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SYSTEMATIC REVIEW

THE RELATIONSHIP BETWEEN TRAUMATIC BRAIN INJURY AND SUICIDE: A SYSTEMATIC REVIEW OF RISK FACTORS

Rosaria De Luca, Andrea Calderone, Maria Grazia Maggio, Antonio Gangemi, Francesco Corallo, Gianluca Pandolfo, Carmela Mento, Maria Rosaria Anna Muscatello, Mirjam Bonanno, Angelo Quartarone, Rocco Salvatore Calabrò

Abstract

Objective: Traumatic brain injury (TBI) significantly increases the risk of suicidal ideation (SI) and behaviors due to neurobiological changes, cognitive impairments, and emotional dysregulation. This review consolidates current evidence on the relationship between TBI and suicide, identifying key risk factors and underlying mechanisms, and highlights the need for further research, especially in civilian populations.

Method: Studies were identified from an online search of PubMed, Web of Science, Cochrane Library, Embase, and Scopus databases with studies published from 2014 to 2024. This review has been registered on Prospero (number CRD42024574643).

Results: Factors indicated such as external causes of injury, comorbidities like depression and substance use disorders, and post-TBI symptoms consistently influence suicide risk. Advanced predictive models emphasize the role of psychological symptoms, particularly depressive features, in forecasting SI post-TBI, underscoring the need for targeted interventions and early symptom management.

Conclusions: The seriousness of TBI significantly impacts the probability of SI and suicide attempts (SA). Research consistently shows that patients with more severe TBIs tend to have higher rates of SI and SA. Psychological disorders, such as depression and substance abuse disorders, greatly increase the likelihood of suicidal actions after a TBI. These conditions not only raise the occurrence of SI but also lead to earlier and more regular SA.

Key words: neurorehabilitation, TBI, suicidal risk

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1. Introduction

Physical trauma that affects the brain is the reason behind traumatic brain injury (TBI), a matter of public health concern. Damage in cases of TBI can vary from minor, like a concussion, to moderate and severe. It is capable of resulting in extended periods of unconsciousness or amnesia. The World Health Organization reports that annually, 69 million individuals across the globe experience this health issue. Levels of this differ significantly based on location, with higher concentrations often seen in nations with lower to moderate earnings. Road accidents and falls are two of the primary reasons (Hyder et al., 2007; Maas et al., 2017; Menon et al., 2010). TBI affects individuals across various age brackets, with certain groups having an increased likelihood of experiencing its effects. The age categories most commonly observed in emergency departments and hospitalized include children aged 0-4, adolescents aged 15-19, and elderly individuals aged 65 and above. The primary causes of TBI differ across these various age groups. Falls are the top cause of TBI in young children and the elderly, while car accidents are the main reason for teenagers and young adults (Corrigan et al., 2010). The range of clinical and psychological conditions that differentiate TBI can vary based on the type and severity of the injury. Usually, there are physical, cognitive, emotional, and behavioral signs (Masel & DeWitt, 2010). On a physical level, these people might have ongoing headaches, feelings of sickness, or throwing up, as well as sensory issues like blurry vision or ear ringing. They also report dizziness or balance problems, which can significantly affect daily activities and mobility (Coronado et al., 2011). On a cognitive level, head trauma frequently leads to difficulties with concentration and memory. Once routine

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activities become demanding and difficult, there may be a noticeable slowing of mental processes or confusion, especially in complex situations. Some people may struggle with problem-solving abilities, feeling bewildered or unable to fully follow instructions (Levine et al., 2002). Anxiety, sadness, and impatience are just a few of the behavioral and mental mood swings that can be caused by TBI. Sleep disorders, such as insomnia and hypersomnia, are common causes of cognitive and emotional issues. Aside from changes in energy and appetite, additional alterations may have an impact on overall well-being and day-to-day activities (Castriotta & Lai, 2001; Jorge & Robinson, 2003). Even so, a wide range of neuropsychiatric disorders may affect these patients, and research is beginning to show that people with TBI have a higher risk of suicide. This is a concern that requires further investigation and understanding (Ahmed et al., 2017; Halbauer et al., 2009). An official definition of suicide is "the intentional act of ending one's own life." It is a complex phenomenon that is influenced by many different factors, such as biological, social, psychological, and environmental factors (*World Health Organization*, 2014). Suicidal thoughts are often accompanied by intense mental suffering, hopelessness, and a sense of being unable to handle life's challenges. Anxiety, mental health issues, and early life trauma are some of the precipitating factors that influence suicidal behavior, but genetic predisposition and other predisposing factors also play a part (Mann et al., 1999). Suicide thoughts among TBI survivors vary according to injury severity, mental health issues, and demographic factors, as more severe injuries are related to greater suicide thoughts. Anxiety disorders, which are very frequent, are characterized by excessive concern and physiological symptoms, including palpitations and restlessness. After suffering from a TBI, a person may experience intrusive recollections of the damage, avoidance of stimuli linked to the trauma, unfavorable changes in mood and cognition, and elevated arousal. A person's propensity for self-harm is increased by impulsivity and risk-taking behaviors, which are associated with executive dysfunction and injury to the frontal lobes (Bryant et al., 2009; Rao & Lyketsos, 2002; Stein & McAllister, 2009; Whelan-Goodinson et al., 2008).

Data in the literature indicate that people with TBI are much more likely to commit suicide than the general population (Brenner et al., 2011). Neurobiological changes, cognitive dysfunction, and psychosocial stress are among the possible reasons for this increased risk in this clinical population (Wilde et al., 2007). Mental disorders and changes in brain chemical messengers are linked to suicidal thoughts and behaviors (Silver et al., 2001, 2009). This clinical condition can disrupt dopamine and serotonin pathways, potentially leading to depression and SI. Damage to brain regions such as the prefrontal cortex, amygdala, white matter, and hippocampus can impair emotional regulation and decision-making, leading to impulsive actions and suicidal thoughts. All of this can lead to morphological and physiological changes that only increase the risk of psychiatric problems such as depression and anxiety following a head injury, along with an increased potential for suicidal thoughts and behaviors (Baxter & Liddle, 1998; Fazel et al., 2014; McAllister, 2011). Cognitive impairments resulting from TBI, such as impaired decision-making and critical thinking skills, further increase the risk of SI and behaviors. Lesions to the frontal areas of the brain, vital for decision-making, problem-solving, and impulse control, can lead to impulsive actions and poor decision-making, thus increasing the likelihood of suicidal behavior (Barrash et al., 2000; Bush et al., 2000). Head trauma often impairs the speed and efficiency of information processing, affecting how individuals interpret and respond to stressful or traumatic events. Slow cognitive processing can exacerbate feelings of frustration and hopelessness, contributing to the development of suicidal thoughts (Ponsford et al., 2008). Cognitive deficits in memory retrieval and excessive rumination on negative thoughts are prevalent after TBI. These cognitive processes can amplify depressive symptoms and increase the likelihood of SI as individuals' dwell on perceived failures and setbacks (Jorge & Robinson, 2003). Another aspect to take into consideration among the suicide risk factors is the emotional one. TBI disrupts neural circuits crucial for emotional regulation, which can lead to heightened emotional reactivity and difficulty effectively modulating intense feelings of sadness, anger, or hopelessness. The disruption often causes damage to key brain regions responsible for emotional processing and regulation, such as the prefrontal cortex, amygdala, and hippocampus. All these aspects lead to a greater predisposition of the individual towards SI or such behavior (Davidson et al., 2002; Kennedy et al., 2007; LeDoux, 2000; McCauley et al., 2001; Simpson & Tate, 2007; Torregrossa et al., 2023; Vanderploeg et al., 2009). These cognitive, emotional, biological, and structural change aspects just described and which can lead to suicidal risk in TBI are visually summarized in **figure 1**.

Given the wide variety of symptoms, it becomes imperative to evaluate the risk of suicide in individuals with TBI. It requires reliable psychometric tools designed to identify and assess the severity of SI and behavior. Employing psychometric assessments to evaluate suicide risk in TBI enhances clinical decision-making, enables prompt intervention, and supports continual research endeavors. The Patient Health Questionnaire (PHQ), Columbia-Suicide Severity Rating Scale (C-SSRS), Beck Scale for Suicide Ideation (BSS), Suicidal Behaviors Questionnaire-Revised (SBQ-R), and Scale for Suicide Ideation (SSI) are key tools. By employing these resources, healthcare professionals can successfully reduce the risk of suicide and enhance results for individuals with TBI (Beck et al., 1979, 1988; Brown et al., 2000; Kroenke et al., 2001; Osman et al., 2001; Posner et al., 2011). These psychometric tools are briefly described in **table 1**. Despite these findings, the existing literature on the relationship between TBI and suicide is fragmented, with notable gaps requiring further investigation. Previous studies have often varied in their methodologies and population samples, making it difficult to draw definitive conclusions (Simpson & Tate, 2005). Furthermore, while some research has focused on military personnel and veterans, who are particularly at high risk, there is a need to understand this relationship in civilian populations as well (Pietrzak et al., 2010).

This systematic review aims to consolidate current evidence regarding the association between TBI and suicide, focusing on identifying key risk factors and underlying mechanisms.

2. Materials and methods

2.1. Search strategy

A comprehensive literature search was performed using PubMed, Web of Science, Cochrane Library, Embase, and Scopus databases, employing the keywords: (All Fields: "TBI") AND (All Fields: "Suicidal risk"),

Figure 1. *Cognitive, emotional, biological, and structural aspects linked to suicide risk among TBI*

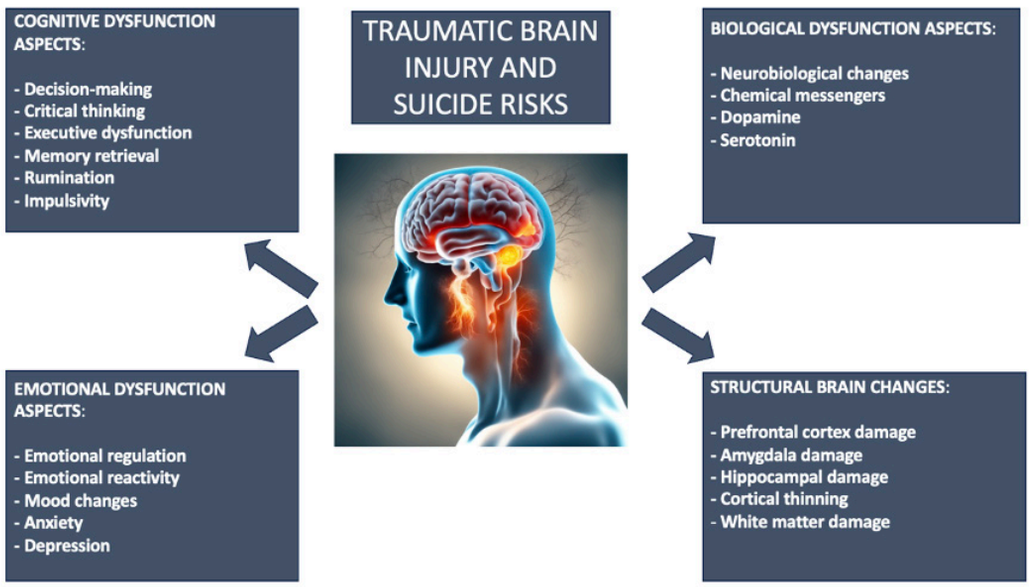


Table 1. *A summary of psychometric tools to assess suicide risk among TBI*

Psychometric tools	Description
Patient Health Questionnaire (PHQ)	The PHQ is a diagnostic instrument individuals can use on themselves in primary care and mental health environments. It aims to identify various mental disorders such as depression, anxiety, and somatoform disorders. The PHQ-9, created to assess depression, is renowned for its accuracy in measuring the severity of depressive symptoms. It can also be used to detect self-harm or suicidal behaviors. The research includes nine questions that prompt patients to evaluate how often they have experienced symptoms such as disinterest in activities, feelings of hopelessness, and thoughts of self-harm within the past two weeks (Kroenke et al., 2001).
Columbia-Suicide Severity Rating Scale (C-SSRS)	The tool C-SSRS is commonly used to evaluate suicidal thoughts and actions. It aids clinicians in assessing the severity and urgency of suicidal risk by inquiring about the strength, frequency, and duration of suicidal thoughts, along with any previous suicidal actions. The structure of the C-SSRS is designed to aid in discussions about suicide risk, helping healthcare providers pinpoint individuals requiring immediate intervention (Posner et al., 2011).
Beck Scale for Suicide Ideation (BSS)	The BSS is a self-report questionnaire with 19 items that assesses the intensity of an individual's suicidal thoughts. It is utilized in both clinical environments and studies to detect individuals who are at risk of suicide. The BSS inquiries about concrete suicide plans, the manageability of suicidal thoughts, and factors that prevent suicide, offering a thorough assessment of the person's intent and risk of suicide (Beck et al., 1979).
Suicidal Behaviors Questionnaire-Revised (SBQ-R)	The SBQ-R is a short tool containing four items that evaluate suicidal thoughts and behaviors. Inquiry covers thoughts of suicide throughout life, frequency of SI in the past year, potential for future suicidal actions, and self-assessed risk of suicide. Both in clinical and research settings, the SBQ-R is highly regarded for its simplicity and effectiveness (Osman et al., 2001).
Scale for Suicide Ideation (SSI)	The SSI is a tool given by clinicians to assess an individual's level of suicidal thoughts, behaviors, and intentions. It consists of 19 items evaluated using a 3-point scale and addresses different aspects of suicidal thoughts, like the wish for death, planning for suicide, and real intent to commit suicide. The SSI is very helpful for assessing how severe someone's suicidal thoughts are over a period of time and is commonly combined with other evaluations to get a more in-depth understanding of a patient's risk of suicide (Beck et al., 1988).

**Legend: Patient Health Questionnaire (PHQ), Columbia-Suicide Severity Rating Scale (C-SSRS), Beck Scale for Suicide Ideation (BSS), Suicidal Behaviors Questionnaire-Revised (SBQ-R), Scale for Suicide Ideation (SSI).*

with studies published from 2014 to 2024. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram was utilized to outline the process (identification, screening, eligibility, and inclusion) for selecting relevant studies, as illustrated in **figure 2**. Titles and abstracts from the database searches were independently reviewed. Articles were evaluated for their relevance based on predefined inclusion criteria. All titles and abstracts that met these criteria were fully reviewed. To minimize bias, multiple expert teams independently selected articles and analyzed data, discussing any discrepancies until consensus was achieved. This review has been registered on Prospero with the number CRD42024574643.

2.2 PICO evaluation

We utilized the PICO (population, intervention, comparison, outcome) model to establish our search terms. The population focused on patients with TBI. The intervention encompassed all studies and rehabilitation methods that included the reduction or detection of suicidal risk. The comparison involved analyzing different forms of interventions that yielded data or effects in patients with TBI both before and during rehabilitation with suicidal risk. The outcome included any data or improvements observed in these patients concerning suicidal risk throughout rehabilitation.

2.3. Inclusion criteria

A study was included if it described or examined the suicidal risk among TBI patients. Only articles written in English were considered. Additionally, studies that described or investigated the functional assessment of these patients were included. We only included studies conducted in human populations and published in English that met the following criteria: (i) original or protocol studies of any kind; and (ii) articles that detail the suicidal risk among TBI patients.

2.4. Exclusion Criteria

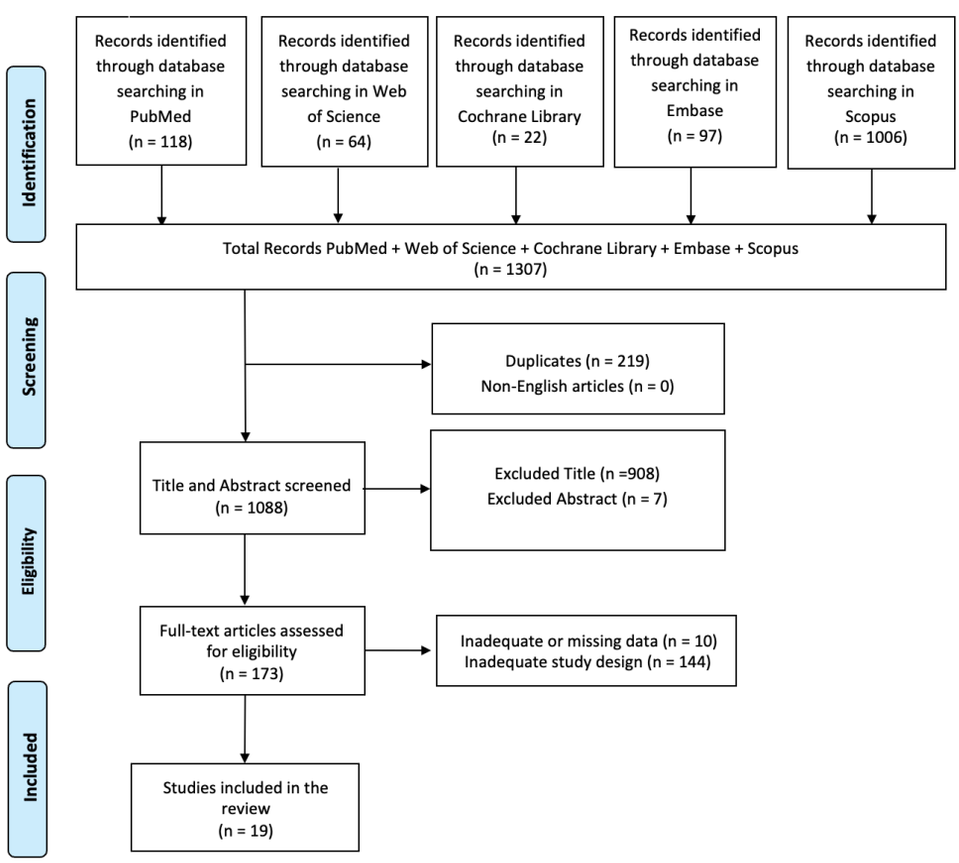
A study was excluded if it lacked data or information regarding the suicide risk among TBI patients. Systematic, integrated, or narrative reviews were also excluded; however, their reference lists were reviewed and included when relevant. Additionally, any articles written in languages other than English were excluded.

3. Results

3.1. Quality of included studies - Risk of bias

Each study was assessed using the Newcastle-Ottawa Scale (NOS) (Stang, 2010) following the Cochrane Non-Randomized Studies Methods Working Group criteria. The NOS, originally designed for observational studies, has been adapted to assess the methodological quality of non-randomized interventional studies. The assessment includes key areas such as participant selection, comparability of groups, and outcome assessment. The NOS allows for a systematic evaluation of potential bias, providing insights into the strengths and limitations of the reviewed studies. The quality assessment was conducted independently by two authors (RDL, AC, and MGM) and the level of agreement between them was calculated by a third author (RSC). The detailed results of this assessment are presented below.

Figure 2. *PRISMA 2020 flow diagram of evaluated studies*



The risk of bias assessment for the included studies indicates generally good methodological quality, though some studies exhibit lower scores in specific domains. In terms of participant selection, studies with the highest scores, such as Brenner et al. 2015 (2015) and Fisher et al. (2023), demonstrate robust methods for participant selection, suggesting a low risk of selection bias. However, studies like Miller et al. (2023) received lower scores in this domain, which may reflect issues with participant recruitment or criteria that could impact the generalizability of the results.

Regarding comparability, most studies encountered challenges in controlling confounding variables and ensuring that study groups are comparable. This is evident from the consistently low scores in this domain. The limited ability to manage differences between groups or confounding factors could compromise the validity of the conclusions. Even studies with higher overall scores, such as those by Brenner et al. 2015 (2015) and Fisher et al. (2023), reveal that comparability remains an area requiring improvement, underscoring the need for more refined methods to manage confounding variables.

Outcome assessment shows notable variability across studies. Studies with higher scores, such as Brenner et al. 2015 (2015) and Fisher et al. ((Fisher et al., 2023), exhibit strong methodologies in measuring and reporting outcomes, ensuring greater reliability of their findings. In contrast, studies like Miller et al. (Miller et al., 2023) and Soberay et al. (2019) received lower scores in this domain, indicating potential weaknesses in how outcomes are measured or reported, which could affect the overall reliability of their findings.

In summary, while most studies demonstrate robust methodological practices, particularly in participant selection and outcome assessment, there remains significant variability, especially concerning comparability and outcome measurement. Consequently, the overall risk of bias is considered low to moderate (see **table 2**).

3.2. Synthesis of evidence

In total, 1307 articles were found: 219 articles were removed due to duplication after screening; 0 articles were excluded because they were not published in English; 915 articles were excluded based on title and abstract screening. Finally, 154 articles were removed based on screening for inadequate and untraceable study designs (**figure 4**). Nineteen research articles met the inclusion criteria and were therefore included in the review. These studies are summarized in **table 3**.

The articles described in this review investigated the current evidence regarding the association between TBI and suicide, focusing on identifying key risk factors and their underlying mechanisms. The first ten studies analyzed the risk factors and pattern of suicidal behaviors (Awan et al., 2021; Blakey et al., 2018; Brenner, Bahraini, et al., 2015; Brenner et al., 2023; Campbell-Sills et al., 2020; Kesinger et al., 2016; Lu et al., 2020; Madsen et al., 2018; Miller et al., 2023; Soberay et al., 2019), while the remaining nine studies explored the psychological factors and predictive models of SI following TBI (Aaronson et al., 2024; Bethune et al., 2017; Campbell-Sills et al., 2021; DeBeer et al., 2017; Fisher et al., 2023; Mackelprang et al., 2014; McKee et al., 2021; Perrin et al., 2022; Wisco et al., 2014).

3.3 Risk factors and patterns of suicidal behaviors post-TBI

TBI is intricately linked to an increased risk of suicidal behaviors, including SI and SA. Studies consistently demonstrate that the severity of TBI can amplify this risk, with more severe injuries often correlating with higher incidences of SI. Kesinger et al. (2016), in a cohort study with 3575 participants with TBI, revealed distinct patterns in suicidal behaviors: participants reported both SI without SA and at least one SA within the initial 5 years post-injury. Severe external causes of injury significantly increased the likelihood of

Table 2. *The table shows the NOS results*

Study	Selection	Comparability	Outcome Assessment	Total Score
Kesinger et al., 2016	3	1	2	6
Lu et al., 2020	3	1	2	6
Madsen et al., 2018	4	1	2	7
Miller et al., 2023	3	1	1	5
Campbell-Sills et al., 2020	3	1	3	7
Brenner et al., 2023	3	1	3	7
Blakey et al., 2018	3	1	2	6
Awan et al., 2021	4	1	2	7
Brenner, Bahraini, et al., 2015	4	1	3	8
Soberay et al., 2019	4	1	1	6
Aaronson et al., 2024	4	1	1	6
Mackelprang et al., 2014	4	1	2	7
Perrin et al., 2022	3	1	2	6
Campbell-Sills et al., 2021b	3	1	3	7
McKee et al., 2021	3	1	2	6
Bethune et al., 2017	3	1	1	5
Wisco et al., 2014	4	1	2	7
DeBeer et al., 2017	3	1	1	5
Fisher et al., 2023	4	1	3	8

Table 3. *Summary of studies included in the research*

Author	Aim	Study Design/Intervention	Treatment Period	Sample Size	Range of Age/Gender Percentage and Suicide Ideation-Attempts Percentage in TBI	Outcomes Measures	Main Findings	Study Limitations	Statistical Analyses.
Kesinger et al., 2016	To assess if the severity of head injuries and ECI is linked to SI or SA following a TBI.	Inception Cohort Study.	Data Collected 1,2 and 5 years post-TBI.	3575 participants with TBI.	Age: Individuals were older than 16 years, with the average age of those expressing SI at 37 years, while the average age for those making SA was 33 years. Gender: not Specificated. SI: 8.2% of participants reported having suicidal thoughts in the two weeks leading up to the planned follow-up interviews. SA: 3.0% of participants made a SA at any time in the year leading up to the follow-up interview.	PHQ-9, Interview, ISS	ECI significantly increases the likelihood of SI nearly threefold after TBI, but these injuries are not associated with SA. Additionally, head injury severity and less severe ECI are not linked to SI or SA.	The study does not identify specific factors associated with severe ECI that contribute to increased SI susceptibility after TBI.	Random effects logit modeling.
Lu et al., 2020	To investigate the relationship between TBI and SR in a Chinese cohort.	Cohort Study.	Not Specificated.	17.504 subjects with TBI.	Age: older than 20 years. Gender: 43.35% were female. SI: not measured in the study. SA: In a median follow-up period of 4.2 years, 0.88% (154 patients) of the TBI group made at least one suicide attempt.	Estimated suicide attempts using Cox proportional hazard regression analysis.	Individuals with TBI have more than twice as high risk of SA compared to those without TBI, with the risk increasing with the severity of the injury. Additionally, depression and alcohol-related diseases further elevate the risk of SA in this group.	The findings are based on a Taiwanese cohort, which may limit the applicability to other populations with different healthcare systems, cultural contexts, and genetic backgrounds.	Cox proportional hazard regression analysis and Kaplan-Meier method.
Madsen et al., 2018	To investigate the association between TBI and the risk of subsequent suicide.	Retrospective Cohort Study.	Data collected from 1980 to 2014.	7,418,391 individuals aged 10 years and older in Denmark. 567,823 individuals (7.6%) had a medical contact for TBI.	Age: Individuals who are 10 years or older, with an average age of 34.3 years at their first TBI. Gender: 41% women and 59% man. SI: not Specificated. SA: 10.2% of people who committed suicide had a previous TBI diagnosis, suggesting an increased risk of SA in this group relative to individuals without TBI.	Suicide recorded in the Danish Cause of Death register until December 31, 2014.	Individuals with TBI face a significantly increased risk of suicide, particularly in severe cases, followed by skull fractures and mild TBI. This risk escalates with more frequent medical contacts for TBI, peaking within 6 months post-injury and remaining elevated beyond 7 years.	The study's retrospective nature and reliance on registry data may introduce bias and limit the ability to control for all confounding variables.	Poisson regression adjusted for covariates, including fractures not involving the skull, psychiatric diagnoses, and deliberate self-harm.

Table 3. *Continued*

Miller et al., 2023	To explore the mediation effects of substance use, psychiatric disorders, and sleep disorders on the relationship between TBI and SI/SA.	A matched case control study.	From October 2015 to December 2018.	Included individuals under 65 years of age from both private health insurance and Medicaid samples.	Age: 10 to 64 years. Gender: Higher percentage of females than males. SI: In the Medicaid sample, individuals with TBI had more than double the likelihood of experiencing suicidal thoughts or attempts within a year, with increased rates observed in younger age groups (10-17). SA: Higher likelihood of SA, particularly among females and younger age demographics exhibiting significantly greater risks.	ICD-10-CM.	Psychiatric disorders significantly mediate the association between TBI and SI/SA with substantial effects observed in both Medicaid and private health insurance samples.	The study's reliance on insurance claims data may limit generalizability, and the retrospective design prevents causal inference.	Mediation analysis to estimate the indirect effects of substance use, psychiatric disorders, and sleep disorders on the relationship between TBI and SI/SA.
Campbell-Sills et al., 2020	To investigate the associations between lifetime TBI characteristics and prospective SA among U.S. Army soldiers.	Observational Study.	Soldiers were followed prospectively after deployment, with a median follow-up period of 30 months.	7,677 baseline respondents who deployed.	Age: Young adults. Gender: predominantly male. SI: not Specificated. SA: 103 soldiers in the sample reported having made at least one SA during the follow-up period, representing a weighted prevalence of 1.31% with a standard error of 0.14%.	SA data were collected from administrative records and post-deployment surveys.	Among the evaluated TBI characteristics, only past-month post-concussive/post-TBI symptoms were significantly associated with an increased risk of SA.	Limitations include reliance on self-report and administrative data, potential recall bias, and the observational nature of the study which limits causal inference.	Logistic regression models were used to estimate associations between TBI characteristics and SA, adjusting for other risk factors including lifetime mental disorders.

Table 3. *Continued*

Brenner et al., 2023	To investigate differences in rates of new-onset mental health conditions among US Army soldiers with and without military-related TBI and to explore how these conditions mediate the association between TBI and suicide.	Retrospective cohort study.	From September to December 2022.	860,892 soldiers, with 108,785 (12.6%) having at least one documented TBI.	Age: Soldiers from 18 to 24 years old and older, up to ≥40 years by the end of their initial deployment. Gender: 89% male soldiers. SI: not Specificated. SA: In soldiers who had previously experienced TBI, the suicide rate was 0.4% (458 soldiers) while it was 0.3% (2237 soldiers) in soldiers without a history of TBI.	Database SUPIC.	TBI was directly associated with suicide risk and also indirectly through these mental health conditions, with substance use disorder showing the strongest mediation effect.	A reliance on retrospective data, the potential for underreporting TBI, and the observational nature restricting causal conclusions.	Mediation analyses using AFT models were employed, alongside the product of coefficients method to assess indirect effects through mental health conditions.
Blakey et al., 2018	The study aimed to investigate whether the polytrauma clinical triad (chronic pain, TBI, and PTSD) increases the risk of SI and violent impulses among veterans, after accounting for other established risk factors.	Cross-Sectional Study.	Not Specificated.	667 veterans who served in the military since September 11, 2001, and reported chronic pain.	Age: Adult participants (veterans). Gender: not Specificated. SI: Around 19.04% of all participants indicated that they were currently experiencing thoughts of suicide. SA: not Specificated.	Interview and self-report measures.	Among veterans with chronic pain, severe pain interference was found to be a more influential predictor of SI and violent impulses than pain intensity. Moreover, PTSD, TBI+PTSD, and co-occurring conditions like alcohol abuse and major depressive disorder as significant contributors to these mental health risks.	The cross-sectional design limits causal inference, and reliance on self-report data, which may introduce bias.	Multiple regression analyses were used to assess predictors of SI and violent impulses, controlling for various covariates.
Awan et al., 2021	To examine the relationships among substance misuse, depression, employment status, and SI following moderate to severe TBI.	Prospective cohort study.	Data were collected at years 1 and 2 post-injury.	1377 individuals aged 18 to 59 years with moderate to severe TBI.	Age: 18-59 years. Gender: both genders with a high prevalence of SI among women. SI: By the first year, over 31% of participants experiencing depression reported having suicidal ideation, while by the second year, over 29% with depression reported experiencing suicidal ideation. In addition, a small percentage, more than 10%, indicated experiencing suicidal ideation without having depression at year 1 and year 2. SA: not Specificated.	Not Specificated.	Substance misuse and unemployment at year 1 were associated with higher rates of depression. Depression, in turn, was linked to concurrent SI at both year 1 and year 2. Greater overall injury severity was associated with higher rates of SI at year 1, which predicted SI at year 2.	Dependence on self-reported data, possible underrepresentation of certain TBI severity levels, and challenges in generalizing findings beyond the study population.	Cross-lagged structural equation modeling was utilized to analyze the relationships among study variables.

Table 3. *Continued*

Brenner, Bahraini, et al., 2015	To explore the relationship between executive dysfunction facets (decision-making, impulsivity, aggression, concept formation) and history of SA in veterans with moderate to severe TBI.	Observational Study Design.	Not Specificated.	133 veterans: 48 without SA or TBI, 51 with TBI only, 12 with SA only, and 22 with both SA and TBI.	Age: The age of participants varied from about 49.5 to 54.2 years, with mean ages for each group being: 54.2 years (±7.6), 53.0 years (±8.5), 51.7 years (±12.0), and 49.5 years (±10.3). Gender: The majority of the participants were male, with the breakdown as follows: 83% male and 17% female in the No SA/No TBI group, 100% male in the No SA/Yes TBI group, 67% male and 33% female in the Yes SA/No TBI group, and 86% male, 9% female, and 5% transgender in the Yes SA/Yes TBI group. SI: not Specificated. SA: Approximately 16.5% of the total sample had both SA and TBI among 133 participants with a history of TBI.	IGT, Immediate and Delayed Memory Test, STAXI-2, WCST.	Veterans with both SA and TBI showed impaired learning during the IGT compared to other groups. No significant differences were found in other measures of executive functioning across groups.	Small sample size, potentially limiting generalizability; lack of longitudinal assessment of executive function and SA history.	Linear regression to assess group differences; varying-coefficient model for analyzing IGT performance over time blocks.
Soberay et al., 2019	To investigate the relationship between insomnia severity, positive TBI screens, and suicidal outcomes across various military branches.	Observational Study Design.	Not Specificated.	1,635 participants from multiple military branches.	Age: not Specificated. Gender: primarily male. SI: There is a significant connection between higher rates of suicidal thoughts and individuals who tested positive for TBI among participants. SA: Likewise, individuals who tested positive for TBI were more likely to SA.	TBI-4, ISI.	Insomnia severity and positive TBI screens independently predicted suicidal outcomes. The impact of insomnia severity on SR varied by military branch, while the effect of a positive TBI screen was consistent across branches.	Potential biases inherent in observational data, reliance on self-report measures for insomnia and TBI screening.	Multiple regression analyses to explore predictors of suicidal outcomes, examining interactions with military branch.
Aaronson et al., 2024	To explore the relationships between TBI and SI/SA among veterans, examining impulsivity and psychiatric diagnoses as potential mediators.	Cross-sectional retrospective chart review study.	Not Specificated.	164 veterans (69 without TBI, 95 with TBI).	Age: 22-65 years. Gender: Of the veterans with TBI, 95% were men, while 84% of those without TBI were male. SI: SI was reported by 58% of veterans with TBI, specifically 55 out of the 95 veterans. SA: 29 out of 95 veterans with TBI, which is equivalent to 30%, disclosed a past of SA.	Not Specificated.	Veterans with TBI were initially more likely to report SI, but this association became non-significant when controlling for mediators. Impulsivity was strongly associated with both SI and SA among veterans with TBI, followed by depression and PTSD.	Retrospective design limits causal inference; reliance on chart review data introduces potential biases.	Chi-square tests, t tests, logistic regression models.

Table 3. *Continued*

Mackelprang et al., 2014	To investigate rates and predictors of SI following TBI within the first-year post-injury.	Prospective cohort study.	Participants were assessed at multiple time points from 1 to 12 months post-injury.	559 adult patients with complicated mild to severe TBI.	Age: The average age of the participants was 42.5 years, with a deviation of 17.9 years. Gender: The majority of the sample consisted of men, with males making up 71.6% of the participants. SI: In the initial year post-injury, a quarter of participants disclosed having SI at least once. SA: Before experiencing a TBI, 12% of the individuals in the sample had attempted suicide at least once.	PHQ-9.	Approximately 25% of patients reported SI during the first-year post-injury. Significant predictors of SI included initial depression severity, history of prior SA, bipolar disorder history, and lower educational attainment.	Potential biases inherent in self-report measures and retrospective recall; single-center study limits generalizability.	Multivariate analysis to identify predictors of SI, likely involving logistic regression given the categorical nature of the outcome.
Perrin et al., 2022	To explore the causal relationships over 10 years among SI, depressive symptoms, and functional independence following TBI.	Prospective longitudinal design study.	Not Specificated.	9,539 individuals enrolled in the TBIMS National Database, with data on SI collected longitudinally.	Age: 16-99 years. Gender: 72.1% male. SI: not Specificated. SA: not Specificated.	PHQ-9, FIM.	Longitudinal analysis indicated bidirectional relationships between SI and depressive symptoms, with depressive symptoms exerting a stronger influence on SI in the earlier years post-injury. Functional independence initially influenced depressive symptoms more than vice versa, but its direct impact on SI diminished over time.	These findings may not accurately reflect the experiences of individuals who do not undergo inpatient rehabilitation following TBI, which is often the case across all severities.	Cross-lagged panel structural equation modeling to assess causal relationships among variables over time.

Table 3. *Continued*

Campbell-Sills et al., 2021b	To identify risk factors associated with SI following mTBI.	Prospective observational study.	Participants were assessed at 2 weeks 3-, 6-, and 12-months post-injury.	A total of 1158 emergency department patients with mTBI.	Age: Individuals who are 17 years old and above, with an average age of 40.5 years (standard deviation = 17.2). Gender: 65.1% male. SI: Across follow-up periods, 10.2% of individuals with mild TBI reported experiencing SI at least once. SA: not Specificated.	PHQ, RPCS.	Preinjury psychiatric history and prior TBI were significant predictors of SI across multiple follow-up periods. Post-TBI symptoms, particularly depression, strongly correlated with SI at all time points, suggesting their role in mediating these associations.	The study may not generalize to patients not treated in level 1 trauma centers or those with severe impairments that could affect self-reporting of symptoms.	Weighted multivariable logistic regression models were employed to adjust for baseline factors and analyze associations between predictors and outcomes.
McKee et al., 2021	To explore the association of SI between individuals with TBI and their primary caregivers in Mexico and Colombia, over a period post-hospitalization.	Longitudinal observational study.	Participants from hospitalization through 4 months post-hospitalization.	A total of 109 individuals with TBI and their primary caregivers participated in the study.	Age: Individuals with TBI had an average age of 35.87 years, with a standard deviation of 14.08. Gender: 82.6% men. SI: Approximately 18.3% to 22.4% of individuals with TBI disclosed having experienced thoughts of death or suicide for a few days within the past two weeks based on their scores on the suicidality item in the PHQ-9. SA: not Specificated,	PHQ-9 (Spanish version).	Both patients and caregivers reported notable levels of SI throughout the study period, with significant continuity of SI observed over time. Specifically, SI in patients during hospitalization predicted similar ideation in caregivers two months later, suggesting a strong interdependence.	The study may be Limited by unaccounted variables that could influence the observed relationships between patient and caregiver SI.	The study likely employed longitudinal data analysis techniques to assess the relationships over time, possibly including methods to account for correlated data within patient-caregiver dyads.

Table 3. *Continued*

Bethune et al., 2017	To investigate the psychosocial and injury-related factors contributing to SI following concussion or mTBI, focusing on the time course of SI development.	Prospective cohort study.	Patients were assessed at 3 and 6 months after their concussion or mTBI.	The study initially involved 2,296 patients with mTBI, of whom 871 completed assessments at 3 months, and 500 returned for follow-up at 6 months.	Age: 18-60 years. Gender: At the 3-month mark, 5.4% of males reported having SI, and this percentage increased to 6.8% by the 6-month mark. In comparison, 7.7% of females had suicidal ideation at 3 months, which rose to 10.1% at 6 months. SI: Three months after the injury occurred, SI were reported by 6.3% of the participants in the overall study. At 6 months after the injury, this number rose to 8.2%. SA: not Specificated.	Psychiatric assessments at 3- and 6-months post-injury.	SI was reported by 6.3% of patients at 3 months and increased to 8.2% at 6 months post-injury. Factors independently associated with SI included speaking English as a second language and being a passenger in a motor vehicle collision at both time points.	Sample bias due to exclusion of patients with milder TBI who did not attend follow-up visits, and the likelihood of more severe cases being overrepresented at later assessments. Additionally, reliance on patient-reported pre-existing conditions without clinical confirmation and incomplete clinical records may impact the accuracy of findings.	Statistical analyses included chi-square tests, t-tests, and logistic regression models to identify associations between variables related to SI and mTBI.
Wisco et al., 2014	To investigate the association between TBI, psychiatric conditions (specifically PTSD and depression), and SI among U.S. veterans deployed to Iraq and Afghanistan, focusing on gender differences.	Observational Study.	Not Specificated.	The study included 824 male and 825 female veterans, totaling 1,649 participants.	Age: The average age of the participants was 38.5 years old (SD = 9.74), ranging from young adults to middle-aged veterans. Gender: Male: Most of the individuals involved were men, with the overall percentage not being specified for the whole group. Female: Women were surveyed at an equal rate to men, but are not as prevalent among veterans overall. SI: It was discovered that having a history of TBI is linked to current thoughts of suicide. The research points out that there was a strong association between TBI and thoughts of suicide in male veterans, although no exact percentage was provided for the whole group. Nonetheless, it implies that experiencing numerous TBIs or TBIs that result in loss of consciousness are more strongly linked to thoughts of suicide. SA: not Specificated.	DRRI, psychiatric assessments.	Current depressive symptoms, PTSD, and history of prior TBI were significantly associated with current SI. After adjusting for psychiatric comorbidities, a history of TBI remained a significant risk factor for SI among male veterans, but not among female veterans.	Limitations include the observational nature of the study, which precludes establishing causality, and potential biases inherent in self-reported data and retrospective assessment of TBI.	Statistical analyses included Cohen's d effect size calculations for continuous variables and Cramers' V coefficients for categorical variables. Regression models, likely logistic regression, were used to examine associations between TBI, psychiatric conditions, and SI.

Table 3. *Continued*

DeBeer et al., 2017	To investigate whether sleep quality mediates the relationship between TBI history and current SI among Iraq/Afghanistan veterans.	Cross-sectional study.	Not Specificated.	The study included 130 Iraq/Afghanistan veterans.	Age: Participants had an average age of 38.0 years, with a standard deviation of 10.76 years. Gender: 84.6% of the participants were male. SI: In the previous two weeks, 18.6% of veterans who have experienced TBI mentioned having SI. SA: not Specificated.	Demographic informations, PSQI, BSS.	The study found that sleep quality mediated the association between TBI history and current SI. Veterans with a history of TBI reported poorer sleep quality, which in turn was associated with higher levels of SI. The indirect effect size was statistically significant.	The study's limitations include its cross-sectional design, reliance on self-reported data for key variables such as sleep quality and SI, and the use of a convenience sample limited to Iraq/Afghanistan-era veterans, which may limit generalizability to other populations and eras.	The study employed mediation analysis to assess whether sleep quality mediated the relationship between TBI history and SI. Confidence intervals were used to estimate the magnitude and significance of the indirect effect.
Fisher et al., 2023	To predict SI one year after moderate to severe TBI using machine learning algorithms and clinical assessment data.	Cross-sectional study.	The study analyzed data collected longitudinally, focusing on outcomes assessed at the one-year follow-up.	4,328 participants.	Age: 16 years and older. Gender: not Specificated. SI: 9.78% of subjects reported having SI according to question 9 of the PHQ-9. SA: not Specificated.	PHQ-9.	A gradient-boosting machine algorithm demonstrated strong predictive performance for SI using predictors such as depression symptoms, anxiety symptoms, and heavy drinking. Depression symptoms were found to be the most significant predictors of SI.	The inability of feature importance analysis to determine the directionality of predictors on SI risk. The sample's restriction to individuals receiving specialized, acute inpatient rehabilitation for moderate-to-severe TBI may limit generalizability, as this subgroup differs socioeconomically and demographically from the broader TBI population.	Statistical analyses included gradient boosting machine learning, 10-fold cross-validation, and calculation of sensitivity, specificity, and accuracy metrics.

*Legend: Extracranial Injuries (ECI), Suicidal Ideation (SI), Suicidal Attempts (SA), Traumatic Brain Injury (TBI), Patient Health Questionnaire- 9 (PHQ-9), Injury Severity Scale (ISS), Suicide Risk (SR), International Classification of Diseases, Tenth Revision, Clinical Modifications (ICD-10-CM), Substance Use and Psychological Injury Combat Study (SUPIC), Accelerated Failure Time (AFT), Posttraumatic Stress Disorder (PTSD), Iowa Gambling Test (IGT), Immediate and Delayed Memory Test, State-Trait Anger Expression Inventory-2 (STAXI-2), Wisconsin Card Sorting Test (WCST), Traumatic Brain Injury-4 (TBI-4), Insomnia Severity Index (ISI), Traumatic Brain Injury Model Systems (TBIMS), Functional Independence Measure (FIM), Mild Traumatic Brain Injury (mTBI), Patient Health Questionnaire (PHQ), Rivermead Post-Concussion Symptoms Questionnaire (RPCS), Deployment Risk and Resilience Inventory (DRRI), Pittsburgh Sleep Quality Index (PSQI), Beck Scale for Suicide Ideation (BSS).

SI, while drug use at the time of injury independently correlated with higher SI rates. Interestingly, external causes of injury severity did not predict SA occurrence. These findings emphasize the importance of identifying specific factors within severe external causes of injury severity that contribute to SI vulnerability post-TBI and guiding targeted interventions and support strategies. Another cohort study compared individuals with and without TBI, with a large sample of 17.504 subjects, in terms of baseline characteristics, comorbidities, and subsequent SA. Patients suffering from TBI showed an elevated prevalence of hypertension, diabetes, hyperlipidemia, and other medical issues in contrast to individuals without TBI. There was a higher rate of SA among TBI patients, with these events occurring sooner than in non-TBI patients. Risk factors for SA in TBI patients included depression and alcohol-related disorders, with the severity of TBI correlating with increased risk. These findings underscore the importance of monitoring and addressing mental health issues in TBI patients to mitigate suicide risk effectively (Lu et al., 2020). An extensive study spanning 34 years in Denmark found that individuals with TBI, particularly those with severe forms, had significantly higher rates of suicide compared to the general population. The risk was notably elevated shortly after the TBI event and remained heightened, especially among younger adults and those with concurrent psychiatric conditions or a history of deliberate self-harm (Madsen et al., 2018). Miller et al. (2023), in a matched case-control study, examined two distinct samples, Medicaid and private health insurance, finding that individuals with TBI are significantly more likely to experience suicidal thoughts or attempts, particularly among women and younger age groups. Psychiatric disorders and substance use disorders, excluding opioid use disorder, were identified as significant mediators of this association in both samples, highlighting their role in influencing post-TBI suicide risk (Miller et al., 2023). An observational study about the association between TBI and SA in a sample of U.S. soldiers has revealed that soldiers with moderate-to-severe TBI in the past 5 years had approximately twice the odds of SA compared to those without TBI. However, those with very mild TBI showed a reduced risk of SA. Additionally, post-concussive/post-TBI symptoms mediated the association between recent moderate-to-severe TBI and SA. These findings highlight the importance of assessing TBI severity and timing in suicide risk assessments among military personnel, thereby informing targeted interventions and prevention strategies (Campbell-Sills et al., 2021). A retrospective cohort study investigated 860,892 soldiers, revealing that 12.6% had at least one documented TBI in their military health records. Soldiers with TBI showed significantly increased rates of mental health diagnoses post-injury compared to those without TBI, particularly for mood and substance use disorders. Time-to-suicide estimates were faster for soldiers with TBI, with adjustment disorders accelerating time to suicide by 16.7%. Indirect effects were notable, particularly through new-onset substance use disorder, accelerating the time to suicide by 63.8% (Brenner et al., 2023). Blakey et al. (2018) examined a sample of veterans experiencing chronic pain, revealing high prevalence rates of comorbid conditions such as TBI, post-traumatic stress disorder (PTSD), and their co-occurrence, known as the polytrauma clinical triad. Significant associations were found between these conditions and adverse mental health outcomes, including current SI and violent impulses. Specifically, chronic pain with co-occurring PTSD or the polytrauma triad emerged as strong predictors of SI, while chronic pain with TBI alone did not show significant associations. Similarly, variables such as pain interference, younger age, alcohol and drug abuse, and major depressive disorder were identified as significant predictors of SI and violent impulses among veterans with chronic pain (Blakey et al., 2018). A prospective cohort study indicated that demographic and clinical factors such as older age, female sex, unemployment, substance misuse, and depression were significantly linked to higher rates of SI at both year 1 and year 2 post-injury. Employment was consistently associated with lower SI risk, while substance misuse and depression were associated with increased SI likelihood across both time points. Complex relationships were also identified, including the influence of depression on subsequent SI and the stability of employment and substance misuse statuses over time (Awan et al., 2021). An observational study design recruited and analyzed data from 133 veterans to explore the impact of TBI and suicidal behavior on executive functioning using the Iowa Gambling Task. Despite consistent demographic profiles between groups, significant clinical differences were found, particularly in executive functioning measures. The study did not observe significant interactions for primary and secondary hypotheses but highlighted learning deficits in the TBI and suicidal behavior cohorts during the Iowa Gambling Task. Control for current psychiatric diagnoses did not alter the findings. These insights underscore the nuanced cognitive challenges faced by veterans with histories of TBI and suicidal behavior, suggesting targeted interventions are crucial for improving cognitive outcomes in this population (Brenner, Bahraini, et al., 2015). Soberay et al. (2019) examined differences among military branches (Army, Navy, Marine, National Guard/Reserve) regarding insomnia severity, TBI screening results, and suicidal thoughts, behavior, communication, and likelihood. Marines and Army personnel reported the highest insomnia severity and prevalence of positive TBI screens, with significant variations across branches. Regression analyses indicated that greater insomnia severity and a positive TBI screen independently predicted higher levels of suicidal thoughts and behavior across all groups, though the impact of insomnia severity varied by military branch (Soberay et al., 2019). In summary, these studies indicate that there is a strong connection between TBI and a higher likelihood of suicidal behaviors, particularly in individuals with severe injuries and other conditions like depression and substance use disorders. Those in the military and veterans are at increased risk for suicidal thoughts and actions due to challenges like PTSD and ongoing pain. Factors like being young and female, as well as experiencing unemployment, can add to the heightened risk. Specific actions, timely mental health evaluations, and community backing are crucial in decreasing the likelihood of suicide among this group.

3.4 Psychological factors and predictive models of SI following TBI

A cross-sectional retrospective chart review study compared veterans with and without TBI across several factors. Veterans with TBI were more likely to have PTSD, use psychotropic medications, and experience chronic pain and insomnia. Initial results showed higher rates of SI among those with TBI, although this link disappeared when considering impulsivity, depression, and PTSD as factors. TBI was not significantly linked

to prior SA, but impulsivity, insomnia, depression, and substance abuse were. The study highlighted that TBI combined with depression or PTSD significantly increased impulsivity, emphasizing the need for tailored interventions in suicide prevention among veterans with TBI (Aaronson et al., 2024). In a study by Mackelprang et al. (2014a) found that 25% of individuals with TBI reported SI within the first year post-injury. The strongest predictor of SI was the initial PHQ-8 score, with other significant factors including a prior SA, bipolar disorder, and lower education levels. The study concluded that SI rates in TBI patients are higher than in the general population. Increased knowledge of risk factors for SI may assist health care providers in identifying patients who may be vulnerable to SI after TBI (Mackelprang et al., 2014b). The authors found that 25% of the 559 participants reported experiencing SI within the initial year after the injury, reaching its highest point at 10% between the second and eighth months. Factors linked to SI included being covered by Medicaid, having higher initial depression scores (PHQ-8), a history of depression, bipolar disorder, or anxiety, and previous SA or psychiatric hospitalizations. Being older and no longer working was associated with a reduced chance of SI. The initial PHQ-8 score following the injury was particularly significant in predicting SI, highlighting its effectiveness in identifying people who are at risk (Mackelprang et al., 2014b). Another study (Perrin et al., 2022) employed a cross-lagged panel path model to examine relationships over time among SI, depressive symptoms, and functional independence in a cohort. Results indicated that SI and depressive symptoms influenced each other reciprocally over 10 years, with depressive symptoms showing stronger causal effects initially and SI becoming more bidirectional later on. Functional independence significantly predicted depressive symptoms at earlier intervals, implying a potential protective role (Perrin et al., 2022). A prospective observational study (Campbell-Sills et al., 2021) investigated predictors and temporal patterns of SI among mild TBI patients. Findings revealed that psychiatric history and prior TBI significantly predicted SI across multiple follow-up periods up to 12 months post-injury. Post-TBI symptoms, particularly those related to functional impairment and depressive symptoms, consistently correlated with a higher SI risk. Adjusting for depression attenuated these associations, suggesting a mediating role. Moreover, the severity of post-TBI symptoms early on predicted SI at subsequent time points, highlighting the importance of early symptom management in reducing long-term SI risk post-TBI. A longitudinal observational study (McKee et al., 2021) explored SI among patients with TBI and their caregivers across multiple time points. Findings indicated persistent levels of SI among both groups over time, with significant correlations within and between patients and caregivers. The initial path model highlighted that patient SI at a one-time point positively influenced caregiver SI at the subsequent time point, suggesting a potential dyadic influence. Exploratory analyses incorporating broader depressive symptoms revealed complex relationships, underscoring the interconnected nature of SI and depression post-TBI. Another study examined factors associated with SI among patients following TBI at 3- and 6-months post-injury. Results highlighted that speaking English as a second language, being a passenger in a motor vehicle crash, and having a history of depression were independently linked to higher odds of SI at both time points. Demographic and injury-related variables also showed significant associations with SI expression. Psychometric evaluations underscored substantial differences in cognitive and psychological functioning between patients with and without SI (Bethune et al., 2017). Wisco et al. (2014) investigated factors associated with SI among veterans, finding significant correlations with Hispanic ethnicity, PTSD, alcohol problems, TBI history (especially multiple TBI and TBI with loss of consciousness), severe depressive symptoms, older age, combat exposure, and low social support. Multivariate Poisson regression further confirmed that severe depressive symptoms, PTSD, and Hispanic ethnicity independently increased the risk of SI, with gender-specific analyses revealing TBI as a significant risk factor for men (Wisco et al., 2014). Another paper examined a cohort of 130 veterans, primarily Caucasian and male, with a mean age of 38 years. Nearly half reported experiencing a TBI during deployment, primarily due to blast exposure. Among all veterans, 18.5% endorsed recent SI, with a higher prevalence among those with a history of TBI. Poor sleep quality mediated the relationship between TBI history and SI, indicating that veterans with TBI were more likely to report poor sleep, which in turn increased their likelihood of experiencing suicidal thoughts (DeBeer et al., 2017). A final research project examined 4,328 individuals with TBI to evaluate SI using advanced computer algorithms. The gradient-boosting machine showed the best performance, showcasing its strong predictive accuracy. Depressive symptoms like feeling unhappy and experiencing guilt were found to be the strongest predictors of SI, with anhedonia and other mental factors coming next. Taking into account demographic factors and the severity of TBI did not lead to a noticeable enhancement in model accuracy, underscoring the predominant influence of psychological symptoms on forecasting suicidal thoughts following a brain injury (Fisher et al., 2023). To sum up, veterans who have suffered from TBI often show higher rates of PTSD, depression, and impulsivity, which lead to a higher risk of SI when associated with sleep disturbances and chronic pain. Furthermore, although TBI itself may not directly indicate SI, the existence of coexisting problems such as intense depressive symptoms and PTSD significantly impact suicidal thoughts. The findings highlight the importance of personalized interventions that target early symptom control and provide mental health care to reduce the risk of suicide in long-term TBI patients. Moreover, sophisticated predictive models indicate that psychological symptoms, particularly depression, are the most significant predictors of SI, independent of TBI severity or demographic variables.

4. Discussion

Our review aimed to explore the current evidence regarding the association between TBI and suicide, focusing on identifying key risk factors and their underlying mechanisms. The results included in this systematic review consistently link the severity of TBI to increased risks of SI and SA, especially in cases involving severe external causes. However, while severe injuries heighten vulnerability to SI, they do not reliably predict SA. The association between TBI and suicidal behaviors is influenced by diverse factors such as comorbidities (e.g., depression, PTSD, substance use), demographics (e.g., age, gender), and psychosocial factors (e.g., employment status, social support). Veterans and military personnel with TBI face elevated SI risks, particularly when accompanied

by PTSD or chronic pain (the polytrauma clinical triad). Furthermore, temporal analyses highlight the dynamic nature of SI post-TBI, with early symptoms like functional impairment and depression serving as strong predictors of long-term SI risk. Advanced techniques like machine learning enhance predictive accuracy by emphasizing the role of psychological symptoms, especially depressive features, in forecasting suicidal thoughts (Aaronson et al., 2024; Awan et al., 2021; Bethune et al., 2017; Blakey et al., 2018; Brenner, Bahraini, et al., 2015; Brenner et al., 2023; Campbell-Sills et al., 2020, 2021; DeBeer et al., 2017; Fisher et al., 2023; Kesinger et al., 2016; Lu et al., 2020; Mackelprang et al., 2014b; Madsen et al., 2018; McKee et al., 2021; Miller et al., 2023; Perrin et al., 2022; Soberay et al., 2019; Wisco et al., 2014). The literature supports the strong association between TBI and psychiatric conditions such as depression, anxiety, and psychosis, which significantly increase the risk of suicide. Early psychiatric assessment and intervention are crucial to mitigating long-term suicide risk in individuals with TBI. Additionally, resilience plays a critical role in post-TBI psychological adjustment; lower resilience correlates with higher levels of depression and anxiety, exacerbating suicide risk. Comprehensive neuropsychiatric evaluations and targeted interventions, particularly for military personnel and veterans with combat-related TBIs, are essential to address elevated SI and attempts (Bryant et al., 2009; Kim et al., 2007; Lukow et al., 2015; van der Naalt et al., 2017; van Reekum et al., 2000). Monitoring for depressive symptoms and functional impairments early in mild TBI cases is fundamental, as these issues often lead to persistent neuropsychological challenges and heightened suicide vulnerability. Moreover, adolescents and young adults with TBI are disproportionately prone to SA compared to their counterparts without TBI. Cultural considerations in mental health support within military settings, especially focusing on emotional regulation and depressive symptoms, are vital to reducing suicide vulnerability among individuals with mild TBIs from diverse racial and ethnic backgrounds (Bahraini et al., 2023; Chang et al., 2019; Dreer et al., 2018; O'Neil et al., 2024; Pugh et al., 2019; Shura et al., 2019; Stanley et al., 2017). Executive function deficits post-TBI also contribute to increased suicide risk, underscoring the necessity for tailored cognitive interventions. Studies further highlight higher mortality rates, including suicide and overdose deaths, among individuals with TBI, emphasizing the need for integrated approaches encompassing cognitive, psychological, and community-oriented strategies to prevent suicide in this population (Byers et al., 2020; Crocker et al., 2019; Homaifar et al., 2012; Klyce et al., 2024, 2024; León-Carrión et al., 2001; Schafer et al., 2022; Talaslahti et al., 2024; Tsaousides et al., 2011). Recognizing that individuals with a susceptibility to injury, particularly those with a previous TBI, are at higher risk for both TBI and suicide is of utmost importance. The link has been acknowledged in studies, with Madsen et al. (2018) being highlighted as a notable example. Their study examined the connection between TBI and suicide, considering factors such as prior psychiatric conditions and nonfatal self-harm. Their study reveals that people who have endured TBI are more likely to engage in intentional self-harm and suicide due to the substantial emotional, cognitive, and physical challenges they face following the injury. This approach is crucial because it specifically examines how TBI affects the probability of suicide, reducing the influence of other variables. In this study, researchers compared suicide rates among individuals with TBIs to those with non-central nervous system fractures (e.g. extremity fractures) as a control group to consider overall injury susceptibility and its effect on suicide risk. This comparison allows us to distinguish the specific risk associated with TBI from the overall risk that could be associated with any major injury. The study found that people with TBI were much more likely to commit suicide compared to those with non-central nervous system fractures, showing that TBI is a major factor in suicide risk (Madsen et al. 2018). In rehabilitation environments, a comprehensive and combined method is required to reduce or stop the risk of suicide in people with TBI. Therapeutic methods such as cognitive behavioral therapy and dialectical behavior therapy play a vital role in TBI rehabilitation. These therapies target the underlying mental health problems like depression and anxiety often found in people with TBI, leading to a higher risk of suicidal tendencies. Appropriate psychiatric care, which involves proper use of medications like antidepressants and mood stabilizers, is crucial in stabilizing mood and reducing suicidal thoughts. Having a reliable network of support is essential for safety. Engaging in peer support groups, family therapy, and community-based rehabilitation programs can foster a feeling of belonging and reduce feelings of isolation, both of which are often associated with suicide. Involving the family in treatment planning and providing education can establish supportive settings that aid in recovery and reduce factors that lead to SI. Vocational rehabilitation and programs aimed at assisting individuals in reentering the workforce play a critical role in restoring independence and self-worth. These programs provide skills training, job assistance, and workplace support to aid individuals in their successful reintegration into society and reduce economic stressors associated with suicidal thoughts. It is crucial to push for policy adjustments that support TBI rehabilitation and suicide prevention initiatives on local, national, and international scales. Policy measures can allocate resources, improve healthcare infrastructure, and fund research on new treatments (*An Evaluation of Crisis Hotline Outcomes Part 2: Suicidal Callers - Gould - 2007 - Suicide and Life-Threatening Behavior - Wiley Online Library*, s.d.; Brenner, Betthauser, et al., 2015; Brenner et al., 2009; Fann et al., 2001; Millis et al., 2001; Mooney et al., 2005; Oquendo et al., 2004; Ponsford et al., 2008; Seel et al., 2003). In summary, it is essential to integrate cognitive, psychological, social, and vocational approaches in TBI rehabilitation to reduce the risk of suicide. By acknowledging the complex connection between physical and mental well-being, enhancing social support networks, and endorsing policy changes, we can create environments that promote resilience, recovery, and improved quality of life for individuals affected by TBI.

4.1. Comparative insights on suicidal behavior in TBI vs. general population

Individuals with TBI face a serious and complicated public health problem with regards to the risk of suicide. Compared to the overall population, individuals with TBI are particularly at risk for SI and SA with rates significantly higher regardless of age, gender, or military or civilian background. These increased dangers are caused by a combination of neurobiological, psychological, and environmental elements that all play a role in worsening each other and leading to significant vulnerabilities for individuals

who have suffered from TBI. Examining information from main health databases like the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) Database (Centers for Disease Control and Prevention, 2024), the Suicide Prevention Resource Center (SPRC) (Suicide Prevention Resource Center, 2024), and Italy's Istat (Istituto Nazionale di Statistica, 2024), offers a thorough view of these variations, highlighting the importance of tailored suicide prevention and support plans for this group. Over the last ten years, there has been a consistent increase in suicide rates among the general population. Between 2011 and 2021, the suicide rate in the U.S. rose from 12.3 to 14.1 per 100,000 people, as reported by the CDC's WONDER Database. Suicide rates vary significantly based on demographics, with men consistently displaying higher rates of suicide than women in the majority of age categories. As an example, although suicide ranks as the 10th most common cause of death in the entire U.S. population, it is the second most common cause in individuals aged 10-34, a group considered especially vulnerable by the SPRC. Differences in geography and ethnicity also impact the risk of suicide, as rates can vary based on access to healthcare, cultural attitudes toward mental health, and socio-economic pressures. In Italy, Istat data shows similar worries, indicating variations in suicide rates due to age, gender, and location, highlighting the influence of socio-demographic and regional elements. Rural and financially deprived regions show significantly elevated suicide rates, demonstrating the impact of both location and economic conditions on mental health results. These findings from nationwide data create a comparison point for better understanding the heightened risks in patients with TBI. Research has shown a notable increase in both SI and SA among individuals with TBI compared to the general population. Studies consistently indicate that individuals with traumatic brain injuries have SI rates reaching 8.2% and SA rates at approximately 3.0% in the first year after the injury, which are similar to or higher than the suicide rates in the general American population during that timeframe (Kesinger et al., 2016). These heightened percentages highlight the significant emotional impact TBI has on people, impacting their psychological well-being, overall life satisfaction, and extended rehabilitation. For TBI military veterans, the risk is even more noticeable. Recent research conducted by Aaronson et al. (2024) shows extremely concerning levels of SI at 58% and SA at 30%. These rates stand in sharp opposition to those seen in the general population, emphasizing the increased dangers veterans encounter (Aaronson et al., 2024). In Italy, Istat data shows that around 2.5% of the population has had suicidal thoughts at some point in their lives. This figure is much lower than the rates found in TBI populations, such as the 10.2% SI rate found by Campbell-Sills et al. (2020) among U.S. soldiers with TBI, indicating that individuals with TBI are at a higher risk compared to the general population (Campbell-Sills et al., 2020). In terms of veterans, Brenner et al. (2023) found that 0.4% of soldiers with TBI had died by suicide, compared to 0.3% of soldiers without TBI. This suggests that while TBI increases suicide risk, the increase might not be as pronounced as in other studies that show much higher SA rates (Brenner et al., 2023). In the military context, Blakey et al. (2018) found that nearly 19% of veterans with chronic pain, TBI, and post-traumatic stress disorder reported SI, which is consistent with Kesinger's conclusion that mental health conditions often exacerbate the risk of suicide in TBI survivors. In addition, there are notable differences in suicide risk among TBI patients based on age and gender compared to what is seen in the general population (Blakey et al., 2018). As an example, young adults with TBI have suicide rates up to 25% in the first year after the injury (Kesinger et al., 2016), which is much higher than suicide rates for individuals of the same age in the general population, according to the SPRC. This difference highlights the significant effect that TBI has on younger patients, who are already juggling important life changes like education, career growth, and forming relationships. Gender differences in individuals with TBI are especially significant as well. Research indicates that women with TBI are at a much greater risk of experiencing both SI and SA compared to women without TBI, despite men generally having higher suicide rates than women in the general population. The heightened risk could be due to several factors such as the additional psychological stress of managing a disability, hormonal fluctuations, and societal expectations. The deviation from the normal gender-related trends in suicide risk indicates that TBI could worsen or modify the gender stereotypes usually seen in the overall population (Kesinger et al., 2016). Females who have suffered from traumatic brain injury encounter a distinct array of emotional and psychological obstacles. They might find it difficult to come to terms with a feeling of loss regarding their previous self-identity and responsibilities, particularly in relation to family, caregiving, or work, all of which are frequently impacted or gone after the injury. In the end, the increased risk of suicide in patients with TBI is caused by a complicated mix of physical limitations, emotional effects, lack of social contact, and existing mental health issues. Targeted interventions are needed to specifically address the unique needs of young adults and women who show increased vulnerability. Preventing suicide requires a comprehensive approach that addresses the physical, cognitive, psychological, and emotional needs of TBI patients, taking into account age and gender differences.

5. Strengths and limitations

This systematic review has several strengths. It provides a thorough and systematic review of the literature on the association between TBI and suicide, covering a wide range of studies, including cohort studies, observational studies, and systematic reviews, which strengthens the reliability of the findings. Furthermore, it considers various factors influencing suicide risk post-TBI, including the severity of injury, demographic variables, and comorbidities such as depression and PTSD. In addition, it discusses practical implications for clinical practice, such as the use of psychometric tools for assessing suicide risk, early psychiatric intervention, and tailored rehabilitation programs. This makes it valuable for healthcare professionals working with TBI patients. It emphasizes the importance of integrating cognitive, psychological, social, and vocational approaches in TBI rehabilitation to mitigate suicide risk. Nevertheless, a significant drawback is the limited number of articles meeting the criteria, as only nineteen studies have centered on the correlation between suicide risk and TBI. The presence of this restriction, along with variations in methods and diverse study groups, complicates the ability to come to definite conclusions on this important subject. Furthermore, there was variability in sample sizes, with some being large and others being small, and inconsistency in the measured parameters. While

the review identifies associations between TBI and suicide risk factors, it is challenging to establish causal relationships due to the multifactorial nature of suicide. Factors like pre-existing mental health conditions or life circumstances could also contribute independently. Another constraint is the inability to conduct a comprehensive meta-analysis due to the studies solely focusing on either SI or SA, with restricted data on both. The assessment highlighted bias risk in nineteen studies, which improved the review's reliability and quality, as well as its conclusions.

6. Conclusions and future directions

In conclusion, the seriousness of TBI significantly impacts the probability of SI and SA. Research consistently shows that patients with more severe TBIs tend to have higher rates of SI and SA. Psychological disorders, such as depression and substance abuse disorders, greatly increase the likelihood of suicidal actions after a TBI. These conditions not only raise the occurrence of SI but also lead to earlier and more regular SA. Treating these coexisting conditions with integrated care models uniting neurology and psychiatry might enhance results for TBI patients. Long-term studies show that the likelihood of suicidal actions remains increased for extended lengths of time after TBI, particularly in younger adults and individuals with coexisting psychiatric disorders. Continuous monitoring and extensive support systems are required to effectively handle and decrease suicide risk. Research focused on the military has shown distinct difficulties experienced by soldiers, such as traumatic brain injuries from combat and stress from deployments. Customized methods to prevent and intervene are essential in military environments to tackle the intricate relationship between TBI severity, post-concussive symptoms, and suicidal behaviors among personnel. Improvements in predictive modeling, like machine learning algorithms, hold the potential to recognize individuals at increased risk of SI following TBI. Incorporating these instruments into clinical settings may improve early identification and intervention, leading to better patient results and lower suicide rates. Studying the neurobiological mechanisms that cause suicidal behavior after TBI could lead to breakthroughs. This involves examining how changes in brain structure and functioning following TBI lead to changes in mood regulation, impulsivity, and decision-making, all linked to suicidal thoughts and behaviors. Furthermore, there is growing recognition of the significance of inflammation and neuroinflammatory mechanisms in both TBI and mental health conditions such as depression. Future research may further explore these inflammatory pathways to identify possible targets for therapeutic interventions to reduce suicide risk in TBI patients. Another crucial area of focus involves enhancing predictive models to identify individuals with an increased risk of suicidal thoughts after experiencing TBI. Although machine learning algorithms have potential in this area, more improvements and validation are needed to improve their precision and usefulness in clinical environments. Incorporating these predictive tools with thorough assessment protocols may allow for the early identification of suicide risk factors and support prompt interventions. Ultimately, the progress in these areas of research shows great potential for bettering our comprehension of suicide risk related to TBI and boosting results for those impacted by these difficult circumstances. By using scientific advancements and interdisciplinary collaboration, we can work towards better prevention, early intervention, and support strategies designed for TBI patients who are at risk for suicide.

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