Psychiatric Illness Following Traumatic Brain Injury in an Adult Health Maintenance Organization Population

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Background: Psychiatric illness after traumatic brain injury (TBI) has been shown to be prevalent in hospitalized and tertiary care patient populations.

Objective: To determine the risk of psychiatric illness after TBI in an adult health maintenance organization population.

Design: Prospective cohort study.

Setting: Large staff-model health maintenance organization.

Participants: Nine hundred thirty-nine health plan members diagnosed as having TBI in 1993 and enrolled in the prior year, during which no TBI was ascertained. Three health plan members per TBI-exposed subject were randomly selected as unexposed comparisons, matched for age, sex, and reference date.

Main Outcome Measure: Psychiatric illness in the 3 years after the TBI reference date, determined using computerized records of psychiatric diagnoses according to the *International Classification of Diseases, Ninth Revision, Clinical Modification*, prescriptions, and service utilization.

Results: Prevalence of any psychiatric illness in the first year was 49% following moderate to severe TBI, 34% following mild TBI, and 18% in the comparison group. Among subjects without psychiatric illness in the prior year, the adjusted relative risk for any psychiatric illness in the 6 months following moderate to severe TBI was 4.0 (95% confidence interval [CI], 2.4-6.8) and following mild TBI was 2.8 (95% CI, 2.1-3.7; $P<.001$) compared with those without TBI. Among subjects with prior psychiatric illness, the adjusted relative risk for any psychiatric illness in the 6 months following moderate to severe TBI was 2.1 (95% CI, 1.3-3.3) and following mild TBI was 1.6 (95% CI, 1.2-2.0; $P=.005$). Prior psychiatric illness significantly modified the relationship between TBI and subsequent psychiatric illness ($P=.04$) and was a significant predictor ($P<.001$). Persons with mild TBI and prior psychiatric illness had evidence of persisting psychiatric illness.

Conclusions: Both moderate to severe and mild TBI are associated with an increased risk of subsequent psychiatric illness. Whereas moderate to severe TBI is associated with a higher initial risk, mild TBI may be associated with persistent psychiatric illness.

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HIGH RATES OF MOOD, PSY-chotic, and substance abuse disorders following traumatic brain injury (TBI) have been found in hospitalized trauma and tertiary care referral populations.[1-5] A population-based secondary analysis of the New Haven portion of the National Institute of Mental Health Epidemiologic Catchment Area Study[6] by Silver and colleagues examined patients at varying time points after self-reported "severe head injury that was associated with a loss of consciousness or confusion,"[7(p937)] making the TBI exposure susceptible to recall bias. The study found that adjusted odds ratios (ORs) for all psychiatric diagnoses ex-cept bipolar disorder were increased in the group reporting a history of head injury compared with the group reporting no history of head injury. Data on injury severity and time since injury were not available. Few data exist on the longitudinal risk of psychiatric disorders in large, population-based ambulatory primary care settings following the entire spectrum of TBI severity, particularly mild TBI.

Studies have confirmed that disability caused by psychiatric disorders may contribute to the disability associated with TBI.[2,8] Identifying the extent of psychiatric problems following TBI, particularly mild TBI, may assist in targeting secondary and tertiary prevention efforts for TBI-related disability.

Psychiatric history has been shown to be a risk factor for post-TBI psychiatric illness in some but not all studies.[1,9-11] Similarly, the relationship between TBI severity and prevalence of subsequent psychiatric disorders has been inconsistent.[2,10-14] The effects of psychiatric history and TBI severity on risk of psychiatric problems following TBI have not been systematically and longitudinally studied in large TBI and comparison samples.

The goals of this study were to determine the prevalence of psychiatric illness following mild as well as moderate to severe TBI in an adult health maintenance organization (HMO) population, the ORs for prevalent psychiatric illness and relative risks (RRs) for incident psychiatric illness following TBI compared with patients without TBI, and the effect of prior psychiatric illness on the relationship between TBI and subsequent psychiatric illness.

METHODS

This prospective cohort study was conducted using computerized records from the Group Health Cooperative of Puget Sound (GHC), a consumer-governed regional HMO that serves approximately 450 000 members in the Puget Sound area of western Washington State. As a staff-model HMO, it builds and owns its facilities, and the physicians and other staff are employees of the health plan. The GHC population is broadly representative of the greater Seattle population in terms of age, sex, race, and marital status; GHC enrollees have slightly higher educational attainment and less representation at the high end of income distribution.[15] This study used data obtained in conjunction with a previously reported case-control study of psychiatric risk factors for TBI.[16] Subjects received medical care from one of GHC's facilities, located in 6 counties. Data on health plan members were derived from GHC's computerized databases, which included information on all inpatient and outpatient visits and diagnoses, all prescriptions dispensed from GHC pharmacies, age, sex, and insurance type (Medicare, Medicaid, GHC individual or family plan, GHC group plan, or other plan), which was used as a proxy for socioeconomic status. Each GHC member has a unique and permanent number that makes linkage of all utilization possible; GHC tracks enrollment closely and has a low rate of member disenrollment (13.1% for 1992 through 1993), which made it possible for us to maintain a stable study base. Diagnoses in 1992 were recorded on 95% of all visit records.[15] Only about 7% of GHC members had dual insurance coverage, so ascertainment of utilization was nearly complete. The study was approved by the institutional review boards of GHC and the University of Washington, Seattle.

TBI-EXPOSED GROUP

The TBI-exposed group included patients 15 years or older diagnosed at an emergency department, hospital, or outpatient clinic as having a TBI in 1993. The following diagnostic categories and codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*)[17] were used to identify TBI: fracture of the vault or base of the skull (800.0-801.9); other, unqualified, and multiple fractures of the skull (803.0-804.9); and intracranial injury, including concussion, contusion, laceration, and hemorrhage (850.0-854.1). These diagnostic categories for TBI were used by the Centers for Disease Control and Prevention in their TBI surveillance studies.[18] If a person received a TBI diagnosis at more than 1 visit in 1993, the first diagnosis was considered the incident TBI. The reference date for cases was the date of this incident

TBI diagnosis. Patients with TBI were required to have been continuously enrolled at GHC for the year prior to their TBI diagnosis to ensure that records were available to assess indicators of prior psychiatric illness. We included patients from 6 counties in the Puget Sound area that provided complete health service utilization data. To maximize the likelihood of ascertaining incident TBI cases, subjects who had an *ICD-9-CM* diagnosis of TBI in the year prior to their reference date were excluded from the TBI-exposed group.

Severity of TBI was dichotomized into mild TBI and moderate to severe TBI using the categorization criteria of the Centers for Disease Control and Prevention.[19] The TBI exposure was considered to be mild if *ICD-9-CM* codes indicated brief (<1 hour) or no loss of consciousness and no documented traumatic intracranial lesions. The TBI exposure was considered to be moderate to severe if *ICD-9-CM* codes indicated prolonged loss of consciousness or a documented traumatic intracranial or brain lesion. Persons whose TBI severity was undetermined were excluded from the study.

TBI-UNEXPOSED COMPARISON GROUP

To compare the effects of recent incident TBI exposure with no recent TBI exposure, 3 subjects per TBI-exposed patient were selected at random from GHC enrollment files and were frequency matched with TBI-exposed patients by sex, age in 5-year groups (15-19 years up to ≥95 years), and enrollment at the time of the TBI-exposed patient's reference date. Similar to the patients with TBI, TBI-unexposed patients had to be GHC members on their assigned reference date as well as continuously during the year prior to this date and could not have received a TBI diagnosis during that year.

PSYCHIATRIC ILLNESS INDICATORS

Psychiatric illnesses in the year prior to and 3 years following the reference date were ascertained using 3 separate indicators: presence of a psychiatric diagnosis, filling of a prescription for psychiatric medication, or utilization of psychiatric services. Presence of a psychiatric illness was recorded in 6-month blocks for the 3 years following the reference date. The denominator for each period was the number of subjects who were enrolled at any time during that period. Therefore, except for those who were disenrolled as a result of death on the reference date all patients had psychiatric illness outcome data in the first 6 months after the reference date.

Psychiatric diagnoses were determined using *ICD-9-CM* codes and were categorized as follows: acute reaction to stress or adjustment reaction (308, 309); alcohol or drug intoxication, withdrawal, or dependence (291.0-292.9, 303.0, 303.9, 304, 305); anxiety (300.0, 300.2, 300.3, 799.2); depression (296.2, 296.3, 296.82, 296.9, 300.4, 311); hyperkinetic syndrome of childhood (314); malaise or fatigue (300.5, 780.7); organic psychotic mental disorders (290.0-290.9, 293.0-294.9); organic nonpsychotic mental disorders (310, 780.09); schizophrenia, hallucinations, or paranoia (295, 297.0-299.9, 780.1); somatoform disorders (300.1, 300.6-300.9, 306, 307.8, 307.89); or other psychiatric disorders (307, 316, V40.2-V40.9, V62.81, V62.89, V65.9).

Subjects were considered to have filled a psychiatric medication prescription if automated GHC pharmacy data indicated that a prescription for a psychiatric medication in any of the following classes was filled in the 3 years after the reference date: antidepressants, lithium, anxiolytics, antipsychotics, or psychostimulants. Surveys in 1985 and 1986 showed that more than 90% of all medications prescribed at GHC were filled in GHC pharmacies, and a study found that 97.6% of patients treated with antidepressant medications between 1991 and 1992 filled their prescriptions at GHC pharmacies.[15] Because anti-

depressants are commonly used for other conditions, they were considered to be for a psychiatric indication only if the prescription was filled within 60 days of a depression diagnosis. Anxiolytics were considered to be for a psychiatric indication if the prescription was filled within 60 days of an anxiety diagnosis. Psychostimulants were excluded if there was a diagnosis of narcolepsy in the year prior to the reference date.

Utilization of psychiatric services was ascertained based on computerized records of inpatient psychiatric hospitalizations, outpatient mental health clinic visits, and inpatient stays or outpatient visits for alcohol or drug treatment in the year before and 3 years after the reference date. Out-of-plan mental health care use is rare owing to comprehensive mental health services with small copayments in GHC.

To maximize clinical validity, the psychiatric illness indicators were further divided into the following clinical categories: (1) affective disorders (depressive or anxiety disorder diagnosis; antidepressant, lithium, or anxiolytic prescription), (2) psychotic disorders (schizophrenia, hallucinations, or paranoia or organic psychotic disorder diagnosis; antipsychotic prescription), (3) substance abuse disorders (alcohol or drug intoxication, withdrawal, or dependence diagnosis), (4) adjustment reaction (acute reaction to stress, adjustment reaction, malaise, or fatigue), (5) somatoform disorder, (6) organic nonpsychotic mental disorder, (7) hyperactivity (hyperkinetic syndrome of childhood; psychostimulant prescription), and (8) other psychiatric disorder. An overall summary determination of psychiatric illness was made based on the presence of any psychiatric diagnosis, psychiatric medication prescription, or psychiatric utilization during the year before and 3 years after the reference date.

INJURY AND MEDICAL COMORBIDITY

Comorbid injuries associated with incident TBI were determined using *ICD-9-CM* codes for fractures (805-829), internal injuries (860-869), open wounds (870-897), crushing injuries (925-929), injury to the nerves or spinal cord (950-957), and other injuries (958-959) during the 6 months before and 6 months following the reference date.

To adjust for medical comorbidity, we initially considered the Johns Hopkins Ambulatory Care Group (ACG) Case Mix Adjustment System,[20] a measure of relative health status designed to be indicative of expected resource consumption. This system uses age, sex, and *ICD-9-CM* diagnoses to assign a person to 1 of 106 mutually exclusive categories.[21] Although adjustment with the ACG system may be considered for continuous or large-count outcomes, its many categories make it less useful for dichotomous outcomes. Consistent with the cost-prediction design goal of the ACG, we used the logarithm of total costs in the year prior to TBI as a proxy for medical comorbidity and compared it with ACG adjustment. With the most prevalent outcomes, in which ACG adjustment was possible, logarithm of total costs and ACG adjustment were nearly interchangeable as adjustments to the effect of TBI, with logarithm of total costs tending to be a slightly stronger confounder.

STATISTICAL ANALYSIS

The proportion of subjects with psychiatric illness indicators within a particular period (p=prevalence) reveals the cumulative effects of exposure regardless of time of onset. Adjusted exposure effects are estimated with the OR (odds=p/[1-p]; OR=odds [exposed]/odds [unexposed]). Because of the potential for correlation among the psychiatric illness indicators for each subject, OR estimates were computed using generalized estimating equations. Separate regression analyses were reported for subgroups with and without psychiatric illness in the prior year. We used SAS version 8 statistical software (SAS Institute Inc, Cary, NC) for this analysis.

The proportion of subjects whose first psychiatric illness indicator occurs during a particular period (incidence) shows the effect of exposure on new cases. The RR expresses incidence among exposed subjects as a proportion of the incidence among unexposed subjects. The RR estimates were computed using complementary log-log generalized linear models for fixed-interval, interval-censored data.[22] Based on the a priori hypothesis of strong early effects of TBI with decreasing risk thereafter, we modeled the first 6-month RR separately along with a linear trend in RR for intervals 2 through 6. Because of the small number of substance abuse outcomes, the ORs and RRs for substance abuse are reported for a combination of mild TBI exposure and moderate to severe TBI exposure. Inferences are based on omnibus tests of any effect of TBI and nested tests for trends in RR across time. In addition, descriptive tests and confidence intervals (CIs) for individual periods are reported for comparison of the relative strength of TBI effects across time. Stata version 7 (Stata Corp, College Station, Tex) and S-PLUS version 6.1 (Insightful Corporation, Seattle) statistical software were used for this analysis.

RESULTS

PATIENT AND TBI CHARACTERISTICS

In 1993, 939 GHC members who were enrolled in the 6-county study region were diagnosed as having a TBI. These members had been enrolled in GHC for at least 1 year prior to their index TBI and had no evidence of a TBI in that year. Most TBIs were classified as mild (n=803; 85.5%) and were diagnosed in an outpatient setting (n=410; 43.7%) or in the emergency department (n=388; 41.3%), whereas 141 (15.0%) were diagnosed in the hospital. The overall annual incidence rate of TBI at GHC among all ages was 475.2 per 100 000 person-years.[16]

Although 531 (57%) of all TBI-exposed subjects and 494 (62%) of mild TBI–exposed individuals were aged 15 to 44 years, 77 (57%) of those with moderate to severe TBI were 65 years or older. There were slightly more women (51%) than men. The TBI and comparison groups were similar with regard to insurance type; 74% were group plan subscribers or dependents, 4% received Medicare, and less than 1% received Medicaid. The TBI events were distributed evenly across months, although there was a slightly lower proportion in the winter months.

PREVALENCE AND ORs FOR PSYCHIATRIC ILLNESS

The prevalence of psychiatric illness categories for the year prior to and the 3 years following the reference date are shown in **Table 1**. Participants with TBI generally had higher rates of psychiatric illness indicators compared with those without TBI. Among subjects with moderate to severe TBI, 49% had evidence of a psychiatric illness in the year following TBI compared with 34% in those with mild TBI and 18% in non-TBI comparisons. The prevalence for subjects with TBI gradually dropped during subsequent years but usually remained greater than for the comparison group. Most psychiatric diagnoses were made by non–mental health professionals, with 48% made

Table 1. Prevalence of Psychiatric Illness Indicators in the Year Before and 3 Years After TBI Among HMO Enrollees 15 Years or Older*

Psychiatric Indicator	Prior Year (n = 3756)	1-12 mo (n = 3704)	13-24 mo (n = 3230)	25-36 mo (n = 2892)
Total No. in each exposure category†				
Mild TBI	803 (21.4)	788 (21.3)	691 (21.4)	620 (21.4)
Moderate to severe TBI	136 (3.6)	108 (2.9)	88 (2.7)	76 (2.6)
No TBI	2817 (75.0)	2808 (75.8)	2451 (75.9)	2196 (75.9)
Affective disorder				
Mild TBI	69 (8.6)	89 (11.3)	90 (13.0)	89 (14.4)
Moderate to severe TBI	15 (11.0)	13 (12.0)	10 (11.4)	7 (9.2)
No TBI	143 (5.1)	155 (5.5)	150 (6.1)	180 (8.2)
Psychotic disorder				
Mild TBI	20 (2.5)	24 (3.0)	20 (2.9)	24 (3.9)
Moderate to severe TBI	18 (13.2)	14 (13.0)	8 (9.1)	11 (14.5)
No TBI	42 (1.5)	52 (1.9)	48 (2.0)	60 (2.7)
Substance abuse				
Mild TBI	29 (3.6)	45 (5.7)	35 (5.1)	33 (5.3)
Moderate to severe TBI	5 (3.7)	9 (8.3)	4 (4.5)	3 (3.9)
No TBI	48 (1.7)	46 (1.6)	47 (1.9)	72 (3.3)
Adjustment reaction				
Mild TBI	67 (8.3)	57 (7.2)	46 (6.7)	60 (9.7)
Moderate to severe TBI	14 (10.3)	8 (7.4)	4 (4.5)	5 (6.6)
No TBI	118 (4.2)	128 (4.6)	123 (5.0)	132 (6.0)
Somatoform disorder				
Mild TBI	15 (1.9)	12 (1.5)	10 (1.4)	12 (1.9)
Moderate to severe TBI	2 (1.5)	2 (1.9)	1 (1.1)	2 (2.6)
No TBI	13 (0.5)	9 (0.3)	10 (0.4)	14 (0.6)
Organic nonpsychotic mental disorder				
Mild TBI	8 (1.0)	37 (4.7)	5 (0.7)	9 (1.5)
Moderate to severe TBI	1 (0.7)	11 (10.2)	0 (0.0)	4 (5.3)
No TBI	6 (0.2)	7 (0.2)	3 (0.1)	2 (0.1)
Hyperactivity				
Mild TBI	3 (0.4)	4 (.5)	6 (0.9)	8 (1.3)
Moderate to severe TBI	1 (0.7)	3 (2.8)	1 (1.1)	1 (1.3)
No TBI	14 (0.5)	15 (0.5)	15 (0.6)	15 (0.7)
Other				
Mild TBI	40 (5.0)	30 (3.8)	30 (4.3)	44 (7.1)
Moderate to severe TBI	10 (7.4)	9 (8.3)	7 (8.0)	5 (6.6)
No TBI	77 (2.7)	87 (3.1)	89 (3.6)	89 (4.1)
Psychiatric diagnosis				
Mild TBI	176 (21.9)	201 (25.5)	166 (24.0)	159 (25.6)
Moderate to severe TBI	42 (30.9)	41 (38.0)	24 (27.3)	20 (26.3)
No TBI	328 (11.6)	364 (13.0)	344 (14.0)	386 (17.6)
Psychiatric medication				
Mild TBI	61 (7.6)	81 (10.3)	81 (11.7)	82 (13.2)
Moderate to severe TBI	23 (16.9)	19 (17.6)	12 (13.6)	8 (10.5)
No TBI	126 (4.5)	144 (5.1)	141 (5.8)	158 (7.2)
Psychiatric utilization				
Mild TBI	102 (12.7)	132 (16.8)	101 (14.6)	78 (12.6)
Moderate to severe TBI	15 (11.0)	24 (22.2)	12 (13.6)	6 (7.9)
No TBI	239 (8.5)	223 (7.9)	191 (7.8)	157 (7.1)
Any psychiatric illness indicator				
Mild TBI	229 (28.5)	268 (34.0)	209 (30.2)	173 (27.9)
Moderate to severe TBI	51 (37.5)	53 (49.1)	29 (33.0)	20 (26.3)
No TBI	479 (17.0)	510 (18.2)	459 (18.7)	439 (20.0)

Abbreviations: HMO, health maintenance organization; TBI, traumatic brain injury.
*Data are presented as number (percentage). Percentages are among all subjects in each exposure category during the specified 12-month period.
†Data are given as the denominator, or the number of enrollees for each exposure category at midyear.

by family practice physicians (46% of TBI-exposed subjects and 50% of comparisons). During the 3 years, 60 subjects (44%) who had moderate to severe TBI, 183 (23%) who had mild TBI, and 621 (22%) without TBI were dropouts as a result of death or GHC disenrollment. Death on the reference date accounted for 47% (n=28) of all dropouts in the moderate to severe TBI group compared with 8% (n=15) in the mild TBI group and 1% (n=9) in the comparison group.

Table 2 summarizes the adjusted OR estimates during the 3 years following TBI, stratified by psychiatric illness in the prior year, for prevalent affective disorders, psychotic disorders, and substance abuse disorders as well as diagnostic, medication prescription, utilization, and

Table 2. Estimated TBI vs No TBI Odds Ratios and 95% Confidence Intervals for Prevalent Psychiatric Illness Indicators in the 3 Years After TBI Among HMO Enrollees 15 Years or Older*

Psychiatric Indicator	P Value for Any Effect of TBI	1-12 mo	13-24 mo	25-36 mo
Affective disorder				
No prior psychiatric illness	.02			
Mild TBI		2.0 (1.3-3.1)†	1.8 (1.2-2.8)†	1.5 (1.0-2.3)
Moderate to severe TBI		1.9 (0.6-5.8)	1.6 (0.6-4.7)	0.5 (0.2-1.7)
Prior psychiatric illness	.05‡			
Mild TBI		1.2 (0.8-1.8)	2.1 (1.4-3.1)†	1.4 (0.9-2.2)
Moderate to severe TBI		1.0 (0.4-2.2)	1.0 (0.4-2.7)	0.9 (0.3-2.2)
Psychotic disorder				
No prior psychiatric illness	.54			
Mild TBI		2.3 (0.9-5.8)	1.0 (0.3-3.5)	1.1 (0.4-3.1)
Moderate to severe TBI		2.8 (0.5-14.9)	5.9 (1.6-22.1)†	3.6 (1.0-12.3)†
Prior psychiatric illness	.19			
Mild TBI		1.7 (0.8-3.4)	2.1 (1.0-4.3)†	2.3 (1.1-4.8)†
Moderate to severe TBI		2.9 (1.3-6.9)†	1.9 (0.6-5.9)	2.2 (0.8-6.3)
Substance abuse				
No prior psychiatric illness	<.001			
Any TBI		4.5 (2.6-7.6)†	1.8 (1.0-3.3)	1.4 (0.8-2.3)
Prior psychiatric illness	.05‡			
Any TBI		1.7 (0.9-3.1)	2.4 (1.2-4.8)†	0.9 (0.5-1.9)
Psychiatric diagnosis				
No prior psychiatric illness	<.001			
Mild TBI		2.2 (1.7-2.9)†	1.9 (1.4-2.4)†	1.5 (1.1-1.9)†
Moderate to severe TBI		3.5 (2.0-6.2)†	1.7 (0.9-3.1)	0.9 (0.4-2.0)
Prior psychiatric illness	.07			
Mild TBI		1.4 (1.1-1.9)†	1.5 (1.1-2.0)†	1.5 (1.1-2.2)†
Moderate to severe TBI		1.4 (0.8-2.5)	0.9 (0.5-1.7)	1.0 (0.5-2.1)
Psychiatric prescription				
No prior psychiatric illness	.18			
Mild TBI		1.8 (1.1-2.9)†	1.8 (1.1-2.8)†	1.6 (1.0-2.5)
Moderate to severe TBI		2.1 (0.7-6.2)	1.3 (0.4-4.7)	1.1 (0.3-3.6)
Prior psychiatric illness	.04			
Mild TBI		1.2 (0.8-1.8)	1.9 (1.3-2.8)†	1.5 (1.0-2.3)
Moderate to severe TBI		1.6 (0.8-3.3)	1.6 (0.7-3.5)	0.7 (0.3-1.8)
Psychiatric utilization				
No prior psychiatric illness	<.001			
Mild TBI		2.1 (1.4-3.0)†	1.7 (1.2-2.4)†	1.4 (0.9-2.2)
Moderate to severe TBI		4.5 (2.2-9.0)†	2.7 (1.1-6.5)†	0.6 (0.1-3.7)
Prior psychiatric illness	.19			
Mild TBI		1.3 (0.9-1.8)	1.5 (1.0-2.3)†	1.7 (1.1-2.7)†
Moderate to severe TBI		1.3 (0.7-2.6)	0.8 (0.3-1.9)	0.7 (0.2-1.9)
Any psychiatric illness indicator				
No prior psychiatric illness	<.001			
Mild TBI		2.1 (1.6-2.6)†	1.8 (1.4-2.3)†	1.3 (1.0-1.7)
Moderate to severe TBI		3.4 (1.9-5.8)†	1.7 (0.9-3.1)	0.9 (0.4-2.0)
Prior psychiatric illness	.02			
Mild TBI		1.4 (1.1-1.9)†	1.6 (1.2-2.1)†	1.4 (1.0-2.0)†
Moderate to severe TBI		1.6 (1.0-2.7)	1.0 (0.6-2.0)	0.8 (0.4-1.6)

Abbreviations: HMO, health maintenance organization; TBI, traumatic brain injury.

*Data are adjusted for age, sex, comorbid injuries, and logarithm of costs in the year prior to the reference date. *P* values for any effect of TBI represent tests for overall effect of TBI for each prior psychiatric illness stratum during the 3-year follow-up period.

†Represents statistical significance at *P*<.05 at the specific time point.

‡*P* value has been rounded up.

any psychiatric illness indicator categories. Time points for which *P*<.05 are marked with a dagger for comparison of the strength of effect across time. Adjusted ORs for subjects with prior psychiatric illness were computed separately so that the TBI effect estimates and all adjustments accounted for the effect modification due to prior psychiatric illness. For most outcomes, the estimated effects caused by TBI were greater among those without prior psychiatric illness and were often stronger for mild TBI. With a few exceptions, primarily in subjects with prior psychiatric illness who sustained mild TBI, the OR estimates decreased across time.

Among subjects without prior psychiatric illness, the OR estimates for prevalent affective disorder after mild TBI were greatest in the first 2 years. In those with prior psychiatric illness, the estimated ORs for affective disorder were not individually significant until the second year after mild TBI. In the first year after TBI, the
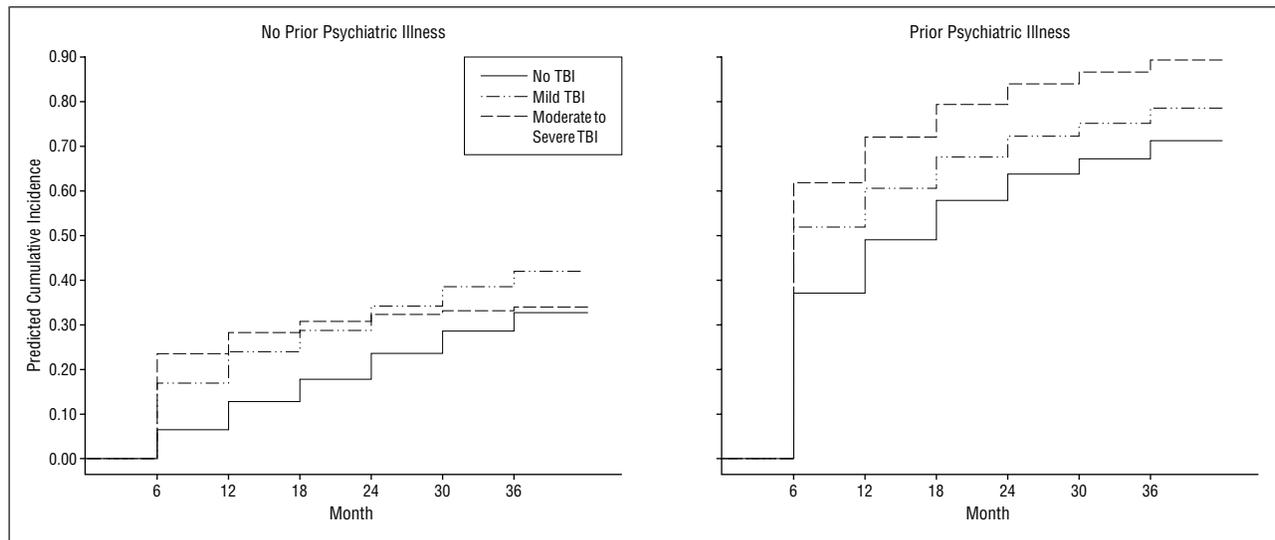
Estimated proportions of health maintenance organization enrollees 15 years or older with any psychiatric illness indicator. Estimates for each 6-month block are for the prior 6 months. Predicted proportions are for women aged 40 to 44 years with median index month (6), median log cost, and no comorbid injuries. The lines for the 3 traumatic brain injury (TBI) exposure groups overlap between the reference date and the end of the first 6-month period, for which the observed incidence is 0 by definition.

estimated OR for psychotic disorder was greatest for moderate to severe TBI exposure. However, the OR estimate increased in subjects with moderate to severe TBI without a psychiatric history and in those who had mild TBI with a psychiatric history. Although substance abuse was rare among GHC enrollees, precluding stratification by TBI severity, the OR estimate was highest in the first year among subjects without a psychiatric history and in the second year in those with a psychiatric history.

In examining the major psychiatric illness indicators (diagnosis, prescription, utilization, and any indicator), the OR estimates for prevalent psychiatric illness conferred by mild TBI were individually statistically significant at 18 of 24 time points compared with 4 of 24 time points in the moderate to severe cohort. Among subjects with mild TBI without prior psychiatric illness, the estimates tended to decrease; however, in those with prior psychiatric illness, they tended to increase.

INCIDENCE AND RR FOR PSYCHIATRIC ILLNESS

The **Figure** shows the predicted cumulative incidence of any psychiatric illness within the TBI exposure groups for subjects with and without prior psychiatric illness. As expected, those with prior psychiatric illness had a higher incidence of subsequent psychiatric illness. This may explain the smaller OR and RR estimates (**Table 3**) for the additional effect due to TBI in this subgroup. Subjects who sustained a moderate to severe TBI also developed subsequent psychiatric illness at a higher rate, particularly in the first 6 months. However, among those without prior psychiatric illness, there seems to be a "catch-up" phenomenon whereby those with no TBI and those with mild TBI close the gap in proportions at later time points. This may explain OR and RR estimates that are lower than 1 at the later time points.

Adjusted estimates of the RR for incidence of affective, psychotic, and substance abuse disorders and any psychiatric illness indicator are presented in Table 3. Statistically significant effects of TBI on incident affective disorders were seen in patients without prior psychiatric illness, particularly in the mild TBI cohort. However, RR estimates for incident psychotic disorders were greater for the moderate to severe TBI cohort compared with subjects who had mild TBI; CIs were large owing to the rarity of the outcomes. The estimated RR for substance abuse was significant in the group with no prior psychiatric illness, with individual significance continuing through month 30. In the category of any psychiatric illness, the estimated increase in risk of subsequent psychiatric illness conferred by TBI was initially greater in subjects without prior psychiatric illness and in those with moderate to severe TBI compared with mild TBI. However, nominally statistically significant risks were sustained longer in the mild TBI group.

For subjects without prior psychiatric illness, being female (adjusted RR=1.2; 95% CI, 1.1-1.4) and having higher costs in the prior year (adjusted RR=1.4; 95% CI, 1.3-1.6, for groups differing by a factor of 10) were associated with a higher risk of any psychiatric illness indicator in the 3 years following TBI. For those with prior psychiatric illness, sex was not a significant risk factor, but costs were (adjusted RR=1.3; 95% CI, 1.1-1.6). Comorbid injuries were not associated with higher risk of psychiatric illness in either psychiatric history stratum. Prior psychiatric illness significantly modified the effect of TBI on subsequent psychiatric illness (P=.04) and was also a strong predictor of subsequent psychiatric illness (P<.001). The RRs for any psychiatric illness in the 3-year follow-up period for prior vs no prior psychiatric illness were 2.9 (95% CI, 2.4-3.3) for the TBI-unexposed group, 2.5 (95% CI, 2.0-3.1) for the mild TBI group, and 3.0 (95% CI, 1.7-5.0) for the moderate to severe TBI group.

Table 3. Estimated TBI vs No TBI Relative Risks and 95% Confidence Intervals for Incident Psychiatric Illness Indicators in the 3 Years After TBI Among HMO Enrollees 15 Years or Older*

Psychiatric Indicator	P Value for Any Effect of TBI	P Value for Trend	1-6 mo	7-12 mo	13-18 mo	19-24 mo	25-30 mo	31-36 mo
Affective disorder								
No prior psychiatric illness	<.001	.03						
Mild TBI			2.7 (1.5-4.8)†	2.2 (1.4-3.6)†	1.9 (1.3-2.6)†	1.6 (1.2-2.1)†	1.3 (0.9-1.9)	1.1 (0.6-1.9)
Moderate to severe TBI			1.0 (0.1-7.6)	4.6 (1.8-11.7)†	2.2 (1.0-4.9)†	1.1 (0.4-3.0)	0.5 (0.1-2.3)	0.2 (0.0-1.9)
Prior psychiatric illness	.78	NA						
Mild TBI			1.3 (0.9-1.19)	1.0 (0.6-1.7)	1.1 (0.7-1.6)	1.1 (0.8-1.7)	1.2 (0.7-2.1)	1.4 (0.7-2.7)
Moderate to severe TBI			1.1 (0.5-2.5)	0.4 (0.1-2.6)	0.6 (0.2-2.0)	0.7 (0.3-1.9)	1.0 (0.4-2.8)	1.4 (0.3-5.9)
Psychotic disorder								
No prior psychiatric illness	.07	NA						
Mild TBI			2.6 (0.8-8.6)	3.0 (0.9-9.3)	2.5 (1.0-6.0)†	2.1 (1.0-4.4)	1.7 (0.8-4.0)	1.5 (0.5-4.3)
Moderate to severe TBI			2.0 (0.2-17.6)	9.2 (2.2-38.7)†	6.1 (1.8-20.3)†	4.0 (1.1-14.5)†	2.7 (0.5-13.4)	1.8 (0.2-14.3)
Prior psychiatric illness	.04	.76						
Mild TBI			1.6 (0.8-3.2)	1.4 (0.5-3.9)	1.7 (0.8-3.5)	2.0 (1.0-3.9)	2.3 (1.0-5.4)	2.7 (0.8-8.6)
Moderate to severe TBI			3.5 (1.5-8.1)†	1.2 (0.2-8.4)	2.0 (0.5-8.1)	3.1 (1.0-10.1)	5.0 (1.3-19.3)†	8.0 (1.3-50.1)†
Substance abuse								
No prior psychiatric illness	<.001	.17						
Any TBI			6.3 (3.1-12.8)†	2.0 (1.0-4.0)†	1.9 (1.2-3.2)†	1.8 (1.2-2.8)†	1.7 (1.1-2.8)†	1.6 (0.8-3.3)
Prior psychiatric illness	.20	NA						
Any TBI			2.3 (1.1-4.8)†	1.4 (0.6-3.4)	1.3 (0.7-2.5)	1.2 (0.7-2.1)	1.1 (0.5-2.2)	1.0 (0.4-2.6)
Any psychiatric illness indicator								
No prior psychiatric illness	<.001	<.001						
Mild TBI			2.8 (2.1-3.7)†	1.3 (0.9-1.7)	1.2 (1.0-1.5)	1.2 (0.9-1.4)	1.1 (0.8-1.4)	1.0 (0.7-1.5)
Moderate to severe TBI			4.0 (2.4-6.8)†	1.5 (0.7-3.2)	0.9 (0.5-1.8)	0.6 (0.2-1.4)	0.3 (0.1-1.3)	0.2 (0.0-1.2)
Prior psychiatric illness	.005	.24						
Mild TBI			1.6 (1.2-2.0)†	0.9 (0.6-1.5)	1.0 (0.7-1.4)	1.0 (0.7-1.5)	1.1 (0.6-1.8)	1.1 (0.5-2.3)
Moderate to severe TBI			2.1 (1.3-3.3)†	1.5 (0.5-4.3)	1.5 (0.76-3.3)	1.6 (0.7-3.6)	1.7 (0.5-5.6)	1.7 (0.3-9.8)

Abbreviations: HMO, health maintenance organization; NA not applicable; TBI, traumatic brain injury.

*Data are adjusted for age, sex, reference date, comorbid injuries, and logarithm of costs in the year prior to the reference date. *P* values for any effect of TBI represent tests for overall effect of TBI for each prior psychiatric illness stratum during the 3-year follow-up period. *P* values for trend represent nested tests for trend in relative risk.

†Represents statistical significance at *P*<.05 at the specific time point.

COMMENT

We found that the risk of psychiatric illness, ascertained using several different indicators, was significantly increased following both mild and moderate to severe TBI in an adult HMO population. The magnitude and pattern of risk for subsequent psychiatric illness was modified by whether patients had a history of psychiatric illness in the year prior to their TBI. The already high risk of subsequent psychiatric illness in those with prior psychiatric illness may have diluted the increase in risk due to TBI, accounting for the smaller RR estimates in this subgroup. The risk of incident psychiatric illness was greatest in the first 6 to 12 months after TBI. In patients without prior psychiatric illness, decreasing trends were generally evident in RR estimates across time. A few studies found that psychiatric history was a significant risk factor for psychiatric problems after TBI.[1,11]

The literature on the relationship between TBI severity and subsequent psychiatric disorders is inconsistent, with study findings ranging from positive or inverse to no relationship.[2,10-14,23,24] We found that although survivors of moderate to severe TBI with no prior illness had a greater initial elevation in risk of any psychiatric illness, the mild TBI cohort exhibited a more prolonged pattern of elevated risk that eventually surpassed that of the moderate to severe cohort. Our findings also suggest that the TBI-associated RR for incident psychiatric illness is highest shortly following injury in persons with no psychiatric history, whereas it may remain high or even increase in subsequent years in persons with prior illness.

Some psychiatric illnesses appear to persist after TBI. Table 2 shows sustained elevation and a delayed increase in ORs for certain prevalent psychiatric illnesses, particularly in patients who have mild TBI with prior psychiatric illness. This population often perplexes health care professionals with their persistent symptoms and disability.[25-27] The TBI may precipitate the expression of underlying psychiatric distress, which may initially appear as nonspecific somatic or postconcussive symptoms such as headache, decreased memory, or irritability.[2,28] Our data suggest the need to control for medical comorbidity when studying the relationship between TBI and psychiatric illness, although comorbid injuries did not confound this relationship.

Affective disorders were common in this HMO population with TBI. We found that patients with mild TBI had higher ORs and RRs for affective disorders than those with moderate to severe TBI. This finding is consistent with various reports that more severe TBI is not necessarily associated with a higher risk of depression.[2,10,12,13,24] Moreover, patients with a psychiatric history who sustained mild TBI had higher ORs for preva-

lent psychiatric illness in the second and third years after TBI compared with the first year. This subgroup seems to be at particularly high risk for persistent psychiatric morbidity.

There was also a pattern of delay for the relatively higher risk of psychotic disorder in TBI-exposed subjects with prior psychiatric illness. A psychotic disorder in the first year after moderate to severe TBI may represent delirium due to the TBI or to intensive care unit–related psychosis. However, RR increases in the second and third years in those with prior psychiatric illness, particularly with moderate to severe TBI, are consistent with findings from other reports of delayed psychosis after TBI.[3,29]

Substance abuse disorders have been found to initially decrease after moderate to severe TBI, but there may be a delayed increase after the first year.[4,30] Our OR data replicated this finding in patients with prior psychiatric illness, although those with no prior psychiatric illness had an initial increase that decreased with time. Relative risk estimates of incident substance abuse consistently decreased across time for both groups. The different OR patterns of substance abuse between those with and without prior psychiatric illness may be related to an initial heightened emphasis on alcohol abstinence among health care professionals toward prior substance abusers. Nearly all substance abusers with TBI had mild TBI.

From our findings, we hypothesize that psychiatric symptoms arising immediately after TBI may be etiologically related to the neurophysiological effects of the injury, as supported by an early relationship between TBI severity and psychiatric risk. However, other factors such as psychological vulnerability (eg, personality and attribution styles), self-awareness of deficits, social influences, and secondary gain may play subsequent roles, particularly in subjects with prior psychiatric illness and mild injury. These possible etiological correlates, which have been proposed by other investigators,[8,23,31,32] likely interact in complex ways and require further research.

Psychiatric diagnosis, prescriptions filled, and health care utilization were all recorded at the time of medical service. Therefore, possible bias due to differential recall between TBI-exposed and TBI-unexposed subjects was eliminated. Because of the completeness and uniformity of the database, the determination of psychiatric illness was not subject to the limitations of incomplete recall or information bias.[33] Also, because providers at GHC are not influenced by the risk that a psychiatric diagnosis may not receive full reimbursement, as may be the case in fee-for-service settings, reporting bias of psychiatric diagnoses owing to reimbursement rates was unlikely. Use of a comparison group allowed us to control for baseline fluctuations in psychiatric illness detection; there was a 1% increase per year in overall psychiatric illness in the comparison group during the 4-year study period, perhaps representing improved detection and coding efforts at GHC.

A limitation of this study is the possible lack of precision in TBI exposure measurement. Our study population had a higher proportion of women than other TBI populations; this may have been an ambulatory population with more women reporting mild TBI. This higher representation of women may have afforded the statistical power to find the association between female sex and risk of subsequent psychiatric illness. Insurance type was used as a proxy measure for socioeconomic status. Although it was not shown to be a confounder, there could be residual confounding by socioeconomic status that was not controlled for in the analyses.

Incident RR estimates that decline lower than 1, particularly for moderate to severe TBI exposure, suggest that TBI may advance the identification of psychiatric illness in groups that might have been diagnosed at a later date. The plot for no prior psychiatric illness best depicts this catch-up effect. Because individuals with TBI may visit their physician more frequently, such as for postconcussive symptoms, it is more likely that a psychiatric illness in these persons would be recognized and recorded; a person without TBI may not go to a GHC clinic, and thus a psychiatric illness might not be recognized. Those with TBI would be more likely to have a subsequent TBI,[34] further increasing the risk of psychiatric illness; therefore, our RR estimates may include risk associated with subsequent TBIs.

The method used to determine psychiatric illness may have been subject to misclassification. Psychiatric diagnoses assigned by non–mental health professionals may be less sensitive and specific than those made by mental health professionals. Subjects could have been incorrectly assigned to diagnostic categories or may not have received a diagnosis when a psychiatric illness was present. However, this potential nondifferential misclassification due to type of specialist would likely bias TBI effect estimates toward the null.

Moderate to severe TBI–exposed subjects were at higher risk for dropout, particularly resulting from higher injury-related fatality, than those with mild TBI and comparison subjects. It is possible that losses to follow-up may have affected the estimates of ORs and RRs, especially for later periods. When comparing these results with those in other populations, consideration should be given to differences in the distributions of disenrollment, death, and exposure severity within categories. The incident RR estimates may have been more resistant to disenrollment effects because they relied on incident vs prevalent psychiatric illness.

Despite these limitations, we found both mild and moderate to severe TBI to be significant risk factors for subsequent psychiatric illness. Evidence of psychiatric illness in the year prior to TBI significantly modified this relationship. Subjects with a psychiatric history had a substantially greater risk of post-TBI psychiatric illness. Their RR due to the effect of TBI was smaller compared with those without prior illness; the already high incidence among controls with prior illness left little room for other effects. The clinical implications of this study include evidence that patients should be screened for psychiatric morbidity within the first 6 to 12 months following TBI. However, continued vigilance for up to 3 years, particularly in patients with mild TBI and prior psychiatric illness, is also supported. Health care professionals working in primary care settings may have the best opportunity to identify and treat psychiatric morbidity in patients with mild TBI. It is also important to inquire about psychiatric history before attributing psychiatric symptoms to TBI.

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