Assessing Pre-Injury Health Status of Older Adults Who Have Sustained a Traumatic Brain Injury Compared to Matched Controls

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Abstract

Traumatic brain injuries (TBI) are a major public health burden with approximately 2 million individuals receiving hospital treatment annually. Large heterogeneity exists among individuals who sustain a TBI concerning the clinical representation and post-TBI disease progression. Additionally, older adults tend to have worse post-injury outcomes compared to younger cohorts and research surrounding this difference in clinical prognoses is limited. It remains unknown whether the decline seen post-TBI in older adults can be attributed to a continuation of a pre-existing disease process or whether the TBI was the causal trigger for the cognitive and physical decline. We performed conditional logistic regression analyses that examined pre-index injury physical and behavioral risk factors in inpatient TBI cases from the TBI Health Study compared to matched, non-TBI controls from MIDUS Study populations. We found the odds of having prior year, pre-index injury depression was 3.98 times higher in TBI cases compared to matched controls (OR=3.98, 95% CI=1.71-9.27, p-value=0.001). Subgroup analyses found the odds of having prior year exposure of depression was significant in *male* TBI cases versus male controls (OR=6.92, 95% CI=2.19-21.90, p-value=<0.001). Additionally, the odds of having prior year exposure of depression was significant in >=65 years TBI cases versus >=65 years controls (OR=6.54, 95% CI=1.72-24.84, p-value=0.006). While most prior year risk

factors reported insignificant differences between TBI cases and controls, the null findings suggest that post-TBI disease progression may *not* be a continuation of prior health conditions. In fact, traumatic brain injuries may be the causal agent for the cognitive and physical health decline experienced after injury. The public health significance is that these results will lead to better categorization of post-TBI disease progression, thus helping improve TBI prevention methods and traumatic brain injury clinical care.

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Preface

I would like to thank my essay mentors Dr. Kristen Dams-O'Connor, Dr. Andrea Rosso, Dr. Ada Youk, and my department advisor, Dr. Nancy Glynn. Additionally, I would like to thank my friends, Epidemiology faculty, and University of Pittsburgh Graduate School of Public Health faculty for guiding and allowing me to receive such an amazing education. To my teacher parents, thank you for instilling the love of learning within a younger me. I am forever grateful for your constant support.

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1.0 Introduction

Traumatic brain injuries (TBI) are a major public health burden and are often referred to as a 'silent epidemic' occurring throughout the United States (US). There are 5.3 million Americans estimated to be living with disabilities related to traumatic brain injuries.[1] Estimates of the economic effects of TBI reach well into the billions with approximately 2 million individuals receiving hospital treatment for TBI annually within the US.[1,2] Knowledge of risk factors and long-term consequences of TBI remain limited, and large heterogeneity exists among survivors over the long-term clinical course. TBIs affect all age cohorts, but growing hospitalization rates and worse long-term prognoses for older adults make this demographic of utmost public health importance.[3] Older adults who experience TBI have greater cognitive decline and do not respond as well to rehabilitation efforts compared to younger adults.[3,4] Even within older adults, clinical representation and prognoses of TBI can differ dramatically; some older individuals experience normal aging patterns while others have accelerated cognitive decline and premature death.[5] One major gap in knowledge is the extent to which this accelerated cognitive decline due to traumatic brain injury can be attributed to a pre-existing disease process occurring prior to the head injury. Understanding whether individuals who sustained a TBI had pre-existing conditions that increased their risk for a head injury and that may serve as independent risk factors for cognitive and functional decline could better target TBI prevention and intervention methods and help improve health outcomes for at-risk groups.

1.1 Understanding TBI

Over the 20th century, stigma and characterization of traumatic brain injury, especially milder cases, has changed dramatically. The physiological understanding of TBI has lead to the increase of research and public concern surrounding this 'silent epidemic'.[6] To begin, traumatic brain injuries refer to damage to the brain from an external force; this does *not* include brain injuries resulting from internal events like stroke or anoxia. For a head injury to be categorized as a TBI, the external force has to result in at least one of the following criteria:

1. A loss of consciousness
2. Any loss of memory for events before or after incident
3. Alteration in mental state at the time of the incident
4. Focal neurological deficits that may or may not pass[7]

Or 5. A post-traumatic seizure, skull fracture, or abnormal brain scan[8]

1.2 TBI Classification

Traumatic brain injuries can be further categorized into closed vs. open TBI and injury processes can be characterized as primary vs. secondary. In a closed head injury, the skull and brain have not been penetrated from the external force. An open head injury refers to the skull and brain being penetrated (i.e. a gunshot wound) by some external force. Within these two overarching TBI categories, injuries can be further categorized as primary or secondary injuries. Primary injuries occur at the moment of external impact like fractures or hemorrhages, while secondary injuries can occur minutes or even days later, like swelling, hypoxia, and ischemia. [8]

1.3 Causes of TBI

Traumatic brain injuries stem from a plethora of causes; some occur from single incidents while others are compounded events. Every year, an estimated 2.5 million TBIs occur within the United States.[9] The leading causes of TBIs occur from: falls, collisions with an object, motor vehicle accidents, assaults, and sports and military-related injuries.[1] Among older adults (65 and older), falls account for approximately 80% of all TBIs annually, while falls account for only 45% of TBIs in younger adults.[10,11] While the causes of approximately 25% of all incident falls within older adults are unknown or cannot be specifically recalled, falls in older adults are often related to a pre-existing medical comorbidity and frailty.[12] The varying distributions of TBI etiology by age suggests there may be different risk factors within age cohorts. Moreover, the clinical presentation of TBI can also vary, not only between age cohorts but within age groups; TBIs unfold heterogeneously across individuals. Finding clinical predictors of TBI outcome and response to treatment are critical for improving short- and long-term prognoses, especially in older adults. Some evidence is beginning to suggest that understanding pre-injury health status of individuals with TBI may actually be a better predictor for the clinical course post-TBI.[13,14]

1.4 Clinical Presentation of TBI

The severity of traumatic brain injuries can range from mild (commonly referred to as a concussion) to moderate and severe. One clinical predictor of TBI severity is the duration of loss of consciousness (LOC). LOC requires that either 1.) loss of bilateral function within the brain or 2.) disruption in the reticular activating system, the brain's main center for regulating

wakefulness and the sleep-wake cycle.[15] Clinically, moderate TBIs are defined as having a <24 hour period of LOC and a sustained dazed/confused state for at least 24 hours. Severe TBIs have LOC periods of more than 24 hours and can even lead to a medical coma.[7,13] TBI severity indices like the Glasgow Coma Scale (GCS) are commonly used to describe the severity of TBI on a 15-point scale immediately following injury. Within the GCS, the three components individuals are scored on are: eye-opening response, verbal response, and motor response. On the GCS scale, mild TBIs (mTBI) range in score from 13 to 15, moderate TBIs from 9-12, and severe TBIs can reach a score as low as 3 indicating a deep coma. [8,16]

Traumatic brain injuries can also be diagnosed through computed tomography (CT) or magnetic resonance imaging (MRI) scans that are able to display problems like bruises, swelling, and/or blood products post-injury.[8] Another diagnostic difference between mild and moderate/severe TBI is that neuroimaging CT or MRI methodology usually cannot detect milder cases, while most moderate/severe TBI incur detectable, physiological evidence of injury.[17] Even within this 3-level TBI categorization, there is heterogeneity that blurs the lines among classifications, especially within mTBI.[18] A sub-categorization of mTBI, referred to as "complicated mild TBI" (cmTBI), refers to an injury that results in a 'mild' GCS score but have intracranial abnormalities are present on neuroimaging.[19] Older adults have higher incidence rates of cmTBI, which can complicate long-term clinical prognoses in this already at-risk group.[20] While the categories are not homogeneous, the purpose of the 3-level TBI categorization is, not only understanding the initial impact of the head injury, but to gauge the long-term clinical course. Understanding the severity of TBI is a critical component for determining potential injury sequelae.

1.5 Injury Sequelae Post-TBI

In most mild TBI cases, common sequelae like cognitive impairments and physical symptoms resolve within weeks. These impairments can be long-standing in more severe cases.[21] Many moderate and severe TBI cases report long-term cognitive impairments and neurologic symptoms like headache and sensory changes.[21,22] The relationship between TBI severity and objective cognitive sequelae is approximately linear with longer durations of loss of consciousness.[23] Nonetheless, individuals who experience a TBI with a loss of consciousness period of more than 30 minutes are at a higher risk for exacerbated cognitive impairments and worse long-term prognoses.[23]

These cognitive changes associated with TBI can limit activities of daily living, social integration, and work performance. Approximately half of severe TBI cases reporting these cognitive impairments experience these effects for longer than six months.[24] Over time, these cognitive impairments can manifest in behavioral and mood changes, and individuals with TBI experience higher rates of depression compared to non-TBI controls. [25] Additionally, recent reports have also claimed that long-term consequences of TBI can lead to various neurodegenerative diseases like Alzheimer's and Parkinson's. [26] The pathophysiology behind cognitive impairments can include a host of factors such as:

1.) Rupturing of the cellular and vascular membranes within the brain

2.) Axonal damage due to rapid shifts of the brain

3.) Changes in cerebral blood flow from neuronal damage and compensation.

Thus, this physiological damage to the brain can lead to widespread metabolic depletion and the initiation of programmed cell death.[27] While the body has repair mechanisms to restore the initial damage to the brain, individuals with moderate to severe TBI experience such

detrimental biological damage that compensatory mechanisms may not be sufficient for a full recovery.

Besides debilitating and life-long cognitive impairments, more severe TBI cases can result in long-term physical disabilities that reduce an individual's quality of life. Common physical and psychiatric comorbidities include but are not limited to: Post-traumatic stress disorder (PTSD), substance abuse, depression, hypertension, visual problems, and general decline in physical motility.[28] Additionally, compared to age-matched healthy controls, both young and old TBI age cohorts report problems with metabolic and endocrine system functioning.[22] The biologic mechanism behind this reported physical health sequelae of TBI may be due to a prolonged inflammatory response and compensatory efforts within the body.[29] The effects of TBI are not limited to the brain; they affect the entire body and its physical functioning ability. While the consequences of TBI affect all age groups, older adults experience greater congitive and physical decline post-TBI compared to younger cohorts.

1.6 TBI in Older Adults

As mentioned previously, the main causes of TBI in older adults are distributed differently compared to younger cohorts. Falls account for approximately 60% of all TBIs experienced in adults ages 65 and older, while being struck by an object is the main cause in younger adults.[1] Older adults have a higher risk for an accelerated cognitive decline and may be more limited in their capacity to recover from TBIs compared to younger adults. Younger adults who sustained a TBI showed a significant improvement in cognitive and physical functioning one and five years post-injury, while older counterparts did not experience the same

improvement. [4] While the mechanism for this difference between age cohorts is not known, it may be attributed to the reduced cognitive reserve that occurs in aging populations.[30] Additionally, it has yet to be determined whether this increased decline in cognitive and physical health is a continuation of a pre-existing disease process or whether the traumatic brain injury *caused* the decline in functioning in what was a previously healthy individual. Distinguishing between whether TBIs exascerbate pre-existing pathology or initiate non-neurological medical conditions is necessary for identifying the exact consequences of TBI and improving the quality of post-injury care. Ultimately, the dramatic and unfortunate cognitive and physical decline seen in older individuals sustaining a TBI leads to a reduce lifespan compared to healthy counterparts.[31,32]

1.7 Mortality Associated with TBI

One of the most pressing issues regarding the long-term effects of TBI is that mortality rates are significantly higher in those sustaining a TBI compared to the general population. On average, individuals with a TBI carried about 2.5 times the risk of death, resulting in a reduced life expectancy by 6-7 years.[32] TBIs account for 20% of symptomatic epilepsy, and follow-up studies have found that individuals one year post-TBI were 37 times more likely to die from seizures compared to healthy controls.[33] Older adults (55+) with TBI have greater risk of death from external causes like motor vehicle accidents, being hit by an object, and falls.[34] Other causes of death in which TBI individuals are at increased risk compared to the general population include: pneumonia, digestive system diseases, stroke, and circulatory diseases.[35] In particular, older adults with TBI have a greater increased risk of death from pneumonia,

aspiration pneumonia, and sepsis compared to the younger cohorts with TBI.[34] As stated previously, these studies on mortality support the notion that the pathophysiology and stress put on the body when an individual sustains a TBI is not limited to the brain. Understanding the host of factors contributing to this increased risk of mortality post-TBI is crucial for narrowing this life expectancy gap and improving TBI care.

1.8 Falls and TBI: Pre-Injury Health

As mentioned above, falls account for approximately 80% of all traumatic brain injuries in adults 65 years or older.[1] This is especially concerning considering falls, especially injurious falls, are usually attributed to prior declining cognitive and physical health. Previous literature has shown older adults with diabetes and peripheral nerve damage experienced higher rates of injurious falls compared to healthy counterparts.[12] Additionally, both older males and females who reported having at least one mental health disorder experienced an increased number of falls.[36] Certain behavioral risk factors like illicit drug use and excessive alcohol consumption are also associated with higher injurious fall rates.[36,37]

Since pre-existing conditions can lead to higher rates of falls, it is necessary to understand whether falls resulting in a TBI are attributed to pre-existing disease processes. It remains unknown whether individuals who sustain a TBI have an overall poorer health status compared to non-TBI sustaining counterparts.

1.9 Other TBI-Associated Risk Factors

The risk for having a TBI and the heterogenity of disease progression varies due to different causes of injury, severity, and individual health and demographic characteristics.[8,31,38] As stated previously, TBIs have different long-term clinical courses if they are mild versus moderate/severe. Moderate and severe TBIs characterized by a loss of consciousness episode >=30 minutes lead to worse long-term prognoses and an increased risk for sustaining a subsequent TBI.[15,23] After an initial TBI incident, the risk for a second head injury is three times higher compared to non-TBI individuals; this risk jumps to eight times higher for a third TBI incident.[39] One prospective cohort study found 20% of the population risk for TBI with loss of consciousness in older adulthood was attributable to baseline history of TBI with LOC.[40] Concerning the clinical progression of TBI, individuals who sustain a moderate to severe TBI have significantly worse one year post-injury outcomes compared to their healthy counterparts. Additionally, older adults tend to have poorer post-injury outcomes compared to healthy counterparts.[4] These poorer health outcomes include: worse psychiatric state, increased risk for many chronic illness, and pre-mature death.[23,35] Nonetheless, while these risk factors contribute to TBI severity and long-term prognosis, incidence rates of TBI do not occur equally throughout the population.

Traumatic brain injuries disproportionately affect individuals based on demographic characteristics. Males are more likely to experience a brain injury at almost every age group compared to females and are more likely to experience a TBI that results in death and/or hospitalization.[41,42] Age is also a major risk factor for sustaining a TBI with older adults and younger kids having higher TBI incidence rates than middle-aged adults.[4] Also, some studies suggest African Americans have a higher risk of TBI and TBI-associated mortality compared to

non-Hispanic Whites.[43,44] Traumatic brain injuries do not discriminate and affect all individuals, but the heterogenity of this injury leaves many opportunities for future research. It is imperative to assess all gaps in knowledge concerning TBI in hopes to improve clinical outcomes and reduce the overall public health burden.

1.10 Gaps in Knowledge

While TBI research efforts have grown in recent years, the explanation behind the heterogeneity of symptomology and clinical course remains largely unknown. As mentioned previously, one major difference that exists for long-term TBI prognoses is the poorer health outcomes older adults experience compared to younger cohorts.[4,34] This gap is particularly concerning considering the high incidence rate of TBIs within older adults.[9] Additionally, the number of older adults in the United States is increasing, so the public health burden will only grow.[45] It remains unknown whether the poorer long-term clinical course in older adults who sustained a TBI is attributed to a pre-existing disease process, or if the TBI was the causal trigger for this poorer clinical course. Certain prior health conditions may predispose an individual to be at a greater risk for a TBI (i.e. falling due to poor, prior physical health), and/or these conditions may interact with the pathology of a traumatic brain injury to accelerate cognitive and physical decline.

Most TBI treatments focus on tertiary prevention; this targets the clinical and outcome stages of individuals who have already sustained an injury. Understanding the behavioral and physiological risks an individual has for sustaining a TBI are critical for improving secondary TBI prevention methods, the subclinical/screening phase of prevention care.[46] Physicians would

be able to assess pre-TBI conditions and discern which subset of individuals is at greatest risk for exascerbated TBI-related consequences. This identification will lead to earlier and hopefully more effective treatments to improve TBI prognoses and secondary prevention methods. Additionally, because TBI survivors experience higher rates of mortality, understanding any pre-existing risk factors could better characterize TBI-associated mortality and improve long-term prognoses. The health decline experienced in many older individuals post-TBI is incredibly burdensome, and the long-term clinical course of TBI is very heterogeneous, making tertiary prevention methods difficult for healthcare providers. Identifying pre-existing conditions increasing the risk for sustaining a TBI can lead to better targeted and effective injury prevention initiatives

1.11 Public Health and Economic Burden

Approximately, 16% of all injurious visits to the emergency department (ED) record TBIs as either the primary or secondary reason for admission. From 2002 to 2006, of the approximately 2 million TBI-related emergency department (ED) visits: 40% were attributed to falling, 19% due to being struck by an object, 15% from motor vehicle accidents, 11% from assault/homicide, and 15% from other or unknown causes. 2% of all TBI-related ED visits (or ~ 50,000 individuals) resulted in a death noting the head injury as one of the primary causes.[1] It should be noted that these percentages of TBI-related ED visits are underestimating the overall public health burden of TBI. This underestimation can be attributed to individuals who decide not to seek out medical care, potentially due to mild TBI symptomology and/or lack of education surrounding head injuries.[6] Within the 21st century, the public interest and awareness concerning

traumatic brain injuries, especially milder cases like concussion, has grown.[6] One qualitative study compared the perception and knowledge of TBIs between youth athletes and their parents, and they showed younger individuals to be more receptive and understanding to messages about concussions. However, a majority of parents did note a lifetime change in their perception of TBI/concussions.[47]

Concerning the annual economic burden of TBI within the United States, one study estimated an approximate $37.8 billion in costs broken down as: $4.5 billion on direct healthcare costs, $20.6 billion as injury and work-related losses, and $12.7 billion due to earlier mortality.[2,48] Individually, the cost per case of a mild TBI is estimated to average around $34,000, while a moderate TBI can fluctuate from $25,174 to $81,153 per case. These costs were estimated from acute care.[49] These estimate failed to capture the emotional and physical burden that family members and loved ones experience as a result of an individual sustaining and living with a TBI. But some quality of life studies have found that individuals with more severe TBI have lower self-value and more dismal outlooks on life.[50]

All in all, traumatic brain injuries are a major financial, social, and public health burden, and assessing factors that could reduce hospitalizations and better health outcomes is needed to improve treatment and prevent traumatic brain injuries. If an individual had pre-injury health and behavioral TBI risk factors, then the individual or a physician could identify and targetpotential changes to those risk factors. The ability to prevent a life-altering head injury or improve an individual's clinical course could drastically reduce TBIs' substantial healthcare and societal burden.

2.0 Objective / Hypothesis

2.1 Objective

The objective of this essay is to discern whether there is evidence that individuals over 40 years old who sustained a traumatic brain injury had greater risk of pre-existing health conditions and/or behaviors compared to no-TBI matched controls.

2.2 Hypothesis

Older adults who sustain a traumatic brain injury have poorer health status and riskier health behaviors in the year *prior to* head injury compared to demographically-matched controls with no reported traumatic brain injury.

3.0 Methods

3.1 Study Populations

3.1.1 Individuals with TBI

Individuals with traumatic brain injuries were recruited via the TBI and Health in Older Adults study (i.e. TBI Health Study) out of the Mount Sinai Brain Injury Rehabilitation Unit (MSBIRU). The MSBIRU is a part of the Mount Sinai Hospital System in New York, New York, and annually they admit approximately 125 patients with TBI. To receive inpatient care at the MSBIRU, individuals needed physician referral and to be clinically deemed to require in-patient rehabilitative care. To be eligible for the TBI Health Study, individuals either had:

1. An abnormal computed tomography (CT) scan consistent with TBI pathology

2. Normal CT, but post-resuscitation GCS score between 3-12

3. Loss of consciousness >30 minutes

Or 4. Post-TBI amnesia longer than 24 hours[51]

All participants who enrolled into the TBI and Health in Older Adults study via the MSBIRU were above the age of 40 at the time of injury and consented to study participation. Data were collected via in-person and phone interviews with the individual who sustained the TBI and/or a close family member familiar with the patient's medical history. During data collection, individuals were asked to respond to questions about their health status and lifestyle in the year prior to injury, as well as at the time of admission. Interview protocols and questions regarding past-year health status were exactly replicated from the Midlife in the United States

(MIDUS) Study Health Questionnaire. The statement "*In the year prior to injury"* was added to the MIDUS Health Questionnaires for the TBI Health Study to assess the index injury.[51] TBI exposure, mechanisms and severity was assessed via the Brain Injury Screening Questionnaire (BISQ). The BISQ is a 20-item questionnaire that uses contextual and etiological cues to facilitate recall of injuries to the head, occurrence of a loss of consciousness (LOC) and presence of altered mention status (feelings of being "dazed and confused" (DAC)), and duration of the LOC and DAC.[52]

An original TBI cohort of N=87 was recruited, and due to incomplete questionnaires and missing exposure information (see Methods Section 3.3), this initial sample size was reduced from N=87 to N=64 prior to matching protocol (see Appendix: Figure 2). The matching rate stated in Section 3.3 does not incorpate the N=23 individuals excluded due to incomplete risk factor information.

3.1.2 Non-TBI Controls

As stated above, non-TBI controls were pulled from the Midlife in the United States (MIDUS) Study, a longitudinal, random-digit-dialing study of cognitive aging in mid-life launched in 1994-1995. The goal of this study was to better characterize and investigate the roles of psychological and social factors in regards to the heterogeneity, both physically and mentally, that exists within the aging process. The initial cohort ranged in age from 25 to 74 and were eligible if they were non-institutionalized, English-speaking adults in the continguous United States, N=7,108. This cohort completed a host of baseline and lifetime assessments conducted via phone and self-administered questionnaires. MIDUS II study was initiated in 2004 to reassess baseline questionnaires and expand cognitive assessments of the original cohort, N=4,963 and

age range from 35 to 86. This wave expanded African-American enrollment with an additional N=592 added to the MIDUS II cohort.[53] To add to the original MIDUS cohort, the MIDUS Refresher recruited new participants (N=3,577) from 2011-2014 with identical (and additional) comprehensive assessments and questionnaires to MIDUS I & II.[54] The average response rate (adjusted for individuals who died) was 86%, thus compiling a comprehensive and representative cohort of older individuals throughout the United States.

For this project, both MIDUS 2 and MIDUS Refresher cohorts were used as non-TBI controls to assess health conditions and behaviors. If the MIDUS participant reported 'Yes' to having a 'history of serious head injury', they were excluded as controls. Because both the TBI and Health in Older Adults and the MIDUS studies used identical structured interview questions, complete and direct comparisons of self-reported health conditions and behavioral factors between TBI individuals and matched controls was performed.

3.2 Matching Protocol

A matched case control study was used as the study design for assessing pre-index injury health conditions of TBI individuals with controls. The specific method of matching used between TBI cases and controls was a 'greedy matching' or nearest neighbor matching without replacement.[55] The TBI cases were matched with up to three control participants by the following demographics: age (caliper width +/- 5 years), sex, education, employment, and race. Sex was defined as "Male/Female". Employment was characterized as "Employed/Working for Pay" or "Unemployed: (Retired, Student, Disabled, Etc.)". Education was defined on four levels: "Less than High School", "High School", " Some College" , and "Completed College Degree".

Finally, Race, was defined as “White”, “Black”, or “Other: (Asian, Native American, Etc.)”. The greedy matching algorithm was to find the closest control (up to 3 per case) for each TBI case, which produced a matched sample with balanced covariates across the two groups. The matching rate of TBI to controls was 96.88%, N=2 were lost due to matching unavailability. N=62 TBI individuals and N=171 MIDUS controls. were included in the final cohort (See Appendix: Figure 2). While not included in the matching algorithm, ethnicity and marital status of participants were also assessed as potential demographic confounders.

3.3 Pre-Injury Health Measures

Risk factor measures in the TBI Health Study included the statement “*In the year before your injury*” to prompt the individual to only answer in regards to the year *prior*. For the analyses, there were three main categories of health measures: physical health, behavioral health, and other self-reported risk factor measures. To understand multidimensional concepts like physical and behavioral health, a composite score was created for both exposures. Components of the composite score were also assessed independently.

3.3.1 Physical Health Composite Score

In both the TBI Health Study and MIDUS Study, participants endorsed either: 1=yes or 0=no for “being treated for any of the following [30 conditions] in the year prior to injury.” [53,54] Examples of conditions include: asthma, urinary incontinence, autoimmune diseases, high blood pressure, mental illness, and migraine headaches (see *Marmot et al.* for further explanation of

these categories).[56] To examine whether there was evidence of poorer health status compared to matched controls in the year prior to index injury, a single-item, physical health composite score was generated by summing individual health condition responses.

Thus, the physical health composite score ranged from 0=indicating *no* health conditions to 30=indicating having *all* conditions in the year prior to index injury. Previous literature from Piazza et al. has shown success using this physical health composite variable with MIDUS populations.[57]

3.3.2 Behavioral Health Composite Score

The behavioral risk factor composite score consisted of four health behaviors: alcohol use, smoking status, physical inactivity, and substance use. Each of the four behavioral health risk factors were assessed individually, along with the composite score. This composite score was created by summing the four binary variables for risky health behaviors: 'Alcohol Use', 'Smoking Status', 'Physical Inactivity', and 'Substance Use'. Ranging from 0-4: 0=indicating no risky health behaviors and 4=indicating extremely risky health behaviors. Results of literature searching suggest that these MIDUS measures have not been previously combined into a behavioral health composite score. However, abundant literature supports the prevalence and consequences of these 4 health behaviors among individuals with TBI, justifying their inclusion in a composite score.

The **'Alcohol Use'** variable was defined as "*having alcohol related problems during the past 12 months*". If participants answered "*Yes*" to the following four questions, then they would have a positive value for "Alcohol Use": emotional or psychological problems relating to alcohol, strong desire or urge to use alcohol, period of a month or more frequently using alcohol,

use more alcohol to get the same effect. [58] 0=indicated *no* alcohol related problems, while 1=indicated alcohol-related problems based on the four criterion above,.

The **'Smoking Status'** variable was defined as "*smoking cigarettes regularly in the year prior to injury*". 0=did *not* smoke cigarettes regularly in year prior, 1=did smoke cigarettes regularly in year prior to injury.

The **'Substance Use'** variable was defined as "any use of drugs or medications without a doctor's prescriptions, in larger amounts than prescribed, or for a longer period in the year prior to injury". Examples of substances included: sleeping pills, amphetamines, marijuana, hallucinogens, and heroin.[53] If the individual marked 'Yes' for any of the 10 substances in the questionnaire, then the 'Substance Use' variable would equal 1=indicating substance abuse. Thus, if the individual marked 'No' for all substances, then the 'Substance Use' variable would equal 0=indicating no substance abuse.

The **'Physical Inactivity'** risky behavior variable was created in the following manner. Physical activity was assessed in the year prior to injury across three locations: while at [a] paid job, while performing chores in and around home, and during leisure or free. To be considered physically active, the individual would have to engaged in vigorous and/or moderate physical activity several times a week.[59,60] Vigorous activity was defined as '…activity that caused sweat…and breathing heavily…and heart to beat rapidly. Moderate activity was defined as 'activity that was not physically exhausting, but caused heart rate to increased…and sweat to work up'.[53] If individuals met this criteria above and were considered physically active, they were reverse scored for 'Physical Inactivity' in the composite score. This is because physical activity is a behavioral protective factor, while physical inactivity is a behavioral risk factor. For

scoring, 0=indicated *no* physical *inactivity*, while 1=indicated physical *inactivity*, positive for the 'Physical Inactivity' risk factor.

3.3.3 Additional Pre-Injury Health Measures

To further understand factors that are more prevalent in individuals with TBI various self-reported questions were included as exposure measures. **'Self-Reported Physical Health'** in the year prior to injury was assessed on a 5-point Likert Scale ranging from poor to excellent. Responses were assessed on a binary level as 'excellent/very good/good' and 'fair/poor'. Additionally**, 'Self-Reported Chronic Pain'** in the year prior to injury was included as a yes/no exposure and defined as 'pain that persisted beyond the time of normal healing and has lasted anywhere from a few months to many years'. Lastly, to further assess whether depression alone was a risk factor for TBI, the variable **'Self-Reported Depression'** was included and defined as 1.) Endorsing depression or 2.) Currently on treatment for depression. These three risk factors were assessed separately from the physical and behavioral health composite scores.

3.4 Statistical Analyses

All statistical analyses were performed using SAS enterprise guide SAS Enterprise Guide (version 7.1, SAS Institute Inc, Cary, NC) and $p\text{-}value<0.05$ was considered statistically significant. Univariate descriptive analyses were perfomed all on variables to assess for data entry errors, presence of outliers, and variable distribution. Descriptive counts and proporitions

of demographic and outcome variable by presence of TBI were conducted to describe both cases and controls. Differences between TBI cases and controls were assessed via one-way ANOVA, Kruskal-Wallis, and Chi-Square tests as appropriate. As stated in section 3.3, demographic balance between two groups was achieved by matching TBI cases to controls based on nearest neighbor without replacement matching on age (caliper width +/- 5 years), gender, race, education, and employment status at the time of interview. A pre-determined matching ratio of up to 3:1, controls to cases, was established. To assess the balance of variables after matching, standardized differences were reported, and differences >10% were considered as meaningful difference.

Primary and secondary analyses were conducted using conditional logistic regression modeling with 95% confidence intervals and Odds Ratio (OR) reporting.[61] ORs were estimated to assess the odds of prior year physical health and behavioral exposure in TBI cases compared to matched controls.[62] Models were conditional on the matched strata. Subgroup analyses were conducted by age and sex to examine if the association differs by subgroups. Age was stratified as >=65 years and <65 years at the time of interview.

4.0 Results

Table 1 presents the overall demographic characteristics of the TBI and No TBI samples after the nearest neighbor matching protocol. For TBI individuals, the mean age was 66.53 ± 12.81 with a median age of 69 and an IQR of 59-75 years. The mean age of 'No TBI' individuals was 65.30 ± 11.95 with a median age of 68 and inner-quartile range (IQR) of 58-74 years old. The age standardized differences were greater than 10% (0.18 for mean and 0.16 for median), but the ranges for cases and controls were extremely similar. Nonetheless, age was adjusted for in the final model for potential residual confounding. The standardized differences for sex, race, employment, and education, the other matched demographic variables, were all less than 10%. For descriptive purposes, marital status and Spanish ethnicity of the cohort were also reported in Table 1. The majority of both TBI and 'No TBI' participants were married, and the majority reported 'No Spanish Ethnicity'.

Table 2 shows the proportions and balance of the self-reported past-year health and behavioral outcomes included in the analyses after matching. All cases reported on the year prior to index TBI, and controls were asked about their prior year health status. A majority of cases (80.7%) and controls (84.1%) reported their previous years' health status to be in excellent, very good, or good conditions. More 'No TBI' individuals reported chronic pain in the year prior (33.3%), while individuals who sustained a TBI had 17.7% reporting this chronic pain. A higher proportion of individuals sustaining a TBI had self-reported depression in the year prior (27.4%), with only 9.9% of controls reporting this mental illness. Table 2 shows the physical health composite score dichotomized as >=3 medical conditions or <3 conditions. There was one outlier, not shown, in the controls that reported 28 medical conditions, but upon closer

inspection, the data appeared to be correct with the individual reporting all medical conditions but hay fever and high blood pressure. Along with proportions of the number of behavioral risk factors, the number of individuals reporting excessive alcohol use, current smoking status, physical inactivity, and substance abuse is also shown in Table 2.

Tables 3 and 4 describe the type of head injury within the TBI individuals, with information based off of the Brain Injury Screening Questionnaire (BISQ). Four TBI cases did not have completed BISQ forms and were excluded from these TBI descriptive reports. Table 3 gives the frequency of each of the 20 head injury etiologies within the BISQ questionnaire. Columns do not sum to 100% because individuals reported lifetime TBIs and could identify multiple TBIs; 40% of TBI individuals reported having multiple head injuries. The three most common TBI etiologies in descending order were: falling down stairs (28.3%), falling from other cause (21.7%), and other cause (20.0%). Within the BISQ, individuals could report any loss of consciousness (LOC) and/or dazed and confused (DAC) state associated with a traumatic injury to the head. Table 4 shows the longest lifetime period of LOC and DAC. For LOC, approximately a third of individuals reported never having a period of loss of consciousness, while approximately a quarter of individuals reported never having a dazed and confused state post-TBI. Further, 23.2% could not recall the duration of their loss of consciousness episode, while that percentage was 14.3% for DAC. It was less common for participants to report LOC durations longer than one week, while over 30% of participants reported having a dazed and confused state longer than one week post-TBI.

For the primary analyses of physical and behavioral health factors, Tables 5 a-e show the results of the conditional logistic regression with nearest neighbor matching of TBI cases and non-TBI controls. These values in the 2x2 Tables 5-6 represent the matched pairs and do not

equal the descriptive, unmatched values in Table 1. The prior-year, self-reported risk factors were: poor health status, chronic pain, depression, physical health composite score, and behavioral health composite score. The only statistically significant matched odds ratio was prior-year (or pre-index injury for TBI cases) depression or have been/are being treated for depression, OR=3.98 (95% CI=1.71-9.27) with a p-value=0.001. In other words, the odds of having prior year, pre-index injury depression was 3.98 times higher in TBI cases compared to matched controls. In Table 5.d, the physical health composite score was dichotomized on whether the individual had >=3 or <3 conditions, but the reported matched odds ratio was not significant at OR=1.52 (95% CI=0.82-2.81) and p-value=0.183. Likewise, the behavioral health composite score reported not significant differences in odds in prior-year health exposures between TBI cases and controls, OR=1.48 (95% CI=0.75-2.91) and p-value=0.254

Since the creation of the behavioral health composite score and summing the number of behavioral risk factors was a novel approach for these cohorts, the four components of this score were analyzed in the regression model separately. All behavioral health risk factors: excessive alcohol use, current smoking status, physical inactivity, and abuse of control/illegal substance, reported insignificant differences in prior year odds of exposure between TBI cases and controls.

Sub-group analyses were performed for each of the primary outcomes stratified on sex and age (>=65 years or <65 years). Tables 6.a-6.b show only the significant results of the sub-group analyses based on sex and age; non-significant results were not reported. When stratified by sex, the odds of having prior year, pre-index injury exposure of depression was significant in *male* TBI cases versus male controls (OR=6.92, p-value=<0.001). The odds of having prior year, pre-index injury exposure of depression was *not* significant in female cases versus female controls (OR=1.68, 95% CI=0.43-6.67), p-value=0.459. Additionally, when stratified by age, the

odds of having prior year, pre-index injury exposure of depression was significant in TBI cases >=65 years compared to controls >=65 years (OR=6.54, 95% CI=1.72-24.84, p-value=0.006). For cases and controls below the age of 65, there was no significant difference in odds of prior year exposure to depression in TBI cases compared to matched controls (OR=2.40, 95% CI=0.74-7.78), p-value=0.143).

5.0 Discussion

The results of my project assessing the pre-index injury health measures of TBI individuals with matched controls suggest the odds of having depression in the year prior was significantly higher in cases compared to controls. When stratified by sex, male TBI cases had increased odds of having depression in the year prior compared to male controls. Additionally, when stratified by age, TBI cases >=65 years had increased odds of having depression in the year prior compared to <65 years controls.

When matched on age, sex, race, education, and employment, conditional logistic regression models showed the odds of having depression in the year prior to injury for TBI cases was 3.98 times higher compared to non-TBI controls. Previous literature has shown that individuals who sustained a TBI have higher rates of depression compared to general population.[25] Approximately half of all people with TBI report depressive symptoms one-year post TBI, which can be partially attributed to physical changes within the brain and the emotional response to the TBI.[9] But the results above show TBI individuals having higher odds of depressive symptoms *prior* to injury, suggesting a potential association between depression and risk for sustaining a traumatic brain injury. Stratified sub-group analyses by age, defined as >=65 or <65 years, showed that individuals >=65 years with a TBI had a significant 6.53 times odds of having depression compared to matched controls. One explanation for this finding may be the higher rates of frailty and poorer physical health in individuals who have depression, especially older adults. Previous work has shown that older adults with depression have higher incident and overall frailty as measured by a short performance physical battery.[63,64] The higher rates of frailty in older individuals with depression can lead to an increased risk for injurious

falls that could potentially result in a TBI. Additional sub-group analyses by gender showed that males with TBI had a 6.98 times higher odds of having depression prior to injury compared to matched controls, *p-value*=<.0001. And while individuals with traumatic brain injuries have increased rates of depression irrespective of gender, this result is inconsistent with current depression estimates stating females have a higher risk of depression compared to male counterparts.[65]

Besides the findings surrounding depression, the remaining prior year, pre-index injury health and behavioral factors reported insignificant differences between TBI cases and matched controls. The goal of these analyses was to determine if post-TBI disease burden was a continuation of a pre-existing disease process, or whether TBIs were causative of post-injury health problems including non-neurological conditions. These analyses addressed this question through the novel approach of utilizing the same standardized and structured interview to assess pre-index TBI in cases compared to nearest-neighbor matched controls. The findings support the notion that post-TBI disease progression is *not* simply a continuation of prior health conditions, but that TBIs may be the causal agent for the cognitive and physical health decline experienced after injury. So while most findings were null, they help elucidate the long-term clinical course of traumatic brain injuries and individuals most at-risk to sustain a TBI.

One conflicting finding was the suggested trend that chronic pain in the year prior was more common among those with TBI compared to non-TBI controls, OR=0.52 (95% CI 0.25-1.07) and p-value=0.076. In other words, individuals who sustained a TBI had a 48% reduced odds in having chronic pain in the year prior to injury compared to non-TBI, matched controls. This result goes against the initial hypothesis that individuals with a TBI have *worse* self-reported health. More specifically, chronic pain is most often reported as one of the most

common chronic health problem after TBI, and this finding suggests that the high rates of chronic pain do *not* precede TBI but reflect post-injury, new-onset pain.[52] While new-onset pain may be the case, this finding may be attributed to a form of information bias called "good-old-days" bias. [66] Previous research has shown that TBI individuals do not accurately recall past problems, leading to an underestimation of pre-injury health conditions. This "good-old-days" bias has higher underestimation of prior health status at the 1-month post-TBI compared to 3-months post-TBI.[67] Since the TBI Health Study gave cases the health questionnaire soon after injury, participants may have underreported their previous pain levels due to their worse physical and cognitive health immediately following TBI.

In regards to the limitations of this exploratory analysis, the small sample of TBI cases prevents more accurate estimation and modeling the odds of having these physical and behavioral health conditions in the year prior to injury. The TBI Health Study was limited to those who received inpatient rehabilitative care and for moderate/severe TBI. Individuals who present mild TBI symptoms or do not seek or require extensive medical treatment were not recruited into the study. Additionally, in the initial TBI cohort, 25 of the individuals were missing one or both of the questionnaires, i.e. the primary/secondary outcomes, due to non-response and incomplete answers, so they were excluded from analyses. This reduced the TBI cases sample size, thus lowering power and the ability to detect significant differences in prior year health status between cases and matched controls. One limitation for the MIDUS control population was that this cohort did not have an index injury to enroll them into the study. Research has shown that in injury case-control studies, there are certain factors that govern the selection as an injury case.[68] We are assuming the factors that make an individual *not* have a head injury are the same as the factors that make an individual sustain a TBI. Additionally, the

retrospective study design in both the TBI Health Study and MIDUS Study are subject to recall bias in the reporting of prior year health conditions. Both cases and controls in this historical case-control design will have increased recall bias and controls would not have be subjected to 'good-old-days' bias as compared to nested case-controls study designs. Although, these biases would likely be differential with TBI cases having increased recall bias due to cognitive impairment and more likely to under-report pre-index injury health conditions and behaviors. This differential information bias may further contribute to the null findings between TBI cases and controls.

Another limitation of the analytic strategy was the use of composite scores in the primary analyses. Since the analyses for assessing pre-injury health conditions in TBI cases were exploratory, our group decided to use composite scores to increase power and reduce the number of planned analyses. Although previous work suggests a precedence for using MIDUS physical health composite scores, this may have obscured differences between groups in the constellation of health conditions experienced in the prior year.[56] This limits the understanding of whether TBI cases have increased odds for individual health conditions compared to controls. Concerning the behavioral health composite score, other than for physical inactivity, the number of 'yes' respondents for alcohol use, substance use, and smoking status was quite low, thus the current study likely lacks the power necessary to detect a significant difference for these individual components. Additionally, since TBI cases were matched to controls based on age, sex, race, employment, and education, we were unable to explore the possible association between demographic characteristics and sustaining a TBI.

There are several important strengths to the design of this project was chosen based on the strengths provided. The questionnaires used in the TBI Health Study were exactly based off

the MIDUS Health Questionnaires, only adding the "prior to injury" clause. This standardized, structured interview improved accuracy and completeness of outcome assessments to concatenate TBI cases with controls. Additionally, the TBI case definition was well established based on the criterion for enrolling into the study; all were incident TBI diagnoses. Case-control studies require homogenous case definitions, and MSBIRU clinicians validated that all TBI cases required rehabilitative care for their injury.[51] Likewise, the use of random population controls instead of hospital or deceased individuals reduced the amount of selection bias in the control group. Demographically-matched TBI cases and controls ensured the two groups were similar, providing a more precise estimate of association of prior year health conditions and sustaining a TBI.

Future directions will involve using these exploratory analyses to specifically understand more about the prior year health conditions in incident TBI cases. While the odds of more physical health conditions was not significantly associated with sustaining a TBI, investigating the individual components of the physical health composite may provide insight on specific health conditions and their relationship to sustaining a TBI. Additionally, certain behavioral health conditions like physical inactivity were dichotomized to fit the logistic regression model, but assessing these risk factors on multiple levels would likely improve estimates. Since the BISQ assessed the etiology of TBI and presence/duration of LOC and DAC, a future direction would involve understanding if pre-injury health status differs by cause and severity of TBI. As mentioned previously, the small sample of TBI cases precludes these more detailed analyses at the present time. Finding ways to increase the sample size of this cohort will improve power for additional future analyses.

In summary, individuals who sustain a TBI appear to have higher odds of pre-injury depression compared to matched, non-TBI controls. Additionally, when stratified by sex and age, the results suggest older individuals and males who sustain a TBI have even higher odds of prior year depression than do younger individuals and women. These analyses contribute to understanding whether sustaining a traumatic brain injury is a direct result of a pre-existing disease process, or if TBIs are the *cause* of injury sequelae and long-term health consequences. Improving secondary and primary prevention methods for TBIs are pertinent in reducing the enormous economic and public health burden these injuries place on the population and individual. With both the percentage of older adults and incidence rates of TBI estimated to continue rising, identifying all pre-injury conditions and risk factors for TBI will improve long-term prognoses for individuals with traumatic brain injuries for generations to come.

Appendix A Tables

Table 1: Demographic Characteristics of Individuals with and without Traumatic Brain Injury at Baseline (N=233).

Participants Demographic Characteristics	**TBI** N=62	**No TBI** N=171	**Total** N=233	**Standardized Differences**
Age*				
Mean ± SD	66.53 ±12.81	65.30 ± 11.95	65.62 ±12.17	0.18**
Median (IQR)	69 (59-75)	68 (58-74)	68 (58-75)	0.16**
Sex*				
Male	42 (67.7%)	118 (69.0%)	160 (68.7%)	0.03
Female	20 (32.3%)	53 (31.0%)	73 (31.3%)	0.03
Race*				
Caucasian	47 (75.8%)	130 (76.0%)	177 (76.0%)	0.01
African-American	6 (9.7%)	17 (9.9%)	23 (9.9%)	0.01
Other	9 (14.5%)	24 (14.0%)	33 (14.2%)	0.01
Employment*				
Employed	30 (48.4%)	90 (52.6%)	120 (51.5%)	0.08
Unemployed	32 (51.6%)	81 (47.4%)	113 (48.5%)	0.08
Education*				
<High School	6 (9.7%)	17 (9.9%)	23 (9.9%)	0.01
High School	9 (14.5%)	26 (15.2%)	35 (15.0%)	0.02
Some College	7 (11.3%)	19 (11.1%)	26 (11.2%)	0.01
College Degree	40 (64.5%)	109 (63.7%)	149 (63.9%)	0.02
Marital Status				
Married	36 (58.1%)	112 (65.5%)	148 (63.5%)	0.15
Separated	2 (3.2%)	3 (1.8%)	5 (2.1%)	0.09
Divorced	2 (3.2%)	20 (11.7%)	22 (9.4%)	0.33
Widowed	9 (21.0%)	22 (12.9%)	31 (13.3%)	0.05
Never Married	13 (21.0%)	13 (7.6%)	26 (11.2%)	0.39
Missing Info	2 (3.2%)	1 (0.6%)	1 (0.4%)	0.11
Spanish Ethnicity				
Yes	10 (16.1%)	9 (5.3%)	19 (8.2%)	0.36
No	50 (80.6%)	162 (94.7%)	212 (91.0%)	0.44
Missing Info	2 (3.2%)	0 (0.00%	2 (0.9%)	0.26

*Demographic Variables Used in Nearest Neighbor Matching Protocol

** Standardized Differences >10%, adjusted for residual confounding in final model

Table 2: Frequency of Self-Reported Risk Factors in Individuals with and without Traumtic Brain Injury in the Year prior to Injury (TBI) or Interview (no TBI).

Participant Self-Reported Outcomes	**No TBI** N=171	**TBI** N=62	**Total** N=233	**Standardized Differences**
Health Status				
Fair/Poor	27 (15.7%)	11 (17.7%)	38 (16.3%)	0.11
Excellent/Very Good	144 (84.1%)	50 (80.7%)	194 (83.3%)	0.28
Missing Info	0 (0.00%)	1 (1.6%)	1 (0.4%)	0.18
Chronic Pain				
Yes	57 (33.3%)	11 (17.7%)	68 (29.2%)	0.36
No	114 (66.7%)	50 (80.6%)	164 (70.4%)	0.32
Missing Info	0 (0.00%)	1 (1.6%)	1 (0.4%)	0.18
Depression				
Yes	17 (9.9%)	17 (27.4%)	34 (14.6%)	0.46
No	154 (90.1%)	44 (71.0%)	198 (85.0%)	0.5
Missing Info	0 (0.00%)	1 (1.6%)	1 (0.4%)	0.18
Physical Health Composite				
<3 Conditions	100 (58.5%)	29 (46.7%)	129 (55.4%)	na
>=3 Conditions	71 (41.5%)	42 (53.3%)	104 (44.6%)	na
Behavioral Health Composite				
0	66 (38.6%)	19 (30.6%)	85 (36.5%)	0.17
1	87 (50.9%)	32 (51.6%)	119 (51.1%)	0.01
2	14 (8.2%)	10 (16.1%)	24 (10.3%)	0.24
3	4 (2.3%)	0 (0.00%)	4 (1.7%)	0.22
4	0 (0.00%)	1 (1.6%)	1 (0.4%)	0.18
Excessive Alcohol Use				
Yes	10 (5.9%)	7 (11.3%)	17 (7.3%)	na
No	161 (94.2%)	55 (88.7%)	216 (92.7%)	na
Currently Smoking				
Yes	12 (7.0%)	7 (11.3%)	19 (8.2%)	na
No	159 (93.0%)	55 (88.7%)	214 (91.8%)	na
Physically Inactive				
Yes	90 (52.6%)	33 (53.3%)	123 (52.8%)	na
No	81 (47.4%)	29 (46.8%)	110 (47.2%)	na
Substance Abuse				
Yes	15 (8.8%)	9 (14.5%)	24 (10.3%)	na
No	156 (91.2%)	53 (85.5%)	209 (89.7%)	na

*na= standardized difference values not available currently

Table 3: Frequency of Traumatic Brain Injury Etiologies in Cases (N=60) according to Brain Injury Screening Questionnaire (BISQ)

TBI Etiology (N=60)	**YES** N (%)
Motor Vehicle Accident	2 (3.33%)
Motorcycle/ATV	1 (1.67%)
Pedestrian Hit by Vehicle	6 (10.00%)
Hit by Falling Object	2 (3.57%)
Hit by Equipment	1 (1.67%)
Falling Down Stairs	17 (28.33%)
Falling from High Place	3 (5.00%)
Falling during a Fainting Spell	7 (11.67%)
Falling during Drug/Alcohol Blackout	4 (6.67%)
Falling from Other Cause	13 (21.67%)
Biking/Skateboarding/Rollerblading	8 (13.33%)
Horseback Riding	1 (1.67%)
Skiing/Snowboarding	0 (0.00%)
In Organized Sports	5 (8.33%)
Playground	1 (1.67%)
Diving into Water	0 (0.00%)
Being Assaulted or Mugged	1 (1.67%)
Being Physically Abused	0 (0.00%)
While in Combat	0 (0.00%)
Other Cause	12 (20.00%)
Multiple Reported Lifetime TBIs	24 (40.00%)

N=2 Missing BISQ

Table 4: Individuals with Traumatic Brain Injury Longest Lifetime Loss of Consciousness and/or Dazed and Confused State Duration

TBI Loss of Consciousness / Dazed and Confused Duration (N=56)	**Max LOC** N (%)	**Max DAC** N (%)
No Reported LOC/DAC period	18 (32.14%)	14 (25.00%)
Less than 1 minute	2 (3.57%)	1 (1.79%)
1-10 minutes	5 (8.93%)	2 (3.57%)
11-20 minutes	2 (3.57%)	0 (0.00%)
21-30 minutes	1 (1.79%)	3 (5.36%)
31-45 minutes	2 (3.57%)	1 (1.79%)
46-60 minutes	0 (0.00%)	2 (3.57%)
1 hour-23 hours	4 (7.14%)	3 (5.36%)
1 day-1 week	5 (8.93%)	5 (8.93%)
1 week-1 month	4 (7.14%)	6 (10.71%)
More than 1 month	0 (0.00%)	11 (19.74%)
Don’t Know	13 (23.21%)	8 (14.29%)

N=2 Missing BISQ , N=4 Missing LOC/DAC Reports

Primary Analyses

Table 5a: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Poor Health Status

	Control		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Poor Health Status	No Self-Reported Poor Health Status		
TBI Self-Reported Poor Health Status	6	25	1.43 (0.59-3.47)	0.423
TBI No Self-Reported Poor Health Status	21	116		

Table 5b: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Chronic Pain

	Control		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Chronic Pain	No Self-Reported Chronic Pain		
TBI Self-Reported Chronic Pain	8	25	0.52 (0.25-1.07)	0.076
TBI No Self-Reported Chronic Pain	48	85		

Table 5c: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Depression

	Control		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Depression	No Self-Reported Depression		
TBI Self-Reported Depression	5	43	3.98 (1.71-9.27)	0.001**
TBI No Self-Reported Depression	12	108		

**significant with p-value>0.05

Table 5.d: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Physical Health Composite Score

	Control		Pair matched odds ratio (95%)	*p-value*
	Physical Health Composite Score >=3 Conditions	Physical Health Composite Score <3 Conditions		
TBI Physical Health Composite Score >=3 Conditions	38	53	1.52 (0.82-2.81)	0.183
TBI Physical Health Composite Score <3 Conditions	33	47		

Table 5.e: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Behavioral Health Composite Score

	Control		Pair matched odds ratio (95%)	\ *p-value*
	Behavioral Health Composite Score >0 Risk Factors	Behavioral Health Composite Score =0 Risk Factors		
TBI Behavioral Health Composite Score >0 Risk Factors	75	47	1.48 (0.75-2.91)	0.254
TBI Behavioral Health Composite Score =0 Risk Factors	30	19		

Table 5.e.1: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Alcohol Use

	Control		Pair matched odds ratio (95%)	*p-value*
	Excessive Alcohol Use	No Excessive Alcohol Use		
TBI Excessive Alcohol Use	1	21	2.053 (0.738-5.714)	0.1682
TBI No Excessive Alcohol Use	10	140		

Table 5.e.2: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Smoking Status

	Control		Pair matched odds ratio (95%)	*p-value*
	Currently Smoking	Not Currently Smoking		
TBI Currently Smoking	2	17	1.929 (0.670-5.554)	0.2235
TBI Not Currently Smoking	10	142		

Table 5.e.3: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Substance Abuse

	Control		Pair matched odds ratio (95%)	*p-value*
	Reported Abuse of Illegal/Control Substances	No Reported Abuse of Illegal/Control Substances		
TBI Reported Abuse of Illegal/Control Substances	3	24	2.216 (0.878-5.590)	0.0920
TBI No Reported Substances	12	132		

Table 5.e.4: Comparison of Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Physical Inactivity

	Control		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Physical Inactivity	No Self-Reported Physical Inactivity		
TBI Self-Reported Physical Inactivity	49	43	0.924 (0.492-1.734)	0.8058
TBI No Self-Reported Physical Inactivity	41	38		

Subgroup Analyses

Table 6.a.1: Male Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Depression

**Males*	**Male Controls**		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Depression	No Self-Reported Depression		
Male TBI Self-Reported Depression	3	32	6.92 (2.19-21.90)	<0.001**
Male TBI **No** Self-Reported Depression	5	75		

Table 6.a.2: Female Individuals with Traumatic Brain Injuryand Matched Controls: Prior-Year Depression

**Females*	**Female Controls**		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Depression	No Self-Reported Depression		
Female TBI Self-Reported Depression	2	11	1.68 (0.43-6.67)	0.459
Female TBI No Self-Reported Depression	7	33		

Table 6.b.1: >= 65 Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Depression

*>=65 years	**>= 65 Years-Old Controls**		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Depression	No Self-Reported Depression		
>= 65 Years-Old TBI Self-Reported Depression	2	26	6.54 (1.72-24.84)	0.006**
>= 65 Years-Old TBI No Self-Reported Depression	5	65		

Table 6.b.2: < 65 Individuals with Traumatic Brain Injury and Matched Controls: Prior-Year Depression

*<65 years	**<65 Years- Old Controls**		Pair matched odds ratio (95%)	*p-value*
	Self-Reported Depression	No Self-Reported Depression		
<65 Years- Old TBI Self-Reported Depression	3	17	2.40 (0.74-7.78)	0.143
<65 Years- Old TBI No Self-Reported Depression	7	43		

Appendix B Figures

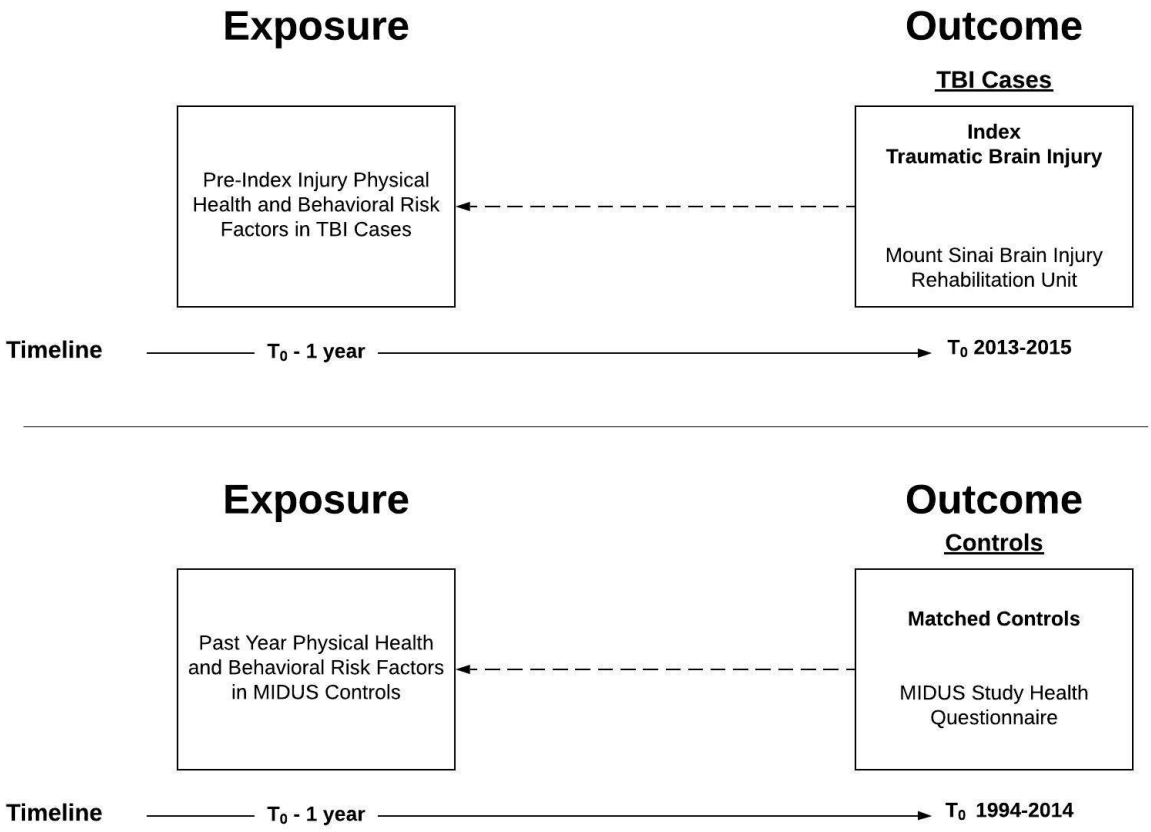

Figure 1. Study Timeline of Risk Factor and Outcome Assessment of Individuals with Traumatic Brain Injury Compared to Matched Controls in the Prior Year

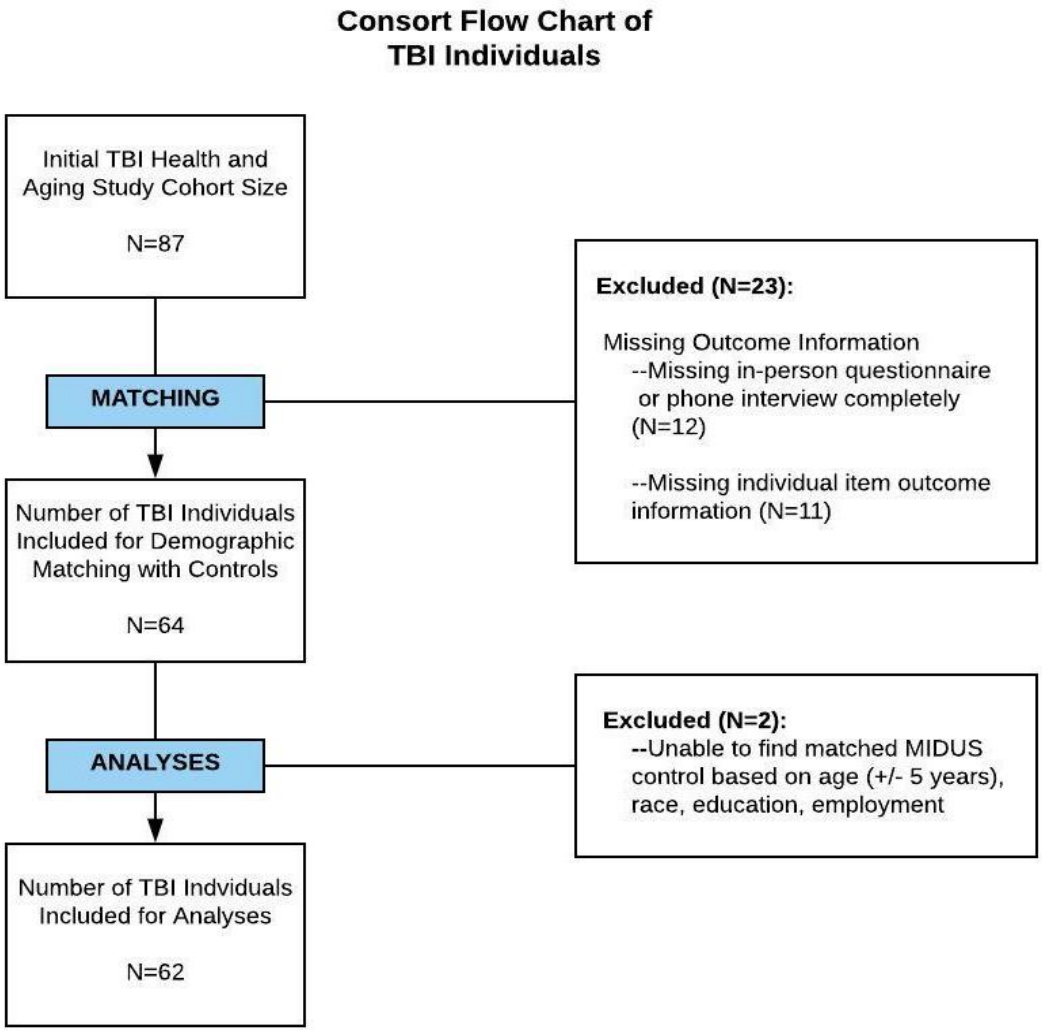

Figure 2 Consort Flowchart Showing the Sample of Individuals with Traumatic Brain Injuries During Beginning Assessments, Matching, and Final Analyses N=62

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