



Association between Traumatic Brain Injury and Suicidality using a Mediation approach and MarketScan

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Abstract

Introduction: Negative outcomes, including suicidal ideation/attempts, are a major public health concern, particularly among individuals who sustain a traumatic brain injury (TBI). TBI is associated with high rates of post-injury substance use, psychiatric disorders, post-traumatic stress disorder, and sleep disturbances. This study examines the mediation effects of substance use, psychiatric disorder, and sleep disorder on the associations between TBI and suicidal ideation/attempts.

Methods: A matched case control study using data from MarketScan databases for private health insurance and Medicaid from October 2015 to December 2018 estimated the association between TBI and suicidal ideation/attempts using a mediation approach. Individuals less than 65 years of age were included.

Results: In the Medicaid sample, psychiatric disorders mediated 22.2% of the total effect between TBI and suicidal ideation/attempt, while substance use disorders other than opioid use disorder mediated 7.46%. In the private health insurance sample, psychiatric disorders mediated 4.18% of the total effect, opioid use disorders mediated 2.17% of the total effect, and sleep disorder mediated 1.25% of the total effect.

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Conclusions: Mediators explained less than 30% of the relationship between TBI and suicidal ideation/attempt. Findings reinforce the importance of primary prevention of TBI and monitoring patients with a TBI for risk of suicide in the first 6-12 months following injury.

Keywords

TBI; Suicide; Mediation; Substance Use; Opioid Use; Psychiatric Disorder; Sleep Disorder

Introduction

There is a well-recognized association between traumatic brain injury (TBI) and suicidal thoughts and behaviors^{1, 2} however, few studies have provided quantifiable estimates to support the mechanistic hypotheses underpinning this relationship.³ Research has supported the idea that TBI is associated with a range of psychiatric disorders observed following TBI which may impact suicidal behaviors.^{4, 5}

Negative physical and psychiatric health outcomes, including suicidal ideation, attempts, and suicide, are a major public health concern, particularly among individuals who sustain a TBI. Systematic reviews report an increased suicide risk among people with a history of TBI.⁶⁻⁸ Measuring definitive rates of suicidal ideation/attempts among those with a history of TBI is challenging due to variable follow-up periods post-TBI, reliance on retrospective data (e.g., existing medical records), and differing strategies for measuring outcomes. One study of 559 adults, who denied prior suicide attempts and sustained complicated mild to severe TBI, reported that 20% of the study population experienced suicidal ideation during their first year post-TBI,⁹ a rate at least double those of the general population (2.1% to 10%) based on a systematic review of epidemiological studies.¹⁰ Prevalence of past year suicide attempts among a similar cohort receiving care within the TBI Model Systems, a program sponsored by the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR), Administration for Community Living, U.S. Department of Health and Human Services, was approximately 1-2%,¹¹ while the prevalence was 0.6% of adults aged 18 years or older in the general population.¹² Although research has identified several risk factors and predictors of suicidal ideation/attempts among those with TBI, few studies have examined the mechanisms that underlie such associations.

TBI is also significantly associated with high rates of post-injury substance use,¹³⁻¹⁷ psychiatric disorders,¹⁸⁻²⁰ post-traumatic stress disorder,²¹ and sleep disturbances;²²⁻²⁴ each of these conditions may have a bidirectional relationship with suicidal ideation/attempts. Most studies examining predictors of suicidal ideation/attempts among those with TBI employ some type of multiple regression to identify variables that contribute independently to poor suicide-related outcomes. During the first year post-TBI, documented predictors of suicidal ideation include history of prior suicide attempt, history of bipolar disorder or manic depression, and having less than a high school education.⁹ Significant predictors of a suicide attempt post-TBI include post-injury substance use, hopelessness, and post-injury psychiatric history, or emotional distress.^{25, 26} Closer examination of the inter-relationships among these variables using mediation analyses have not been conducted and could provide

greater illumination of the relationship between TBI and suicidal thoughts and behaviors by way of potential mediator variable(s) (e.g., substance use, psychiatric disorders/emotional distress, sleep disturbances). Findings from mediation analyses can identify modifiable factors that could have practical implications for public health and clinical practice.

We used a mediation approach to investigate indirect effects of conditions known to be associated with both TBI and suicidal ideation/attempt among patients with and without a diagnosed nonfatal TBI, within 1 year of the TBI. The purpose of testing for mediation was to identify potentially modifiable conditions that could improve long-term outcomes of TBI, particularly suicidal ideation/attempts. To our knowledge, this is the first study to examine the mediation effects of opioid use disorders (OUD), sleep disorder, psychiatric disorder, and substance use disorders other than OUD on the association between TBI and suicide.

Methods

Data and study sample

This research did not require IRB approval as data were deidentified and available from IBM MarketScan Research databases. We used deidentified IBM MarketScan Research databases for private health insurance and Medicaid to identify cases and matched controls. Both inpatient and outpatient records were included in this analysis. The study period was January 2016 to December 2018. Patients with continuous enrollment during the study period, aged between 10 to 64, having coverage for mental health/substance abuse, and prescription drug coverage were included. The main predictor variable was TBI. Patients were identified with initial TBI encounters (ICD-10-CM: S02.0, S02.1, S02.8, S02.91, S04.02, S04.03, S04.04, S06, S07.1, excluding T74.4)²⁷ occurring from January 2016 to December 2017. T74.4 was excluded due to it being specific to infants. We identified 37,703 patients with TBI from Medicaid and 62,290 patients from private health insurance. For the comparison group, we conducted a randomized exact match for Medicaid (by age group, sex, and race) and private insurance (by age group, sex, and region) among the sample of patients without TBI as a 5:1 comparison group. Controls were assigned the same visit date as their matched patients with a TBI.

Measures

International Classification of Diseases, Tenth Revision, Clinical Modifications (ICD-10-CM) codes were used to identify visits with the outcome or mediator variables. Detailed definitions are provided below and are listed in Appendix table A.

Outcome variable

The study outcome variable comprised both suicidal ideation (ICD-10-CM: R45.851) and self-harm/suicide attempt (ICD-10-CM: T14.91, T71, T36-T65, X71-X83) documented in the medical record. We removed patients with documented suicidal ideation/attempt before initial TBI encounter or with documented suicide ideation/attempt more than one year following the initial TBI encounter from the sample population.

Mediator variables

Mediator variables and corresponding ICD-10-CM codes included opioid use disorder (F11), sleep disorder (G47), psychiatric disorder (F20, F25, F31-F33, F39, F41, F43, F60, F91), and substance use disorders other than OUD (F10, F12-F16, F18, F19) documented in the medical record.

Mediating variables had to occur between the TBI and suicide: cases where outcome variables or mediating variables preceded initial visit for TBI were excluded. To avoid including controls with history of recent TBI prior to the study period, patients with first TBI visit in 2015 were removed from the sample.

Demographic variables

Covariates were identified through a review of the literature and included sex (female, male), age group (10-17, 18-24, 25-34, 35-44, 45-54, 55-64 years), race/ethnicity (white, black, Hispanic, other/missing), plan type (comprehensive, other), region (northeast, north central, south, west, unknown), Basis of Eligibility (BOE) (adults, children, unknown), source (inpatient, outpatient), and Charlson Comorbidity Index (CCI) (0, 1-3, 4+).^{9, 26, 28, 29} The Charlson Comorbidity index was used to capture information on comorbidities, those with a score of 0 had no comorbidities.^{30, 31} Included variables were based on what was available in each of the datasets.

Statistical Analysis

We conducted multiple logistic regression analyses to the direct effect of TBI on suicide ideation/attempt adjusted by demographic variables: sex, age, race/ethnicity, plan type, BOE, inpatient/outpatient source, and CCI score. We also conducted the direct analysis controlling for sleep disorder, opioid use disorder, and substance use disorders other than OUD in addition to the demographic variables. Analysis was conducted separately for the commercial and Medicaid sample.

We conducted mediation analyses to determine the effect of mediators on the association between TBI and suicidal ideation/attempt. Figure 1 provides a depiction of the conceptual model for the mediation. Path c is the direct effect of TBI on suicidal ideation/attempt. Paths a and b together are the indirect effect of TBI on suicidal ideation/attempt. We used the natural effect model (NEM) to examine the association between TBI and suicidal ideation/attempt, the mediating influences of opioid use disorder, sleep disorder, psychiatric disorder, and substance use disorders other than OUD, while controlling for sociodemographic variables.³² The NEM can estimate the indirect effect of TBI on suicidal ideation/attempt. Because there were four mediators, the other three mediators were controlled for while the mediation effect of the remaining one was estimated. It is possible that there is a presence of predictor-mediator interaction. We used the counterfactual approach, which allows one to carry out mediation analysis when interaction between predictor and mediator is present.³² The CAUSALMED procedure in SAS 9.04.01M5 was used to conduct the mediation analyses allowing for predictor-mediator interactions.³² CAUSALMED procedure fitted generalized linear regression models with specified binary distributions. The mediation effects were computed using the odds ratio and excess relative risk (ERR). The ERR of

total effect is equal to the sum of ERR of the direct and indirect effect. The Percentage Mediated = $100 * \text{ERR}(\text{NID}) / \text{ERR}(\text{Total effect})$.

The public was not involved in the design of this study, as it was not appropriate for this study.

Results

The descriptive statistics of the two samples are reported in Table 1. In the Medicaid sample, among those who had a TBI and a suicidal ideation/attempt there was a higher percentage of females than males, those aged 10-17 years compared with other age groups, and who were white compared with other races. The majority (92.81%) of those with a TBI and suicidal ideation/attempt had a psychiatric disorder present within the study period. While only 14.75% had a documented opioid use disorder, 43.71% had presence of substance use disorders other than OUD; 16.77% had a sleep disorder. In the private health insurance sample, among those who had a TBI and a suicidal ideation/attempt there was a higher percentage of females than males and those aged 10-17 years compared with other age groups. Less than half of the private health insurance sample who had a TBI and suicidal ideation/attempt had opioid use disorder (6.12%), sleep disorder (1.65%), psychiatric disorder (15.98%), or substance use disorders other than OUD (41.19%).

In both the Medicaid and private health insurance samples, patients with a TBI had at least 2 times higher odds of suicidal ideation/attempt in the preceding 12 months. Males had lower odds than females of suicidal ideation/attempt (Table 2). In the Medicaid sample, those aged 55-64 years had lower odds than other age groups of suicidal ideation/attempt. The same is true among the private health insurance sample, although the odds ratios are much higher for those aged 10-17 and 18-24 years. Both the Medicaid and private health insurance samples showed that individuals with a CCI of 1 or higher had higher odds of a suicidal ideation/attempt than those without comorbidities.

Table 3 contains the estimates of the direct association of TBI on suicidal ideation/attempt while controlling for opioid use disorder, sleep disorder, psychiatric disorder, substance use disorders other than OUD, sex, age, race/ethnicity, plan type, BOE, inpatient/outpatient source, and CCI score. When controlling for the mediators, those with a TBI had 1.49 and 1.73 times higher odds to have a suicidal ideation/attempt in the Medicaid and private health insurance samples, respectively. In both samples those with sleep disorder, psychiatric disorder, and substance use disorders other than OUD had higher odds of suicidal ideation/ attempts.

Table 4 presents the mediation analysis results. In the Medicaid sample psychiatric disorders partially mediated the association between TBI and suicide (indirect AOR = 1.16; CI = 1.15-1.17), as did substance use disorders other than OUD (AOR = 1.03; CI = 1.03-1.03). Psychiatric disorders mediated 22.40% of the total effect, while opioid use disorder mediated 7.47%. Similarly, in the private health insurance sample psychiatric disorders partially mediated the association between TBI and suicide (indirect AOR = 1.03; CI = 1.03-1.03), as did substance use disorders other than OUD (AOR = 1.01; CI = 1.01-1.01).

Psychiatric disorders mediated 3.97% of the total effect and substance use disorders other than OUD mediated 2.08% of the total effect. Among those in the private health insurance sleep disorder mediated 1.03% of the total effect.

Discussion

In this study of more than 600,000 Medicaid and privately insured patients over a 12-month period, those with a documented TBI were over 2 times more likely to have documented suicidal ideation/attempt compared with those without a TBI. The association between TBI and suicide was revealed to take place, in part, with mediators, with 22.2% of the association mediated by psychiatric disorders and 7.46% mediated by substance use disorders other than OUD in patients with Medicaid; and among those with private health insurance, 4.18% of the association was mediated by psychiatric disorders and 2.17% by substance use disorders other than OUD. After controlling for mediators, patients in both the Medicaid and private health insurance sample were at least 1.49-1.73 times more likely to have suicidal ideation/attempt when compared to patients without TBI, respectively. While results trended in the same direction for both Medicaid and privately insured patients, we observed a general increase in the percentage of mediated associations among patients with Medicaid insurance. Given differences in socioeconomic status between individuals with Medicaid and private insurance, this finding may reflect unique contributions of socioeconomic status to the relationship between TBI, suicidal ideation/attempt, and mediators. Further research integrating data sources with additional socioeconomic indicators would be helpful to better understand this potential relationship. Taken together, our results emphasize the important direct associations between TBI and suicidal ideation/attempt. While psychiatric disorders, substance use disorders other than OUD, and sleep disorders contribute indirect effects to this relationship (1.25–22.2%), direct effects from TBI had the largest impact on suicidal ideation/attempt, indicating that close monitoring of patients with TBI for suicidal ideation/attempt is important, even in the absence of psychiatric, substance use, or sleep comorbidities.

Previous studies have posited that post-TBI psychiatric disorders may act as mediators between TBI and suicide;³³ our study affirms that psychiatric disorders partially mediate the relationship between TBI and suicide. Our study echoes previous findings that depression,^{3, 34} PTSD,³⁵ and sleep quality³⁶ mediate associations between TBI and suicide. Fonda et al.'s study of TBI and attempted suicide among U.S. veterans of the Iraq and Afghanistan wars found that 83% of the association between attempted suicide and TBI was mediated through comorbid psychiatric conditions and 51.4% through substance use disorder.³⁵ In contrast, our study found that psychiatric disorders only mediated 22.2% and substance use disorders other than OUD mediated 7.46% of the TBI-suicide association in our Medicaid sample and 4.18% mediated by psychiatric disorders and 2.17% mediated by substance use disorders other than OUD in patients with private health insurance. This difference in mediation effect may be due to differences in study populations (e.g., general public versus veterans) and outcomes, as we included both suicidal ideation/attempts.

Our study findings have important implications for clinical practice. Identifying treatable conditions that increase risk for suicide among patients with a TBI—and quantifying their

impact—provides actionable information for suicide prevention efforts. Treatment of opioid use disorders, sleep disorders, psychiatric disorders, and substance use disorders other than OUD among patients with TBI may minimize risk of suicidal ideation/attempt. Other suicide prevention strategies (e.g., reducing access to lethal means, ensuring coverage of psychiatric health conditions by health insurance policies, ensuring continuity of care among those at risk within health systems) may also help address issues underlying some of the risk conferred by conditions associated with TBI.³⁷ However, in our study, mediators did not address the majority of the relationship between TBI and suicidal ideation/attempt, suggesting there are other factors that contribute to suicide risk among patients with a TBI that are not yet fully understood. Further, there is a direct relationship between TBI and suicidal ideation that may not be improved by treatment of mediators like psychiatric disorders or substance use disorders other than OUD. The mechanism for this direct relationship between TBI and suicide is not yet understood; further studies, including those that examine biomarkers and conduct neuroimaging, are needed to elucidate this relationship. Overall, our findings reinforce the importance of primary prevention of TBI and the need for close monitoring of patients with a TBI for risk of suicide in the 12 months following injury.

There are several limitations to this study. First, patients with mediators that occurred outside of the 3 months that were controlled for may be included in the study. Patients may have experienced one of the mediators prior to the TBI and outside the study timeframe, which may result in results that are overestimated. Second, survey weights were not used and therefore these results cannot be generalized to the national population. Third, the analysis included all cases with ICD 10-CM codes related to intentional self-harm, but these codes do not differentiate between events that were suicide attempts and events in which the self-harm was intentional but there was no intent to die.³⁸ However, there is some research that suggests that most ED visits for self-harm are suicidal in nature.³⁹ Fourth, our study is reliant on medical coding to capture clinical diagnoses and may underrepresent cases of TBI, suicidal ideation/attempt, sleep disorders, psychiatric disorders, and substance use disorders; given the known associations between TBI and other disorders, healthcare providers may be more likely to assess suicidal behaviors and sub-clinical sleep, psychiatric, and substance use disorders in patients with a known TBI diagnosis, which may bias our results away from the null. Additionally, at the time of this analysis, we were unable to stratify TBI encounters by injury severity due to a lack of uniform criteria for injury severity established for ICD-10-CM coding. Finally, we did not conduct analyses looking at suicidal ideation/attempts separately, due to the small size of the sample.

Conclusion

Sleep disorders, psychiatric disorders, and substance use disorders other than OUD partially mediate the relationship between TBI and suicidal ideation/attempt. However, the direct effect between TBI and suicidal behaviors accounts for the largest associations. These results suggest that closely monitoring patients with TBI for suicidal ideation/attempts, even in the absence of psychiatric, substance use, or sleep comorbidities, could help prevent suicides. Further research is needed to understand the direct relationship between TBI and suicidal ideation/attempt.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Data Availability:

Data is available through IBM MarketScan Research.

References

1. Tsasouides T, Cantor JB, Gordon WA. Suicidal ideation following traumatic brain injury: prevalence rates and correlates in adults living in the community. *The Journal of head trauma rehabilitation* 2011;26(4):265–275. [PubMed: 21734510]
2. Simpson GK, Tate RL. Preventing suicide after traumatic brain injury: implications for general practice. *Medical journal of Australia* 2007;187(4):229–232. [PubMed: 17708726]
3. Gradus JL, Wisco BE, Luciano MT, Iverson KM, Marx BP, Street AE. Traumatic brain injury and suicidal ideation among US Operation Enduring Freedom and Operation Iraqi Freedom veterans. *Journal of Traumatic Stress* 2015;28(4):361–365. [PubMed: 26179483]
4. Taylor C, Jung H. Disorders of Mood After Traumatic Brain Injury. In: *Seminars in clinical neuropsychiatry*; 1998; 1998. p. 224–231.
5. Hesdorffer DC, Rauch SL, Tamminga CA. Long-term psychiatric outcomes following traumatic brain injury: a review of the literature. *The Journal of head trauma rehabilitation* 2009;24(6):452–459. [PubMed: 19940678]
6. McIntire KL, Crawford KM, Perrin PB, Sestak JL, Aman K, Walter LA, et al. Factors Increasing Risk of Suicide after Traumatic Brain Injury: A State-of-the-Science Review of Military and Civilian Studies. *Brain injury* 2021;35(2):151–163. [PubMed: 33460350]
7. Bahraini NH, Simpson GK, Brenner LA, Hoffberg AS, Schneider AL. Suicidal ideation and behaviours after traumatic brain injury: a systematic review. *Brain Impair* 2013;14(1):92–112.
8. Dreer LE, Tang X, Nakase-Richardson R, Pugh MJ, Cox MK, Bailey EK, et al. Suicide and traumatic brain injury: a review by clinical researchers from the National Institute for disability and independent living rehabilitation research (NIDILRR) and Veterans health administration traumatic brain injury model systems. *Current opinion in psychology* 2018;22:73–78. [PubMed: 28963946]
9. Mackelprang JL, Bombardier CH, Fann JR, Temkin NR, Barber JK, Dikmen SS. Rates and predictors of suicidal ideation during the first year after traumatic brain injury. *AJPH* 2014;104(7):e100–e107.
10. Nock MK, Borges G, Bromet EJ, Cha CB, Kessler RC, Lee S. Suicide and suicidal behavior. *Epidemiologic reviews* 2008;30(1):133–154. [PubMed: 18653727]
11. Fisher LB, Pedrelli P, Iverson GL, Bergquist TF, Bombardier CH, Hammond FM, et al. Prevalence of suicidal behaviour following traumatic brain injury: longitudinal follow-up data from the NIDRR traumatic brain injury model systems. *Brain inj* 2016;30(11):1311–1318. [PubMed: 27541868]
12. National Institutes of Mental Health. Statistics - Suicide. 2021 [cited 2021 August 16]; Available from: https://www.nimh.nih.gov/health/statistics/suicide#part_154973
13. Pagulayan KF, Temkin NR, Machamer JE, Dikmen SS. Patterns of alcohol use after traumatic brain injury. *Journal of neurotrauma* 2016;33(14):1390–1396. [PubMed: 26530335]
14. McKinlay A, Corrigan J, Horwood LJ, Fergusson DM. Substance abuse and criminal activities following traumatic brain injury in childhood, adolescence, and early adulthood. *The Journal of head trauma rehabilitation* 2014;29(6):498–506. [PubMed: 24263173]
15. Corrigan JD, Adams RS. The intersection of lifetime history of traumatic brain injury and the opioid epidemic. *Addictive behaviors* 2019;90:143. [PubMed: 30391775]
16. Adams RS, Corrigan JD, Dams-O'Connor K. Opioid use among individuals with traumatic brain injury: a perfect storm? *Journal of neurotrauma* 2020;37(1):211–216. [PubMed: 31333067]

17. Kolakowsky-Hayner SA EVG III, Kreutzer JS, Marwitz JH, Meade MA, Cifu DX. Post-injury substance abuse among persons with brain injury and persons with spinal cord injury. *Brain injury* 2002;16(7):583–592. [PubMed: 12119077]
18. Bombardier CH, Fann JR, Temkin NR, Esselman PC, Barber J, Dikmen SS. Rates of major depressive disorder and clinical outcomes following traumatic brain injury. *Jama* 2010;303(19):1938–1945. [PubMed: 20483970]
19. Rapoport MJ. Depression following traumatic brain injury. *CNS drugs* 2012;26(2):111–121. [PubMed: 22296315]
20. Koponen S, Taiminen T, Portin R, Himanen L, Isoniemi H, Heinonen H, et al. Axis I and II psychiatric disorders after traumatic brain injury: a 30-year follow-up study. *American journal of Psychiatry* 2002;159(8):1315–1321. [PubMed: 12153823]
21. Alway Y, Gould K, Johnston L, McKenzie D, Ponsford J. A prospective examination of Axis I psychiatric disorders in the first 5 years following moderate to severe traumatic brain injury. *Psychological medicine* 2016;46(6):1331–1341. [PubMed: 26867715]
22. Rao V, Spiro J, Vaishnavi S, Rastogi P, Mielke M, Noll K, et al. Prevalence and types of sleep disturbances acutely after traumatic brain injury. *Brain injury* 2008;22(5):381–386. [PubMed: 18415718]
23. Kempf J, Werth E, Kaiser PR, Bassetti CL, Baumann CR. Sleep–wake disturbances 3 years after traumatic brain injury. *Journal of Neurology, Neurosurgery & Psychiatry* 2010;81(12):1402–1405. [PubMed: 20884672]
24. Weymann KB, Rourke JM. Sleep after traumatic brain injury. *Nursing Clinics* 2021;56(2):275–286. [PubMed: 34023121]
25. Simpson G, Tate R. Clinical features of suicide attempts after traumatic brain injury. *The Journal of nervous and mental disease* 2005;193(10):680–685. [PubMed: 16208164]
26. Simpson G, Tate R. Suicidality after traumatic brain injury: demographic, injury and clinical correlates. *Psychological medicine* 2002;32(4):687–697. [PubMed: 12102383]
27. Hedegaard H, Johnson R, Warner M, Chen L, Annett J. Proposed Framework for Presenting Injury Data Using the International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) Diagnosis Codes. *National health statistics reports* 2016(89):1–20.
28. Steele IH, Thrower N, Noroian P, Saleh FM. Understanding suicide across the lifespan: a United States perspective of suicide risk factors, assessment & management. *Journal of forensic sciences* 2018;63(1):162–171. [PubMed: 28639299]
29. Fisher LB, Pedrelli P, Iverson GL, Bergquist TF, Bombardier CH, Hammond FM, et al. Prevalence of suicidal behaviour following traumatic brain injury: longitudinal follow-up data from the NIDRR traumatic brain injury model systems. 2016;30(11):1311–1318.
30. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of chronic diseases* 1987;40(5):373–383. [PubMed: 3558716]
31. Beyrer J, Manjelienskaia J, Bonafede M, Lenhart G, Nolot S, Haldane D, et al. Validation of an ICD-10 coding adaptation for the Charlson Comorbidity Index in United States healthcare administrative data. In: *ISPOR*; 2020.
32. Valeri L, VanderWeele TJ. Mediation analysis allowing for exposure–mediator interactions and causal interpretation: theoretical assumptions and implementation with SAS and SPSS macros. *Psychological methods* 2013;18(2):137. [PubMed: 23379553]
33. Madsen T, Erlangsen A, Orlovskaya S, Mofaddi R, Nordentoft M, Benros ME. Association between traumatic brain injury and risk of suicide. *JAMA* 2018;320(6):580–588. [PubMed: 30120477]
34. Stanley IH, Joiner TE, Bryan CJ. Mild traumatic brain injury and suicide risk among a clinical sample of deployed military personnel: Evidence for a serial mediation model of anger and depression. *Journal of psychiatric research* 2017;84:161–168. [PubMed: 27743528]
35. Fonda JR, Fredman L, Brogly SB, McGlinchey RE, Milberg WP, Gradus JL. Traumatic brain injury and attempted suicide among veterans of the wars in Iraq and Afghanistan. *American journal of epidemiology* 2017;186(2):220–226. [PubMed: 28472407]

36. DeBeer BB, Kimbrel NA, Mendoza C, Davidson D, Meyer EC, La Bash H, et al. Traumatic Brain Injury, Sleep Quality, and Suicidal Ideation in Iraq/Afghanistan-Era Veterans. *The Journal of nervous and mental disease* 2017;205(7):512. [PubMed: 28590264]
37. Stone DM, Holland KM, Bartholow BN, Crosby AE, Davis SP, Wilkins N. Preventing suicide: a technical package of policies, programs, and practice. In: National Center for Injury Prevention and Control, Centers for Disease Control and Prevention, editors. Atlanta, GA; 2017.
38. Hedegaard H, Schoenbaum M, Claassen C, Crosby A, Holland K, Proescholdbell S. Issues in developing a surveillance case definition for nonfatal suicide attempt and intentional self-harm using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) coded data. *National health statistics reports* 2018(108):1–19.
39. Centers for Disease Control and Prevention. Nonfatal self-inflicted injuries treated in hospital emergency departments--United States, 2000. *MMWR: Morbidity and mortality weekly report* 2002;51(20):436–438. [PubMed: 12056500]

What is already known on this subject

- There is an association between Traumatic Brain Injury (TBI) and suicidal thoughts and behaviors, however there is little research on the mechanistic hypothesis underpinning the relationship.
- TBI is associated with post-injury substance abuse, psychiatric disorders, PTSD, and sleep disturbances, however there may be a bidirectional relationship with suicidal thoughts and behaviors.

What this study adds

- The association between TBI and suicide was revealed to take place, in part, with mediators. However, mediators such as psychiatric, substance use, or sleep comorbidities did not explain the entirety of the relationship between TBI and suicidal ideation/attempt.
- Identifying treatable conditions that increase risk for suicide among patients with a TBI—and quantifying their impact—provides actionable information for suicide prevention efforts.

How this study might affect research, practice, or policy

- Closely monitoring patients with TBI for suicidal ideation/attempts, even in the absence of psychiatric, substance use, or sleep comorbidities, could help prevent suicides, based on these results.
- Further research is needed to understand the direct relationship between TBI and suicidal ideation/attempt.

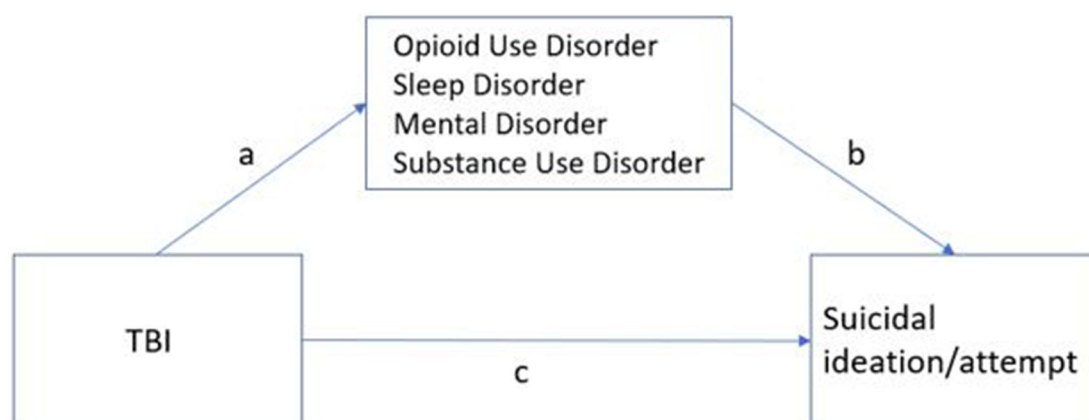


Figure 1:
Concept model of mediation relationship

Table 1:

Descriptive Statistics, MarketScan January 2016–December 2018

Characteristics	Medicaid				Private Health Insurance			
	TBI (N=37703)		Non-TBI (N=190141)		TBI (N=62290)		Non-TBI (N=323150)	
	Yes (N=1837)	No (N=35866)	Yes (N=3772)	No (N=186369)	Yes (N=607)	No (N=61683)	Yes (N=1498)	No (N=321652)
Suicidal Ideation/Attempt	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Sex								
Male	813(44.26)	18966(52.88)	1802(47.77)	96351(51.7)	251(41.35)	31270(50.69)	818(54.61)	163943(50.97)
Female	1024(55.74)	16900(47.12)	1970(52.23)	90018(48.3)	356(58.65)	30413(49.31)	680(45.39)	157709(49.03)
Age								
10-17	716(38.98)	19685(54.88)	1914(50.74)	100336(53.84)	277(45.63)	29549(47.9)	745(49.73)	149941(46.62)
18-24	262(14.26)	4002(11.16)	488(12.94)	21269(11.41)	197(32.45)	11060(17.93)	552(36.85)	58001(18.03)
25-34	275(14.97)	4058(11.31)	479(12.7)	22092(11.85)	27(4.45)	3105(5.03)	47(3.14)	16425(5.11)
35-44	241(13.12)	2919(8.14)	372(9.86)	16070(8.62)	31(5.11)	4835(7.84)	56(3.74)	25522(7.93)
45-54	208(11.32)	2706(7.54)	322(8.54)	14511(7.79)	45(7.41)	6853(11.11)	50(3.34)	36809(11.44)
55-64	135(7.35)	2496(6.96)	197(5.22)	12091(6.49)	30(4.94)	6281(10.18)	48(3.2)	34954(10.87)
Race/Ethnicity								
White	1254(68.26)	21067(58.74)	2468(65.43)	110212(59.14)	NR	NR	NR	NR
Black	363(19.76)	10521(29.33)	906(24.02)	53521(28.72)	NR	NR	NR	NR
Hispanic	56(3.05)	1520(4.24)	94(2.49)	7764(4.17)	NR	NR	NR	NR
Other, Missing	164(8.93)	2758(7.69)	304(8.06)	14872(7.98)	NR	NR	NR	NR
Plan type								
Comprehensive	617(33.59)	13936(38.86)	1576(41.78)	81637(43.8)	45(7.41)	2582(4.2)	60(4.02)	12094(3.78)
Other ^a	1220(66.41)	21929(61.14)	2196(58.22)	104731(56.2)	562(92.59)	58830(95.8)	1432(95.98)	307825(96.22)
Region								
Northeast	NR	NR	NR	NR	139(22.9)	15030(24.37)	297(19.83)	78142(24.29)
North Central	NR	NR	NR	NR	175(28.83)	14929(24.2)	429(28.64)	78034(24.26)
South	NR	NR	NR	NR	172(28.34)	22345(36.23)	539(35.98)	116485(36.21)
West	NR	NR	NR	NR	121(19.93)	9301(15.08)	231(15.42)	48589(15.11)
Unknown	NR	NR	NR	NR	0(0.0)	78(0.13)	2(0.13)	402(0.12)
Basis of Eligibility								

Characteristics		Medicaid				Private Health Insurance			
		TBI (N=37703)		Non-TBI (N=190141)		TBI (N=62290)		Non-TBI (N=323150)	
Suicidal Ideation/Attempt		Yes (N=1837)	No (N=35866)	Yes (N=3772)	No (N=186369)	Yes (N=607)	No (N=61683)	Yes (N=1498)	No (N=321652)
		N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Source									
Adults		997(54.27)	15629(43.58)	2058(54.56)	93844(50.35)	NR	NR	NR	NR
Children		701(38.16)	18408(51.32)	1669(44.25)	88252(47.35)	NR	NR	NR	NR
Unknown		139(7.57)	1829(5.1)	45(1.19)	4273(2.29)	NR	NR	NR	NR
Inpatient		180(9.8)	2625(7.32)	425(11.27)	8146(4.37)	36(5.93)	2612(4.23)	722(48.2)	18737(5.83)
Outpatient		1657(90.2)	33241(92.68)	3347(88.73)	178223(95.63)	571(94.07)	59071(95.77)	776(51.8)	302915(94.17)
Charlson Comorbidity Index Score									
0		657(35.76)	18706(52.16)	1876(49.73)	119114(63.91)	303(49.92)	39443(63.94)	985(65.75)	233041(72.45)
1-3		896(48.78)	14070(39.23)	1526(40.46)	55539(29.8)	265(43.66)	19852(32.18)	482(32.18)	79136(24.6)
4+		284(15.46)	3090(8.62)	370(9.81)	11716(6.29)	39(6.43)	2388(3.87)	31(2.07)	9475(2.95)
Presence of Opioid Use Disorder									
No		1566(85.25)	34303(95.64)	3413(90.48)	181102(97.17)	537(93.88)	58474(95.94)	1320(92.7)	311357(98.26)
Yes		271(14.75)	1563(4.36)	359(9.52)	5267(2.83)	35(6.12)	2474(4.06)	104(7.3)	5518(1.74)
Presence of Sleep Disorder									
No		1529(83.23)	32391(90.31)	3284(87.06)	174230(93.49)	597(98.35)	61467(99.65)	1467(97.93)	321257(99.88)
Yes		308(16.77)	3475(9.69)	488(12.94)	12139(6.51)	10(1.65)	216(0.35)	31(2.07)	395(0.12)
Presence of Psychiatric disorder									
No		132(7.19)	21764(60.68)	306(8.11)	136174(73.07)	510(84.02)	59869(97.06)	1174(78.37)	319691(99.39)
Yes		1705(92.81)	14102(39.32)	3466(91.89)	50195(26.93)	97(15.98)	1814(2.94)	324(21.63)	1961(0.61)
Presence of Other Substance Use Disorders									
No		1034(56.29)	31093(86.69)	2464(65.32)	175952(94.41)	357(58.81)	55580(90.11)	431(28.77)	304431(94.65)
Yes		803(43.71)	4773(13.31)	1308(34.68)	10417(5.59)	250(41.19)	6103(9.89)	1067(71.23)	17221(5.35)

Note: NR=Not Reported.

^aOther plan type is defined as HMO, EPO, PPO, POS with Capitation, CDHP, and HDHP.

Table 2:

Direct effect of TBI on Suicidal Ideation and Attempt, adjusted by selected variables, MarketScan, January 2016 - December 2018

Variable	Medicaid		Private Health Insurance	
	AOR	95% CI	AOR	95% CI
TBI				
No		Ref		Ref
Yes	2.29	2.16, 2.42	2.31	2.10, 2.55
Sex				
Male	0.85	0.81, 0.90	0.74	0.68, 0.81
Female		Ref		Ref
Age				
10-17	1.82	1.57, 2.11	11.72	9.13, 15.06
18-24	2.27	1.96, 2.61	13.64	10.66, 17.45
25-34	1.89	1.64, 2.17	3.75	2.71, 5.21
35-44	1.85	1.61, 2.13	2.65	1.94, 3.62
45-54	1.51	1.31, 1.73	1.64	1.21, 2.23
55-64		Ref		Ref
Race/Ethnicity				
White		Ref	NR	NR
Black	0.69	0.64, 0.73	NR	NR
Hispanic	0.64	0.54, 0.75	NR	NR
Other, Missing	0.89	0.81, 0.99	NR	NR
Plan Type				
Comprehensive		Ref		Ref
Other ^a	1.12	1.06, 1.19	0.81	0.66, 0.99
Region				
Northeast	NR	NR		Ref
North Central	NR	NR	1.29	1.14, 1.47
South	NR	NR	0.94	0.83, 1.06
West	NR	NR	1.25	1.08, 1.44
Unknown	NR	NR	0.90	0.22, 3.69
Basis of Eligibility				
Adults		Ref	NR	NR
Children	0.98	0.89, 1.07	NR	NR
Unknown	0.95	0.82, 1.11	NR	NR
Source				
Inpatient		Ref		Ref
Outpatient	0.52	0.48, 0.57	0.05	0.05, 0.06
Charlson Comorbidity Index Score				
0		Ref		Ref
1-3	1.76	1.66, 1.87	1.47	1.34, 1.62

Variable	Medicaid		Private Health Insurance	
	AOR	95% CI	AOR	95% CI
4+	2.54	2.29, 2.83	1.25	0.96, 1.62

Note: NR=Not Reported; Ref=Referent group.

Models were adjusted for opioid use disorder, sleep disorder, psychiatric disorder, substance use disorder other than OUD, sex, age, race/ethnicity , type of plan, region, basis of eligibility category, inpatient/outpatient source, and Charlson Comorbidity Index score.

^aOther plan type is defined as HMO, EPO, PPO, POS with Capitation, CDHP, and HDHP

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Table 3:

Direct effect of TBI on Suicidal Ideation and Attempt, adjusted by all covariates: MarketScan, January 2016 - December 2018

Variable	Medicaid		Private Health Insurance	
	AOR	95% CI	AOR	95% CI
TBI				
No		Ref		Ref
Yes	1.49	1.40, 1.58	1.73	1.56, 1.93
Opioid Use Disorder				
No		Ref		Ref
Yes	1.09	0.98, 1.20	0.71	0.47, 1.07
Sleep disorder				
No		Ref		Ref
Yes	1.08	1.00, 1.17	1.34	1.09, 1.63
Psychiatric disorder				
No		Ref		Ref
Yes	24.29	21.96, 26.86	18.28	16.55, 20.19
Substance Use Disorders Other than OUD				
No		Ref		Ref
Yes	4.67	4.36, 5.01	4.5	3.86, 5.23
Sex				
Male	0.91	0.86, 0.96	0.77	0.70, 0.85
Female		Ref		Ref
Age				
10-17	3.84	3.28, 4.49	12.27	9.32, 16.14
18-24	3.08	2.66, 3.58	10.45	7.96, 13.71
25-34	1.71	1.48, 1.98	3.15	2.19, 4.54
35-44	1.58	1.37, 1.83	2.33	1.65, 3.29
45-54	1.23	1.06, 1.42	1.73	1.25, 2.39
55-64		Ref		Ref
Race/Ethnicity				
White		Ref	NR	NR
Black	0.94	0.88, 1.00	NR	NR
Hispanic	0.95	0.80, 1.13	NR	NR
Other, Missing	1.08	0.98, 1.20	NR	NR
Plan Type				
Comprehensive		Ref		Ref
Other ^a	1.10	1.04, 1.17	0.91	0.73, 1.14
Region				
Northeast	NR	NR		Ref
North Central	NR	NR	1.18	1.03, 1.36
South	NR	NR	0.93	0.81, 1.06

Variable	Medicaid		Private Health Insurance	
	AOR	95% CI	AOR	95% CI
West	NR	NR	1.21	1.03, 1.41
Unknown	NR	NR	0.93	0.21, 4.22
Basis of Eligibility				
Adults		Ref	NR	NR
Children	1.10	1.00, 1.21	NR	NR
Unknown	1.13	0.96, 1.33	NR	NR
Source				
Inpatient		Ref		Ref
Outpatient	0.68	0.62, 0.75	0.08	0.07, 0.09
Charlson Comorbidity Index Score				
0		Ref		Ref
1-3	1.21	1.14, 1.29	1.36	1.23, 1.51
4+	1.39	1.24, 1.55	1.24	0.93, 1.65

Note: AOR= adjusted odds ratio; CI= confidence interval; NR=Not Reported; Ref=Referent group.

Models were adjusted for opioid use disorder, sleep disorder, psychiatric disorder, substance use disorder other than OUD, sex, age, race/ethnicity , type of plan, region, basis of eligibility category, inpatient/outpatient source, and Charlson Comorbidity Index score.

^aOther plan type is defined as HMO, EPO, PPO, POS with Capitation, CDHP, and HDHP.

Mediation Effect of Opioid Use Disorder, Sleep Disorder, Psychiatric Disorder, and Substance Use Disorder Other than OUD on the Association between TBI and Suicide, MarketScan, January 2016 - December 2018

Table 4:

Insurance	Mediator	Total Effect		NIE		Percent Mediated
		AOR (95%CI)	ERR (95%CI)	AOR (95%CI)	ERR (95%CI)	
Medicaid	Opioid Use Disorder	1.44(1.35,1.54)*	0.44(0.35,0.54)*	1.00 (1.00,1.00)*	0.00(0.00, 0.00)	0.00(0.00,0.00)
	Sleep Disorder	1.49(1.39,1.58)*	0.49(0.39,0.58)*	1.00 (1.00,1.00)*	0.00(0.00,0.00)	0.26(−0.09,0.6)
	Psychiatric Disorder	2.62(2.10,3.15)*	1.62(1.10,2.15)*	1.16(1.15,1.17)*	0.36(0.29,0.44)*	22.40(19.51,25.3)*
	Substance Use Disorder Other than OUD	1.67(1.54,1.79)*	0.67(0.54,0.79)*	1.03(1.03,1.03)*	0.05(0.04,0.06)*	7.47(6.53,8.4)*
Private Health Insurance	Opioid Use Disorder	1.73(1.54,1.91)*	0.73(0.54,0.91)*	1.00(1.00,1.00)*	0.00(0.00,0.00)	−0.02(−0.05,0.01)
	Sleep Disorder	1.80(1.61,2.00)*	0.80(0.61,1.00)*	1.00(1.00,1.01)*	0.01(0.01,0.01)*	1.03(0.66,1.39)*
	Psychiatric Disorder	4.35(3.71,4.98)*	3.35(2.71,3.98)*	1.03(1.03,1.03)*	0.13(0.11,0.15)*	3.97(3.64,4.31)*
	Substance Use Disorder Other than OUD	1.92(1.71,2.14)*	0.92(0.71,1.14)*	1.01(1.01,1.01)*	0.02(0.02,0.02)*	2.08(1.79,2.37)*

Note: NIE= Natural Indirect effect; AOR= adjusted odds ratio; CI= confidence interval; ERR=Excess Relative Risk; Percent Mediated=100*ERR(NIE)/ERR(Total effect).

All models were adjusted for sleep disorder, opioid use disorder, substance use disorder other than OUD, psychiatric disorder, sex, age, race, type of plan, basis of eligibility category, inpatient/outpatient source, and Charlson Comorbidity Index score. Models included an interaction term between the mediator and TBI.

* Indicates statistical significance at $p<.0001$.