Prevalence of Medical and Psychiatric Comorbidities Following Traumatic Brain Injury

Flora M. Hammond, MD, **John D. Corrigan, PhD**, **Jessica M. Ketchum, PhD**, **James F. Malec, PhD**, **Kristen Dams-O'Conner, PhD**, **Tessa Hart, PhD**, **Thomas A. Novack, PhD**, **Jennifer Bogner, PhD**, **Marie N. Dahdah, PhD**, and **Gale G. Whiteneck, PhD**

Indiana University School of Medicine, Indianapolis

Abstract

Objective: To examine the prevalence of selected medical and psychiatric comorbidities that existed prior to, or up to 10 years following, traumatic brain injury (TBI) requiring acute rehabilitation.

Design: Retrospective cohort.

Setting: Six TBI Model Systems centers.

Participants: 404 participants in the TBI Model System National Database who experienced TBI 10 years prior.

Interventions: Not applicable.

Main Outcome Measure: Self-reported medical and psychiatric comorbidities and the onset time of each endorsed comorbidity.

Results: At 10 years post-injury, the most common comorbidities developing post-injury, in order, were: back pain, depression, hypertension, anxiety, fractures, high blood cholesterol, sleep disorders, panic attacks, osteoarthritis, and diabetes. Comparing those 50 years and older to those less than 50 years, diabetes (OR = 3.54; $p = 0.0016$), high blood cholesterol (OR = 2.04; $p = 0.0092$), osteoarthritis (OR = 2.02; $p = 0.0454$), and hypertension (OR = 1.84; $p = 0.0175$) were significantly more prevalent in the older cohort while panic attacks (OR = 0.33; $p = 0.0022$) were significantly more prevalent in the younger cohort. No significant differences in prevalence rates between the older and younger cohorts were found for back pain, depression, anxiety, fractures, or sleep disorders.

Conclusions: People with moderate-severe TBI experience other medical and mental health comorbidities during the long-term course of recovery and life after injury. The findings can inform further investigation into comorbidities associated with TBI and the role of medical care, surveillance, prevention, lifestyle, and healthy behaviors in potentially modifying their presence and/or prevalence over the life span.

Corresponding Author: Flora M. Hammond, MD, Indiana University School of Medicine, 4141 Shore Dr, Indianapolis, IN 46254 (flora.hammond@rhin.com).

Keywords

prevalence; traumatic brain injury; rehabilitation; outcomes; medical conditions; comorbidities

Introduction

A growing body of evidence suggests that individuals who survive a traumatic brain injury (TBI) are at elevated risk for long-term chronic health conditions.[1–3] Persons who experience TBI may have one or more pre-existing medical comorbidities at the time of injury; some evidence suggests premorbid health problems (such as alcohol use and depression) can be a risk factor for TBI, particularly among older adults.[4–9] Other medical conditions may occur simultaneously with TBI, such as orthopedic trauma, or develop afterward as a direct consequence of the TBI, such as epilepsy. Still other medical comorbidities may begin months or years following injury, and their associations with the TBI may be difficult to distinguish from age-related health changes. Health comorbidities, regardless of time of onset, can further complicate recovery from TBI and long-term health maintenance, increase health care costs, and shorten life expectancy.[10]

Comorbidities strongly associated with TBI include chronic pain,[11] headaches[12–14] neuroendocrine dysfunction,[15,16] fatigue or sleep disturbance including insomnia,[17] incontinence or other urinary disturbance,[18] new onset stroke,[19] and posttraumatic seizures or epilepsy.[20] In fact, in comparison to uninjured control groups, studies have suggested that individuals with TBI have more than twice the rates of pain,[21] growth hormone deficiency,[22] insomnia and fatigue,[23] new onset stroke,[19] urinary incontinence,[24] and epilepsy.[25] A review of published data was convened by the National Academy of Medicine to assess the association between TBI and long-term health in civilian or military populations, spanning all injury mechanisms and severities.[26,27] Sufficient evidence was found that moderate-severe TBI is associated with depression, aggression, psychosis, endocrine dysfunction, Alzheimer-type dementia, and parkinsonism emerging years after injury, as well as premature death. Moderate-severe TBI and open or penetrating TBI was found to be a cause of unprovoked seizures. Many studies investigating TBI and dementia have revealed that those with a history of TBI compared to those without TBI history tended to have significantly higher rates of diabetes, hypertension, myocardial infarction, cerebrovascular disease, peripheral vascular disease, chronic pulmonary disease, renal disease, psychiatric diagnoses, and substance use disorders, and they demonstrate slower recovery following TBI.[9,28–30]

Individuals with moderate-severe TBI may also be at ongoing risk of rehospitalization and premature death. Causes of rehospitalization and mortality vary over time post-injury. Longitudinal modeling of rehospitalization following moderate-severe TBI suggests rehospitalization risk begins to increase around 5 years post-injury.[31] Common reasons for rehospitalization after TBI include infectious, neurological, neurosurgical, traumatic, psychiatric events, and orthopedic disorders, as well as medical reasons typical for the general population.[32–34] People with moderate-severe TBI are at risk of the same comorbidities as the general population while also at uniquely higher risk for death due to

seizure, accidental poisoning, infection (aspiration pneumonia, pneumonia, septicemia), respiratory disorder, suicide, homicide, mental/behavioral disorder, nervous system conditions, falls, vehicular collisions, and other external causes of injury and poisoning.[10]

Previous studies have investigated cohorts with diverse characteristics, making rates of comorbidities difficult to compare across samples. Moreover, most prior studies have been cross-sectional, leaving it unknown whether the medical comorbidities pre- or post-dated the TBI. Therefore, the prevalence rates of comorbidities that co-occur with TBI remain unclear.

Individuals living with the effects of TBI face multiple challenges to effective health management, including cognitive impairment, limited financial resources, reduced participation in society, and variable access to specialized care,[35–38] making it particularly difficult to manage multiple chronic health comorbidities. Whether those health problems are pre-existing or arise after injury, the intersection of TBI-related impairments with chronic health problems can have a mutually exacerbating effect on overall health and life quality. Yet, it is important to know more about the nature and timing of the onset of medical comorbidities among individuals with TBI to inform the development of optimal health management and prevention strategies. The purpose of this study is to assess the prevalence of selected medical and psychiatric comorbidities, as well as the timing of onset in relation to the index TBI, using a cohort of the TBI Model Systems (TBIMS) longitudinal National Database participants who had survived to 10 years post-injury. The longitudinal nature of this study with a focus on timing of onset and inclusion of both medical and psychiatric comorbidities offers a unique contribution to the literature. Prior studies have generally examined the associations between TBI and one or two other medical or psychiatric conditions among patients seen in a single center. This study builds on this prior research by examining 44 medical and psychiatric conditions that have been previously shown or hypothesized to be associated with TBI in a large sample drawn from multiple centers representing diverse regions of the continental United States.

Methods

Participants

Participants included individuals within the TBIMS National Database at six TBIMS centers: The Ohio State University (Columbus, OH); University of Texas Southwest Medical school/Baylor Scott and White Institute for Rehabilitation (Dallas, TX); Craig Hospital (Englewood, CO); Icahn School of Medicine at Mount Sinai (New York, NY); Moss Rehabilitation Research Institute (Elkins Park, PA); University of Alabama at Birmingham (Birmingham, AL). Each center received approval for human subjects research from their respective Institutional Review Boards. The TBIMS National Database enrollment criteria include: age at least 16 years at time of injury; moderate-severe TBI [defined as post-traumatic amnesia greater than 24 hours, trauma-related intracranial neuroimaging abnormalities, loss of consciousness exceeding 30 minutes, or GCS in the emergency department of less than 13]; and received acute care hospitalization within 72 hours followed by inpatient rehabilitation in designated TBIMS facilities. An additional inclusion criteria for the current study was that participants needed to be eligible for their 10-year follow-up window between 7/1/2013 and 9/30/2017 and had FIM™ data collected during at least 2 of

the three prior follow-up interviews (at 1, 2, and 5-years post-injury); the FIM data criterion was used for a different investigation with the same cohort. Eligible participants were consecutively enrolled in this study when they were contacted for their 10-year TBIMS telephone follow-up interview.

Outcome Measures

Medical and Mental Health Comorbidities Interview (MMHCI).—The MMHCI interview recorded the presence of 44 medical and mental health comorbidities during an individual's lifetime, and if present, whether the diagnosis occurred before or after the TBI that qualified them for TBIMS participation. The interview was modeled after national health surveys, using the National Health and Nutrition Examination Survey (NHANES) for the medical comorbidities and the National Comorbidity Survey Replication (NCS-R) for the mental health comorbidities.[39] All items used the stem "Has a doctor ever told you that you had …". The national survey questions were utilized given their widespread use in the general population. The 44 comorbidities were chosen by the investigators based on those conditions collected through the two national survey tools; investigators' clinical experience in TBI; and information gleamed through prior TBI research suggesting a higher than normal rate after TBI, uncertainty about the relationship with TBI, or the possibility to screen and/or treat the condition with potential to positively impact life after TBI.

Procedures

Participants were asked the MMCHI questions after the standard 10-year follow-up interview. For MMHCI comorbidities endorsed by the respondent, participants were asked whether the comorbidity was diagnosed before, at the same time, or after their TBI (the index TBI that occurred 10 years prior to this interview). Per TBIMS follow-up interview protocols, information was obtained from the best source, either the participant with TBI or a significant other. Missing data on the medical comorbidities ranged from 0 to 2.5% (0 to 10 participants).

Statistical Analysis

All data was analyzed using SAS v.9.4[40] assuming a 5% level of significance unless otherwise noted. The prevalence of each of the 44 medical comorbidities was estimated along with 95% confidence intervals (CIs). Prevalence rates for each comorbidity were estimated in three different time frames: (1) those having the comorbidity diagnosed before the index TBI, (2) those having the comorbidity diagnosed at either the same time or after their TBI, and (3) those having the comorbidity diagnosed ever in their lifetime (before, same time, or after their TBI). Each of these ways of defining onset corresponds with potentially important parameters for informing proactive medical management in the years after serious TBI. Finally, the percentages and 95% CIs of the 10 most prevalent medical comorbidities occurring at the same time or after TBI were estimated for participants in two age groups: those with 10-year post-injury follow-ups occurring before age 50, and those with 10 year follow-up at age 50 or older. Logistic regression models were used to compare prevalence rates between the older and younger cohorts. Prior publications have utilized varied age cut-offs in the comparison of younger to older age cohorts in TBI, with the most

common cut-points being 50, 60, and 65 years.[41] Fifty years was chosen for the present study based on literature suggesting this age cohort has higher rates of comorbidities and complications, including deterioration in cognitive and emotional function.[42–47]

Results

Data were collected from 404 participants. Characteristics of the sample are shown in Table 1.

The estimated prevalence rates before TBI, at the same time or after TBI, and ever (before, same time or after TBI) for the medical and psychiatric comorbidities and the associated 95% confidence intervals are summarized in Table 2. The most common comorbidities occurring ever in participants' lifetimes, in order, were hypertension, back pain, depression, high blood cholesterol, anxiety, and fractures (hip/wrist/spine) (see Table 3). Each of these comorbidities affected approximately one-fourth to one-third of the cohort. There was a significant drop in prevalence from fractures (~ 23%) to the next most common, osteoarthritis, which affected less than 15%.

The 10 most common comorbidities developing at the same time or after injury largely reflected those most common in one's lifetime. One exception was alcoholism, which was among the 10 most prevalent comorbidities before TBI, but dropped off the list at the same time or after TBI. It was instead replaced by diabetes at the time of/after TBI. For hypertension, high blood cholesterol, depression and anxiety, more than half of participants who had ever had the comorbidities developed them at the same time or post-injury; two-thirds or more of those with sleep disorders, diabetes and panic attacks were diagnosed at the same time or post-injury. The only comorbidity diagnosed in more than 10% of cases before the TBI was hypertension; comorbidities diagnosed before the TBI in 5–10% of the cases were hay fever, high blood cholesterol, alcoholism, back pain, depression, attention-deficit (hyperactivity) disorder, and anxiety.

Table 4 displays the 10 most prevalent medical and psychiatric comorbidities diagnosed at the same time or after the TBI separately for the younger and older participants. Odds ratios were computed to express the relative magnitude of the prevalence of comorbidities in the older group compared to the prevalence in the younger group. Diabetes (OR = 3.54; p = 0.0016), high blood cholesterol (OR = 2.04; p = 0.0092), osteoarthritis (OR = 2.02; p = 0.0454), and hypertension (OR = 1.84; p = 0.0175) were significantly more prevalent in the older cohort, while panic attacks (OR = 0.33; p = 0.0022) were significantly more prevalent in the younger cohort. There were no significant differences in prevalence rates between the older and younger cohorts for back pain, depression, anxiety, fractures, or sleep disorders.

Discussion

This study represents an initial attempt to characterize the medical and psychiatric comorbidities experienced by people who sustained TBI severe enough to warrant inpatient rehabilitation, and who have survived for at least 10 years. One-fifth of our sample reported a diagnosis of anxiety, depression, hypertension, or back pain. Other comorbidities with high prevalence included high cholesterol, fractures, sleep disorder, and panic attacks. The

presence of all of these comorbidities doubled from before TBI to time of TBI or after. Diagnoses of alcoholism did not substantially increase after TBI.

While disease onset post-injury does not indicate a causal relationship with TBI (i.e., 10 years of aging had occurred at the time of assessment), there is reason to suspect that some later-developing comorbidities are causally related to the injury. TBI not only disrupts central nervous system (CNS) function, but can potentially have short and long-term effects on the autonomic nervous system (ANS)[48–52] as well. Chronic inflammation, insulin resistance, and metabolic syndrome are consequences of CNS and ANS dysfunction that can lead to the development of chronic disease.[53–57] Disruption of ANS (in addition to the CNS) is also associated with the dysregulation of emotions and behavior,[58,59] which may be sufficiently severe to be diagnosed as a psychiatric disorder. Moreover, TBI-related cognitive and behavioral symptoms may pose challenges for health self-management such that a TBI influences medical health through non-biological pathways. Regardless of causality, however, interventions currently known to help prevent the most likely comorbidities should be recommended, including those targeting exercise, diet, and stress management, as well as treatments supporting the maintenance of meaningful and pleasurable activity in the community.

The prevalence rates for comorbidities first occurring after TBI are essentially incidence rates over the decade between injury and the 10-year follow-up data collection. Four of the 10 most frequent comorbidities occurring in the first decade after the TBI were significantly more frequent in older individuals than younger individuals. During the decade after TBI, the new onset diabetes rate was 4.3% for the younger group (less than age 40 at the start of the decade and less than age 50 at the end of the decade) compared to 13.6% for the older group (age 40 and older at the start of the decade and age 50 and older at the end of the decade). This is only slightly higher than new onset diabetes in the general population (3.1% per decade for age 18–44, 10.9% per decade for age 45–64, and 9.6% per decade for age 65 and over).[60] Since the TBI and general population rates both increase sharply with age but do not differ substantially from each other, diabetes seems to be more strongly associated with aging than with TBI.

New onset hypertension, high blood cholesterol, and osteoarthritis all occurred about twice as frequently in the older group as in the younger group, indicating they too may be associated with age. In 2013–2014, 55.9% of community-dwelling adults aged 65 and older in the United States reported having a diagnosis of hypertension, 29.4% reported heart disease, 20.8% reported diabetes, and 49% reported having arthritis.[61,62] Data from the National Health and Nutrition Examination Survey indicate that 70% of older adults have hypertension, compared to only 32% for adults aged 40–59 years.[63] Given the association of these conditions with age in the general population combined with this study's findings of similar age relationships with these conditions may suggest the rates observed herein are reflective of aging more so than TBI-related health changes. Because the effects of a TBI are overlaid upon the effects of aging, their relative contributions cannot be readily disentangled.

On the other hand, new onset panic attacks were three times more frequent in the decade after TBI in the younger group than in the older group. This finding highlights the

importance of screening for depression and anxiety disorders and specifically for panic attacks after TBI, particularly among relatively younger TBI survivors, with referral of positive cases for further evaluation and treatment. No significant age effects were identified for back pain, depression, anxiety, fractures, or sleep disorders, suggesting a potentially stronger association with TBI than aging. The absolute and relative magnitude of these comorbidity rates provides initial insight into the association these comorbidities have with the combination of TBI and aging.

Our findings highlight the need for careful screening for comorbid comorbidities in survivors of moderate-severe TBI. Psychiatric comorbidities including anxiety and depression are strongly comorbid with TBI, as suggested by prior TBI Model System research,[64,65] and warrant special attention for prevention as well as detection and treatment. With regard to medical comorbidities, people with moderate-severe TBI frequently have long-term cognitive dysfunction that may interfere with the ability to manage those comorbidities, e.g., to take medications accurately and to arrange follow-up appointments. Healthcare providers may need to engage relatives in health management tasks and/or provide extra supports such as written information and reminders.

Limitations:

In this study, as is the case in most longitudinal studies of health conditions, the outcome required the use of self-report, raising questions of accuracy. While it was not possible to verify self-report against medical records in the current investigation, a recent study using the TBIMS cohort showed good to excellent test-retest reliability for the same questions about health conditions when readministered.[66] Studies have found positive congruence of self-report and physician ratings and stability of ratings overtime, with occurrences of incongruity to be towards an individual overestimating one's health and self-report better predicting future physician ratings.[67] There may be other conditions common among the TBI population not represented in this study as the interview included a only subset of possible conditions. The TBIMS is comprised of specialized centers for TBI inpatient rehabilitation, and thus, our findings may not generalize to individuals with TBI who are treated at less specialized centers or who do not receive inpatient rehabilitation. It is important to note that this study does not assess for causal relationships between the TBI and the subsequent comorbidities. No control (non-injured) group was available for comparison. Comparisons to the literature on the general population are challenging for many reasons including potential population differences, and limited general population prevalence data for individuals younger than 65 years. We did not exclude participants who had previously incurred TBI, for whom some of the comorbid conditions identified as occurring prior to a TBI may have occurred after a (previous) TBI. Finally, it is important to consider that the current study only included individuals who survived at least 10 years post moderate-severe TBI, and therefore excludes those who likely experienced the most significant increases in TBI-related disease morbidity. Results from the current study and their implications for the chronic disease management needs among TBI survivors should be interpreted in this context.

Directions for future research:

Since only individuals who received inpatient rehabilitation were included in our sample, further examination of differences in comorbidities between those who received inpatient rehabilitation and those that did not is of interest. Differences in the types of comorbidities and their prevalence between a subsample of TBI survivors with multiple TBIs prior to index injury and those with a single TBI would also be valuable, particularly if the presence of multiple TBIs served to modify the above treatment suggestions. Controlled studies that include a cohort without TBI are needed to evaluate the possibility of causal relationships between TBI and subsequent comorbidities. Of particular interest in this regard is exploration of the possible role of disruption of CNS and ANS function by TBI in the development of chronic disease through either metabolic and/or behavioral pathways. Future research is also needed to evaluate the potential positive impact of a chronic disease management approach to TBI that includes surveillance, prevention and treatment of medical and psychiatric comorbidities on community re-integration and satisfaction with life in the long term.

Conclusion

Individuals recovering from a moderate-severe TBI are at risk for medical and mental health comorbidities during long-term course of recovery and life after injury. The findings can inform further investigation into comorbidities associated with TBI and the role of medical care, surveillance, prevention, lifestyle and healthy behaviors in potentially modifying their presence and/or prevalence over TBI survivors' life span.

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Table 1:

Summary of Sample Characteristics ($N = 404$)

Continuous Characteristics	N	Mean (SD)	Median (IQR)
Age at Injury (years)	404	37.8 (16.0)	37 (23 – 49.5)
Age at 10 year FU (years)	404	47.9 (15.9)	48 (33 – 59)
Glasgow Coma Scale	304	9.5 (4.7)	9 (5 – 14)
FIM Motor Discharge	403	69.2 (18.1)	72 (60 – 83)
FIM Cognitive at Discharge	403	23.5 (6.6)	25 (20 – 28)
Post Traumatic Amnesia (days) [†]	388	31.7 (31.7)	23 (10.5 – 44)
Time to Follow Commands (days) [†]	400	10.5 (20.2)	3 (0.5 – 12)
Rehabilitation Length of Stay (days) [†]	404	26.1 (19.7)	21 (13 – 33)

Nominal Characteristics	N	Count (Percent)
Sex	404	
Female		97 (24.0%)
Male		307 (76.0%)
Race	404	
White		280 (69.3%)
Black		78 (19.3%)
Hispanic		31 (7.7%)
Other		15 (3.7%)
Marital Status at injury	404	
Married		141 (34.9%)
Not Married		263 (65.1%)
Education Level	404	
Less than High School		138 (34.2%)
High School		109 (27.0%)
Some College		91 (22.5%)
College		66 (16.3%)
Employment at injury	404	
Employed		277 (68.6%)
Not Employed		127 (31.4%)

IQR = interquartile range, SD = standard deviation, FU = follow-up

[†] Distributions markedly skewed thus median and IQR are more appropriate measures of center and spread than mean and SD

Table 2:

Prevalence of Medical Comorbidities Listed by Body System

	Before TBI			Same Time / After TBI			Ever		
	X / N	Percent	95% CI	X / N	Percent	95% CI	X / N	Percent	95% CI
Cardiovascular									
Hypertension	46/394	11.7	(8.5, 14.9)	79/394	20.1	(16.1, 24.0)	133/402	33.1	(28.5, 37.7)
Congestive Heart Failure	3/401	0.8	(0.0, 1.6)	5/401	1.2	(0.2, 2.3)	9/402	2.2	(0.8, 3.7)
Myocardial Infraction/Heart Attack	8/401	2.0	(0.6, 3.4)	7/401	1.7	(0.5, 3.0)	16/402	4.0	(2.1, 5.9)
Other Heart Conditions	16/398	4.0	(2.1, 6.0)	20/398	5.0	(2.9, 7.2)	40/402	10.0	(7.0, 12.9)
Stroke	2/401	0.5	(0.0, 1.2)	13/401	3.2	(1.5, 5.0)	16/402	4.0	(2.1, 5.9)
High Blood Cholesterol	31/398	7.8	(5.1, 10.4)	68/398	17.1	(13.4, 20.8)	101/401	25.3	(21.0, 29.5)
Endocrine									
Diabetes	10/402	2.5	(1.0, 4.0)	35/402	8.7	(5.9, 11.5)	45/402	11.2	(8.1, 14.3)
Goiter	0/401	0.0	-	1/401	0.2	(0.0, 0.7)	1/401	0.2	(0.0, 0.7)
Other Thyroid Disease	10/401	2.5	(1.0, 4.0)	11/401	2.7	(1.1, 4.3)	21/401	5.2	(3.0, 7.4)
Gastrointestinal									
Liver Disease	9/402	2.2	(0.8, 3.7)	10/402	2.5	(1.0, 4.0)	19/402	4.7	(2.6, 6.8)
Genitourinary									
Kidney Stones	13/400	3.3	(1.5, 5.0)	13/400	3.3	(1.5, 5.0)	26/400	6.5	(4.1, 8.9)
Musculoskeletal & Rheumatologic									
Rheumatoid Arthritis	8/401	2.0	(0.6, 3.4)	21/401	5.2	(3.0, 7.4)	30/402	7.5	(4.9, 10.0)
Osteoarthritis	18/400	4.5	(2.5, 6.5)	38/400	9.5	(6.6, 12.4)	58/402	14.4	(11.0, 17.9)
Fractures (Hip/Wrist/Spine)	19/400	4.8	(2.7, 6.8)	73/400	18.3	(14.4, 22.1)	93/401	23.2	(19.0, 27.3)
Back Pain	30/399	7.5	(4.9, 10.1)	87/399	21.8	(17.7, 25.9)	119/401	29.7	(25.2, 34.2)
Osteoporosis	4/401	1.0	(0.0, 2.0)	5/401	1.2	(0.2, 2.3)	9/401	2.2	(0.8, 3.7)
Lupus	4/401	1.0	(0.0, 2.0)	1/401	0.2	(0.0, 0.7)	5/401	1.2	(0.2, 2.3)
Neurologic									
Sleep Disorder	8/400	2.0	(0.6, 3.4)	47/400	11.8	(8.6, 14.9)	56/401	14.0	(10.6, 17.4)
Movement Disorder	0/401	0.0	-	3/401	0.7	(0.0, 1.6)	3/401	0.7	(0.0, 1.6)

	Before TBI			Same Time / After TBI			Ever		
	X / N	Percent	95% CI	X / N	Percent	95% CI	X / N	Percent	95% CI
Dementia	0/401	0.0	-	9/401	2.2	(0.8, 3.7)	9/401	2.2	(0.8, 3.7)
Ophthalmologic									
Cataracts	11/402	2.7	(1.1, 4.3)	26	6.5	(4.1, 8.9)	37	9.2	(6.4, 12.0)
Psychiatric or Mental Health									
Alcoholism	31/399	7.8	(5.1, 10.4)	14/399	3.5	(1.7, 5.3)	45/399	11.3	(8.2, 14.4)
Drug Addiction	19/398	4.8	(2.7, 6.9)	11/398	2.8	(1.1, 4.4)	30/398	7.5	(4.9, 10.4)
Anorexia	3/399	0.8	(0.0, 1.6)	0/399	0.0	-	3/399	0.8	(0.0, 1.6)
Bulimia	1/398	0.3	(0.0, 0.7)	0/399	0.0	-	1/399	0.3	(0.0, 0.7)
Other Eating Disorder	0/399	0.0	-	3/399	0.8	(0.0, 1.6)	3/399	0.8	(0.0, 1.6)
Anxiety	20/398	5.0	(2.9, 7.2)	78/398	19.6	(15.7, 23.5)	98/398	24.6	(20.4, 28.9)
Obsessive Compulsive Disorder	10/397	2.5	(1.0, 4.1)	7/397	1.8	(0.5, 3.1)	17/397	4.3	(2.3, 6.3)
Panic Attacks	10/397	2.5	(1.0, 4.1)	44/397	11.1	(8.0, 14.2)	55/398	13.8	(10.4, 17.2)
Post-Traumatic Stress Disorder	6/398	1.5	(0.3, 2.7)	24/398	6.0	(3.7, 8.4)	31/399	7.8	(5.1, 10.4)
Depression	25/396	6.3	(3.9, 8.7)	83/396	21.0	(16.9, 25.0)	109/397	27.5	(23.0, 31.9)
Bipolar Disorder	13/395	3.3	(1.52, 5.1)	23/395	5.8	(3.5, 8.1)	38/397	9.6	(6.7, 12.5)
ADD/ADHD	24/400	6.0	(3.7, 8.3)	18/400	4.5	(2.5, 6.5)	42/400	10.5	(7.5, 13.5)
Narcolepsy	0/399	0.0	-	3/396	0.8	(0.0, 1.6)	3/399	0.8	(0.0, 1.6)
Psychosis	3/398	0.8	(0.0, 1.6)	2/398	0.5	(0.0, 1.2)	5/398	1.3	(0.2, 2.4)
Schizophrenia	2/400	0.5	(0.0, 1.2)	2/400	0.5	(0.0, 1.2)	4/400	1.0	(0.0, 2.0)
Autism	1/400	0.3	(0.0, 0.7)	0/400	0.0	-	1/400	0.0	(0.0, 0.7)
Respiratory									
Asthma	20/404	5.0	(2.8, 7.1)	9/404	2.2	(0.8, 3.7)	29/404	7.2	(4.7, 9.7)
Emphysema	3/404	0.7	(0.0, 1.6)	1/404	0.2	(0.0, 0.7)	4/404	1.0	(0.0, 2.0)
COPD	2/404	0.5	(0.0, 1.2)	6/404	1.5	(0.3, 2.7)	8/404	2.0	(0.6, 3.3)
Chronic Bronchitis	9/402	2.2	(0.8, 3.7)	7/402	1.7	(0.5, 3.0)	16/402	4.0	(2.1, 5.9)
Hay Fever	32/402	8.0	(5.3, 10.6)	2/402	0.5	(0.0, 1.2)	34/402	8.5	(5.7, 11.2)
Cancer									
Skin Cancer	2/403	0.5	(0.0, 1.2)	7/403	1.7	(0.5, 3.0)	9/403	2.2	(0.8, 3.7)

| | Before TBI | | Same Time / After TBI | | Ever | |
	X / N	Percent	95% CI	X / N	Percent	95% CI	X / N	Percent	95% CI
Other Cancer	5/403	1.2	(0.2, 2.3)	11/403	2.7	(1.1, 4.3)	16/403	4.0	(2.1, 5.9)

X = number of patients reporting comorbidity, N = total number of patients with and without the comorbidity; CI = confidence interval

Sample size (N) varies due to missing data about specific medical comorbidities and onset (before, same time, or after TBI)

Abbreviations: ADD/ADHD = Attention Deficit Disorder / Attention Deficit Hyperactivity Disorder; COPD = Chronic Obstructive Pulmonary Disorder

Table 3:

Most Prevalent Medical Comorbidities

Before TBI (4.8% – 11.7%)	Same Time / After TBI (8.7% – 21.8%)	Ever (11.3% – 33.1%)
Hypertension 11.7%	Back Pain 21.8%	Hypertension 33.1%
Hay Fever 8.0%	Depression 21.0%	Back Pain 29.7%
High Blood Cholesterol 7.8%	Hypertension 20.1%	Depression 27.5%
Alcoholism 7.8%	Anxiety 19.6%	High Blood Cholesterol 25.3%
Back Pain 7.5%	Fractures (Hip/Wrist/Spine) 18.3%	Anxiety 24.6%
Depression 6.3%	High Blood Cholesterol 17.1%	Fractures (Hip/Wrist/Spine) 23.2%
Attention Deficit Disorder 6.0%	Sleep Disorder 11.8%	Osteoarthritis 14.4%
Asthma 5.0%	Panic Attacks 11.1%	Sleep Disorder 14.0%
Anxiety 5.0%	Osteoarthritis 9.5%	Panic Attacks 13.8%
Fractures (Hip/Wrist/Spine) 4.8%	Diabetes 8.7%	Alcoholism 11.3%

Table 4:

Percent of Cases Developing the 10 Most Frequent Medical Comorbidities in the Decade after TBI by Age Cohort

Same Time / After TBI

	<50 Years at 10 Year FU			50 Years at 10 Year FU			50 vs. <50 Years Comparison		
	X / N	Percent	95% CI	X / N	Percent	95% CI	OR	95% CI	p-value
Back Pain	47/209	22.5	(16.8, 28.2)	40/190	21.1	(15.2, 26.9)	0.92	(0.57, 1.48)	0.7288
Depression	48/207	23.2	(17.4, 29.0)	35/189	18.5	(12.9, 24.1)	0.75	(0.46, 1.23)	0.2549
Hypertension	32/207	15.5	(10.5, 20.4)	47/187	25.1	(18.9, 31.4)	1.84	(1.11, 3.03)	0.0175
Anxiety	40/208	19.2	(13.8, 24.6)	38/190	20.0	(14.3, 25.7)	1.05	(0.64, 1.72)	0.8469
Fractures (Hip/Wrist/Spine)	41/209	19.6	(14.2, 25.0)	32/191	16.8	(11.4, 22.1)	0.82	(0.49, 1.37)	0.4594
High Blood Cholesterol	26/210	12.4	(7.9, 16.9)	42/188	22.3	(16.3, 28.3)	2.04	(1.19, 3.48)	0.0092
Sleep Disorder	20/210	9.5	(5.5, 13.5)	27/190	14.2	(2.5, 9.2)	1.57	(0.85, 2.91)	0.1485
Panic Attacks	33/208	15.9	(10.9, 20.9)	11/189	5.8	(2.5, 9.2)	0.33	(1.16, 0.67)	0.0022
Osteoarthritis	14/210	6.7	(3.3, 10.1)	24/190	12.6	(7.9, 17.4)	2.02	(1.01, 4.04)	0.0454
Diabetes	9/211	4.3	(1.5, 7.0)	26/191	13.6	(8.7, 18.5)	3.54	(1.61, 7.76)	0.0016

X = number of patients reporting comorbidity, N = total number of patients with and without the comorbidity; CI = confidence interval; OR = odds ratio