and outpatient care interventions.

Limitations

This study has limitations. Our findings are applicable to populations where cranial imaging is indicated to rule out traumatic intracranial hemorrhage but may not be generalizable to patients who do not present to the ED. Participants with assessments at 1 and 3 to 7 years were more likely to be female, non-Hispanic, have greater educational attainment, and less socioeconomic disadvantage, which limit overall generalizability. The OSU TBI-ID is a validated and reliable self-reported measure for lifetime TBI history; however, self-reported measures are inherently limited by recall bias. While out of scope of our study, between-center variability in outcomes is another factor worth examining for comparative effectiveness research in this burdened population. We were unable to evaluate associations between multiple postindex TBIs and outcomes at 1 year, as these data were not captured until 3 to 7 years. Because we sought to review the largest sample size at each time point, the cohorts with assessments at 1 year and 3 to 7 years have slightly different baseline characteristics. Future hypothesis-driven analyses may consider using a common sample across time points. We did not assess associations between postindex TBI and deaths due to small numbers, which warrant future investigation in larger and more diverse samples. While we controlled for major confounders of outcomes, residual confounding related to procedural interventions, complications, and postdischarge care may remain. These limitations constitute relevant next steps.

Using linear regressions to model scalar outcome measures constituted another limitation. While the BSI-18 conformed to normality, the other measures demonstrated some degree of skew.

Given that skews were generally mild, we proceeded with linear regression to prioritize the reporting of coefficient units in their original interpretable outcome scores, which aligns with the methodology in prior published reports on outcome measures in large multicenter TBI studies. We recognize that skew may decrease the validity of linear regression models. As such, our results should be interpreted with a commensurate level of caution and await validation studies in this understudied and at-risk population.

Conclusions

In a prospective multicenter cohort of patients with acute TBI, postindex TBI was associated with functional, PCS, mental health, and HRQOL symptomatology at 1 year and 3 to 7 years postinjury. Sustaining multiple postindex TBIs was associated with additional increases in symptomatology compared with sustaining 1 postindex TBI. These results highlight the profound cumulative deficits acquired after repetitive TBI and underscore the imperative need to establish institutional programs to support TBI prevention, education, counseling, and follow-up for at-risk patients.

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SUPPLEMENT 1.

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SUPPLEMENT 3.
Data Sharing Statement

JAMA Network Open

原始研究|神经病学

重复性创伤性脑损伤后的纵向恢复

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摘要

一个创伤性脑损伤(TBI)增加了继发TBI的风险。对平民重复性创伤性脑损伤的纵向结果的研究是有限的。

目的:调查研究注册后维持1个或多个tbi(即指数tbi)与1年和3 - 7年多维结局之间的关系。

设计、背景和参与者:本队列研究包括在创伤性脑损伤24小时内到急诊科就诊的参与者，这些参与者参加了前瞻性、18个中心的创伤性脑损伤转化研究和临床知识(TRACK-TBI)研究(注册时间:2014年2月至2020年7月)。包括在1年和3 - 7年完成结果评估的参与者。分析了2022年9月至2023年8月的数据。

暴露指数后TBI。

主要结果和测量人口统计学和临床因素，创伤前(即指数前TBI)和功能(格拉斯哥预后扩展量表[GOSE])，脑震荡后(Rivermead脑震荡后症状问卷[RPQ])，心理困扰(简要症状量表-18 [BSI-18])，抑郁(患者健康问卷-9 [PHQ-9])，创伤后应激障碍(PTSD;评估DSM-5的PTSD检查表(PCL-5)和与健康相关的生活质量(脑损伤后生活质量-总体量表[qolibrio - os])结果。调整后的平均差异(aMDs)和调整后的相对风险报告为95%的ci。

2417名TRACK-TBI参与者中，1572人在1年后完成了结果评估(1049人[66.7%]男性;平均[SD]年龄41.6[17.5]岁，3 - 7岁时完成预后评估的有1084人(714人[65.9%]男性;mean [SD]年龄，40.6[17.0]岁)。一年后，共有60名参与者(4%)是亚洲人，255名(16%)是黑人，1213名(77%)是白人，39名(2%)是其他种族，5名(0.3%)是未知种族。在3 - 7岁时，39人(4%)是亚洲人，149人(14%)是黑人，868人(80%)是白人，26人(2%)有其他种族，2人(0.2%)有未知种族。共有50例(3.2%)和132例(12.2%)分别在1年和3至7年报告了1例或1例以上的tbi。指数后TBI的危险因素为精神病史、指数前TBI和颅外损伤严重程度。在1年的时间里，与那些没有指数后创伤性脑损伤的人相比，指数后创伤性脑损伤的参与者有更差的功能恢复(GOSE评分为8:调整相对风险，0.57;95% CI, 0.34-0.96)和与健康相关的生活质量(QOLIBRI-OS: aMD，−15.9;95% CI，−22.6至−9.1)，以及更大的脑震荡后症状(RPQ: aMD, 8.1;95% CI, 4.2-11.9)，心理困扰症状(BSI-18: aMD, 5.3;95% CI, 2.1-8.6)，抑郁症状(PHQ-9: aMD, 3.0;95% CI, 1.5-4.4)和创伤后应激障碍症状(PCL-5: aMD, 7.8;95%可信区间，3.2-12.4)。在3 - 7年，这些相关性仍然具有统计学意义。多个(2个或更多)术后tbi与所有领域的较差预后相关。

(续)

重点

指数后创伤性脑损伤(TBIs)的成年人在损伤后1年和3 - 7年的功能、脑震荡后、心理健康和与健康相关的生活质量结果是什么?

在这项2417名TBI患者的队列研究中，与那些没有TBI的患者相比，在1年和3 - 7年的TBI患者在功能、脑震荡后、心理健康和与健康相关的生活质量领域中有更多的症状，在多重TBI患者中观察到最大的症状负担。

在本研究中，指数后tbi患者是长期恢复的症状队列，需要对这些高危患者进行预防、教育、咨询和随访护理。

+补充内容

作者所属机构和文章信息列在这篇文章的结尾。

摘要(续)

在这项对急性TBI患者的队列研究中，创伤后TBI在损伤后1年和3 - 7年的结局域与更严重的症状相关，且多个创伤后TBI存在剂量依赖性反应。这些结果强调了为高危患者提供脑外伤预防、教育、咨询和随访护理的迫切需要。

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简介

在美国和世界范围内，创伤性脑损伤(TBI)是死亡和残疾的主要原因，仅在美国，每年就有280万例与TBI相关的急诊科(ED)就诊，28万例住院，6.4万例死亡。[1-3] 承受1次创伤性脑损伤的个体承受另一次创伤的风险显著增加。[4-7] 重复性创伤性脑损伤常发生在接触运动运动员和军事人员身上。多次脑震荡的病史与抑郁有关，[8,9] 延迟恢复，[10,11] 认知障碍，[12,13] 还有慢性创伤性脑病。[14] 然而，关于重复性脑损伤及其与一般人群预后的纵向关联的研究是有限的。

TBI可由原发性损伤发展为慢性疾病。重复性创伤性脑损伤的发生率在7%到23%是平民。[4-6,15-18] 先前的创伤性脑损伤增加了精神症状的风险[4,5] 对生活的满意度也降低了。[19] 在2013年美国的一项多中心研究中，有创伤性脑损伤病史的参与者报告了更严重的脑震荡后6个月的症状(PCS)、心理痛苦、非文字记忆和处理速度。[6] 在新西兰进行的一项以人群为基础的研究[18] 研究发现，TBI持续后，1年内的研究登记TBI指数与恶化的PCS相关。[20] 在一项大型TBI模型系统研究中，中度或重度TBI指数后评分较差，在TBI指数后1年、2年和5年认知依赖较差。[21]

为了更好地描述重复性创伤性脑损伤与恢复的关系，我们调查了指数后TBI与1年和3 - 7年的功能性、PCS、心理困扰、创伤后应激障碍(PTSD)、抑郁和健康相关的生活质量(HRQOL)结局之间的相关性。我们假设，术后创伤性脑损伤与较差的预后相关，且3 - 7年的多次术后创伤性脑损伤与较多的不良预后相关。

方法

参与者和研究设计

该研究于2014年2月26日至2018年7月3日在美国18个I级创伤中心招募了TBI患者。[22-24] 符合美国康复医学协会TBI诊断标准[25] 在急诊室接受了临床诊断的头部计算机断层扫描[26] 创伤性脑损伤后24小时内。排除标准包括监禁、怀孕、无法存活的身体创伤、精神拘留、使人衰弱的精神健康障碍、神经疾病以及非英语或非西班牙语，具体取决于地点。TRACK-TBI研究在每个地方都获得了机构审查委员会的批准。参加者或其合法授权的代表在登记前提供书面知情同意。2019年，TRACK-TBI纵向亚研究被批准在受伤后2年或更长时间与TRACK-TBI参与者进行年度电话交谈。

数据来自17岁及以上的参与者，他们在1岁和3岁至7岁时完成了结果评估这一分析包括年份;死亡被排除在外。如果在研究注册后3 - 7年完成了一次以上的纵向评估，则对最新的结果评估进行分析。

根据美国国立卫生研究院TBI通用数据元素收集研究变量。[27-30]
功能、PCS、心理困扰、创伤后应激障碍、抑郁和HRQOL结果被选为我们分析的主要结果。本研究遵循《加强流行病学观察性研究报告(STROBE)报告指南》。

基线测量

通过自我报告和病历回顾，在基线时收集社会人口特征(年龄、性别、种族和民族、教育、保险)、病史和伤害特征。种族类别包括亚洲人、黑人、白人、其他种族(包括美国印第安人和阿拉斯加原住民、因纽特人、夏威夷原住民和其他太平洋岛民)，以及未知种族。种族分类包括西班牙裔和非西班牙裔。我们调整了参与者的邻里不利指数(NDI)得分(范围为0-100)，这是一个基于4个美国人口普查区指标的社会经济不利得分。[31,32]
损伤相关特征包括格拉斯哥昏迷量表(GCS)、[33]意识丧失，护理水平，损伤严重程度评分，[34]对于急性创伤性颅内病变，计算机断层扫描编码为阳性或阴性。为了探讨泛化性，我们将纳入本研究的TRACK-TBI参与者在1年和3 - 7年的描述性特征与被排除的参与者进行了比较(附录1中的表1)。

前索引和后索引TBI病史

在入学时，使用俄亥俄州立大学创伤性脑损伤识别方法(OSU TBI-id)评估终身创伤性脑损伤史，这是一种有效的结构化访谈，用于检测以往的创伤性脑损伤。[35,36]
在随访时间点，通过OSU TBI-id短表收集索引后的TBI信息，以确定参与者是否自索引后持续了另一次TBI。3 - 7年的访谈增加了一个关于后索引tbi数量的问题。

主要终点测量格拉斯哥终点扩展量表

8点格拉斯哥预后扩展量表(GOSE)[20,37]
通过与参与者或看护人的结构化访谈来评估创伤性脑损伤后的功能障碍。[38,39]
得分为1表示死亡;2、植物状态;3、降低严重残疾;4、上部严重残疾;5、低中度残疾;6、上中度残疾;7、较低回收率好;8、上肢恢复良好。8分表示完全恢复基线功能;得分低于8表示功能恢复不完全。

里弗米德脑震荡后症状调查表

Rivermead脑震荡后症状问卷(RPQ)测量了4个领域(身体、认知、情绪和睡眠)中16pcs的严重程度，并与受伤前的水平(范围从0[没有经历过]到4[严重问题])进行了比较。[40];根据接受的协议，1被重新编码为0。[41]总分最多64分;0～12分、13～24分、25～32分和33分以上分别表示轻度、轻度、中度和重度PCS。[41]

简要症状清单-18

简要症状表-18 (BSI-18)[42]
通过18个问题评估心理压力，涵盖躯体化、抑郁和焦虑领域，得分从0(完全没有)到4(极端)。The

全球严重性指数T评分和各个领域的反应按年龄和性别归一化(最高评分，72分)[42,43];63分或以上表示临床显著的痛苦。

DSM-5的创伤后应激障碍检查表

DSM-5的PTSD检查表(PCL-5)根据精神障碍诊断和统计手册(第五版)标准测量PTSD症状。[44]
20个项目从0开始打分(不是0

总分)至5分(满分80分);得分33分或更高表明可能与临床相关的创伤后应激障碍。[45,46]

病人健康调查表-9

病人健康问卷-9 (PHQ-9)[47]
是一种自我报告的量表，使用9个以精神障碍诊断和统计手册(第五版)为重点的项目，从0分(完全不得分)到3分(几乎每天得分)来测量抑郁症状。[48] 分数范围从0到27;5～9分、10～14分、15～19分、20～27分分别代表轻度、中度、中度、重度抑郁症。

脑损伤后生活质量-总体量表

脑损伤后生活质量量表(qolibrii - os)[49]
是一项对经常受TBI影响的6个领域(身体状况、认知、情绪、日常生活功能、个人生活和社会生活)的HRQOL的自我报告测量，得分从1(完全没有)到5(非常)。分数转换为QOLIBRI总分(范围0 - 100);小于52分表示HRQOL受损。[50,51]

统计分析

对连续变量采用Mann-Whitney
U检验，对分类变量采用Fisher精确检验，评估了社会人口特征、病史和损伤相关特征的差异。使用逆概率加权来解释由于缺失结果而产生的潜在偏差。基于所有基线社会人口学、医疗史和伤害相关特征的增强回归算法用于建模缺失，并通过倒置和调整产生的倾向估计来获得统计权重(中的方法)

采用线性回归对自我报告的预后指标(RPQ、BSI-18、PCL-5、PHQ-9和qolibi - os)进行建模，采用log-
二项回归对完全功能恢复的概率(GOSE评分为8)进行建模。所有回归分析分别对每个时间点建模，并根据社会人口特征(年龄、性别、种族、民族、教育程度)、GCS、指数前TBI和精神病史进行调整。所有分析均采用双侧显著性阈值$P < .05$，多重比较后进行Benjamini-
Hochberg校正后对结果进行解释。[52]
我们使用箱线图和每个结果测量的主要模型的残差图来评估正态性。所有的结果测量明显是单峰的一般高斯形状。BSI-18具有正态性，而RPQ、PCL-5和PHQ-
9表现出轻度右偏(1年:分别为1.04、1.07和1.20;3至7年:0.95、0.98和1.18)，qolibria - os显示轻度左偏(1年:−0.47;3～
7年:−0.61)。使用兰德公司的非等效组别加权和分析工具集软件进行增强回归建模。[53]
其他统计分析使用SAS版本9.4 (SAS Institute)和SPSS版本26 (IBM)进行。

结果

基线和伤害相关特征

在2417名TRACK-
TBI参与者中，1572人在1年后完成了结果评估(1049人[66.7%]为男性;平均[SD]年龄41.6[17.5]岁，3 - 7岁时完成预后评估的有1084人(714人[65.9%];mean
[SD]年龄，40.6[17.0]岁)。一年后，共有60名参与者(4%)是亚洲人，255名(16%)是黑人，1213名(77%)是白人，39名(2%)是其他种族，5名(0.3%)是未知种族。在3 - 7岁时，39人(4%)是亚洲人，149人(14%)是黑人，868人(80%)是白人，26人(2%)有其他种族，2人(0.2%)有未知种族。纳入和排除的参与者(1岁时845人，3 - 7岁时1315人)之间的比较显示出性别、种族和民族、教育和社会经济劣势的差异(附录1表1)。流程图如图1所示。具体的登记情况见附录1的表9。指数后TBI患者(1572人中的50人[3.2%]在1年;1084例(3 - 7年)中132例(12.2%)无指数后创伤性脑损伤(1522例)

1年1572 [96.8%];1084人中有952人(3 - 7岁)在社会人口和伤害特征方面具有可比性(表1)。

有tbi和没有tbi的参与者在统计学上有显著差异

随访1年和3 - 7年的基线精神病史患者比例较高(1年:19 / 50 [38%]vs 344 / 1522 [23%];*P* = *.02;*3至7岁:132人中有45人[34%]，而952人中有214人

[22%];*P = .009)，需要急诊科或住院(1年:急诊科*

入院时，46人中有12人[26%]，1416人中有171人[12%];住院，46例中有6例[13%]vs 1416例中有101例[7%];*P = .001;*3 - 7年:急诊科，123例中31例[25%]vs 888例中90例[10%];住院率为10例(8%)vs 59例(7%);*P < .001)，更低的平均(SD)损伤严重程度评分(1年:3.5 [5.9]vs 6.0 [7.3];P = .002;*3 - 7岁:4.3 [6.0]vs 5.7 [7.3];*P = .01)*。

指数后TBI和结果

图2总结了我们的主要结果。1年后，指数后TBI组表现出更差的跨领域结局(表2)。与那些没有指数后TBI的参与者相比，指数后TBI参与者实现完全功能恢复的可能性更小(GOSE评分为8;调整后的相对风险[aRR]， 0.57;95% CI, 0.34-0.96)， HRQOL下降(qolibria - os:校正平均差异[aMD]，−15.9;95% CI，−22.6至−9.1)，以及其他结果的症状严重程度增加，包括PCS (RPQ: aMD, 8.1;95% CI, 4.2-11.9)，心理困扰(BSI-18: aMD, 5.3;95% CI, 2.1-8.6)，创伤后应激障碍(PCL-5: aMD, 7.8;95% CI, 3.2-12.4)和抑郁(PHQ-9: aMD, 3.0;95%可信区间，1.5-4.4)。在3 - 7年，指数后TBI患者的症状仍然较多，但程度降低(QOLIBRI-OS: aMD，−7.3;95% CI，−11.4至−3.2;RPQ: aMD, 4.3;95%可信区间，1.9-6.6;BSI-18: aMD, 3.0;95% ci, 0.9-5.1;PCL-5: aMD, 6.5;95% ci, 3.4-9.7;PHQ-9: aMD, 1.8;95% ci, 0.8-2.8)。在指数后TBI患者中，GOSE评分达到8分的可能性较低(42 / 131 [32%]vs 416 / 917[45%])，尽管这一发现在3 - 7岁时不显著(aRR, 0.78;95%可信区间，

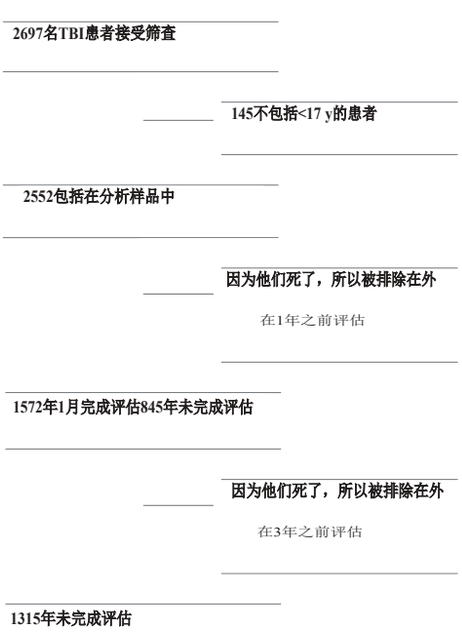
0.61-1.00)。在伴有意识丧失的指数后TBI与无意识的TBI中也观察到了类似的结果(附录1中的表2和表3)。在伴有指数前TBI的参与者中，有无指数后TBI组间的RPQ差异(aMD, 8.6;95% CI, 2.1-15.1)， BSI-18 (aMD, 6.9;95%可信区间，

1.5-12.3)， PHQ-9 (aMD, 4.80;95% CI, 2.26-7.33)和QOLIBRI-OS (aMD，−19.8;95% CI，−30.9至−8.8)在1年和QOLIBRI-OS (aMD，−8.8;95% CI，−16.1 ~−1.6)，3 ~ 7年(附录1表4和表5)。

我们评估了1084例患者中26例(2.4%)和26例(2.4%)的多发性术后tbi之间的相关性

3到7年的结果。postindex TBIs数量(0 vs 1,1 vs 2或更多，以及2或更多vs 0)

图1。CONSORT流程图



TBI表明创伤性脑损伤。

表1。基线和损伤特征

变量	没有。(%)					
总计	1岁的评估	50 (3.2)	na	评估在3-7年	132 (12.2)	na
	41.6 (17.5)	42.7 (17.4)	.84	40.6 (16.9)	40.7 (17.2)	.92
	后索引创伤性脑损伤			后索引创伤性脑损伤		
男性		29 (58)	*P值*	634 (67)	80 (61)	
女性	502 (33)	21 (42)	.28			.19
亚洲	59 (4)	1 (2)		1 (1)		
黑色	245 (16)	10 (20)		14 (11)		
	1522 (96.8)		.73			.16
年龄，平均(SD)，y						
性别						
	1020 (67)					
				318 (33)		
比赛[a]						
				38 (4)		
				135 (14)		

	1175 (77)					
其他种族[b]						
未知，没有。						
白色		38 (76)		754 (79)	114 (86)	
	38 (3)	1 (2)		23 (2)	3 (2)	
	5	0	na	2	0	na
西班牙语裔	263 (17)	6 (12)			20 (15)	
	1253 (83)	44 (88)	.16	776 (82)	111 (85)	.19
种族[a]	6	0		3	1	
	13.7 (2.8)	13.3 (2.2)	.19	13.8 (2.8)	14.0 (2.6)	.46
	33	0	na	21	3	na
				173 (18)		
非西班牙裔						
未知，没有。						
教育						
均值(SD)， y						
未知，没有。						

社会经济劣势[c]						
平均(SD)	10.7 (6.4)	11.2 (6.0)	.35	10.9 (6.4)	9.7 (5.4)	0.0
未知，没有。	57	0	na	27	1	na
精神病史						
不	1178 (77)	31 (62)	.02	738 (78)	87 (66)	0.00
请	344 (23)	19 (38)		214 (22)	45 (34)	
前索引脑损伤						
任何前索引TBI						
不	768 (53)	20 (43)	.09	515 (57)	51 (41)	<.001
可以，不可	392 (27)	13 (28)		230 (25)	37 (30)	
是的，LO	281 (20)	14 (30)		163 (18)	35 (28)	
未知，没有。	81	3	na	44	9	na

前索引tbi, No。[d]

0.67 (1.14)

1047 (70)

178 (19)

16 (12)

未知，没有。

平均(SD)	0.46 (0.92)		.10	0.41 (0.87)	0.67 (1.03)	<.001
0		29 (59)		691 (74)	72 (56)	
1	308 (21)	13 (27)	.17		41 (32)	<.001
≥2	137 (9)	7 (14)		71 (8)		
	30	1	na	12	3	na
均值(SD)， y						
	22.3 (15.1)	28.6 (17.9)	0.0	21.6 (14.4)	24.3 (15.3)	.19
< 15y		4 (20)		87 (35)	16 (29)	
	294 (66)		.32		40 (71)	.43

149 (34)

年龄第一指标前TBI

		160 (65)				
未知，没有。						
TBI前指数最高的护理水平						
	1144 (81)					
	171 (12)					
住院						
未知，没有。		16 (80)				
	30	1	na	14	4	na
没有		28 (61)		739 (83)	82 (67)	
仅限ED		12 (26)	.001	90 (10)	31 (25)	<.001
	101 (7)	6 (13)		59 (7)	10 (8)	
	106	4	na	64	9	na

(续)

表1。基线和损伤特征(续)

变量	没有。(%)					
	1岁的评估			评估在3-7年		
	后索引创伤性脑损伤			后索引创伤性脑损伤		
	不	请讲	*P值*	不	请讲	*P值*
指数损伤因素						
GCS到达ED						
平均(SD)	13.3 (3.5)	13.7 (3.1)	.12	13.1 (3.7)	14.0 (2.6)	.003
严重(3-8)	184 (12)	5 (10)		131 (14)	8 (6)	
中等(9-12)	58 (4)	1 (2)	.76	45 (5)	3 (2)	0.01
温和(13-15)	1251 (84)	42 (88)		754 (81)	117 (91)	
未知，没有。	29	2	na	22	4	na
现场						
不	179 (12)	4 (8)		109 (12)	15 (12)	
怀疑	76 (5)	1 (2)	.30	51 (6)	10 (8)	.68
请讲	1186 (82)	44 (90)		747 (82)	103 (80)	
未知，没有。	81	1	na	45	4	na
最高水平的护理						
埃德	350 (23)	7 (14)		209 (22)	31 (23)	
沃德	548 (36)	24 (48)	.69	335 (35)	57 (43)	.11
icu	624 (41)	19 (38)		408 (43)	44 (33)	
最初CT表现						
阴性	803 (54)	27 (55)		483 (52)	79 (60)	
阳性	682 (46)	22 (45)	.88	438 (48)	53 (40)	.25
未知，没有。	37	1	na	31	0	na
重大颅外损伤						
不	1233 (81)	44 (88)		779 (82)	111 (84)	
请讲	289 (19)	6 (12)	.27	173 (18)	21 (16)	.47
ISS(所有系统)						
平均(SD)	15.0 (10.1)	10.9 (8.5)		15.1 (10.2)	12.2 (9.1)	
中位数(IQR)	13 (8-21)	10 (5-14)	0.005	14 (9-21)	10 (5-17)	.002
未知/仅ED，否。	377	10	na	231	35	na

所有经秩回归评估的结果均显示出剂量依赖相关性(表3)。与那些没有指数后TBI的患者相比，那些指数后TBI 1例的患者PCL-5升高(aMD, 3.6;95% CI, 0.2-7.0)和较低QOLIBRI-OS (aMD，−4.8;95% CI，−9.3~−0.3)。2或以上的患者比1例，2或以上的患者比0例，获得完全功能恢复的可能性更小(GOSE评分为8;2或以上vs 1: aRR, 0.31;95% ci, 0.10-0.96;2或以上vs 0:

aRR, 0.28;95% CI, 0.09-0.84)，并且在结局域内症状更严重，包括QOLIBRI-OS(2或以上vs 1: aMD，−12.6;95% CI，−22.2 ~−3.0;2及以上vs 0: aMD，−17.4;95% CI，−26.1至−8.7)，RPQ(2或更多vs 1: aMD, 10.1;95%可信区间，4.6-15.6;2或以上vs 0: aMD, 12.4;95% CI, 7.4-17.4)， BSI-18(2或以上vs 1: aMD, 6.7;95%可信区间，1.8-11.5;2或以上vs 0: aMD, 8.4;95% CI, 4.0-12.8)， PCL-5(2或以上vs 1: aMD, 14.7;95% ci, 7.4-22.0;2或以上vs 0: aMD, 18.3;95% CI, 11.7-25.0)和PHQ-9(2或以上vs 1: aMD, 4.88;95%可信区间，2.53-7.23;2或以上vs 0: aMD, 5.71;95%可信区间，3.57-7.85)。

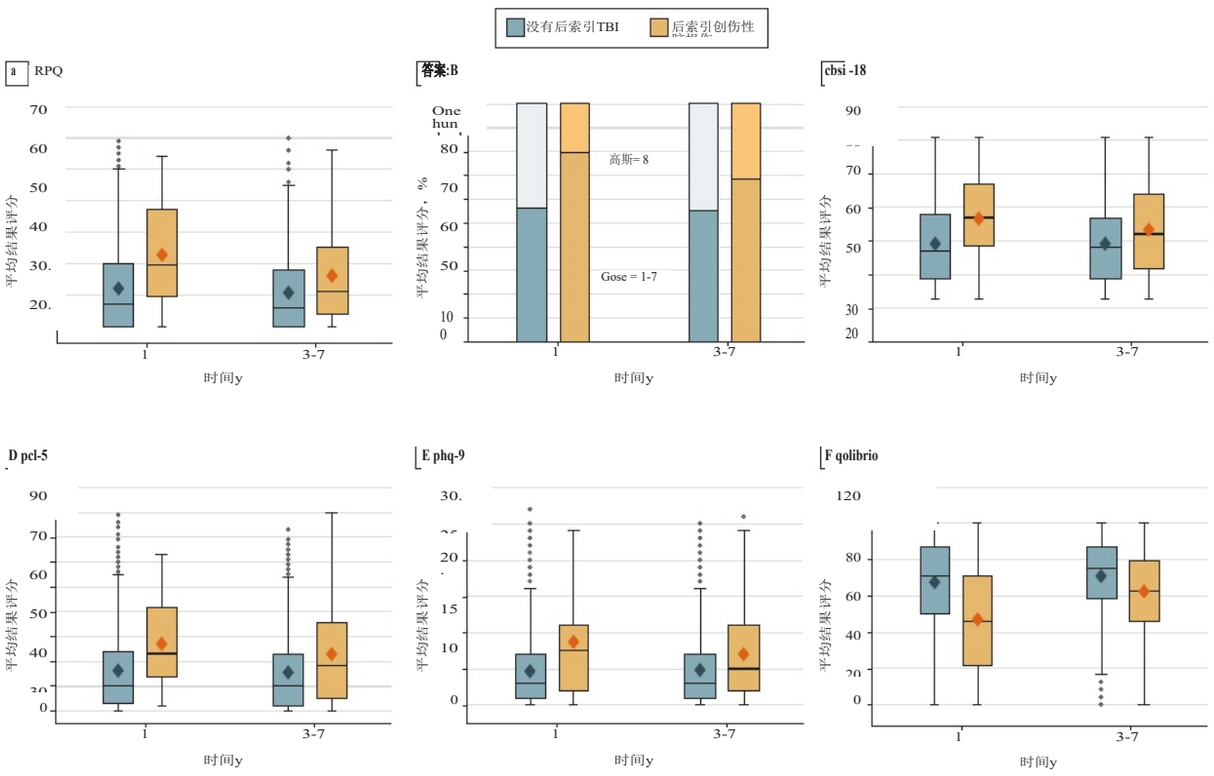
我们进一步研究了指数后创伤性脑损伤发生的时间和预后之间的关系

1年观察到无差异(附录1表6)。附录1表7总结了指数后TBI和3 - 7年结果之间的年数。我们观察到评估的时机与症状减轻之间存在关联(RPQ, BSI-18, PCL-5, PHQ-9, qolibi - os)，在调整时机后，原始的关联仍然显著(附录1中的表8)。

讨论

在这项多中心研究中，创伤后TBI患者在损伤后1年的PCS、心理健康和HRQOL域的不完全功能恢复风险较高，症状更明显。这些发现保存了3到7年。值得注意的是，3 - 7年的多个tbi指数后增加了功能不完全恢复的风险和跨领域的症状负担。这些结果表明，指数后tbi患者在长期康复中构成了一个症状明显的队列，而风险患者可能会从有针对性的预防和随访护理中受益。

图2。1年和3 - 7年组状态的未加权平均预后评分



菱形表示平均值;中线，中位数;box表示IQR;胡须，范围;数据点，离群值。BSI-18表示简要症状清单-18;GOSE，扩大格拉斯哥预后量表;PCL-5, DSM-5的PTSD检查表;PHQ-9，患者健康问卷9;qolibrii - os，脑损伤后生活质量量表;RPQ, Rivermead脑震荡后症状问卷;TBI，创伤性脑损伤。

指数后TBI危险因素

两个时间点的指标后TBI的危险因素包括基线精神病史、指标前TBI的频率和严重程度，以及指标较轻的外周损伤。精神病史[54,55]和前索引TBI[4,5]是众所周知的TBI的危险因素。这一发现表明，在没有创伤后脑损伤的个体中，外周损伤更为严重，这表明这些个体可能因损伤太严重而无法恢复容易发生脑损伤的高风险活动。3 - 7年的特定风险因素包括较轻的TBI指数(较高的GCS)和社会经济劣势。先前的研究表明，指数前和指数后TBI患者的指数TBI较轻。[5,6,17]

指数后TBI和结果

在1年后，控制主要混杂因素的多元回归分析表明，指数后TBI患者有完全功能恢复降低的风险(GOSE评分为8;aRR, 0.57;95% CI, 0.34-0.96)，症状性(PCS、心理困扰、创伤后应激障碍、抑郁和HRQOL)较多。平均预后评分显示临床显著的轻度PCS、抑郁、HRQOL受损。在指数前TBI参与者中，指数后TBI患者在PCS、心理痛苦、抑郁和HRQOL结果中表现出更多症状，且效应量相当，进一步支持指数后TBI与结果的相关性。我们的研究结果与文献中表明伴有前指数创伤性脑损伤的平民PCS、PTSD和心理健康恶化的结果一致[6]并使指数后TBI患者的PCS恶化。[18]

在3 ~ 7年，指数后创伤性脑损伤组仍然有更多的症状(PCS，心理

抑郁、创伤后应激障碍(PTSD)、抑郁和HRQOL)。在多变量回归分析后，功能恢复和指数后TBI之间没有显著联系，这可能反映了3 - 7年的较低的综合症状。在指数前tbi患者中，指数后tbi患者的HRQOL更差，但在其他效果量减少的结果中没有差异，这表明指数前和指数后tbi都对3 - 7年的结果有影响。

3 - 7年的术后tbi(0、1、2或更多)数量呈剂量依赖性

所有领域(功能、个人信息、心理健康和HRQOL)的关联。较低比例的

表2。指数后创伤性脑损伤(TBI)与预后的关系[a]

	没有后索引TBI		后索引创伤性脑损伤		效应大小[b]	
结果测量	总，不。	平均(SD)	总，不。	平均(SD)	测量(95% CI)	*P值*
1 y						
GOSE得分8，排名第一。(%)	1446	638 (44)	48	10 (21)	平均回收率，0.57 (0.34 - 0.96)	0.03
RPQ	1456	12.1 (13.9)	48	22.7 (16.0)	aMD, 8.1(4.2至11.9)	<.001
bsi-18	1453	49.1 (11.6)	48	56.6 (12.0)	aMD, 5.3(2.1至8.6)	.001
pcl-5	1433	16.1 (16.6)	48	26.9 (16.7)	aMD, 7.8(3.2至12.4)	.001
phq-9	1451	4.6 (5.3)	48	8.7 (7.3)	aMD, 2.96(1.49至4.44)	<.001
qolibrio	1452	67.6 (24.5)	48	47.0 (28.4)	aMD，−15.9(−22.6 ~−9.1)	<.001
3-7 y						
GOSE得分8，排名第一。(%)	917	416 (45)	131	42 (32)	平均回收率，0.78 (0.61 - 1.00)	.06
RPQ	917	10.8 (12.7)	130	16.1 (15.1)	aMD, 4.3(1.9至6.6)	<.001
bsi-18	916	49.3 (11.0)	130	53.3 (12.6)	aMD, 3.0(0.9至5.1)	0.004
pcl-5	889	15.5 (16.5)	128	22.8 (20.1)	aMD, 6.5(3.4至9.7)	<.001
phq-9	918	4.8 (5.3)	130	7.0 (6.3)	aMD, 1.78(0.77至2.78)	.001
qolibrio	919	70.8 (21.9)	130	62.2 (24.5)	aMD，−7.3(−11.4 ~−3.2)	<.001

缩略语:aMD，调整后均值差;aRR，调整后相对风险;BSI-18，简要症状清单-18;GOSE，扩大格拉斯哥预后量表;PCL-5, DSM-5的PTSD检查表;PHQ-9，患者健康问卷9;qolibrii - os，脑损伤后生活质量量表;瑞弗米德脑震荡后症状问卷 [a]对标量结局指标(BSI-18、PCL-5、PHQ-9、qolibi - os和RPQ)进行多变量线性回归，对完全功能恢复(GOSE评分为8)进行多变量logistic回归。

[b] 所有回归分析都根据年龄、性别、种族和民族、教育、格拉斯哥昏迷量表、创伤性脑损伤前护理水平和精神病史进行了调整，并对失踪进行了倾向加权。

[c] 所有显著P值(P < .05)在调整多重比较后仍然显著(Benjamini-Hochberg;M = 12)。

表3。多发性创伤性脑损伤(TBIs)与3 - 7年预后的关系

	没有。后索引tbi						效果大小b				
	0 tbi		1 tbi		≥2个tbi		1对0 TBIs		≥2比1 TBI	≥2比0 TBIs	
结果测量	总，不。	平均(SD)	总，不。	平均(SD)	总，不。	平均(SD)	测量 (95% ci)	*P值*	测量 (95% CI) P值	测量 (95% CI) P值	整体 *P值，d*
GOSE得分为8，没有。(	917	416 (45)	105	39 (37)	26	3 (12)	aRR, 0.90 (0.70至1.15)	.21	aRR, 0.31 .04 (0.10至0.96)	aRR, 0.28 .02 (0.09至0.84)	0.0
RPQ	917	10.8 (12.7)	104	14.1 (14.1)	26	24.0 (16.9)	aMD, 2.3 (−0.3 ~ 4.9)	0.0	aMD, 10.1 <.001 (4.6至15.6)	aMD, 12.4 <.001 (7.4至17.4)	<.001
bsi-18	916	49.3 (11.0)	104	52.0 (11.6)	26	58.5 (15.1)	aMD, 1.7 (−0.6至4.0)	.14	aMD, 6.7 .007 (1.8至11.5)	aMD, 8.4 <.001 (4.0至12.8)	.003
pcl-5	889	15.5 (16.5)	102	20.1 (18.2)	26	33.5 (24.0)	aMD, 3.6 (0.2至7.0)	0.0	aMD, 14.7 <.001 (7.4至22.0)	aMD, 18.3 <.001 (11.7至25.0)	<.001
phq-9	918	4.8 (5.3)	104	6.1 (5.8)	26	10.5 (7.0)	aMD, 0.83 (−0.27 ~ 1.93)	.14	aMD, 4.88 <.001 (2.53至7.23)	aMD, 5.71 <.001 (3.57至7.85)	<.001
qolibrio	919	70.8 (21.9)	104	64.7 (23.3)	26	52.4 (26.9)	aMD，−4.8 (−9.3 ~−0.3)	0.0	aMD，−12.6 .01 (−22.2 ~−3.0)	aMD，−17.4 <.001 (−26.1 ~−8.7)	<.001

缩略语:aMD，调整后均值差;aRR，调整后相对风险;BSI-18，简要症状清单-18;GOSE，扩大格拉斯哥预后量表;PCL-5, DSM-5的PTSD检查表;PHQ-9，病人健康问卷-9;qolibrii - os，脑损伤后生活质量量表;RPQ，里弗米德脑震荡后对标量结果测量进行了多变量线性回归分析(BSI-18、PCL-5、PHQ-9、qolibria - os和RPQ)，并进行多变量logistic回归以实现完全功能恢复(GOSE得分8)。

b所有回归分析均根据年龄、性别、种族和民族、教育程度、格拉斯哥昏迷量表、指数前TBI水平进行调整和精神病史，并倾向于失踪。

c P < .05。没有对多次比较进行调整。

d总体显著性假设指数后TBI类别有序数性，并采用秩回归进行评估。

2个或更多的tbi患者报告完全功能恢复(GOSE评分为8;aRR, 0.31;95% CI, 0.10-0.96)，与1个指数后TBI的参与者相比，其平均结局得分超过PTSD、轻度PCS和中度抑郁的临床阈值。我们的研究结果与接触运动文献一致，这些文献表明，持续的多次创伤性脑损伤会导致PCS恶化、心理健康症状和恢复延迟。[10,11,56,57]

我们对术后TBI时机的分析进一步证实了这些结果。虽然没有重大意义

在1年观察到相关性，较短的损伤间隔与3 - 7年RPQ、BSI-18、PCL-5、PHQ-9和QOLIBRI-OS恢复较差相关。重要的是，在经过3 - 7年的敏感性分析，调整时间后，所有指数后TBI和结果之间的相关性仍然显著。这些结果促使预防、教育和后续护理的努力，以减少短间隔伤害的风险。

对临床实践的影响

缺乏后续护理对就业和经济结果是有害的。[58,59]
标准化的TBI教育、咨询、筛查、分诊和转介到有重复损伤风险的患者的护理系统可以减少再损伤并提高康复的可能性。我们的结果显示了收集指标前和指标后TBI病史的重要性，因为重复的TBI是多维预后较差的危险因素。

生物-心理-社会-生态模型的应用将为预防和后续护理提供信息

努力。[60,61]
生物因素、伤前和伤后的心理健康、健康的社会决定因素(种族和族裔以及教育)以及急性期后护理的获得等因素的综合影响着每位患者的康复。经历1个或多个创伤性脑损伤指数后的风险因素和后遗症包括生物学因素(如创伤性脑损伤)、心理因素(如创伤后心理症状学、创伤前修饰因素)和社会/社会经济因素(如社区不利指数)，此外还有生态因素和本研究未评估的其他因素。因此，指数后TBI可能是TBI后长期恢复和/或预后不良的整体表型的一部分，更深入地了解这些重复性损伤的中介因素可以减轻这些风险，并降低单次TBI后的发病率。临床医生在咨询和后续研究中同时应用生物-心理-社会-生态模型，可以更全面地评估潜在的风险因素，并扩大预防、教育和门诊治疗干预的影响。

局限性

本研究存在局限性。我们的研究结果适用于那些通过颅脑成像来排除外伤性颅内出血的人群，但可能不适用于未到急诊室就诊的患者。在1岁和3岁至7岁接受评估的患者更有可能是女性，非西班牙裔，受教育程度更高，社会经济劣势更少，这限制了总体的普遍性。OSU TBI-id是一种验证和可靠的自我报告的创伤性脑损伤历史测量;然而，自我报告的方法本身就受到回忆偏差的限制。虽然超出了我们的研究范围，但中心间的结果变异是另一个值得在这一负担沉重的人群中进行比较有效性研究的因素。我们无法评估多个术后tbi与1年结果之间的关联，因为这些数据直到3 - 7年才被捕获。因为我们试图在每个时间点回顾最大的样本量，在1年和3至7年评估的队列有轻微不同的基线特征。未来的假设驱动分析可能会考虑使用跨越时间点的共同样本。由于数量较少，我们没有评估指数后TBI与死亡之间的关联，这需要在未来更大、更多样化的样本中进行调查。虽然我们控制了主要混杂因素的结果，但与程序干预、并发症和出院后护理相关的残余混杂因素可能仍然存在。这些限制构成了相关的后续步骤。

使用线性回归模型的标量结果措施构成了另一个限制。

BSI-18符合正态分布，其他指标表现出一定程度的偏态。

考虑到偏倚一般比较轻微，我们继续进行线性回归，以优先在原始可解释的结果评分中报告系数单位，这与之前发表的大型多中心脑外伤研究中结果测量方法的方法一致。我们认识到，倾斜可能会降低线性回归模型的有效性。因此，我们的结果应该在相应的谨慎水平下进行解释，并等待在这一研究不足和风险人群中的验证研究。

结论

在一项前瞻性的多中心急性脑损伤队列研究中，创伤后脑损伤与损伤后1年和3 - 7年的功能、PCS、心理健康和HRQOL症状相关。与维持1次术后TBI相比，维持多次术后TBI与症状增加相关。这些结果强调了重复性脑损伤后的严重累积缺陷，并强调了建立机构项目来支持脑损伤预防、教育、咨询和高危患者随访的迫切需要。

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组信息:TRACK-TBI调查人员列于附录2。

数据共享声明:见补充3。

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补充1。

方法。逆概率加权法

表1。在1年和3 - 7年被跟踪的预测因素

表2。指数后TBI与LOC基线和损伤特征

表3。术后TBI与LOC及预后的关系

表4。指数后TBI与指数前TBI患者预后的关系

表5。TBI后指数与LOC的关系及TBI前指数参与者的预后术后TBI时间与1年预后的相关性

表7。指数后TBI的时间与3 - 7年的预后相关

表8。指数后TBI时间与3 - 7年转归之间的关系

表9。按站点登记的患者数量

补充2。

群组信息。TRACK-TBI调查人员

补充3。数据共享声明