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## Using Machine Learning to Examine Suicidal Ideation After TBI: A TBI Model Systems National Database Study

## Lauren B. Fisher, Ph.D.\*,

Department of Psychiatry, Massachusetts General Hospital, Boston, MA; Department of Psychiatry, Harvard Medical School, Boston, MA

## Joshua E. Curtiss, Ph.D.\*,

Department of Psychiatry, Massachusetts General Hospital, Boston, MA; Department of Psychiatry, Harvard Medical School, Boston, MA

## Daniel W. Klyce, Ph.D.,

Central Virginia Veterans Affairs Health Care System, Richmond, VA; Sheltering Arms Institute, Richmond, VA; Virginia Commonwealth University Health System, Richmond, VA

## Paul B. Perrin, Ph.D.,

Central Virginia Veterans Affairs Health Care System, Richmond, VA; Department of Psychology and Department of Physical Medicine and Rehabilitation, Virginia Commonwealth University, Richmond, VA

## Shannon B. Juengst, Ph.D.,

Department of Physical Medicine and Rehabilitation, UT Southwestern Medical Center, Dallas, TX

## Kelli W. Gary, Ph.D.,

Department of Rehabilitation Counseling, Virginia Commonwealth University, Richmond, VA

## Janet P. Niemeier, Ph.D.,

Department of Psychology, University of Alabama, Birmingham, AL

## Flora McConnell Hammond, M.D.,

Department of Physical Medicine and Rehabilitation, Indiana University School of Medicine, Indianapolis, IN; Rehabilitation Hospital of Indiana, Indianapolis, IN

## Thomas F. Bergquist, Ph.D.,

Mayo Clinic College of Medicine and Science, Rochester, MN

## Amy K. Wagner, M.D.,

Departments of Physical Medicine & Rehabilitation and Neuroscience, Center for Neuroscience, Safar Center for Resuscitation Research, Clinical and Translational Science Institute, University of Pittsburgh, Pittsburgh PA

\*These authors contributed equally to this work and claim co-first authorship CONFLICTS OF INTEREST:

The authors have no conflicts of interests to disclose.

**CORRESPONDING AUTHOR:** Lauren B. Fisher Ph.D., 1 Bowdoin Square, 6<sup>th</sup> Floor, Boston, MA 02114, Phone: (617) 643-0877, fisher.lauren@mgh.harvard.edu.

#### Amanda R. Rabinowitz, Ph.D.,

Moss Rehabilitation Research Institute, Elkins Park, PA

#### Joseph T. Giacino, Ph.D.,

Department of Physical Medicine and Rehabilitation, Spaulding Rehabilitation Hospital, Boston, MA; Department of Psychiatry, Massachusetts General Hospital, Boston, MA

#### Ross D. Zafonte, D.O.

Department of Physical Medicine and Rehabilitation, Spaulding Rehabilitation Hospital, Boston, MA; Massachusetts General Hospital, Boston, MA; Brigham and Women's Hospital, Boston, MA; Harvard Medical School, Boston, MA

#### Abstract

**Objective:** To predict suicidal ideation one year after moderate to severe traumatic brain injury (TBI).

**Design:** Cross-sectional design with data collected through the prospective, longitudinal TBI Model Systems (TBIMS) network at hospitalization and one year after injury. Participants who completed the Patient Health Questionnaire-9 (PHQ-9) suicide item at year one follow-up (N=4,328) were included.

**Results:** A gradient boosting machine (GBM) algorithm demonstrated the best performance in predicting suicidal ideation one year after TBI. Predictors were PHQ-9 items (except suicidality), Generalized Anxiety Disorder-7 (GAD-7) items, and a measure of heavy drinking. Results of the 10-fold cross-validation GBM analysis indicated excellent classification performance with an AUC of 0.882. Sensitivity was 0.85, and specificity was 0.77. Accuracy was 0.78 (95% CI: 0.77 - 0.79). Feature importance analyses revealed that depressed mood and guilt were the most important predictors of suicidal ideation, followed by anhedonia, concentration difficulties, and psychomotor disturbance.

**Conclusions:** Overall, depression symptoms were most predictive of suicidal ideation. Despite the limited clinical impact of the present findings, machine learning has potential to improve prediction of suicidal behavior, leveraging electronic health record data, to identify individuals at greatest risk, thereby facilitating intervention and optimization of long-term outcomes following TBI.

#### Keywords

traumatic brain injury; suicidal ideation; depression; anxiety; alcohol use; machine learning

Risk of suicidal ideation (SI) and behavior is 3-5 times higher for persons with traumatic brain injury (TBI) than the general US population.<sup>1–3</sup> Rates of SI after TBI range from 7-33%<sup>4–6</sup>, and one quarter of individuals may experience SI in the first year.<sup>4</sup> Modifiable risk factors of SI after TBI include depression, anxiety, and alcohol use,<sup>7,8</sup> all of which are observed at higher rates among people with a history of TBI than in the general population.<sup>9</sup> Greater than 50% of individuals experience depression in the first year after TBI,<sup>10</sup> with high comorbid occurrence of post-TBI anxiety (31-61%) among people with

TBI and depression.<sup>11</sup> Alcohol use is both a risk factor for sustaining a TBI and a health behavior that can complicate chronic recovery.<sup>12,13</sup>

In addition to comorbid psychological disorders, pre-injury history of depression and suicide attempts are potential risk factors for suicidal thoughts and behaviors (STB) after TBI.<sup>7</sup> Yet, despite the high prevalence and persistence of STB after TBI,<sup>5</sup> there is limited understanding of the complex factors that contribute to the onset and maintenance of post-TBI STB and ultimately put individuals at risk for death by suicide. Very little research has examined factors that predict STB after TBI, and many of these studies are hindered by small sample sizes, absence of standard measurement tools, and variable assessment time frames.<sup>7</sup> Furthermore, traditional approaches to identifying risk factors for STB among the general population have historically focused on isolated measures at one moment in time, resulting in the identification of variables that are weak and inaccurate predictors of STB, thus predicting suicide risk with near-chance accuracy.<sup>14</sup>

To address the limitations of traditional approaches to the identification of suicide risk, researchers studying suicidal behavior in the general population have called for a shift in focus from *a priori* risk factors to machine-learning based algorithms.<sup>14</sup> With large datasets, machine learning approaches offer several advantages, including the use of techniques that can promote clinical significance and generalizability through modeling complex associations among variables, as well as computational strategies that automatically learn methods for optimizing prediction algorithms rather than being dependent on researchers' *a priori* hypotheses.<sup>14,15</sup> Machine learning approaches can be advantageous in predicting outcomes that are heterogeneous and of rare occurrence (i.e., suicidal thoughts and behaviors), which are often associated with class imbalances. Specifically, sampling procedures, including downsampling, can be implemented in conjunction with traditional machine learning procedures to predict imbalanced outcomes. Using a combination of surveys, administrative data, and electronic health records, machine learning has shown promise in identifying short- and long-term risk for suicidal behaviors (in non-TBI populations) with greater accuracy than traditional approaches, up to several years before they occur and across a variety of settings, including the US Army,<sup>16,17</sup> Veterans Health Administration,<sup>18</sup> independent health care systems,<sup>15,19,20</sup> and population-wide studies.<sup>21,22</sup> One machine learning study found that history of TBI was one of several pre-deployment risk factors for suicide attempts during and after Army deployment.<sup>23</sup> A recent metaanalysis suggests that when compared to theoretically-driven models, machine learning models provide superior prediction of suicidal ideation and behavior.<sup>24</sup>

Given the complex, chronic cognitive, emotional, and behavioral sequelae of TBI, and the limitations of traditional statistical approaches in the prediction of suicide, machine learning offers the potential to optimize predication algorithms that are learned from existing, complex data, which may be critical in examining suicide risk after TBI. However, to our knowledge, there have been no published studies examining risk for STB after TBI with machine-learning methods. Utilizing the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) TBI Model Systems (TBIMS) National Database, the aim of the present study was to employ machine learning to predict suicidal ideation one year after moderate-to-severe TBI. Specifically, several different machine

learning algorithms were evaluated and compared to determine which procedure evidenced the best classification performance in predicting the presence of suicidal ideation.

## Method

#### Participants

Participants were enrolled in the NIDILRR-funded TBIMS multi-site prospective study. Participants were enrolled during inpatient rehabilitation after sustaining a TBI caused by an external mechanical force and meeting one or more of the following severity criteria: (a) Glasgow Coma Scale (GCS) score <13 on emergency department admission, (b) loss of consciousness >30 minutes, (c) posttraumatic amnesia >24 hours, or (d) trauma-related intracranial abnormality on neuroimaging. Additional eligibility criteria were: age 16 years or older, medical care received in a TBIMS-affiliated trauma center within 72 hours of injury with direct transfer to a TBIMS-affiliated inpatient TBI rehabilitation program, and written, informed consent from the patient or legal proxy. The current study utilized follow-up data from the period in which the Patient Health Questionnaire-9 (PHQ-9) was administered. Specifically, participants in the study (n = 4,328) completed the PHQ-9 at the one-year follow-up assessment October 2007 through September 2013 and October 2017 through October 2019.

#### Procedure

This study conforms to all STROBE guidelines and reports the required information accordingly (see Supplementary Checklist). The study was approved and overseen by institutional review boards at all TBIMS centers. Demographic data and psychosocial history were gathered from medical records or participant/family interview. Follow-up data were collected via telephone or in-person interview. Interviews were conducted as close to the anniversary of injury as feasible, within a  $\pm$  8-week window. In the TBIMS study, self-report measures such as the PHQ-9 and GAD-7 are only administered to individuals who are determined by the local study team to have capacity to participate in research. For individuals with diminished capacity or who were consented by a legally authorized representative, information is collected by proxy and does not include the self-reported measures of emotional status. All predictor and outcome variables were measured at oneyear follow-up.

#### Measures

**Predictor Variables**—*Patient Health Questionnaire 9 (PHQ-9)*<sup>25</sup> is a 9-item self-report measure of the frequency of depressive symptoms (i.e., anhedonia, depressed mood, sleep problems, fatigue, appetite problems, guilt, concentration difficulties, psychomotor retardation or agitation, and suicidal ideation) over the past two weeks. Participants also rate the amount of difficulty and interference caused by depressive symptoms. Item responses range from 0 (not at all) to 3 (nearly every day), and total scores range from 0 to 27. Except for item 9 (suicidal ideation), all other items of the PHQ-9, including the difficulty and interference item, were retained as predictors. Strong evidence supports the validity of the PHQ-9 as a depression screener among individuals with TBI.<sup>26,27</sup>

*Generalized Anxiety Disorder Assessment (GAD-7)*<sup>28</sup> is a 7-item self-report measure of the frequency of generalized anxiety symptoms (anxiety/nervousness, worry, inability to control worry, trouble relaxing, restlessness, irritability, being afraid), as well as an item rating difficulty and interference caused by anxiety. All items, including the interference item, were included as predictors. The GAD-7 has demonstrated adequate psychometric properties among individuals with TBI.<sup>29</sup>

*Heavy drinking* days was assessed. Participants were asked to indicate the number of times they consumed five or more drinks on one occasion (regardless of gender) in the past month.

Demographic and injury-related variables were collected through interview and chart review, including participant age at injury, sex, race, marital status, employment at time of injury, and Glasgow Coma Scale (GCS) score in emergency department.

**Outcome Variable**—The primary outcome of interest was the presence of suicidal ideation (0 = absent and 1 = present). The dichotomous suicidal ideation outcome was determined using item 9 of the PHQ-9, which measures the frequency of "thoughts that you would be better off dead or of hurting yourself" over the past two weeks. A PHQ-9 item 9 score of 0 indicated no suicidal ideation, whereas a score of 1 or greater indicated suicidal ideation was present. The reason this definition of suicidal ideation was employed was twofold: 1) to be sensitive enough to encompass any degree of suicidal ideation, and 2) to optimize the number of people in each group as fewer patients endorsed PHQ-9 item 9 scores above 1. The original breakdown of PHQ-9 item 9 responses was as follows: 3,905 people (90.2%) endorsed a 0, 271 people (6.3%) endorsed a 1, 80 people (1.9%) endorsed a 2, and 72 people (1.7%) endorsed a 3.

#### **Data Analyses**

To predict suicidal ideation one year after TBI, machine learning algorithms were evaluated using all the primary predictor variables (i.e., 18 total predictors, including all PHQ-9 items except suicidality, the PHQ-9 interference item, all GAD-7 items, the GAD-7 interference item, and the heaving drinking variable). A number of machine learning approaches were implemented to predict suicidal ideation, including support vector machine (SVM), random forest (RF), gradient boosting machine (GBM), and logistic regression. Although a full description of each algorithm is beyond the purview of this paper, each approach is derived from a different supervised learning family.<sup>30</sup> SVM is a non-linear approach that uses hyperplanes to best classify the outcome within the predictor feature space.<sup>30</sup> RF is an ensemble approach that uses collections of decision trees to predict an outcome.<sup>30</sup> GBM is an ensemble technique that optimizes prediction by training weak trees successively with each tree learning and improving on the previous one.<sup>30</sup> Binary logistic regression is a traditional generalized linear model procedure using the logit link function. The best performing model was used as the primary model. After the final model was selected, a secondary analysis was conducted that included the 18 primary predictor variables listed above, as well as demographic variables (i.e., age, race, sex, marital status, and employment status) and injury severity (GCS) to determine whether they have any predictive utility.

Machine learning models were examined using ten-fold cross-validation, which partitions the sample into ten subsets, of which nine were used in the training process and predictions were made in the remaining subset. This process was repeated for each of the remaining subsets, and results were averaged to produce a single estimate. Furthermore, feature importance analyses were conducted to determine the ranked order of predictors in terms of predictive power. Feature importance analyses calculated the individual area under the curve value for each individual predictor.

When categorical outcome variables exhibit class imbalances (i.e., one value is far less frequent than others), difficulties can sometimes arise in machine learning performance insofar as the algorithms may yield poor predictive performance for the minority value of the variable. One way to address such class imbalances is a procedure referred to as downsampling, which involves randomly removing observations from the majority class to prevent its signal from dominating the learning algorithm. This procedure was adopted for the current study, as suicidal ideation was endorsed by 9.78% of the sample.

To appraise classification performance, receiver operator characteristics (ROC) and area under the curve (AUC) metrics were calculated. AUC values greater than 0.5 denote successful classification (i.e., maximize the true positive rate and minimize the false positive rate). The following AUC framework was adopted as an interpretive guideline: AUC = 0.50 reflects no discrimination, 0.70 AUC 0.80 reflects acceptable discrimination, and AUC 0.80 reflects excellent discrimination.<sup>31</sup> It is important to note that feature importance does not indicate directionality in prediction. Also, standard ROC metrics, sensitivity (i.e., proportion of positives correctly identified) and specificity (i.e., proportion of negatives correctly identified), were evaluated. These metrics range between 0 and 1 such that larger values indicate better performance. Accuracy, which is the percentage of total items classified correctly, was estimated as well. Analyses were performed in the R Caret package.<sup>32</sup>

## Results

#### **Participant Characteristics**

A total of 4,328 participants with TBI completed item 9 of the PHQ-9 at the year one follow-up assessment. Sociodemographic, injury-related, and mental health characteristics of the sample are summarized in Table 1.

#### Machine Learning Prediction of Suicidal Ideation

Results revealed that the 10-fold cross-validation GBM model evidenced the best performance overall (i.e., having the highest AUC). The GBM model had excellent classification performance with an AUC of 0.882. Sensitivity was 0.85, specificity was 0.77, and accuracy was 0.78 (95% CI: 0.77 - 0.79). The RF model exhibited the second-best classification performance, with an AUC of 0.881. Sensitivity was 0.84, specificity was 0.77, and accuracy was 0.78 (95% CI: 0.77 - 0.79). SVM analysis indicated excellent classification performance with an AUC of 0.87. Sensitivity was 0.82, specificity was 0.78, and accuracy was 0.78 (95% CI: 0.77 - 0.79). Finally, the logistic regression model

exhibited an AUC of 0.87, as well as a sensitivity of 0.77, a specificity of 0.81, and accuracy of 0.80 (95% CI: 0.79 - 0.81). Results of the feature importance analysis produced individual AUC values for each predictor and revealed that depressed mood and guilt were the most important predictors of suicidal ideation, with AUC values above .80, indicating excellent discrimination (Table 2). Anhedonia, concentration difficulties, and psychomotor disturbance were the next most important predictors of suicidal ideation, with AUC values above .70, indicating acceptable discrimination (Table 2). Overall, depressive symptoms were most predictive of suicidal ideation one-year post injury, followed by generalized anxiety symptoms and heavy drinking.

When demographic variables and TBI severity were included in the final GBM model, performance was not improved, with an AUC of 0.77. Sensitivity was 0.68, specificity was 0.71, and accuracy was 0.70 (95% CI: 0.66 - 0.74). Furthermore, the feature importance results indicated the demographic variables were the least associated with suicidal ideation, exhibiting AUC values indicating classification performance not much different from chance (Table 3).

## Discussion

The purpose of this study was to utilize machine learning to predict suicidal ideation in individuals with TBI one year after injury. The machine learning model found that at one year after TBI, depressed mood and guilt were the best predictors of suicidal ideation, followed by anhedonia, concentration difficulties, and psychomotor disturbance. The selected gradient boosting machine (GBM) algorithm achieved successful classification of suicidal ideation with a high AUC of 0.882, as well as good sensitivity and specificity. Paired with feature importance analyses, the model determined a ranked order of predictor power, illuminating depressed mood as the most important predictor of suicidal ideation within the model. Downsampling procedures, like those performed in this study, address potential issues of class imbalance in categorical outcome variables that occur infrequently but are critically important to understand, such as suicidal ideation.

Although there are limited and mixed findings on predictors of suicidal ideation following TBI, depression, anxiety, and substance use are clearly associated with suicidality after TBI.<sup>6,13,33,34</sup> The current results highlight that depressed mood was the most important predictor of SI one-year post-TBI, which is consistent with previous research reporting comorbid depression as the most significant risk factor for STB after TBI.<sup>4,7</sup> Similarly, DSM-IV diagnosis of depression or anxiety more than one-year post-TBI was significantly related to SI in a community-dwelling sample.<sup>6</sup> The current analysis of PHQ-8 features revealed the predictive power of specific depressive symptomology compared to dichotomized reports of depression in prior research. The majority of individuals with depression do not experience suicidal ideation one year after TBI,<sup>5</sup> so although a diagnosis of depression is a strong predictor of suicidal ideation, it is very sensitive without being specific. By identifying the depressive symptoms that are most associated with suicidal ideation (i.e., depressed mood, guilt, and anhedonia), clinicians can better identify high-risk individuals and target intervention.

The current findings highlight the importance of assessment and intervention for depressive symptoms in the rehabilitation setting and the potential for using machine learning algorithms to identify high-risk individuals. Of note, the most important features in the algorithm that predicted SI did not directly ask about suicidal thoughts, which may be appealing for several reasons. For example, STB are not routinely assessed in the rehabilitation setting, which may partly be impacted by deficiencies in institutional policies or systemic challenges around availability of adequately trained clinicians to assess, monitor, and intervene, when appropriate. The current findings highlight the potential for using machine-learning algorithms to monitor risk for STB with measures (e.g., PHQ-8 or brief depression screeners) that are more commonly used in healthcare systems than suicidespecific measures and may be easier to implement on a broad scale via patient portals integrated within electronic health records. Although a machine learning algorithm to predict STB cannot replace a suicide risk assessment conducted by a trained clinician, algorithms can help facilitate referrals to providers when a direct assessment is not part of routine care or when variables in the model are aggregated across multiple encounters through a digital health application.

To improve understanding, assessment, and prevention of suicide after TBI, machine learning has the potential to address the dynamic and temporal nature of risk with the use of technological advances, including real-time data from connected devices, social-behavioral interactions from social media and internet, and longitudinal clinical trends from electronic health records.<sup>35</sup> Mental health symptom profiles have been successfully tracked in a community-dwelling population with TBI using a mobile phone health app platform and demonstrated rich temporal variability that could be useful with machine learning models in defining temporal symptom patterns most associated with STB.<sup>36,37</sup>

## Limitations

To our knowledge, this is the first published study to utilize machine learning to predict suicidality among individuals with a history of moderate-to-severe TBI. Nevertheless, the current approach is limited in that feature importance analysis does not provide information about the directionality of the effect of predictors of suicidal ideation. Although feature importance analyses provide an overall ranking of the predictors that accomplish the best classification, it cannot be concluded that an increase or decrease in a specific predictor (e.g., depressed mood, guilt) increases or decreases an individual's risk of suicidal ideation. The current study utilized a large, well-defined cohort; however, the sample was limited to individuals who received specialized, acute inpatient rehabilitation for moderateto-severe TBI. Individuals who receive inpatient rehabilitation represent 7% of all persons hospitalized with moderate-to-severe TBI, are less likely to be a member of a racial/ethnic minority group, and are more likely to have health insurance compared to individuals who are hospitalized and do not receive inpatient rehabilitation.<sup>38</sup> Further, the TBIMS National Database does not account for potential deficits in self-awareness in the self-report data, which may have resulted in inaccurate or under-reported symptoms, though an inverse relationship between impaired self-awareness and self-report of depressive symptoms<sup>39-41</sup> may minimize this limitation in the current study. Although it would be profitable to examine the predictive relevance of additional variables, the TBIMS National Database

contains a limited number of variables that are theoretically likely to contribute to risk for suicidal ideation. For several variables that are theoretically associated with suicidal ideation, there was a high degree of missing data, which undermines the ability of a machine learning model to converge on a solution. Importantly, the predictors representing depression symptoms originated from the same scale (i.e., PHQ-9) as the main outcome variable. Although items from the same scale might exhibit stronger associations with one another due to method artifact, it would not be theoretically justifiable to omit the depression items from the model due to the overwhelming conceptual justification of depression as a predictor of suicidal ideation. Social supports, social determinants of health, employment status, physical mobility, comorbidity burden, common post-TBI impulsivity coupled with impaired problem-solving, and premorbid psychiatric history may have a "root-causal" role to play when delineating depression, ideation, and attempt relationships. Thus, the clinical impact of this study is limited by a relatively small set of predictor variables. Future research would benefit from considering a larger set of predictor variables, thereby facilitating the development of more rigorous suicide screening procedures using machine learning.

The current study examined predictors of suicidal ideation, not suicide attempts or deaths. Most individuals who endorse suicidal ideation do not attempt suicide.<sup>42</sup> Moreover, many robust predictors of suicidal ideation do not meaningfully distinguish individuals with suicidal ideation who do and do not attempt suicide,<sup>43</sup> limiting the ability to draw conclusions from current analyses about risk for suicide attempts or deaths after TBI. Furthermore, evidence to support the ability of the PHQ-9 item 9 to detect suicidal ideation and behaviors is limited and mixed, warranting a more detailed discussion of the limitations of PHQ-9 item 9. One study demonstrated that the PHQ-9 item 9 was a robust predictor of suicide attempts and deaths, regardless of age, in a large and diverse sample of nearly 300,000 outpatients.<sup>44</sup> However, findings from other studies have suggested that PHQ-9 item 9 is an insufficient assessment tool for suicide ideation when compared to a brief electronic version of the Columbia Suicide Severity Rating Scale (eC-SSRS)<sup>45</sup> and questions from a diagnostic interview among patients with coronary artery disease.<sup>46</sup> The PHQ-9 does not distinguish between active and passive ideation, intent, and plans, and may over-estimate suicide risk compared to more comprehensive assessments of suicidal thoughts and behaviors (e.g., Columbia Suicide Severity Rating Scale<sup>47</sup>). In one large Veterans Health Administration (VHA) study, over 70% of completed suicides occurred among individuals who responded "not at all" on their most recent PHO-9,48 which is reflective of a consistent problem with diagnostic accuracy across suicide risk assessment tools.<sup>49</sup> Given these challenges, the clinical impact of the current findings is limited, and suicide risk models are likely to be most useful when predicting suicide attempts and deaths, despite the challenges inherent in the feasibility of studying suicidal behaviors with low base rates. Furthermore, the limitations outlined above underscore the need for changing the way suicide risk is assessed, and machine learning may provide a pathway to improving diagnostic accuracy when predictive models include suicide attempts and deaths. Future models examining suicide risk after TBI could include a combination of electronic health record data and information passively obtained from connected devices (e.g., activity data, call and text usage) collected within large healthcare systems or large-scale registries, as has been explored in recent studies predicting suicide attempts<sup>15</sup> and deaths<sup>17,18</sup> in different

populations. Careful consideration can be given to when and how to use different predictive models; that is, early models to predict later risk for suicidal behavior could inform prevention efforts and may rely more on premorbid and injury-related factors, whereas concurrent models to predict immediate risk may inform intervention and monitoring in chronic settings and may rely more on concurrent mood symptoms and social factors. Machine learning approaches could be successfully deployed to develop these different predictive models. In addition, future research should examine the potential impacts of suicidal ideation on long-term rehabilitation and functional outcomes after recovery from TBI.

## Conclusions

Utilizing the TBIMS, a machine learning model revealed that depressed mood and guilt were the strongest predictors of suicidal ideation one year after moderate-to-severe TBI, followed by anhedonia, concentration difficulties, and psychomotor disturbance. Limitations to the present study, including the use of a one-item screening tool assessing suicidal ideation and a limited set of predictors, minimize the clinical impact of present findings. However, machine learning approaches can appropriately handle distributions of low base-rate events, including suicidal thoughts and behaviors, and facilitate the identification of the most important predictors of these outcomes. Future directions could include the use of machine learning to develop and refine suicide behavior prediction calculators for individuals with TBI, which can better facilitate identification of patients at risk of suicide, assist clinical decision making and treatment planning, and optimize long-term outcomes following TBI.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## References

 Dreer LE, Tang X, Nakase-Richardson R, 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. Curr Opin Psychol. 2018;22:73–78. doi:10.1016/j.copsyc.2017.08.030 [PubMed: 28963946]

- Harrison-Felix CL, Whiteneck GG, Jha A, DeVivo MJ, Hammond FM, Hart DM. Mortality over four decades after traumatic brain injury rehabilitation: a retrospective cohort study. Arch Phys Med Rehabil. 2009;90(9):1506–1513. doi:10.1016/j.apmr.2009.03.015 [PubMed: 19735778]
- 3. Madsen T, Erlangsen A, Orlovska S, Mofaddy R, Nordentoft M, Benros M. Association between traumatic brain injury and risk of suicide. JAMA. 2018;320(6):580–588. [PubMed: 30120477]
- 4. 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. Am J Public Health. 2014;104(7):e100–107. doi:10.2105/AJPH.2013.301794
- Fisher LB, Pedrelli P, Iverson GL, 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. doi:10.1080/02699052.2016.1195517 [PubMed: 27541868]
- Tsaousides T, Cantor JB, Gordon WA. Suicidal ideation following traumatic brain injury: prevalence rates and correlates in adults living in the community. J Head Trauma Rehabil. 2011;26(4):265–275. doi:10.1097/HTR.0b013e3182225271 [PubMed: 21734510]
- McIntire KL, Crawford KM, Perrin PB, et al. Factors increasing risk of suicide after traumatic brain injury: A state-of-the-science review of military and civilian studies. Brain Inj. 2021;35(2):151–163. doi:10.1080/02699052.2020.1861656 [PubMed: 33460350]
- Awan N, DiSanto D, Juengst SB, et al. Evaluating the cross-sectional and longitudinal relationships predicting suicidal ideation following traumatic brain injury. J Head Trauma Rehabil. 2021;36(1):E18. doi:10.1097/HTR.00000000000588 [PubMed: 32769828]
- Ponsford J, Alway Y, Gould KR. Epidemiology and natural history of psychiatric disorders after TBI. J Neuropsychiatry Clin Neurosci. 2018;30:262–270. [PubMed: 29939106]
- 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]
- Guillamondegui O, Montgomery S, Phibbs F, et al. Traumatic Brain Injury and Depression. Comparative Effectiveness Review No. 25 (Prepared by the Vanderbilt Evidence-Based Practice Center under Contract No. 290-2007-10065-I.). Agency for Healthcare Research and Quality; 2011. www.effectivehealthcare.ahrq.gov/reports/final.cfm
- Weil ZM, Corrigan JD, Karelina K. Alcohol Use Disorder and Traumatic Brain Injury. Alcohol Res. 2018;39(2):171–180. [PubMed: 31198656]
- Kesinger MR, Juengst SB, Bertisch H, et al. Acute trauma factor associations with suicidality across the first 5 years after traumatic brain injury. Arch Phys Med Rehabil. 2016;97(8):1301– 1308. doi:10.1016/j.apmr.2016.02.017 [PubMed: 26987622]
- 14. Franklin JC, Ribeiro JD, Fox KR, et al. Risk factors for suicidal thoughts and behaviors: A metaanalysis of 50 years of research. Psychol Bull. 2017;143(2):187–232. doi:10.1037/bul0000084 [PubMed: 27841450]
- Walsh CG, Ribeiro JD, Franklin JC. Predicting risk of suicide attempts over time through machine learning. Clin Psychol Sci. 2017;5(3):457–469. doi:10.1177/2167702617691560
- Bernecker SL, Rosellini AJ, Nock MK, et al. Improving risk prediction accuracy for new soldiers in the U.S. Army by adding self-report survey data to administrative data. BMC Psychiatry. 2018;18(1):87. doi:10.1186/s12888-018-1656-4 [PubMed: 29615005]
- Kessler RC, Stein MB, Petukhova MV, et al. Predicting suicides after outpatient mental health visits in the Army Study to Assess Risk and Resilience in Servicemembers (Army STARRS). Mol Psychiatry. 2017;22(4):544–551. doi:10.1038/mp.2016.110 [PubMed: 27431294]
- Kessler RC, Bauer MS, Bishop TM, et al. Using administrative data to predict suicide after psychiatric hospitalization in the Veterans Health Administration System. Front Psychiatry. 2020;11:390. doi:10.3389/fpsyt.2020.00390 [PubMed: 32435212]
- Barak-Corren Y, Castro VM, Nock MK, et al. Validation of an electronic health record-based suicide risk prediction modeling approach across multiple health care systems. JAMA Netw Open. 2020;3(3):e201262. doi:10.1001/jamanetworkopen.2020.1262 [PubMed: 32211868]
- Su C, Aseltine R, Doshi R, Chen K, Rogers SC, Wang F. Machine learning for suicide risk prediction in children and adolescents with electronic health records. Transl Psychiatry. 2020;10(1):413. doi:10.1038/s41398-020-01100-0 [PubMed: 33243979]

- Gradus JL, Rosellini AJ, Horváth-Puhó E, et al. Prediction of sex-specific suicide risk using machine learning and single-payer health care registry data from Denmark. JAMA Psychiatry. 2020;77(1):25. doi:10.1001/jamapsychiatry.2019.2905 [PubMed: 31642880]
- 22. Garza Á García de la, C Blanco, M Olfson, Wall MM. Identification of Suicide Attempt Risk Factors in a National US Survey Using Machine Learning. JAMA Psychiatry. 2021;78(4):398– 406. doi:10.1001/jamapsychiatry.2020.4165 [PubMed: 33404590]
- 23. Zuromski KL, Bernecker SL, Chu C, et al. Pre-deployment predictors of suicide attempt during and after combat deployment: Results from the Army Study to Assess Risk and Resilience in Servicemembers. J Psychiatr Res. 2020;121:214–221. doi:10.1016/j.jpsychires.2019.12.003 [PubMed: 31865211]
- Schafer KM, Kennedy G, Gallyer A, Resnik P. A direct comparison of theory-driven and machine learning prediction of suicide: A meta-analysis. PLOS ONE. 2021;16(4):e0249833. doi:10.1371/ journal.pone.0249833 [PubMed: 33844698]
- Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. J Gen Intern Med. 2001;16(9):606–613. doi:10.1046/j.1525-1497.2001.016009606.x [PubMed: 11556941]
- Fann JR, Bombardier CH, Dikmen S, et al. Validity of the Patient Health Questionnaire-9 in assessing depression following traumatic brain injury. J Head Trauma Rehabil. 2005;20(6):501– 511. [PubMed: 16304487]
- 27. Cook KF, Bombardier CH, Bamer AM, Choi SW, Kroenke K, Fann JR. Do Somatic and Cognitive Symptoms of Traumatic Brain Injury Confound Depression Screening? Arch Phys Med Rehabil. 2011;92(5):818–823. doi:10.1016/j.apmr.2010.12.008 [PubMed: 21530731]
- Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: The GAD-7. Arch Intern Med. 2006;166(10):1092. doi:10.1001/archinte.166.10.1092 [PubMed: 16717171]
- Teymoori A, Real R, Gorbunova A, et al. Measurement invariance of assessments of depression (PHQ-9) and anxiety (GAD-7) across sex, strata and linguistic backgrounds in a European-wide sample of patients after Traumatic Brain Injury. Journal of Affective Disorders. 2020;262:278– 285. doi:10.1016/j.jad.2019.10.035 [PubMed: 31732280]
- 30. Boehmke B, Greenwell BM. Hands-On Machine Learning with R. CRC Press; 2019.
- 31. Hosmer D, Lemeshow S. Applied Logistic Regression, 2nd Ed. John Wiley & Sons; 1999.
- 32. Kuhn M Building Predictive Models in R Using the caret Package. J Stat Softw. 2008;28(5):1–26. [PubMed: 27774042]
- 33. Anstey KJ, Butterworth P, Jorm AF, Christensen H, Rodgers B, Windsor TD. A population survey found an association between self-reports of traumatic brain injury and increased psychiatric symptoms. J Clin Epidemiol. 2004;57(11):1202–1209. doi:10.1016/ j.jclinepi.2003.11.011 [PubMed: 15567638]
- 34. Mainio A, Kyllönen T, Viilo K, Hakko H, Särkioja T, Räsänen P. Traumatic brain injury, psychiatric disorders and suicide: A population-based study of suicide victims during the years 1988–2004 in Northern Finland. Brain Inj. 2007;21:851–855. doi:10.1080/02699050701504265 [PubMed: 17676442]
- Torous J, Walker R. Leveraging digital health and machine learning toward reducing suicide—From panacea to practical tool. JAMA Psychiatry. 2019;76(10):999. doi:10.1001/ jamapsychiatry.2019.1231 [PubMed: 31290952]
- 36. Juengst SB, Terhorst L, Kew CL, Wagner AK. Variability in daily self-reported emotional symptoms and fatigue measured over eight weeks in community dwelling individuals with traumatic brain injury. Brain Inj. 2019;33(5):567–573. doi:10.1080/02699052.2019.1584333 [PubMed: 30836017]
- Juengst SB, Graham KM, Pulantara IW, et al. Pilot feasibility of an mHealth system for conducting ecological momentary assessment of mood-related symptoms following traumatic brain injury. Brain Inj. 2015;29(11):1351–1361. doi:10.3109/02699052.2015.1045031 [PubMed: 26287756]
- Asemota AO, George BP, Cumpsty-Fowler CJ, Haider AH, Schneider EB. Race and insurance disparities in discharge to rehabilitation for patients with traumatic brain injury. J Neurotrauma. 2013;30(24):2057–2065. doi:10.1089/neu.2013.3091 [PubMed: 23972035]

- 39. Malec JF, Testa JA, Rush BK, Brown AW, Moessner AM. Self-assessment of Impairment, Impaired Self-awareness, and Depression After Traumatic Brain Injury. J Head Trauma Rehabil. 2007;22(3):156–166. doi:10.1097/01.HTR.0000271116.12028.af [PubMed: 17510591]
- 40. Bivona U, Costa A, Contrada M, et al. Depression, apathy and impaired self-awareness following severe traumatic brain injury: a preliminary investigation. Brain Inj. 2019;33(9):1245–1256. doi:10.1080/02699052.2019.1641225 [PubMed: 31304792]
- Goverover Y, Chiaravalloti N. The impact of self-awareness and depression on subjective reports of memory, quality-of-life and satisfaction with life following TBI. Brain Inj. 2014;28(2):174–180. doi:10.3109/02699052.2013.860474 [PubMed: 24304140]
- Klonsky ED, May AM. Differentiating suicide attempters from suicide ideators: A critical frontier for suicidology research. Suicide Life Threat Behav. 2014;44(1):1–5. doi:10.1111/sltb.12068 [PubMed: 24313594]
- 43. May AM, Klonsky ED. What distinguishes suicide attempters from suicide ideators? A metaanalysis of potential factors. Clin Psychol. 2016;23(1):5–20. doi:10.1111/cpsp.12136
- Rossom RC, Coleman KJ, Ahmedani BK, et al. Suicidal ideation reported on the PHQ9 and risk of suicidal behavior across age groups. J Affect Disord. 2017;215:77–84. doi:10.1016/ j.jad.2017.03.037 [PubMed: 28319695]
- 45. Na PJ, Yaramala SR, Kim JA, et al. The PHQ-9 Item 9 based screening for suicide risk: a validation study of the Patient Health Questionnaire (PHQ)–9 Item 9 with the Columbia Suicide Severity Rating Scale (C-SSRS). J Affect Disord. 2018;232:34–40. doi:10.1016/j.jad.2018.02.045 [PubMed: 29477096]
- 46. Razykov I, Ziegelstein RC, Whooley MA, Thombs BD. The PHQ-9 versus the PHQ-8 Is item 9 useful for assessing suicide risk in coronary artery disease patients? Data from the Heart and Soul Study. J Psychosom Res. 2012;73(3):163–168. doi:10.1016/j.jpsychores.2012.06.001 [PubMed: 22850254]
- 47. Posner K, Brown GK, Stanley B, et al. The Columbia-Suicide Severity Rating Scale: Initial validity and internal consistency findings from three multisite studies with adolescents and adults. Am J Psychiatry. 2011;168(12):1266–1277. doi:10.1176/appi.ajp.2011.10111704 [PubMed: 22193671]
- 48. Louzon SA, Bossarte R, McCarthy JF, Katz IR. Does Suicidal Ideation as Measured by the PHQ-9 Predict Suicide Among VA Patients? Psychiatr Serv. 2016;67(5):517–522. doi:10.1176/ appi.ps.201500149 [PubMed: 26766757]
- 49. Runeson B, Odeberg J, Pettersson A, Edbom T, Jildevik Adamsson I, Waern M. Instruments for the assessment of suicide risk: A systematic review evaluating the certainty of the evidence. Abe T, ed. PLoS ONE. 2017;12(7):e0180292. doi:10.1371/journal.pone.0180292 [PubMed: 28723978]

#### What is Known

Rates of suicidal thoughts and behavior (STB) are significantly higher among individuals with TBI than the general population. Historically, methods for detecting suicide risk have been hindered by small sample sizes, absence of standard assessment tools and time frames, and isolated measures at one moment in time, resulting in identification of variables that are weak and inaccurate predictors of STB.

#### What is New

This is the first published study to utilize machine learning to examine risk factors for suicidal thoughts after TBI. Feature importance results highlight depressive symptoms that are most associated with suicidal ideation after TBI.

#### Table 1.

## Sample Characteristics

	Total Sample (n= 4,328)	Suicidal Ideation	
	M (SD) or n	Yes (n=423)	No (n= 3,905)
Variable		M (SD) or n	
Age at Injury	42.61 (19.12)	38.76 (15.89)	43.03 (19.39)
Glasgow Coma Scale Score at ED	11.49 (3.96)	10.9 (4.02)	11.55 (3.95)
Sex			
Male	3,144 (72.7%)	299	2,845
Female		124	1,057
Race/Ethnicity (%)			
White	3,048 (70.5%)	274	2,774
Black	670 (15.5%)	84	586
Asian/Pacific Islander	113 (2.6%)	11	102
Native American	25 (0.6%)	4	21
Hispanic Origin	416 (9.6%)	44	372
Other	53 (1.2%)	6	47
Marital Status			
Single (Never Married)	1909 (44.1%)	199	1710
Married	1445 (33.4%)	107	1338
Divorced	575 (13.3%)	75	500
Separated	171 (4.0%)	28	143
Widowed	223 (5.2%)	14	209
Other	5 (0.1%)	0	5
Years of Education	13.19 (2.74)	12.61 (2.84)	13.25 (2.72)
Suicidal Ideation, past two weeks (% yes)	423 (9.8%)	423 (9.8%)	3,905 (90.2%)
PHQ-9 Total Score (with Item 9)	5.47 (5.82)	14.03 (6.23)	4.55 (4.97)
GAD-7 Total Score	4.12 (5.24)	10.36 (6.23)	3.47 (4.68)
Heavy Drinking Days (past month)	1.34 (4.07)	2.15 (5.45)	1.25 (3.86)

*Note.* Presence of suicidal ideation includes all individuals who endorsed a score of 1 or greater on the PHQ-9 item 9. Heavy drinking days are the number of times a participant consumed 5 or more alcoholic beverages on an occasion in the past month.

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#### Table 2.

#### Feature Importance for Suicidal Ideation

Predictor	FI Value
PHQ: Depressed Mood	0.84
PHQ: Guilt	0.82
PHQ: Anhedonia	0.73
PHQ: Concentration	0.71
PHQ: Psychomotor Disturbance	0.71
PHQ: Fatigue	0.69
PHQ: Sleep Disturbance	0.69
PHQ: Appetite Disturbance	0.68
GAD: Irritability	0.63
GAD: Uncontrollable Worry	0.62
GAD: Worry	0.62
GAD: Inability to Relax	0.62
GAD: Anxiety/Nervousness	0.61
GAD: Afraid	0.60
GAD: Restlessness	0.59
GAD: Anxiety Interference	0.58
PHQ: Depression Interference	0.54
Heavy Drinking	0.51

Note: Values denote the area under curve value of ROC performance for each predictor in predicting outcome. FI = feature importance.

#### Table 3.

Feature Importance for Suicidal Ideation with Demographic Variables

Predictor	FI Value
PHQ: Depressed Mood	0.84
PHQ: Guilt	0.82
PHQ: Anhedonia	0.73
PHQ: Concentration	0.71
PHQ: Psychomotor Disturbance	0.71
PHQ: Fatigue	0.69
PHQ: Sleep Disturbance	0.69
PHQ: Appetite Disturbance	0.68
GAD: Irritability	0.63
GAD: Uncontrollable Worry	0.62
GAD: Worry	0.62
GAD: Inability to Relax	0.62
GAD: Anxiety/Nervousness	0.61
GAD: Afraid	0.60
GAD: Restlessness	0.59
Employment	0.59
GAD: Anxiety Interference	0.58
Age	0.55
PHQ: Depression Interference	0.54
Race	0.53
Sex	0.51
GCS	0.51
Heavy Drinking	0.51
Marital Status	0.50

Note: Values denote the area under curve value of ROC performance for each predictor in predicting outcome. FI= feature importance.