



# Effective Health Care Program

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Comparative Effectiveness Review  
Number 25

## Traumatic Brain Injury and Depression



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# *Comparative Effectiveness Review*

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Number 25

## **Traumatic Brain Injury and Depression**

**Prepared for:**

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## Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see <http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm>.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (<http://www.effectivehealthcare.ahrq.gov>) to see draft research questions and reports or to join an e-mail list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by e-mail to [epc@ahrq.hhs.gov](mailto:epc@ahrq.hhs.gov).

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Mark Hartmann is our technical editor, without whom our evidence tables would not be nearly as consistent. His eye for detail and ability to review a profusion of data and tables is essential.

Michael Tranchina and Rachel Bazan spent hours as our work study students tracking and organizing hundreds of documents for this review. We are grateful for their consistency, positive attitude, and efficiency.

# Traumatic Brain Injury and Depression

## Structured Abstract

**Objectives.** The Vanderbilt Evidence-based Practice Center systematically reviewed evidence addressing key questions on depression after traumatic brain injury, including prevalence, optimizing timing and methods for diagnostic screening, and approaching treatment.

**Data Sources.** We searched MEDLINE via the PubMed interface, PsycINFO, Embase, the Cumulative Index to Nursing and Allied Health Literature and Published International Literature on Traumatic Stress for articles published in English.

**Review Methods.** We included studies published from January 1966 to May 2010. We excluded those with fewer than 50 participants, participants age 16 or younger, or that did not address a key question. We identified 115 included publications: 14 were good quality, 74 were fair, and 27 poor.

**Results.** The prevalence of depression after traumatic brain injury (TBI) was approximately 30 percent across multiple time points up to and beyond a year. Based on structured clinical interviews, on average 27 percent met criteria for depression 3 to 6 months from injury; 32 percent at 6 to 12 months; and 33 percent beyond 12 months. Higher prevalence measures were reported in many study populations.

Data are sparse to assess the relationship of severity, mechanism, or area of the brain injured to risk of depression. Few risk factors for depression have been studied across populations in models that adjust for confounding factors. Alcohol and substance use, coexisting illness or injury, degree of disability, and older age at injury may contribute to increased risk.

The literature is insufficient to determine whether tools validated in other populations for detecting depression appropriately identify individuals with depression after a TBI. Consideration of potential for coexisting psychiatric conditions is warranted. Anxiety disorders were the most common coexisting condition affecting 31 to 61 percent of those with depression after TBI. Post-traumatic stress disorder prevalence in the included literature suggests that it may also be common (37 percent). Little to no high-quality evidence is available about outcomes of treatment of depression after TBI. A single randomized controlled trial of sertraline showed nonsignificant improvements after 10 weeks.

**Conclusions.** Considerable evidence finds depression to be common after all forms and severities of TBI. At all time points from injury, prevalence is higher than the estimated 8–10 percent in the general population. No evidence provides a basis for preferring one timeframe for screening over another, implying repeated screening is imperative. No evidence is available to guide treatment choices for depression after head injury.

Overall the evidence is low to guide screening and care for depression after TBI. Given at least 1.5 million TBIs per year with many potential consequences that impair quality of life and function, substantially greater efforts are warranted to understand the biologic causes, natural history, treatment, and prevention of depression after TBI.

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# Executive Summary

## Introduction

We do not know the extent to which depression contributes to long-term disability following traumatic brain injury (TBI), although depression is one of several potential psychiatric illnesses that may be common following TBI. Major depression may be triggered by physical or emotional distress, and it can deplete the mental energy and motivation needed for both recovering from the depression itself and adapting to the physical, social, and emotional consequences of trauma with brain injury. Depression may be masked by other deficits after head injury, such as cognitive changes and flat affect, which may be blamed for lack of progress in post-trauma treatment but actually reflect underlying depression. Clinicians, caregivers, and patients lack formal evidence to guide the timing of depression screening, which tools to use for screening and assessment, treatment choices, and assessment of treatment success.

## Importance of Depression

Depression is defined by criteria that likely circumscribe a heterogeneous set of illnesses. While no single feature is seen in all depressed patients, common features include sadness, persistent negative thoughts, apathy, lack of energy, cognitive distortions, nihilism, and inability to enjoy normal events in life. Especially in a first episode, individuals and families may not recognize the changes as part of an illness, making identification and self-reporting of the condition challenging. Active screening is essential to recognition, treatment, and prevention of recurrence.

The most salient consequence of depression is suicide. Suicide is usually impulsive and extremely difficult to predict and prevent. At least half of suicides occur in the context of a mood disorder.<sup>1</sup> Depression reduces quality of life, impairs ability to function in social and work roles, and causes self-doubt and difficulty taking action, all of which can delay recovery from TBI. The Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition, (DSM-IV-TR)<sup>2</sup> defines the illness in terms of physiologic disturbances of sleep, appetite, attention and concentration, motor activity, and energy, and of psychological losses of interest in normal activities, hope, and self-worth while ruminating with excessive sadness, guilt, and suicidal thoughts.

The disturbances may also occur following TBI due to other circumstances, such as pain that disrupts sleep, which may mask the recognition that the sleep disturbance is also a part of a burgeoning depression. Depression may be financially costly in undermining physical therapy efforts, treatment compliance in general, and rehabilitation planning and efforts. The need for systematic evaluation of the prevalence and consequences of depression following TBI is imperative, given the potential for mitigating suicide and unnecessary disability.

## Importance of TBI

TBI occurs when external force from an event such as a fall, sports injury, assault, motor vehicle accident, or explosive blast injures the brain and causes loss of consciousness or loss of memory.<sup>3</sup> TBI can result from direct impact to the head as well as from rapid acceleration or deceleration of brain tissue, which injures the brain by internal impact with the skull. Both mechanisms can cause tissue damage, swelling, inflammation, and internal bleeding.<sup>4</sup>

TBI is responsible for roughly 1.2 million emergency department visits each year, with 1 in 4 patients requiring hospitalization.<sup>5</sup> Because most estimates of TBI rates are based on hospital use, some individuals with TBI are not counted because they do not seek care at all, or they seek care in other settings. The Centers for Disease Control and Prevention estimates that up to 75 percent of TBIs are mild in terms of duration of loss of consciousness and other immediate symptoms, meaning substantial underestimation of the number of individuals affected is likely.

Nonetheless, estimates of direct and indirect costs associated with TBI exceed \$56 billion each year.<sup>6</sup> Among individuals who sustain a TBI, approximately 50,000 die each year of their injuries and 80,000 to 90,000 will have a long-term disability. More than 5 million survivors of TBI live with chronic disability.

Military service carries a high risk of TBI. Traumatic brain injury is more common in the military than in civilian populations, even in peacetime. Advances in body protection systems have resulted in fewer deaths and a concomitant rise in TBI that is more often moderate to severe than mild.<sup>4</sup> The military confirms that more than 50,000 veterans who have returned from current theatres have blast-related TBI.<sup>7</sup> As many as 30 percent of those with any injury on active duty have sustained a TBI.<sup>8</sup> Because TBI is common, serious, and has high personal and economic costs, understanding potential consequences of injury is crucial.

## **Relationship of TBI and Depression**

TBIs are associated with a range of short- and long-term outcomes, including physical, cognitive, behavioral, and emotional impairment.<sup>9</sup> Prior estimates, not derived systematically, of depression among individuals with TBI range widely, from 15 percent to 77 percent.<sup>10-12</sup> Depression associated with TBI can manifest shortly after injury or well into the future.<sup>13-14</sup> In their review of rehabilitation for TBI patients, Gordon and colleagues identified 74 studies of psychiatric functioning after TBI.<sup>15</sup> Their assessment was that TBI is associated with high rates of depression—more than half of cases—and other DSM Axis I and Axis II conditions. Depression was noted to coexist with other psychiatric conditions, including addiction or anxiety. Comorbid psychiatric conditions with depression may complicate screening, diagnosis, and management of depression in multiple ways, including masking depression so it remains undiagnosed or affects the individual's followthrough or adherence to treatment. It is likely that such comorbid conditions complicate treatment response and recovery just as they do in non-TBI depressed patients. However, no systematic examination of this question has been done to date.

Triggers for depression after TBI may include biological, psychological, and social factors,<sup>16</sup> and in the post-TBI population, greater attention is often given to biological factors because of the direct injury to the brain. However, many post-TBI patients do not demonstrate radiological or pathological evidence of brain injury,<sup>17</sup> and in the context of current understanding of depression as a biopsychosocial entity, researchers and clinicians generally consider all depression to have a complex etiologic basis. Just as in the non-TBI population, the psychological impact of decreased occupational and functional abilities and its potential to affect the likelihood of becoming depressed should not be overlooked.<sup>18</sup>

## **Focus of This Systematic Review**

In order to compile the literature in a useful fashion, we included publications that provided a clear description of study participants and that used standardized tools and recognized

approaches to identifying depression. We did not address penetrating head injury and did not include research about children younger than 16.

Patients, clinical care providers, families, and support organizations need to know the degree to which depression after TBI is a threat so that anticipatory guidance and care planning can incorporate strategies to address risk of depression or prevent onset. Care providers in a variety of settings need to know when and how best to screen TBI patients for depression. When depression is identified, information about likely outcomes of treatment and about whether certain options are superior is key to informed decisionmaking. This review is focused on pragmatic aspects of these concerns.

## Key Questions

In preparing this report, we have addressed the following key questions (KQs):

**KQ1.** What is the prevalence of depression after traumatic brain injury, and does the area of the brain injured, the severity of the injury, the mechanism or context of injury, or time to recognition of the traumatic brain injury or other patient factors influence the probability of developing clinical depression?

**KQ2.** When should patients who suffer traumatic brain injury be screened for depression, with what tools, and in what setting?

**KQ3.** Among individuals with TBI and depression, what is the prevalence of concomitant psychiatric/behavioral conditions, including anxiety disorders, post-traumatic stress disorder (PTSD), substance abuse, and major psychiatric disorders?

**KQ4.** What are the outcomes (short and long term, including harm) of treatment for depression among traumatic brain injury patients utilizing psychotropic medications, individual/group psychotherapy, neuropsychological rehabilitation, community-based rehabilitation, complementary and alternative medicine, neuromodulation therapies, and other therapies?

**KQ5.** Where head-to-head comparisons are available, which treatment modalities are equivalent or superior with respect to benefits, short- and long-term risks, quality of life, or costs of care?

**KQ6.** Are the short- and long-term outcomes of treatment for depression after TBI modified by individual characteristics, such as age, preexisting mental health status or medical conditions, functional status, and social support?

## Methods

**Literature search.** Our search included examination of results in five databases: MEDLINE via the PubMed interface, the PsycINFO database of psychological and psychiatric literature, Embase, the Cumulative Index to Nursing and Allied Health Literature, and the Published International Literature on Traumatic Stress database. Controlled vocabulary terms served as the foundation of our search in each resource, complemented by additional keyword terms and phrases selected to represent each of the key concepts in the search. We also employed indexing

terms when possible to exclude undesired publication types (e.g., reviews, case reports, letters, etc.) and articles published in languages other than English. We hand-searched reference lists of included articles to identify additional citations. We excluded studies that included fewer than 50 participants, included participants younger than 16 years of age, did not include an operational definition of depression, or were unable to be used to answer any key question.

**Study selection.** Two reviewers separately evaluated abstracts for inclusion or exclusion. If one reviewer concluded the abstract should be included for full review of the article, it was retained. For the full article review, two reviewers read each article and decided whether it met our inclusion criteria. Discordance was resolved by team adjudication.

**Quality assessment.** The research team used a quality assessment approach that ensured capture of key study characteristics most relevant to our key questions. Quality was assessed by two reviewers independently. They resolved differences through discussion, review of the publications, and arrival at consensus with the team.

**Data extraction.** All team members shared the task of entering information into the evidence tables. After initial data extraction, another member of the team reviewed the article and checked all table entries for accuracy, completeness, and consistency. The two abstractors reconciled any discordance in information reported in the evidence tables.

**Evidence synthesis.** We have endeavored to distinguish duplicate populations; however, for a small proportion of publications, the summaries may overrepresent the total number of unique studies available and could doublecount data. In each section, we summarize the yield of the search and key characteristics of the content of the aggregate literature.

We present data in summary tables arranged by key features discussed. Most often this is by the rigor of the TBI definition and depression measurement used in the research. All data extracted is presented in the evidence tables in Appendix C.

In order to characterize estimates of prevalence, and prevalence across time, we calculated weighted averages and reported these as a global aggregate as well as by timing of screening, setting, and severity of injury. If a study included a measurement at more than one time point, the participants in that study contribute to the estimates for each time at which depression was assessed.

## Results

**Literature search yield.** As a result of the search, 2,015 nonduplicate articles were identified. One hundred fifteen articles were included in the review, representing 81 distinct populations, with 112 articles pertaining to KQ1, 113 to KQ2, 9 to KQ3, 2 to KQ4, and none identified for KQ5 or KQ6. Detailed reasons and process for exclusions are described in the full report.

### KQ1. Prevalence of Depression After Traumatic Brain Injury

**Content of literature.** We identified 112 publications<sup>7,12-14,18-125</sup> from 79 distinct study populations. Thirty-eight of the 79 were in the United States, 12 in Canada, 12 in Europe, 9 in Australia, and 8 in other countries. The most common sources of study populations were tertiary care centers, identifying participants from emergency department, intensive care, and inpatient

admissions (n = 33), including those that specifically noted trauma center status (n = 10), and rehabilitation programs (n = 19). Neuropsychology labs, private neuropsychology practices, prisons, veterans' records, databases, and psychiatric care facilities each contributed three or fewer populations.

Criteria for defining and characterizing those classified as having TBI were varied, with more than half of authors (n = 38) using closed head injury in concert with Glasgow Coma Scores (GCS). American Congress of Rehabilitation Medicine criteria were common (n = 13), as were ad hoc operational definitions (n = 12) and failing to clearly define criteria (n = 12). In total, the majority of the literature provides sufficient detail about inclusion and exclusion criteria and TBI definitions to understand and/or replicate the population studied.

Seventy-three percent of studies provided cross-sectional measures of depression, meaning that depression status was assessed at a single point in time after TBI; the balance were prospective with two or more assessments of depression status over time. Structured clinical interviews, done specifically for the research or in the course of standardized clinical care protocols, were the most common means of assessing depression status (n = 29). Among written or administered tools, the Beck Depression Inventory (BDI; n = 13), Hospital Anxiety and Depression Scale (HADS; n = 11), and Center for Epidemiologic Studies Depression Scale (CES-D; n = 8) were most common. A wide variety of other measures and customized uses of subscales (n = 62) were also used.

**Prevalence estimates.** We have considered the Structured Clinical Interview for DSM-IV (SCID) and other formal structured clinical interview protocols that map to the DSM and/or International Classification of Diseases codes to be the measures of depression that are most relevant to clinical care. Among studies that used a SCID or other structured protocol to reach a formal diagnosis of depression, the prevalence of depression after TBI ranged from 12.2 percent<sup>53</sup> to 76.7 percent.<sup>12</sup> If we focus on the subset of studies with both use of the SCID or other clinical interview and clearly operationalized criteria for TBI, the range was 12.2 percent<sup>53</sup> to 54.0 percent.<sup>96</sup>

Across all timeframes and using all depression measures, in studies with clear TBI definitions, the weighted average for prevalence of depression was 31 percent. Among those studies with repeated assessments and/or longer term followup, no clear pattern of expected natural history or peak prevalence emerged. Depression was more common among those with TBI than among normal comparison groups. Household/family members of individuals with TBI may also have increased risk of depression. Results from comparisons to other trauma populations without severe TBI are variable, with some comparison groups also having statistically comparable risk of depression that exceeds expected prevalence in the general population.

**Risk factors.** Data are sparse to assess whether severity of injury influences risk of depression. Using structured interviews among those studies with mild or mild/moderate TBI populations, the overall prevalence of depression was 20.3 percent compared with 32.5 percent in studies that enrolled or followed up populations of all severity. Too few studies isolated a sufficient number of those with mild TBI compared to those with moderate and/or severe injuries to make valid estimates. Likewise, stratification of prevalence by explanatory factors such as age, gender, area of brain injured, or mechanism of injury is not possible within the current body of literature.

Fourteen studies in 13 distinct study populations report results from multivariate models to identify predictors or risk factors for depression after TBI.<sup>13-14,23,38,50,64,78,99,103,118-121,125</sup> Age was reported in a large United States cohort (n = 559) to be an independent risk factor for depression among both those with and without prior depression. In this study, which reflects the full spectrum of severity of TBI, risk decreased with increasing age, such that those age 60 and older were at lowest risk.<sup>125</sup> In another study aiming at predicting risk, when age was grouped with other factors, the combination of older age at injury, CT scan with documented intracranial lesion, and higher 1-week CES-D scores, were sensitive (93 percent) though not specific (62 percent) for identifying those with mild TBI who were depressed by 3 months after their injury.<sup>50</sup> One group has found that women have higher risk (relative risk [RR] = 1.27; 95 percent confidence interval [CI]: 1.07, 1.52) of new but not recurrent depression after TBI after adjusting for other risk factors.<sup>125</sup>

Severity of TBI is not clearly linked with risk. In the sole model that assessed GCS scores, coma length, and duration of post-traumatic amnesia, none of the factors were associated with depression or its severity.<sup>118</sup> Another group using the Injury Severity Score also found no association between severity and prevalence of depression.<sup>121</sup>

History of alcohol and substance abuse increase risk.<sup>14,64,125</sup> Pain, involvement in litigation related to the injury, and perceived stress have been reported as risk factors among those entering rehabilitation care and in prospective cohorts.<sup>23,121</sup> Psychosocial supports were often described in this literature, and data from caregivers, partners, and family members were common. However, few models incorporated social support items. One group reported that “availability of a confidant” reduced risk of depression,<sup>78</sup> and another reported that years married were inversely related to risk, while presence and degree of cognitive disability, motor disability, and social aggression elevated risk.<sup>99</sup> Concepts related to resilience or personality traits have not been widely investigated, but scores on the Adult Hope Scale (p < 0.005) and the Life Orientation Test-Revised (p < 0.05), a measure of dispositional optimism, are both found to contribute independently to predicting depression and its severity as measured by the BDI in a small Israeli study (n = 65).<sup>119</sup> History of depression has been documented as a substantive risk for having depression at followup (RR = 1.54; 95 percent CI: 1.31, 1.82), as was depression at the time of the injury (RR = 1.62; 95 percent CI: 1.37, 1.91).<sup>125</sup>

A cluster of reports was focused on investigating whether incorporating information about the area of the brain affected by the injury helped to identify those at highest risk. Imaging research about the areas of the brain injured and the relationship to depression risk yields inconsistent results. In aggregate for all those with TBI, onset of major depression within 3 months of injury has been reported to be sevenfold as common (95 percent CI: 1.36 to 43.48) among those with abnormal CT scans after injury compared with normal imaging.<sup>50</sup> Focusing on locations of injury, Jorge and colleagues<sup>13,103</sup> have replicated their findings in several CT scan-based studies that left anterior lesions involving the left dorsolateral frontal cortex and/or left basal ganglia are associated with increased risk of acute depression (p = 0.006) when injury location is assessed in multivariate regression models. They also note that frontal lesions, whether left, right, or bilateral, are associated with decreased risk of acute depression (p = 0.04). In contrast, delayed-onset major depression was not associated with lesion location. In a subanalysis of depression types, depression alone was related to left hemisphere injury (p = 0.003), while depression associated with anxiety was more common among those with right hemisphere injury (p = 0.003). A specific assessment of the presence or absence of contusions

found the type of injury was not predictive and that depression was somewhat more common among those with contusions (71 percent) than among those without (62 percent). Using magnetic resonance imaging (MRI) near the time of injury, the findings from CT scan studies are not supported, and the only lesion type to emerge as a significant predictor was the protective effect of temporal lesions compared to other injury locations ( $p = 0.028$ ).<sup>38</sup> Study size and timing in relation make this literature more exploratory than conclusive in beginning to understand the relationship between pathophysiology related to the brain injury and risk and timing of onset of depression. In a study of political prisoners, up to 50 years after injury, TBI-associated cerebral cortical thinning in the left superior frontal and bilateral superior temporal cortex, as assessed by MRI, was associated with depression, and similar effects were not seen in prisoners without a history of TBI with respect to depression risk.<sup>118</sup>

**Summary.** The prevalence of traumatic brain injury is approximately 30 percent across multiple time points up to and beyond a year. Based on structured clinical interviews, on average 27 percent met criteria for depression 3 to 6 months from injury; 32 percent at 6 to 12 months; and 33 percent beyond 12 months. Higher prevalence is reported in many study populations. No strong predictors are available to select a screening window or to advise TBI patients or their providers about risk of depression.

## KQ2. Screening for Depression After TBI

**Content of literature.** We identified 113<sup>7,12-14,18-126</sup> publications in 79 distinct populations that provide information about timing of screening or comparison of tools. Overlap is virtually complete with those publications included in KQ1, adding only one publication from the United States. As a result, study characteristics for this literature are nearly identical.

**Timing of screening.** In all timeframes across all measures, depression is common after TBI. No distinct trend is apparent to suggest a peak time of enhanced risk or a related priority window for screening. In general, the proportion of those assessed as depressed is lower with structured clinical interviews than standardized instruments. Around 1 year and beyond, both categories of assessments converge around 30 percent (27.4 percent with SCID and 33.2 with other tools).

This review cannot distinguish between whether the data suggests that other tools “over-detect” depression relative to structured clinical interviews or whether differences in study design and population create the observed effect. We also cannot distinguish if features unique to a population with TBI make clinical diagnosis more challenging, or whether evaluators in clinical settings are less likely to classify a patient as depressed early after trauma, deferring definitive diagnosis until later in followup as other sequelae of injury subside or stabilize.

**Choice of tools for screening.** Studies often used more than one instrument, reporting different facets of the scores or evaluation, such as correlations among subscales of separate instruments or relationship of scores by different evaluators. Statistical analyses were generally not intended to directly assess clinical utility. Comparison of diagnostic test characteristics, agreement of classification, and use of expert SCID as a gold standard for comparisons were rare. Five publications compared SCID to candidate tools for assessment of depression, the BDI,<sup>90,115</sup> Patient Health Questionnaire (PHQ-9),<sup>126</sup> and HADS.<sup>28,117</sup> None of the tools reported simultaneous sensitivity and specificity above 90 percent. One study identified different optimal

cutoffs of the BDI-II; maximum sensitivity of 87 percent and specificity of 79 percent were obtained with cutoffs of 19 for participants with mild TBI, and 35 for those with moderate or severe TBI. With modification of the scoring algorithm as proposed by the authors, the PHQ-9 achieved a sensitivity of 93 percent, specificity of 89 percent, positive predictive value of 63 percent, and negative predictive value of 99 percent. The BDI had poor sensitivity of 48 percent and 32 percent at specificities of 80 and 90 percent, respectively. The HADS provided 54 percent sensitivity and 76 percent specificity. One team<sup>31</sup> reported results of an expert consensus process to select subscale domains of three screening tools (Neurobehavioral Functioning Index, Profile of Mood States Depression Scale, CES-D) that correspond to the DSM-IV criteria for major depressive episode, and found in application that the three tools were highly correlated ( $r > 0.80$ ) in their identification of depressed individuals. Nonetheless, SCIDs were not actually done in the study.

**Summary.** Prevalence of depression is high at multiple time points after TBI. No evidence provides a basis for targeting screening to one timeframe over another. Likewise, the literature is insufficient to determine whether tools for detecting depression that have been validated in other populations can accurately identify depression in individuals with TBIs. Nor does the literature support any one tool over the others.

### KQ3. Prevalence of Concomitant Psychiatric Conditions

**Content of literature.** We identified nine publications<sup>13,57,59,91,96,98,110,117,125</sup> in eight populations that reported prevalence of concomitant psychiatric conditions within the population of depressed TBI patients,<sup>13,96,98,117</sup> or compared rates of comorbid conditions in those with and without depression.<sup>57,59,91,110,125</sup> Papers that reported the overall prevalence of psychiatric conditions among the general population of TBI patients with no data on their association with depression were excluded.

Study designs included five prospective cohorts,<sup>13,57,59,98,110,125</sup> one retrospective cohort,<sup>91</sup> and two cross-sectional studies.<sup>96,117</sup> Seven studies were conducted in the United States<sup>13,57,59,91,96,98,110,125</sup> and one in Australia.<sup>117</sup> One was conducted at an academic medical center,<sup>57</sup> one at a rehabilitation center,<sup>96</sup> one in the community,<sup>91</sup> one at two hospitals within the same state,<sup>59</sup> one at a tertiary care center,<sup>117</sup> and three at trauma centers.<sup>13,98,110,125</sup> The most common condition studied in combination with depression was anxiety.<sup>13,59,91,96</sup> Depression was diagnosed via clinical interview in most of the studies.<sup>13,57,59,91,96,98</sup>

**Coexisting psychiatric conditions.** Eight percent to 93 percent of depressed participants had one or more concomitant conditions. Anxiety was the most commonly detected coexisting condition. In the studies that compared rates of comorbid anxiety in those with and without depression, it was significantly more common in the depressed group (76.7 percent vs. 20.4 percent in one study; 60 percent vs. 7 percent in the second).<sup>59,125</sup>

The recruitment phase of a clinical trial for sertraline to treat major depressive disorder was described in the largest study, and included 1-year followup of 599 participants, all of whom had GCS scores of  $\leq 12$ .<sup>125</sup> Depression was assessed with a structured interview based on the PHQ-9, and assessment for anxiety disorders also used modules of the PHQ. The 1-year cumulative incidence of Major Depressive Disorder (MDD) in this population was 53.1 percent. During this first year following injury, individuals with MDD had substantially higher rates of a concomitant

anxiety disorder than did participants without MDD (60 percent vs. 7 percent: RR, 8.77; 95 percent CI, 5.56 to 13.83).

Assessing depression with the PHQ-9, and PTSD with the PTSD Checklist-Civilian, 37 percent of individuals who also had depression after TBI had PTSD, compared to none among those who were not depressed.<sup>110</sup> Anxiety and aggression outcomes have been investigated among patients with closed head injury and those with multiple trauma but no central nervous system involvement.<sup>59</sup> One-third of patients had major depressive disorder (mood disorder with major depressive features). Over the course of followup, 23 of 30 (76.7 percent) patients with major depressive disorder also had anxiety, compared with 9 of 44 (20.4 percent) nondepressed patients. Of note, PTSD was included with anxiety in this study, and was the defining psychiatric feature for 7 of the 23 patients diagnosed with anxiety. Similarly, 17 of 30 (56.7 percent) depressed patients exhibited aggression, compared to 10 of 44 (22.7 percent) without depression.

A cohort of 188 individuals with TBI who were enrolled in a larger study of mood disorders and psychosocial functioning after TBI was assessed twice over 12 months for depression and other psychiatric comorbidities. Individuals were divided into four groups for analysis: no depression at any point, resolved depression (present at entry but not 12 months), late-onset depression (present at 12 months but not study entry) and chronic depression (present throughout the study). At study entry, coexisting psychiatric conditions were most frequent among those individuals who would have late-onset depression (74 percent of late-onset patients) and lowest among those in the chronic depression group (26 percent). At reassessment, the presence of psychiatric conditions had increased in every group except those never diagnosed with depression. Among the psychiatric conditions examined, anxiety was most common at both study entry and at 12 months (19 and 16 percent, respectively).

**Summary.** When conditions were reported individually, anxiety disorder was most prevalent and affected from 31 to 61 percent of study participants in four papers.<sup>13,59,96,125</sup> PTSD, a major anxiety disorder, was observed in 37 percent of depressed patients and in no patients without depression,<sup>110</sup> and panic disorder was seen in 15 percent of patients with major depression, but not measured in those without depression.<sup>96</sup> Consideration of potential for coexisting psychiatric conditions is warranted.

#### KQ4. Outcomes of Treatment for Depression After TBI

**Content of literature.** Only two publications<sup>127-128</sup> addressed a treatment for individuals diagnosed with depression after a traumatic brain injury. One of the treatment studies was conducted in the United States<sup>127</sup> and the second was in Canada.<sup>128</sup> Both were studies of antidepressant efficacy, the first being a randomized controlled trial of sertraline, and the second an open-label case series of the effects of citalopram.

The study on sertraline was a double-blind placebo controlled trial with block randomization, in which treatment was administered for 10 weeks.<sup>127</sup> Participants were at least 6 months post-TBI, and TBI included documented loss of consciousness or other evidence, such as pathology or imaging. Diagnosis of depression was established by DSM-IV criteria and a Hamilton Rating Scale for Depression (HAM-D) score higher than 18. Dosage of sertraline was not fixed and could be adjusted at 2-week intervals, with a maximum dosage of 200mg/d. The primary outcome of interest was a change in depression status measured with the HAM-D. A positive response was considered to be a decrease of 50 percent, or a drop below 10 on the HAM-D. Of

those who completed the study, 59 percent of the treated group and 32 percent of the control group had a positive response; the difference in response rates between the two groups was not statistically significant ( $p = 0.08$ ).

The second study<sup>128</sup> investigated the effect of citalopram on depressive symptoms after TBI, using an open-label, single-arm (case series) design. The study was limited to individuals with mild to moderate TBI. Mild TBI was defined as loss of consciousness at time of injury of 20 minutes or less, an initial GCS score of 13–15, and post-traumatic amnesia (PTA) of less than 24 hours. Moderate to severe TBI had a GCS score of less than 13, a PTA greater than 24 hours, or an abnormal CT image. The study intended to evaluate the effects of a 6-week course of treatment in 54 patients; however, low response rates resulted in a study extension for 26 participants to 10 weeks. Therefore, although 6-week data were available for all 54 completers, 10-week data were available for 26 participants. The primary outcome measured was a change on the HAM-D score, with an improvement of 50 percent or more designated a positive response and a score of less than 8 defined as remission. In the 6-week data ( $n = 54$ ), 27.7 percent were classified as responders and 24.1 percent were in remission. Among participants with data at 10 weeks, 46.2 percent were responders and 26.9 were in remission. Of the 11 individuals who dropped out of the study, 6 were in the intended 6-week group and 5 were in the intended 10-week group. Ten of the 11 experienced an adverse event.

## Discussion

The amount of literature about traumatic brain injury is increasing rapidly, with the focus on the relationship between TBI and depression also growing. As is typical of advancing areas of research, early publications about TBI and depression have been predominantly cross-sectional, with little apparent consensus about measures or key covariates and a high degree of variability in quality of publications. Prospective studies of sufficient size to enable multivariate modeling of predictors of outcome or analysis of outcome by factors such as severity are rare. Achieving representative study populations is challenging because enumerating the entire population eligible for followup is hampered by the portion of the population who do not seek care for head injury. While studies in specialized settings like neuropsychiatric clinics or rehabilitation programs can be applicable to estimating risk in those settings, they cannot be generalized to the base population of all those with injuries.

Overall, the content of the current literature is fair to poor, with a preponderance of study designs that do not provide strong evidence. As a result, the strength of the literature is low for understanding the predictors, prevalence, natural history, treatment options, and modifiers of outcomes of depression that follows TBI. Nonetheless, considerable evidence suggests depression after all forms and severity of TBI is common.

We find a concerning lack of high-quality evidence to inform clinical decisionmaking for the 1 to 2 million individuals in the United States who experience traumatic brain injury each year. Lack of treatment studies focused on this population is especially remarkable. Given how common, concerning, and debilitating the combination of TBI and depression can be, a priority on promoting high-quality research in the United States is imperative.

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# Introduction

We do not know the extent to which depression contributes to long-term disability following traumatic brain injury (TBI). Depression is one of several potential psychiatric illnesses that are common following TBI. Major depression may be triggered by physical or emotional distress, and it can deplete the mental energy and motivation needed for both recovering from the depression itself and adapting to the physical, social, and emotional consequences of trauma with brain injury. Depression may be masked by other deficits after head injury, such as cognitive changes and flat affect, which may be blamed for lack of progress in post-trauma treatment but actually reflect underlying depression. Clinicians, caregivers, and patients lack formal evidence to guide the timing of depression screening, which tools to use for screening and assessment, treatment choices, and assessment of treatment success.

## Importance of Depression

Depression is defined by criteria that likely circumscribe a heterogeneous set of illnesses. While no single feature is seen in all depressed patients, common features include sadness, persistent negative thoughts, apathy, lack of energy, cognitive distortions, nihilism, and inability to enjoy normal events in life. Especially in a first episode, individuals and families may not recognize the changes as part of an illness, making identification and self-reporting of the condition challenging. Active screening is essential to recognition, treatment, and prevention of recurrence.

The most salient consequence of depression is suicide. Suicide is usually impulsive and extremely difficult to predict and prevent. At least half of suicides occur in the context of a mood disorder. Depression reduces quality of life, impairs ability to function in social and work roles, causes self-doubts and difficulty taking action, all of which can delay recovery from TBI. The Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition (DSM-IV-TR) defines the illness in terms of physiologic disturbances of sleep, appetite, attention and concentration, motor activity, and energy, and of psychological losses of interest in normal activities, hope, and self-worth while ruminating with excessive sadness, guilt, and suicidal thoughts. The disturbances may also occur following TBI due to other circumstances, such as pain that disrupts sleep, which may mask the recognition that the sleep disturbance is also a part of a burgeoning depression. Depression may be financially costly in undermining physical therapy efforts, treatment compliance in general, and rehabilitation planning and efforts. The need for systematic evaluation of the prevalence and consequences of depression following TBI is imperative, given the potential for mitigating suicide and unnecessary disability.

## Overview of Traumatic Brain Injury (TBI)

TBI occurs when external force from events such as falls, assault, motor vehicle accidents, or blasts injures the brain. It may occur as a result of a direct hit to the head, or from rapidly accelerating and decelerating wind accompanied by pressure changes that can injure the brain directly or propel other objects into the head (as from a blast).<sup>1</sup> TBI is often accompanied by symptoms that may be severe or mild, and in cases of mild TBI (mTBI) can include nausea, headache, balance problems, blurred vision, memory loss, or difficulty concentrating.<sup>2</sup>

## **Impact of TBI**

The Centers for Disease Control and Prevention (CDC) estimates that 1.5 million nonmilitary individuals in the United States sustain a traumatic brain injury each year.<sup>3</sup> Because these estimates are based on hospital utilization data, and some individuals with mild TBI likely do not seek any care or seek care in other settings, they probably underestimate the impact of TBI, particularly in the presence of sports-related injury. They also do not include TBI that occurs in the military setting. Nonetheless, estimates of direct and indirect costs associated with TBI exceed \$56 billion and may be increasing.<sup>4</sup> Among individuals who sustain a TBI, approximately 50,000 die each year of their injuries and 80,000 to 90,000 have a long-term disability. Traumatic brain injuries are considered mild, moderate, or severe and are categorized using the Glasgow Coma Scale (GCS); a GCS score of 13–15 is considered mild, 9–12 moderate, and 3–8 severe. Most TBIs are mild, and CDC estimates that 75 percent of civilian TBI falls into this category (Available at: <http://www.cdc.gov/ncipc/pub-res/mtbi/mtbireport.pdf>).<sup>5</sup> Because of this, many TBIs likely remain unreported and untreated.

## **Military TBI**

Traumatic brain injury is more common in the military than in civilian populations, even in peacetime. Within the military, the risk for TBI varies among specialties. Paratroopers, for example, are reported to be at higher risk for TBI.<sup>6</sup> Over the past decade, advances in body protection systems have resulted in fewer deaths among combat forces, but a concomitant rise in TBI has been observed.<sup>1</sup> Indeed, prevalence of combat-related brain injuries in forces active in Iraq and Afghanistan appears higher than in any prior conflict. Among patients with combat-related injuries at Walter Reed Army Medical Center from 2003 to 2005, 30 percent had sustained a TBI.<sup>7</sup> A major cause of TBI in the current conflicts is blast injury, in which injuries occur as a result of changes to atmospheric pressure, objects hitting people as a result of the blast, or people being thrown against objects.<sup>8</sup> Unlike the civilian population, however, the military population has a higher rate of moderate and severe TBI (56 percent) than mild TBI.<sup>8</sup>

## **Civilian TBI**

Outside of the military theater, TBIs are most commonly associated with falls (28 percent), motor vehicle traffic accidents (20 percent), being struck by objects (19 percent), and assault (11 percent).<sup>9</sup> Much of the research in the nonmilitary population, especially on mild TBI, is derived from the sports injury literature. Because athletes tend to represent a healthier subpopulation, this literature may not be entirely applicable to the general population of individuals who sustain a TBI. However, it is likely the most robust source of information on TBI in civilians in general.

## **Relationship of TBI to Postinjury Psychiatric Conditions**

TBIs are associated with a range of short- and long-term sequelae, including physical, cognitive, behavioral, and emotional outcomes.<sup>10</sup> Symptoms of depression appear common in individuals who have sustained a TBI, with estimates of post-TBI depression ranging from 15 percent to 77 percent in the published literature.<sup>11-13</sup> Depression associated with TBI can manifest shortly after injury or well into the future,<sup>14-15</sup> and rates reported are likely affected by timing of screening and tools used. In their review of TBI rehabilitation, in which they selected studies from MEDLINE via the PubMed interface<sup>®</sup>, the Cumulative Index to Nursing and Allied Health Literature, and PsycINFO, Gordon and colleagues identified 74 studies addressing

psychiatric functioning after a TBI.<sup>16</sup> Their assessment was that TBI is associated with high rates of depression (up to more than half of cases) and other DSM Axis I and Axis II conditions, including paranoid, schizoid, and avoidant personalities. Furthermore, depression was noted to be comorbid with other psychiatric conditions, including addiction or anxiety, in a number of studies.

Depression diagnosed postinjury is thought to be a product of multiple biopsychosocial factors, including neuroanatomical or pathophysiological changes (i.e., brain lesions and specific location of lesions) and psychosocial factors such as concerns about disability or poor functional status.<sup>14,17</sup>

**Mechanism for post-TBI depression and implications for treatment.** The exact mechanism by which individuals with TBI are at greater risk for depression is not known, although several causes seem possible. For example, mechanisms of post-TBI cellular injury include apoptosis and necrosis.<sup>18</sup> It seems likely that such mechanisms would affect the presentation and treatment of depression. For example, a self-reported history of blast exposure was associated with more headache and tinnitus than nonblast exposure injury mechanisms, but depression rates were similar (respectively, 21.2 percent for  $n = 156$  vs. 15.8 percent for  $n = 38$ ,  $p = 0.65$ ).<sup>19</sup>

Lesion types and locations also may be important, but since pharmacologic treatments address widespread network phenomena, they simultaneously target function in multiple regions, suggesting that choice of medical treatment may depend more on potential harms than the mechanism that causes the depression. Cognitive therapy may be contra-indicated in the presence of severe concomitant cognitive deficits, as it is in depression of nontraumatic etiology, but this assumption has yet to be empirically examined in the TBI population. Other psychotherapy model selections may turn out to depend more on cognitive capacity, psychological mindedness and emotional lability than on the involvement of specific biological lesions or magnitude of psychosocial factors.

**Timing of depression onset.** Clinical care providers and families need to know when and how to screen TBI patients for depression. However, literature on the timing of depression onset should be interpreted carefully, since decisions about when and how to conduct screening within the study could bias results. Intuitively, early-onset depressions might seem more likely to have a neuroanatomic source, while later onset might be presumed to be related to patients' realizations of impairment severity and limitations that are likely to become persistent. These differences could influence interpretation of timing and methods of depression screenings, if indeed earlier screening captures the "neurobiological" depressions and misses the later onsets of "situational" reactions associated with ongoing treatments, complications, or unyielding plateaus in improvement.

**Premorbid conditions and TBI.** Also of concern is the way in which preinjury status may have affected both the likelihood of sustaining an injury and the future risk of depressive disorder. For example, the relationship observed between alcohol use or abuse and TBI may be circular in that preinjury use can increase the risk of injury but may also be related to an increased risk of psychiatric sequelae when an injury does occur. Other factors, such as demographics and support systems in place prior to injury may also confound relationships between injury and depression, and may also affect the perceived need for screening, the criteria for diagnosis, diagnostic elements, goal-setting, and successful assessments with treatment.<sup>17</sup>

**Diagnosing depression in patients with TBI.** Significant overlap between the brain regions associated with the core symptoms of depression and those that are often damaged in TBI (especially frontal lobe lesions), makes accurate diagnosis of depression challenging. Symptoms of postconcussion syndrome (PCS), which is common after TBI, may include: cognitive deficits, disordered sleep, irritability, aggression, anxiety, depression, changes in personality, affective lability, and apathy or lack of spontaneity. Many of these symptoms are also commonly present in a variety of mental disorders, such as unipolar and bipolar mood disorders and anxiety disorders. Therefore, it can be difficult to distinguish, especially in a single diagnostic interview, if these symptoms truly reflect an independent psychiatric disorder or whether they are better understood as simply additional symptoms of TBI or PCS.<sup>20</sup> Longer periods of observation may be needed to assess the degree to which an intrinsic variability of post-TBI symptoms over time is associated with, or dissociated from, the sadness and disinterest that is considered a hallmark characteristic of depression. Additionally, atypical presentations of depression are anticipated in the TBI population, where paradoxical laughter may appear in lieu of tears to express sadness. Furthermore, the timing of the assessment may affect whether depression is suspected or preliminarily identified. Reviews should address questions of how and when depression might best be assessed.

## Treatment Options

This review focuses specifically on depression following TBI and the treatment of depression in this context (i.e., not the treatment of the TBI per se). Treatment options for depression after a TBI theoretically include the range of psychotropic medications, including selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, tricyclic antidepressants, monoamine oxidase inhibitors, and other, non-FDA approved uses of both older and novel medications, as well as psychotherapy, neuropsychological rehabilitation, community-based rehabilitation, complementary and alternative medicine and neuromodulation therapies (electroconvulsive therapy and others) that may be routinely or only recently applied to the treatment of non-TBI associated depressions. Decisions about treatment approach may be affected by the clinician's understanding of the etiology of the initial injury as well as issues of timing of onset of the depression and concomitant conditions.<sup>21</sup> As with nonpsychotic, unipolar depression in the general population,<sup>22-23</sup> in TBI an evidence-based modality of psychotherapy would be a first option with the option to initiate antidepressant medications concomitantly or in sequence.

Treatment harms, including well-recognized side effects, may also be of particular concern in this population because systematic evidence for most medications is generally available only for intact, depressed but otherwise healthy individuals. For example, many psychotropic medications can lower the seizure threshold in a population already potentially predisposed to seizure due to TBI. When patients do have seizure disorders or other TBI-related outcomes, they may already be on medication and therefore at risk for potential drug–drug interactions. Other side effects, such as gastrointestinal distress or weight gain, may also occur in this population, and it is not clear if they may occur at lower doses than in the noninjured population. In patients who present with apathy associated with TBI that is misdiagnosed as depression, antidepressants can sometimes worsen this symptom just as they do in the non-TBI depressed population by causing emotional blunting.<sup>21</sup>

# Key Questions and Analytic Framework

## Key Questions

We synthesized evidence in the published literature to address these key questions:

**KQ1.** What is the prevalence of depression after traumatic brain injury, and does the area of the brain injured, the severity of the injury, the mechanism or context of injury, or time to recognition of the traumatic brain injury, or other patient factors influence the probability of developing incident clinical depression?

**KQ2.** When should patients who suffer traumatic brain injury be screened for depression, with what tools, and in what setting?

**KQ3.** Among individuals with TBI and depression, what is the prevalence of concomitant psychiatric/behavioral conditions, including anxiety disorders, post-traumatic stress disorder, substance abuse, and major psychiatric disorders?

**KQ4.** What are the outcomes (short and long term, including harm) of treatment for depression among traumatic brain injury patients utilizing psychotropic medications, individual/group psychotherapy, neuropsychological rehabilitation, community-based rehabilitation, complementary and alternative medicine, neuromodulation therapies, and other therapies?

**KQ5.** Where head-to-head comparisons are available, which treatment modalities are equivalent or superior with respect to benefits, short- and long-term risks, quality of life, or costs of care?

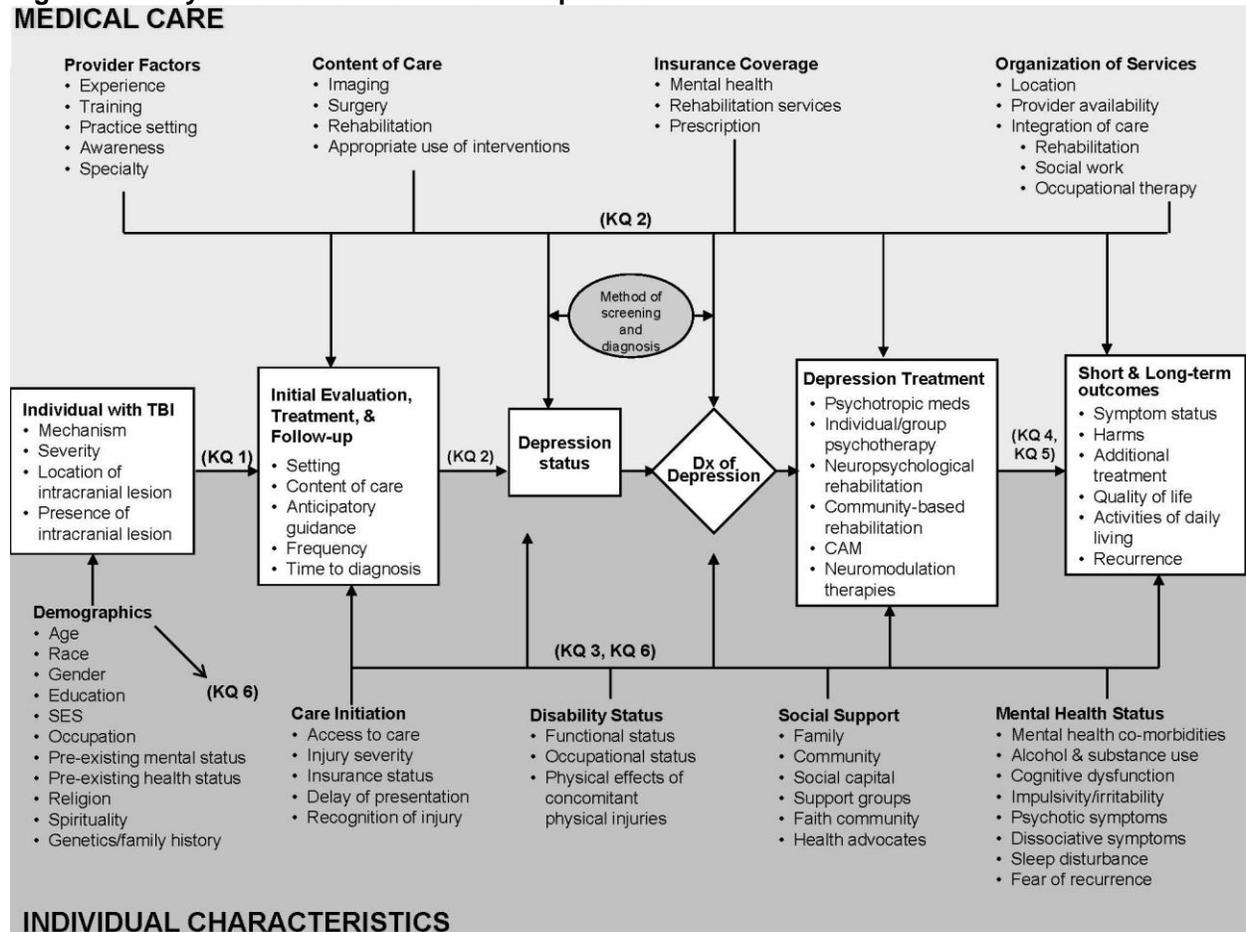
**KQ6.** Are the short- and long-term outcomes of treatment for depression after TBI modified by individual characteristics, such as age, pre-existing mental health status or medical conditions, functional status, and social support?

## Analytic Framework for TBI and Depression

The context in which diagnosis and treatment of depression occurs for individuals after TBI is complex. Our analytic framework emphasizes that care takes place at the interface of the health care system and the individual (Figure 1). The pathway through care is indicated in the boxes along the center line where the person and care meet. Each key question is indicated within the framework at the relevant point of influence in care. Each of the domains listed among individual and system factors, such as demographics, social support, provider factors, and health care coverage status, has been shown to influence care trajectories and outcomes across a range of conditions. Making these domains explicit as they surround and influence the care pathway provides the framework in which the review team and technical expert panel conducted this review. To the degree that individuals or care settings vary in context-specific points of influence, the literature may not always be applicable. We recognized for TBI and depression that there is a dearth of literature for a large portion of these domains and aimed to focus where expert guidance felt evidence was most likely. Overall, we sought to examine factors within the central care pathway as well as in selected contextual domains such as setting (a portion of KQ2), psychiatric comorbidities that could complicate care (KQ 3), and influence of individual characteristics on outcomes as a step toward enhancing applicability of the results (KQ 6).

Portions of the framework that are unexplored in the scientific literature are highlighted in the considerations of future research needs.

**Figure 1. Analytic framework for TBI and depression**



## Organization of This Evidence Report

Chapter 2 describes our methods, including our search strategy, inclusion and exclusion criteria, approach to review of abstracts and full publications, extraction of data into evidence tables, and compilation of evidence. We also describe the approach to grading the quality of the literature and to describing the strength of the literature.

Chapter 3 presents the results of the evidence report by key question, synthesizing the findings across treatment type. We report the number and type of studies identified, and we differentiate between total numbers of publications and unique studies to bring into focus the number of duplicate publications in this literature in which multiple publications are derived from the same study population. Chapter 4 discusses the results in Chapter 3 and enlarges on methodologic considerations relevant to each key question. We also outline the current state of the literature and challenges for future research on depression after TBI.

## **Technical Expert Panel (TEP)**

We identified technical experts on the topic of traumatic brain injury and depression in the fields of trauma surgery, neurology, psychiatry, psychology, military/wartime health care, and patient advocacy to provide assistance during the project. The TEP (see Appendix E) was expected to contribute to the Agency for Healthcare Research and Quality's broader goals of (1) creating and maintaining science partnerships as well as public-private partnerships and (2) meeting the needs of an array of potential customers and users of its products. Thus, the TEP was both an additional resource and a sounding board during the project. The TEP included seven members serving as technical or clinical experts. To ensure robust, scientifically relevant work, we called on the TEP to provide reactions to work in progress and advice on substantive issues or possibly overlooked areas of research. TEP members participated in conference calls and discussions through e-mail to:

- Refine the analytic framework and key questions at the beginning of the project;
- Discuss the preliminary assessment of the literature, including inclusion/exclusion criteria;
- Provide input on the information and categories included in evidence tables;
- Develop a hierarchy of participant characteristics and outcomes to systematically assess;
- Advise about the clinical availability, use, and most common doses for therapeutics.

Because of their extensive knowledge of the literature, including numerous articles authored by TEP members themselves, and their active involvement in professional societies and as practitioners in the field, we also asked TEP members to participate in the external peer review of the draft report.

## **Uses of This Report**

This report is intended to describe the extent to which depression occurs after TBI, appropriate timing and methods for diagnosis, and available evidence for treatment. It should be of use to groups and individuals who treat patients with traumatic brain injury, such as research and clinical psychiatrists; psychologists; physiatrists; trauma surgeons; neurologists; speech, occupational, and physical therapists; and primary care physicians. In particular, evidence in the report could be used to prioritize need for depression screening of those patients. Of particular importance is the role of this report in guiding future research by identifying current gaps, particularly in the treatment literature, given the near absence of research on treatment for depression in TBI-affected populations. Future research recommendations could be helpful to investigators, funders and policymakers, with the goal of advancing understanding of the causes, natural history, and most effective care of individuals with depression after TBI.

# Methods

In this chapter we document the procedures that the Vanderbilt Evidence-based Practice Center used to develop this comprehensive evidence report on the treatment of depression after traumatic brain injury (TBI). We first describe our strategy for identifying articles relevant to our key questions (KQs), our inclusion/exclusion criteria, and the process we used to abstract relevant information from the eligible articles and generate our evidence tables. We also discuss our criteria for grading the quality of individual articles and for rating the strength of the evidence as a whole. Finally, we describe the peer review process.

## Literature Review Methods

### Inclusion Criteria

Our inclusion criteria were developed in consultation with the Technical Expert Panel (TEP) to capture the literature most tightly related to the key questions. Criteria are summarized below.

**Table 1. Inclusion and exclusion criteria for treatment of depression after traumatic brain injury**

Category	Criteria
Study population	Adults age $\geq 16$ years old
Study settings and geography	Developed nations: United States, Canada, United Kingdom, Western Europe, Japan, Australia, New Zealand, Israel, South America
Publication languages	English only
Admissible evidence (study design and other criteria)	<u>Admissible designs</u> Randomized controlled trials, cohorts with comparison, case-control, and case series (n $\geq 50$ )  <u>Other criteria</u> <ul style="list-style-type: none"><li>• Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results</li><li>• Patient populations must include participants that have been diagnosed with depression following a traumatic brain injury received in adulthood</li><li>• Studies must address one or more of the following for depression after traumatic brain injury:<ul style="list-style-type: none"><li>○ Treatment modality</li><li>○ Symptom management approach</li><li>○ Short- and long-term outcomes and quality of life</li></ul></li><li>• Relevant outcomes must be able to be abstracted from data presented in the papers</li></ul>

We limited the review to studies published in developed countries to better approximate the United States health care system in terms of access to screening and treatment services. We did not have translation services available to us to review non-English papers, and our TEP agreed that the vast majority if not all of the relevant literature would be published in English. Furthermore, this review is intended to inform U.S. health care, and most research in this population is published in studies. Empirical evidence on the potential for bias created by excluding non-English studies also suggests little effect.<sup>24</sup> All study designs except individual case reports were included in order to be inclusive and identify all possible prevalence, screening, and treatment studies. The decision to require at least 50 participants in each study was made in concert with our TEP, and resulted in the exclusion of only 36 studies, of which one

was a randomized controlled trial. The adult trauma population is defined at the Level I trauma center as 16 years old or older. Short- and long-term outcomes in traumatic brain injury in children is pathologically distinct from the adult population.<sup>25</sup> We chose to limit this study to the adult population of traumatic brain injury and outcomes associated with depression. In order to ascertain prevalence and to further assess potential modifiers of likelihood of being depressed, it was important that studies use an acceptable means of diagnosing depression. We accepted a structured clinical interview or any validated diagnostic tool, excluding for these questions any studies that relied only on self-report of depressed status or that did not describe their approach to depression diagnosis.

**Additional criteria.** In order to answer KQ1, studies had to provide some measure of prevalence. We excluded studies that did not provide prevalence data (e.g., for which only mean depression scores were available).

In order to answer KQ2, studies had to provide data that allowed prevalence to be assessed in accordance with a specific timeframe, setting, or tool (or some combination of these). Studies that did not provide any information about when depression screening took place relative to injury were excluded from the weighted average for depression prevalence calculations for specific time points.

In order to answer KQ3, we required that studies present data on comorbid psychiatric conditions within the depressed population separately from the nondepressed population, as our intent was not to measure these conditions in the general TBI population but to explain their specific relationship to depression.

This review focused on the prevalence of diagnosed depression in populations that had sustained a documented traumatic brain injury, and on the treatment of those populations. We excluded studies of individuals with penetrating head injuries because penetrating injury, such as gunshot wounds, create specific and severe tissue damage along the course of the injury as well as associated bleeding and inflammation. The mechanism of injury associated with blunt force trauma to the head more often leads to a diffuse pattern of injury that may affect the entirety of the brain. Although long-term outcomes may be similar in some penetrating head injury cases, our focus on the more global nature of blunt-force trauma and its consequences lead us to exclude studies of penetrating head injuries from this review.

## Literature Search and Retrieval Process

**Databases.** Our search included examination of results in five databases: MEDLINE via the PubMed interface, the PsycINFO database of psychological and psychiatric literature, Embase, the Cumulative Index to Nursing and Allied Health Literature (CINAHL), and the Published International Literature on Traumatic Stress (PILOTS) database. We also hand-searched the reference lists of relevant articles to identify additional citations for review.

**Search terms.** Controlled vocabulary terms served as the foundation of our search in each resource, complemented by additional keyword terms and phrases selected to represent each of the key concepts in the search. We also employed indexing terms when possible to exclude undesired publication types (e.g., reviews, case reports, letters, etc.) and articles published in languages other than English.

Tables 2–6 outline our search terms and results yielded by each of the databases. Our searches were executed between March and May 2010. From PubMed, we identified 1,491 items for further review; PsycINFO yielded 319 items; Embase yielded 213 items; CINAHL yielded 109 items; and PILOTS yielded 116 citations. After eliminating duplicate citations, 2,015 citations comprised our pool of citations for review.

**Table 2. PubMed search strategies (last updated June 2009)**

Search #	Terms
#1	(Brain Concussion[mh] OR brain injuries[mh:noexp] OR Brain Hemorrhage, Traumatic[mh] OR Epilepsy, Post-Traumatic[mh] OR Head Injuries, Closed[mh] OR Head Injuries, Penetrating[mh] OR Intracranial Hemorrhage, Traumatic[mh] OR Craniocerebral Trauma[mh] OR TBI[tiab] OR head injuries[tiab] OR head injury[tiab] OR traumatic brain injury[tiab] OR traumatic brain injuries[tiab] OR neurotrauma[tiab] OR diffuse axonal injury[mh] OR diffuse axonal injury[tiab] OR brain trauma[tiab] OR head trauma[tiab])
#2	Depressive Disorder[mh] OR Depression[mh] OR depressive[tiab] OR depression[tiab] OR depressed[tiab] OR sadness[tiab] OR sad[tiab] OR hopelessness[tiab] OR suicidal[tiab] OR suicide[tiab] OR Mental Disorders[mh:noexp] OR mood[tiab]

\* Numbers do not total due to exclusions in more than one category (15 items were indexed as both letter and case report, 2 as comment and case report, 33 as review and case report, 4 as editorial and comment, 12 as letter and comment, 1 as review and comment, and 2 as editorial and review).

**Table 3. PsycINFO search strategies**

Search #	Terms
#1	DE=("head injuries" or "brain concussion" or "traumatic brain injury") or KW=("head injury" or "head injuries" or "traumatic brain injury" or "traumatic brain injuries" OR "craniocerebral trauma" or neurotrauma or "brain trauma" OR "head trauma" OR TBI)
#2	DE=("depression emotion" or "major depression" or "hopelessness" or "sadness" or "suicidal ideation" or "suicide") or KW=(depressive or sad or hopeless or sadness)
#3	#1 AND #2 AND LA=(English) AND PO=(Human)

\* Denotes number of citation retrieved from peer-reviewed journals

**Table 4. Embase search strategies**

Search #	Terms
#1	head injury/ or brain concussion/ or brain contusion/ or diffuse axonal injury/ or postconcussion syndrome/ or traumatic brain injury/ or ("craniocerebral trauma" or "brain trauma" or "head trauma" or TBI or "traumatic brain injury" or "traumatic head injury" or "traumatic brain injuries" or "traumatic head injuries").ab. or ("craniocerebral trauma" or "brain trauma" or "head trauma" or TBI or "traumatic brain injury" or "traumatic head injury" or "traumatic brain injuries" or "traumatic head injuries").ti.
#2	mental disease/ or mood disorder/ or depression/ or major depression/ or suicidal ideation/ or hopelessness/ or (depressive or sad or sadness or hopeless).ti. or (depressive or sad or sadness or hopeless).ab.
#3	1 and 2 and english.lg. and human/

**Table 5. CINAHL search strategies**

Search #	Terms
S1	("traumatic brain injury") or (MH "Brain Injuries+") OR "neurotrauma" OR "brain injuries" OR "TBI" OR "concussion" OR "head injuries" OR "head injury" OR "head trauma" OR "brain trauma"
S2	((MH "Depression+") OR "depressive disorder" OR "sadness" OR "depressed" OR (MH "Suicide") or (MH "Suicide, Attempted") or (MH "Suicidal Ideation") OR "suicide" OR "hopelessness" or (MH "Hopelessness") OR "mood")
S3	S1 AND S2 AND LA English
S4	S3 AND Exclude MEDLINE Records

**Table 6. PILOTS search strategies**

Search #	Terms
#1	(DE="head injuries") or ("brain concussion" OR concussion OR "traumatic brain injury" OR "TBI" OR neurotrauma OR "traumatic brain injuries" OR "head trauma" OR "craniocerebral trauma" OR "brain injury" OR "brain injuries" )
#2	(DE="depressive disorders") or (depression OR depressed OR depressive OR suicidal OR suicide OR sadness OR hopelessness)
#3	#1 AND #2 AND LA=(English)
#4	#3, limited to peer-reviewed journals

**Methods for developing weighted averages for depression prevalence.** The following processes were applied in order to select studies to be used in developing the prevalence histograms in the results section of KQ2:

### Prevalence

- If a study was longitudinal with time since injury greater than 12 months and several followup measures sequentially following initial measure, the study was then included in the spreadsheet duplicate times for each time period (e.g., 2 years, 5 years, 10 years) under the ">12 months" column.
- If a study included different tools with prevalence measure for each, the study was included in the spreadsheet multiple times, once for each tool.

### Glasgow Coma Scale (GCS)

- If a study listed mean GCS score with percentages accounting for each severity group, the study was listed as including all TBI severity groups.
- If a study listed no GCS score, the study was not included in severity analysis.
- If a study did not provide data by TBI severity category, but provided an overall mean and range instead, the study was considered to include participants in each severity grouping representing in the range, and the study contributed to the analysis of each severity level (e.g., GCS mean  $8.0 \pm 3.0$ , range 4–13, then TBI severity groups would be mild to severe, and all TBI severity groups would be included in the spreadsheet).

### Setting

- Setting was extracted from evidence tables.

In addition, studies that explicitly evaluated approaches to diagnosing depression in TBI populations were included for the second part of KQ2. Studies for this subsection were required to compare at least two tools for assessing depression and provide some statistical means of assessing validity and/or reliability.

For KQ3, we required that studies present data on comorbid psychiatric conditions within the depressed population separately from the nondepressed population as our intent was not to measure these conditions in the general TBI population, but to explain their specific relationship to depression.

**Categorization of TBI measures for reporting.** For the purpose of reporting results, we prioritized discussion of papers that adequately described severity levels of TBI in the patient

population. Ideally these are defined by criteria endorsed by professional organizations, including Glasgow Coma Scale, Centers for Disease Control and Prevention, World Health Organization, and American Congress of Rehabilitation Medicine criteria. Studies in which TBI was defined using an ad hoc approach or by patient self-report are presented in Appendix C.

**Categorization of depression diagnoses.** In part due to the heterogeneity in both etiology and expression of depression, descriptions in the literature vary from a strict Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition definition of Major Depressive Disorder diagnosed via a Structured Clinical Interview for DSM-IV (SCID) to a positive response to a simple inquiry asking if the patient has ever felt depressed after their injury. For purposes of the review, therefore, we considered participants to be depressed if they were designated as such by the authors of the studies, and endeavored to document the definition used within each study.

**Identifying duplicate populations.** Because the same study population can be used to do multiple analyses, we developed an algorithm to identify distinct research populations for inclusion in prevalence calculations. We referred to sets of papers that used the same study population as “families” and attempted to identify the “parent” study to provide a representative prevalence estimate.

Most straightforward, of course, were those families of papers in which references were provided that detailed explicitly the relationship between the individual studies, allowing us to identify the parent paper. When such references were not provided, we used a multistep process to cluster papers and then a thorough review of methods and results to identify overlapping or identical populations. Papers were initially clustered by country, then by authors and author affiliations, and potential sets examined together. Within the potential sets of families, we assessed inclusion and exclusion criteria, screening methods, and settings of these studies. In a second step, population descriptors such as average time from injury, age, and population size were examined for identical measures across multiple papers. Of note, it is altogether possible for these characteristics not to match in family papers, particularly in the case of longitudinal studies in which sequential analyses were conducted over time.

Within sets of publications identified as families, individual papers were designated as a “parent” or “child” paper for the purposes of abstracting prevalence data. We attempted to designate the most complete paper as the parent, which meant that it may not have been the earliest or latest publication from the dataset. Factors that played into this determination included assessment of depression as the main outcome, population size (larger populations over smaller populations), inclusion of prevalence information, and inclusion of results over different time periods. Using this approach, we identified 81 unique populations: 62 single studies and 19 parent studies. The 16 parent studies included 34 associated child studies.

Only parent studies were included in summary tables and prevalence calculations for Key Questions 1 and 2. Families are identified in Appendix C, Evidence Tables, with notes in the author field referring to associated studies. Studies utilizing clearly identical populations were combined into a single evidence table when possible.

## **Grey Literature Search Methods**

We conducted a review of the literature for depression in the context of TBI through a systematic search of resources likely to retrieve grey literature and fugitive information items

(Appendix A). Resources were chosen for their relevance to the topic and for their utility in locating unpublished or nontraditional information.

## **Search of the Grey Literature**

We adapted our approach to the published literature for this survey of grey information sources with selected terms related to TBI and depression. Each database and resource searched (Appendix A) has unique features and characteristics that were utilized to improve sensitivity and specificity of our retrieval.

Utilizing the search engine Google, our team searched the Internet using a combination of keywords to identify technical reports and other relevant data. We used the limit “allintext:” to retrieve only information with our keywords included on the Web page and the feature “site: .gov,.org,.edu, .mil” to limit our search to only Web pages from those designations. U.S. and international government resources and registries were employed to locate current clinical trial protocols and newly funded research projects. Given their strength in indexing unpublished resources, PsycINFO, a psychology and psychiatry database, and BIOSIS Previews, a biosciences database, were used to locate current conference proceedings, dissertations, and other grey literature sources. As a means to improve precision of the search strategy, we limited our retrieval to dissertations, meeting abstracts/papers, technical reports, and conference proceedings. To improve the depth of our grey literature review, our team explored several other resources that did not retrieve any additional information.

## **Literature Synthesis**

### **Development of Evidence Tables and Data Abstraction Process**

The staff members and clinical experts who conducted this review jointly developed the evidence tables. We designed the tables to provide sufficient information to help readers understand the studies and determine their quality; we gave particular emphasis to essential information related to our KQs, especially the need to appropriately design evidence tables for prevalence versus treatment studies. We based the format of our evidence tables on successful designs used for prior systematic reviews.

The team was trained to abstract by abstracting several articles into evidence tables and then reconvening as a group to discuss the utility of the table design. We repeated this process through several iterations until we decided that the tables included the appropriate categories for gathering the information contained in the articles. All team members shared the task of initially entering information into the evidence tables. Another member of the team also reviewed the articles and edited all initial table entries for accuracy, completeness, and consistency. The two abstractors reconciled disagreements about the information reported in the evidence tables. The full research team met regularly during the article abstraction period and discussed global issues related to the data abstraction process. In addition to outcomes related to treatment effectiveness, we abstracted all data available on harms. Harms encompasses the full range of specific negative effects, including the narrower definition of adverse events.

The final evidence tables are presented in their entirety in Appendix C. Studies are presented in the evidence tables alphabetically by the last name of the first author. When possible, studies

resulting from the same study population were grouped into a single evidence table. A list of abbreviations and acronyms used in the tables appears at the beginning of that appendix.

Two reporting conventions for describing studies in the evidence table were adopted that warrant explanation, namely those for study design and setting of the study. For settings, we allowed five options, with the operating principle being that the setting should reflect the entity from which the participants were drawn, as this can be a reflection to some degree of injury severity, acuity, or the reason that the individuals were seeking care and thus were identified for the study:

- Tertiary care: academic medical centers and tertiary care hospitals
- Trauma center(s)
- Psychiatric/specialty center(s): psychiatry clinic, disability programs
- Rehabilitation center(s)
- Other: community, private practice, prison, nonacademic Veterans Affairs (VA) facility

Study designs for this review were somewhat more difficult, as “standard” study design definitions for systematic review are most often based on reviews of the treatment literature, and our primary focus was necessarily (due to a paucity of treatment studies) on assessment of prevalence. In this case, we were reviewing studies that may, for example, have been intended as cohort studies in populations with TBI and exposure groups other than depression. The characteristic used to define the cohorts in the study was not relevant for our review, but because the authors captured data on prevalence of depression in the study population, we were able to include the study. Therefore, for our purposes we defined studies in which a group of individuals was systematically described as having a TBI and then “sorted” through diagnosis into depressed and nondepressed groups to be cohort studies, even if there were other exposure groups or no groups defined by the authors. These cohorts could be retrospective or prospective based on the usual definitions about when data were collected. We also allowed for the usual definition of randomized controlled trials for the treatment portion of the review and for cross-sectional studies, in which participants were identified at one time point with no longitudinal collection of data.

## **Assessing Methodological Quality of Individual Studies**

We developed our approach to assessing the quality of individual articles based on our prior experience with conducting systematic reviews. In particular, we used distinct quality rating approaches for the studies used to measure prevalence and those for treatment.

Quality as it relates to prevalence studies is largely a function of appropriately identifying, defining, and enumerating the target population in which prevalence is to be measured. Prevalence estimates may be biased if the study population included has higher or lower rates of the outcome (in this case, depression) than does the population to which the prevalence estimate is intended to apply. Therefore, we based our quality assessment of prevalence studies on the authors’ appropriateness in defining both TBI and depression (including tools used for measurement), in their provision of descriptive information about the TBI (such as mechanism and severity), their followup and retention methods including ability to not lose participants to followup (which would bias estimates if depressed individuals either were or were not lost to

followup at different rates from nondepressed individuals). Therefore, we used eight primary questions with some subquestions to assess quality of the prevalence literature.

## **Prevalence Studies**

*Definition of TBI.* Because no single definition of TBI is consistently used in the literature, we worked with our clinical experts to develop a list of “best” approaches to defining or diagnosing TBI. Studies had to use one of these in order to be awarded the highest quality score under this criterion. Studies that specified an operational definition that was not included on the list of “best” definitions were given one plus. A complete lack of definition, or self-report (i.e., no evidence of clinical diagnosis) received a minus.

*Severity of TBI.* The severity of TBI is known to influence the trajectory of recovery and is thought to affect the risk of post-TBI depression. Therefore, studies should provide measures of TBI severity for included participants.

*Definition of Depression.* As with the definition of TBI, we worked with clinical experts to categorize and rank approaches to diagnosing depression. The full categorization is provided below, and for quality purposes we applied the following:

Was a clinical scale or operational definition provided?

++ = SCID or other structured interview by a trained mental health care provider such as a physician, psychologist, etc.

+ = Operational definition or scale provided, but not a structured interview

- = Other definition, self-report, or not reported (NR)

**Table 7. Categorization of depression measures for reporting**

Category A	SCID or other structured interview by a clinician (e.g., physician or psychologist)
Category B	Validated instruments other than clinical interview, including HAM-D, BDI, HADS, CES-D, NFI, or SCL-90
Category C	Other definition, self report, ad hoc, chart review, or no definition provided

*Participant selection.* For measuring prevalence and comparing studies of prevalence, it is necessary to clearly identify the population from which the cases arise. Therefore, we required that investigators clearly describe the participants, including the source, and that this description be adequate such that another researcher could create a comparable study population.

*Sampling and screening methods.* We used a three-part approach to assessing appropriate sampling and screening methods, requiring first that the pool of potentially eligible participants be clearly enumerated, second that the number meeting eligibility requirements be provided, and third that the number of participants at onset and conclusion of the study (if applicable) also be provided.

*Loss to followup.* For longitudinal studies, we assessed the proportion of participants still in the study at completion. We expected less than 25 percent loss for high quality, between 25 and 50 percent for good quality, and studies that lost more than 50 percent of participants received a low quality (minus) score for this variable.

Two potentially important characteristics of participants that could affect prevalence are prior history of psychological conditions (i.e., psychological conditions in the post-TBI period may not be new onset) and time since injury. Therefore, for adequate quality we required that information on both of these be provided by the authors. We did not specify what information or the degree of information needed.

**Treatment studies.** For treatment studies, we assessed creation and comparability of comparison groups (selection bias), loss to followup and dropout (attrition bias), statistical analysis, including evidence of adequate power, and external validity (also known as applicability).

**Internal validity.** The criteria for assessing internal validity were as follows:

*Randomized allocation to treatment.* This assessment combines randomization and method of randomization into a single criterion with a three-point scale.

**Rationale.** By randomly assigning groups to the intervention of interest, other factors that may confound the results are equally distributed between groups (assuming a large enough sample size). This equal distribution minimizes the chances of over- or underestimation of treatment effect based on unequal distribution of confounding factors.

If randomized, we also evaluated the study for randomization methods, using the rationale described in Matchar and colleagues, 2001.<sup>26</sup> “Pseudo-randomization” methods may be susceptible to bias, as demonstrated by evidence of unequal distribution of subject characteristics<sup>27</sup> and larger effect sizes compared with studies using more rigorous methods.<sup>28</sup> In addition, methods of allocation concealment are also important in preventing bias (e.g., use of prepared sealed envelopes).

We combined these elements into a single operational definition, as described below:

**Operational definition.** Criterion met if randomization methods were not susceptible to bias, such as computer-generated numbers in sealed sequentially numbered envelopes (+). Criterion not met by studies that either used methods more prone to bias, such as alternate medical record numbers, or did not describe randomization methods or methods of allocation concealment (-). Criterion not applicable if treatment was not randomly allocated (NA).

*Masking.*

**Rationale.** Masking, also known as blinding, refers to the concealment of treatment allocation from the care provider, the assessor, and the patient. In certain trials, particularly surgical trials, masking the patient or the surgeon from the treatment allocation can be challenging or impossible. Similarly, masking the assessor assigned to record immediate postprocedural outcomes such as wound healing can also be difficult. Nevertheless, when possible, masking prevents expectations from influencing findings.

**Operational definition.** Criterion was met if assessors and participants were masked to treatment or group (+). Criterion was not met if care provider, assessor, or patient were not masked (-). Criterion not applicable if treatment was not randomly allocated (NA).

*Adequate description of patients and control selection criteria.*

**Rationale.** Patient characteristics that might affect outcomes (such as severity of symptoms, duration of symptoms, failure of prior treatment, or medical comorbidities) are likely to differ between two interventions. If these differences are not characterized, then erroneous conclusions may be drawn.

**Operational definition.** Criterion met if inclusion and exclusion criteria for participation in the study were well described.

We expected that the study population should be adequately described to make clear the potential for confounding in the analysis. We expected the study authors to adequately describe the study population such that it could theoretically be reproducible by another investigator. We expected comparable methods to be used to identify and screen participants across exposure or treatment groups.

*Description of loss to followup.*

**Rationale.** Failing to account for patients lost to followup may lead to erroneous conclusions, especially if the loss to followup is related to either the underlying disease or the intervention (i.e., patients seeking care elsewhere because of continuing symptoms or unacceptable side effects of treatment).

**Operational definition.** Criterion met for adequate followup (+) if (a) loss to followup was explicitly reported and (b) no more than 20 percent of any study arm was lost to followup. Those studies with less than 10 percent lost to followup were given an extra (+). Studies with greater than 20 percent lost to followup were considered inadequate for this measure (-).

*Description of dropout rates.*

**Rationale.** Dropout rates may reflect differences in clinically important variables, such as side effects or treatment response. Failure to account for dropouts may result in erroneous conclusions similar to those seen with failure to account for loss to followup.

**Operational definition.** Criterion met if (a) patients dropping out of the study prior to completion were reported and (b) no more than 20 percent in any study arm left the study for reasons related to the study intervention or withdrawal of consent. Those studies with less than 10 percent dropout were given an extra (+). Studies with greater than 20 percent dropout were considered inadequate for this measure (-).

*Power calculation provided.*

**Rationale.** Many studies, especially case series, lack sufficient power to detect clinically important differences in outcomes or patient characteristics.

**Operational Definition.** Criterion met if a power calculation (pre or post) was provided.

*Recognition and description of statistical issues.*

**Rationale.** Use of inappropriate tests may lead to misleading conclusions. For example, variables such as depression scores are often not normally distributed; use of means instead of medians when data may be affected by outlying observations can be misleading.

**Operational definition.** Criterion met if (a) appropriate statistical tests were used (e.g., nonparametric methods for variables with nonnormal distributions, or survival analysis techniques to account for loss to followup and dropouts) and (b) potential study limitations regarding design and analysis were discussed. Criterion not met if (a) inappropriate statistical tests were used or (b) study limitations were not discussed. An intention-to-treat analysis was required of clinical trials.

**External validity.** The criteria for assessing external validity were as follows:

Baseline characteristics: We created a composite score for adequacy of the description of baseline characteristics. We expected the severity of the TBI and time since the TBI event to be presented. If either of these were omitted, criteria were not met.

## Strength of Available Evidence

Strength of evidence is typically assigned to reviews of medical treatments after assessing four domains: risk of bias, consistency, directness, and precision.<sup>29</sup> Although these categories were developed for assessing the strength of treatment studies, the domains apply also to studies of prevalence and screening. Available evidence for each key question was assessed for each of these four domains; the domains were combined qualitatively to develop the strength of evidence for each key question.

We graded the body of literature for each key question and present those ratings as part of the discussion in Chapter 4. The possible grades were:

**I. High:** High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.

**II. Moderate:** Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

**III. Low:** Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.

**IV. Insufficient:** Evidence is either unavailable or does not permit a conclusion.

## External Peer Review

As is customary for all systematic evidence reviews done for the Agency for Healthcare Research and Quality (AHRQ), this report was reviewed by a wide array of individual outside experts in the field, including our TEP, and from relevant professional societies and public organizations. AHRQ also requested review from its own staff. The Scientific Resource Center sent 8 invitations for peer review. Reviewers included clinicians (e.g., trauma surgeons, military

and combat physicians, physical medicine and rehabilitation physicians, and psychiatrists), representatives of federal agencies, advocacy groups, and potential users of the report.

The Scientific Resource Center charged peer reviewers with commenting on the content, structure, and format of the evidence report, providing additional relevant citations and pointing out issues related to how we had conceptualized and defined the topic and KQs. We also asked reviewers to complete a peer review checklist. The Scientific Resource Center received 4 responses in addition to comments from AHRQ staff. The individuals listed in Appendix E gave us permission to acknowledge their review of the draft. We compiled all comments and addressed each one individually, revising the text as appropriate.

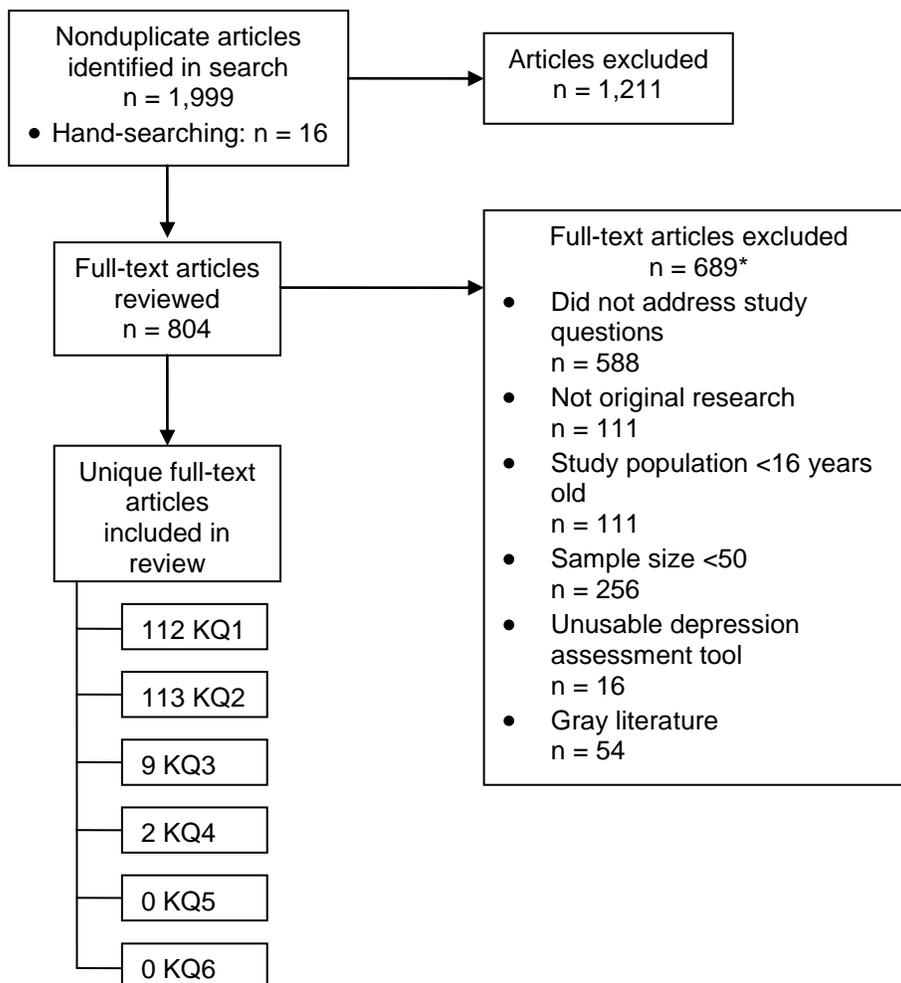
# Results

## Article Selection Process

Once we identified articles through the electronic database searches, review articles, and bibliographies, we examined abstracts of articles to determine whether studies met our criteria. Two reviewers separately evaluated each abstract for inclusion or exclusion using an Abstract Review Form (Appendix B). If one reviewer concluded that the article could be eligible for the review based on the abstract, we retained it. The group included six physicians (KH, OG, RS, SM, FP, SK), and two senior health services researchers (MM, RJ).

Of the entire group of 2,015 articles, 804 required full-text review. For the full article review, two reviewers read each article and decided whether it met our inclusion criteria, using a Full Text Inclusion/Exclusion form. Reasons for article exclusion are listed in Appendix D.

**Figure 2. Disposition of articles for TBI and depression**



KQ = key question

\*The number of articles addressing key question and those excluded exceed the total number of articles in each category because some of articles fit into multiple exclusion categories or addressed more than one key question.

## KQ1. Prevalence of Depression in Traumatic Brain Injury

Understanding the meaning of prevalence estimates requires knowing about both the traumatic brain injury (TBI) population and the method of depression ascertainment. In this section we describe prevalence in the context of the definition of TBI and severity level, as well as the measure of depression used in the research.

### **Prevalence**

We sought publications that provided a defined group of individuals with TBI and used a validated measure of depression to assess the proportion of the population who met specified criteria for depression. We excluded reports relying on simple self-report or single screening items. This key question (KQ) focuses on prevalence because prior and existing depression at the time of head injury are difficult to document in order to formally study incidence.

We identified 112 publications<sup>30,13-15,31-138</sup> from 79 distinct study populations (see Appendix C, Evidence Table 1). Thirty-eight of the 79 were in the United States, 12 in Canada, 12 in Europe, 9 in Australia, and 8 in other countries (Table 8). The most common sources of study populations were tertiary care centers identifying participants from emergency department, intensive care, and inpatient admissions (n = 33), including those that specifically noted trauma center status (n = 10), and rehabilitation programs (n = 19). Neuropsychology labs, private neuropsychology practices, prisons, veterans' records, databases, and psychiatric care facilities each contributed three or fewer populations.

Criteria for defining and characterizing those classified as having TBI were varied with more than half of authors (n = 38) using closed head injury in concert with Glasgow Coma Scores (GCS). American Congress of Rehabilitation Medicine criteria were common (n = 13); as were ad hoc operational definitions (n = 12), and failing to clearly define criteria (n = 12). In total, the majority of the literature provides sufficient detail about inclusion and exclusion criteria and TBI definitions to understand and/or replicate the population studied.

Seventy-three percent of studies provided cross-sectional measures of depression, meaning that depression status was assessed at a single point in time after TBI; the balance were prospective with two or more assessment of depression status over time. Structured clinical interviews, done specifically for the research or in the course of standardized clinical care protocols, were the most common means of assessing depression status (n = 29). Among written or administered tools the Beck Depression Inventory (BDI; n = 13), Hospital Anxiety and Depression Scale (HADS; n = 11) and Center for Epidemiologic Studies Depression Scale (CES-D; n = 8), were most common. A wide variety of other measures and customized uses of subscales (n = 62) were also used. Studies often used more than one instrument, reporting different facets of the scores or evaluation. Comparison of diagnostic test characteristics, agreement of classification, and use of expert Structured Clinical Interview for DSM-IV (SCID) as a gold standard for comparisons were rare (see KQ2), while statistical analyses of correlation of scores or relationships of domains were frequent but generally not intended to directly assess clinical utility.

**Table 8. Characteristics of included TBI and depression studies**

Characteristic	Population Studied				Total (n = 79)
	U.S. (n = 38)	Canada (n = 12)	Europe (n = 12)	Other (n = 17)	
<b>Assessment of depression:</b>					
Cross-sectional	25	9	9	15	58
Prospective	13	3	3	2	21
<b>Setting</b>					
Trauma center(s)	7	0	0	3	10
Tertiary care center(s)	10	7	9	7	33
Rehabilitation center(s)	8	2	3	6	19
Psychiatric/specialty center(s)	2	0	0	0	2
Other	11	3	0	1	15
<b>Operational Definition of TBI*</b>					
CDC Criteria	1	0	0	0	1
WHO Criteria	1	0	0	0	1
ACRM Criteria	7	6	0	0	13
GCS Score	20	5	5	8	38
Self-Report	3	0	0	1	4
Other	2	0	6	4	12
Not Defined	6	1	1	4	12
<b>Depression Tool Used*</b>					
SCID	19	5	1	2	29
Other structured interview	1	0	2	1	4
MMPI	2	2	0	0	4
HAM-D	2	0	2	1	5
BDI	7	1	1	4	13
CES-D	7	0	0	1	8
HADS	2	0	4	5	11
NFI	5	0	0	0	5
SCL-90	2	0	1	1	4
Other	15	8	11	10	44

\* Inclusive: total is greater than number of studies because some publications used multiple definitions or tools.

For this report, we have considered the SCID and other formal structured clinical interview protocols that map to the Diagnostic and Statistical Manual of Mental Disorders (DSM) and/or International Classification of Diseases (ICD) codes to be the measures of depression that are most relevant to clinical care. Ideally patients and care providers want to know what proportion of those with TBI may meet clinical criteria for diagnosis and treatment of depression. Among studies that used a SCID or other structured protocol to reach a formal diagnosis of depression, the prevalence of depression after TBI ranged from 12.2 percent<sup>66</sup> to 76.7 percent.<sup>13</sup> If we focus on the subset of studies with both clearly operationalized criteria for TBI and use of the SCID, the range was 12.2 percent<sup>66</sup> to 54.0 percent.<sup>109</sup> Across all timeframes and depression measures, in studies with clear TBI definitions, the weighted average for prevalence of depression was 31 percent.

Table 9 summarizes context, size of study, measures, and prevalence of depression among studies with clear definitions of TBI. Appendix C includes a similar summary table for studies that provided less information about TBI criteria. In both sets of studies—those with and without optimal definitions of TBI—the observed prevalences are compatible. In these tables, results are

organized by timeframe in which the depression assessment was conducted relative to the injury and by method of assessment. Among those studies with longer term followup, no clear pattern of expected prevalence or natural history emerges:

- Veterans who were hospitalized for TBI approximately 50 years earlier had an 11.2 percent point prevalence of depression, statistically higher than the 8.5 percent among those hospitalized for conditions other than TBI.<sup>15</sup>
- Followup of another group of veterans at an average of 23 years from TBI found 44 percent met criteria for depression.<sup>128</sup>
- Assessment of a group with severe TBI at a mean of 14 years from injury was associated with 44.7 percent prevalence.<sup>31</sup>
- Among studies with assessments 5 to 10 years from TBI, reported prevalences were 9.8 percent,<sup>105</sup> 23 percent,<sup>103</sup> 29.5 percent,<sup>57</sup> and 70 percent.<sup>112</sup>
- Those with assessments three to 5 years from TBI, reported prevalences from 34 to 77 percent.<sup>13,32,38,55,65,85,137</sup>

Among the studies that included comparison groups, 28 reported higher prevalence of depression among those with TBI than those without.<sup>30,13,15,35,43,49,53-55,72,75,83-84,92,97-99,101,112,125,131,133-134,125,129,131,133-134</sup>

Another reported higher mean depression scores among the TBI group (Beck 5-point scale:  $5.5 \pm 5.4$ ) compared to controls ( $2.7 \pm 3.1$ ,  $p = 0.003$ ).<sup>129</sup> Exceptions included: a psychiatric population control group with an equivalent proportion having depression (30 percent);<sup>37</sup> patients with multiple serious injuries from trauma that did not include TBI compared to patients with TBI in which both groups had 76 percent with depression;<sup>48</sup> a prospective cohort in Australia in which those with mild TBI were compared to others hospitalized for similar length trauma admissions without TBI,<sup>134</sup> and a matched control group from the same district in Finland in which both groups had approximately 6 percent prevalence.<sup>61</sup> In no instance was the comparison group significantly more affected by depression.

**Table 9. Prevalence of depression by timing of assessment**

Author Year Country Setting	N with TBI, (% with Depression Measure)	GCS Score	Assessment Method (mean score)	Prevalence %
<b>Unspecified time from injury</b>				
Evans et al. <sup>58</sup> 2005 U.S. Rehabilitation center	96 (100)	3-15	CES-D (NR)	54.0
Hoge et al. <sup>30</sup> 2008 U.S. Other	384 (95.8)	CDC/WHO criteria	PHQ (NR)	13.0

**Table 9. Prevalence of depression by timing of assessment (continued)**

<b>Author Year Country Setting</b>	<b>N with TBI, (% with Depression Measure)</b>	<b>GCS Score</b>	<b>Assessment Method (mean score)</b>	<b>Prevalence %</b>
<b>Unspecified time from injury</b>				
Kant et al. <sup>107</sup> 1998 U.S. Psychiatric/specialty center	83 (100)	3-15	BDI (18.03) AES (38.84)	10.8 60.2
Ruocco et al. <sup>37</sup> 2007 U.S. Other	231 (100)	13-15	MCMI-III Depressive (46.62) MCMI-III Major Depression (56.70)	16.9 30.3
<b>&lt; 3 months since injury</b>				
Gomez-Hernandez et al. <sup>108</sup> 1997 Spain Tertiary care center	65 (100)	3-15	SCID	35.4
Jorge et al. <sup>14,111,114-117</sup> 1993 U.S. Trauma center	66 (100)	3-15	SCID	28.8
Jorge et al. <sup>72,76</sup> 2004 U.S. Other	91 (81.3)	12.3 (mean)	SCID	20.2
McCauley et al. <sup>62-63</sup> 2005 U.S. Trauma center	340 (100)	9-15	SCID	15.0
McCauley et al. <sup>83</sup> 2001 U.S. Tertiary care center	115 (100)	9-15	SCID CES-D (22.5) VAS-D (40.1)	21.7 NR NR
Rao et al. <sup>136</sup> 2009 U.S. Rehabilitation centers	107 (62.6)	3-15	SCID	11.9
Rapoport et al. <sup>77,79</sup> 2003 Canada Tertiary care center	210 (100)	13-15	SCID	16.7

**Table 9. Prevalence of depression by timing of assessment (continued)**

<b>Author Year Country Setting</b>	<b>N with TBI, (% with Depression Measure)</b>	<b>GCS Score</b>	<b>Assessment Method (mean score)</b>	<b>Prevalence %</b>
<b>&lt; 3 months since injury</b>				
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (51.7)	3-15	PHQ-9	31.1 (1 mo)
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (70.0)	3-15	PHQ-9	24.7 (2 mos)
Kashluba et al. <sup>54</sup> 2006 Canada Tertiary care centers	110 (100)	13-15	PCL (NR)	40.0
Rapoport et al. <sup>82</sup> 2002 Canada Tertiary care center	323 (87.3)	3-15	NRS (NR)	Mild/Mod: 34.3
Sherer et al. <sup>40</sup> 2007 U.S. Rehabilitation center	69 (100)	8.0 (mean)	CES-D (11.6)	31.9
<b>3 to 6 months since injury</b>				
Brown et al. <sup>68</sup> 2004 U.S. Trauma center	135 (100)	14.5 (mean)	SCID	16.3*
Bryant et al. <sup>134</sup> 2010 Australia Trauma centers	437 (86.3)	13-15	MINI	17.9
Gomez-Hernandez et al. <sup>108</sup> 1997 Spain Tertiary care center	65 (73.8)	3-15	SCID	37.5
Herrmann et al. <sup>135</sup> 2009 Canada Tertiary care center	200 (100)	ACRM criteria	SCID	48.0

**Table 9. Prevalence of depression by timing of assessment (continued)**

Author Year Country Setting	N with TBI, (% with Depression Measure)	GCS Score	Assessment Method (mean score)	Prevalence %
<b>3 to 6 months since injury</b>				
Jorge et al. <sup>14,111,115-117</sup> 1993 U.S. Trauma center	66 (81.8)	3-15	SCID	29.6
Jorge et al. <sup>72,76</sup> 2004 U.S. Tertiary care centers	91 (81.3)	12.3 (mean)	SCID	32.4
Levin et al. <sup>84</sup> 2001 U.S. Trauma center	69 (100)	9-15	SCID CES-D (22.14) VAS-D (40.79)	17.4 NR NR
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (73.0)	3-15	PHQ-9	24.5 (3 mos)
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (74.2)	3-15	PHQ-9	21.9 (4 mos)
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (75.7)	3-15	PHQ-9	22.9 (5 mos)
Dunlop et al. <sup>119</sup> 1991 U.S. Other	68 (100)	9.2 (mean)	NRS (NR)	50.0
Kashluba et al. <sup>54</sup> 2006 Canada Tertiary care centers	110 (100)	13-15	PCL (NR)	39.1
McCauley et al. <sup>86</sup> 2001 U.S. Trauma centers	210 (100)	ACRM criteria	NRS-R (NR)	51.0
Rapoport et al. <sup>82</sup> 2002 Canada Tertiary care center	323 (87)	3-15	NRS (NR)	Severe: 48.9

**Table 9. Prevalence of depression by timing of assessment (continued)**

<b>Author Year Country Setting</b>	<b>N with TBI, (% with Depression Measure)</b>	<b>GCS Score</b>	<b>Assessment Method (mean score)</b>	<b>Prevalence %</b>
<b>6 to 12 months since injury</b>				
Chamelian et al. <sup>50,67</sup> 2004 Canada Tertiary care center	90 (100)	9-15	SCID GHQ (0.85)	12.9 NR
Gomez-Hernandez et al. <sup>108</sup> 1997 Spain Tertiary care center	65 (64.6)	3-15	SCID	38.1 (6 mos)
Gomez-Hernandez et al. <sup>108</sup> 1997 Spain Tertiary care center	65 (66.2)	3-15	SCID	32.6 (9 mos)
Jorge et al. <sup>14,111,114-117</sup> 1993 U.S. Trauma center	66 (65.2)	3-15	SCID	25.6
Jorge et al. <sup>72,76</sup> 2004 U.S. Tertiary care centers	91 (100)	12.3 (mean)	SCID	40.5
Mooney et al. <sup>87</sup> 2001 U.S. Rehabilitation center	80 (100)	13-15	SCID	44.0
Rapoport et al. <sup>66</sup> 2005 Canada Tertiary care center	74 (100)	9-15	SCID	28.4
Rapoport et al. <sup>49,52</sup> 2006 Canada Rehabilitation center	69 (71)	9-15	SCID Major	12.2 18.8
Bay et al. <sup>44,80</sup> 2002/2007 U.S. Tertiary care center	75 (100)	>8	CES-D (20.5) NFI (30.7)	64.0 14.7
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (77.3)	3-15	PHQ-9	20.8 (6 mos)

**Table 9. Prevalence of depression by timing of assessment (continued)**

<b>Author Year Country Setting</b>	<b>N with TBI, (% with Depression Measure)</b>	<b>GCS Score</b>	<b>Assessment Method (mean score)</b>	<b>Prevalence %</b>
<b>6 to 12 months since injury</b>				
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (68.9)	3-15	PHQ-9	24.2 (8 mos)
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (64.0)	3-15	PHQ-9	27.1 (10 mos)
Bryant et al. <sup>90</sup> 2001 Australia Rehabilitation center	96 (100)	8.0 (mean)	BDI (16.5)	45.8
Dunlop et al. <sup>119</sup> 1991 U.S. Other	68 (100)	9.2 (mean)	NRS (NR)	28.0
Ghaffar et al. <sup>47</sup> 2006 Canada Tertiary care centers	191 (63.9)	14.9 (mean)	GHQ	28.7
Hawley and Joseph <sup>33</sup> 2008 U.K. Rehabilitation centers	563 (7.2)	3-15	HADS (NR)	20.5
Kersel et al. <sup>45,88</sup> 2001 New Zealand Tertiary care center	69 (84)	<9	BDI (NR)	24.0
McCleary et al. <sup>99-101</sup> 1998 U.S. Tertiary care center	105 (100)	3-15	SCL-90 (NR) NRS (NR)	24.4 33.0
Ziino and Ponsford <sup>125</sup> 2006 Australia	46 (100)	3-15	HADS (NR)	39.1

**Table 9. Prevalence of depression by timing of assessment (continued)**

Author Year Country Setting	N with TBI, (% with Depression Measure)	GCS Score	Assessment Method (mean score)	Prevalence %
<b>&gt;12 months since injury</b>				
Al-Adawi et al. <sup>41</sup> 2007 Oman Tertiary care center	68 (100)	3-15	CIDI (NR) HADS (NR)	57.4 19.1
Ashman et al. <sup>70-71</sup> 2004 U.S. Tertiary care center	188 (100)	ACRM criteria	SCID	35.0 (T1: 3 mos - 4 yrs)
Ashman et al. <sup>70-71</sup> 2004 U.S. Tertiary care center	188 (100)	ACRM criteria	SCID	24.0 (12 mos after T1)
Ashman et al. <sup>70-71</sup> 2004 U.S. Tertiary care center	188 (44.1)	ACRM criteria	SCID	21.0 (24 mos after T1)
Bryant et al. <sup>134</sup> 2010 Australia Trauma centers	437 (73.5)	13-15	MINI	17.4
Fann et al. <sup>109</sup> 1995 U.S. Rehabilitation center	50 (100)	3-15	SCID	54.0
Gomez-Hernandez et al. <sup>108</sup> 1997 Spain Tertiary care center	65 (56.9)	3-15	SCID	27.0
Homaifar et al. <sup>128</sup> 2009 U.S. Tertiary care center	52 (100)	3-15	SCID	44.2
Huang et al. <sup>59</sup> 2005 U.S. Tertiary care center	59 (100)	3-15	SCID ZDS (39.6)	13.6 16.9
Jorge et al. <sup>14,111,114-117</sup> 1993 U.S. Trauma center	66 (65.2)	3-15	SCID	25.6

**Table 9. Prevalence of depression by timing of assessment (continued)**

<b>Author Year Country Setting</b>	<b>N with TBI, (% with Depression Measure)</b>	<b>GCS Score</b>	<b>Assessment Method (mean score)</b>	<b>Prevalence %</b>
<b>&gt;12 months since injury</b>				
Kennedy et al. <sup>57</sup> 2005 U.S. Other	78 (30)	9.3 (mean)	SCID	30.0
Rapoport et al. <sup>49,52</sup> 2006 Canada Rehabilitation center	77 (59.7)	9-15	SCID	12.2
Whelan-Goodinson et al. <sup>32,130</sup> 2008 Australia Tertiary care center	100 (100)	<15	SCID	34.0
Bay and Donders <sup>36</sup> 2008 U.S. Rehabilitation center	84 (100)	9-15	NFI-D (31.71)	58.0
Bombardier et al. <sup>138</sup> 2010 U.S. Trauma center	559 (65.3)	3-15	PHQ-9	23.3
Chiu et al. <sup>46</sup> 2006 Taiwan Tertiary care centers	199 (100)	3-15	CES-D (NR)	23.9
Deb et al. <sup>95-96,42</sup> 1999 U.K. Tertiary care center	196 (83.7)	3-15	SCAN (NR) Behavior checklist (NR)	12.8 19.5
Franulic et al. <sup>73</sup> 2004 Chile Tertiary care center	71 (100)	12.5 (mean)	HAMD (NR)	42.3
Frenisy et al. <sup>48</sup> 2006 France Tertiary care center	25 (100)	<8	NRS-R (NR) SCL 90-R (9.72)	76.0 NR
Gagnon et al. <sup>55</sup> 2006 Canada Rehabilitation center	30 (100)	3-13	BDI (10.47)	50.0

**Table 9. Prevalence of depression by timing of assessment (continued)**

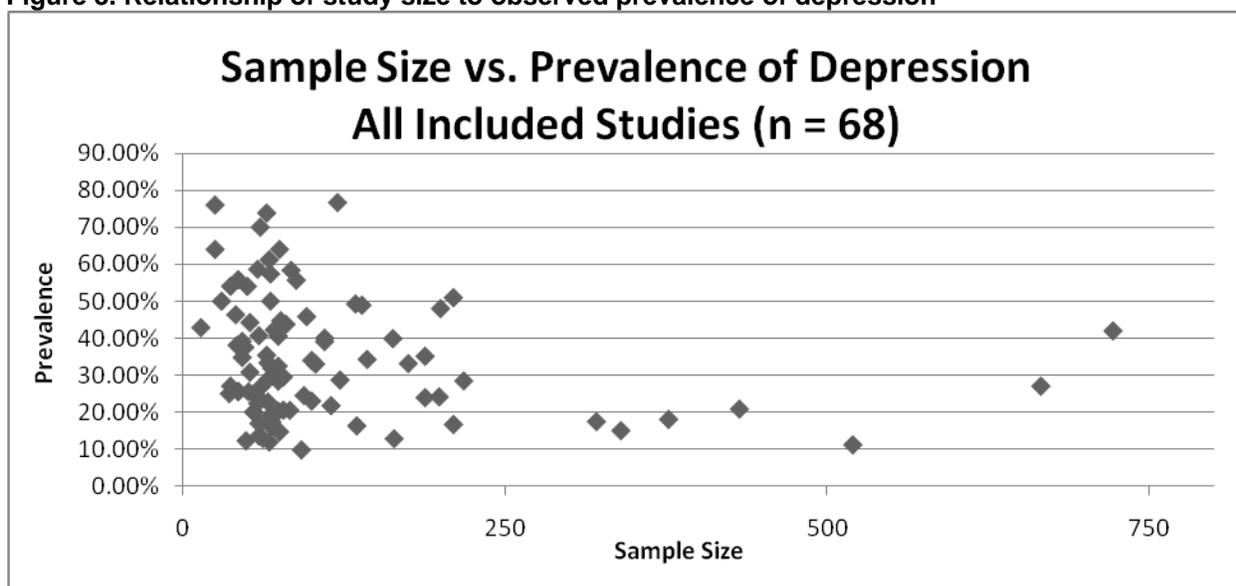
Author Year Country Setting	N with TBI, (% with Depression Measure)	GCS Score	Assessment Method (mean score)	Prevalence %
<b>&gt;12 months since injury</b>				
Hawthorne et al. <sup>133</sup> 2009 Australia Trauma center	66 (100)	3-15	HADS	22.7
Keiski et al. <sup>39</sup> 2007 Canada Other	53 (81.1)	13-15	PAI (NR)	55.8
Kersel et al. <sup>45,88</sup> 2001 New Zealand Tertiary care center	69 (84)	<9	BDI (NR)	24.1
Lima et al. <sup>35</sup> 2008 Brazil Tertiary care center	50 (72)	13-15	HADS (NR)	25.0
McCleary et al. <sup>99-101</sup> 1998 U.S. Tertiary care center	105 (100)	3-15	SCL-90 (NR) NRS (NR)	20.0 33.3
Mooney et al. <sup>60,87</sup> 2005 U.S. Tertiary care center	67 (100)	13-15	BDI-II (22.03)	61.2
Peleg et al. <sup>132</sup> 2009 Israel Rehabilitation centers	65 (100)	3-15	BDI (19.3)	73.9
Ponsford and Schönberger <sup>137</sup> 2010 Australia Tertiary care center	301 (100)	3-15	HADS (NR)	45.0 (24 mos)
Ponsford and Schönberger <sup>137</sup> 2010 Australia Tertiary care center	266 (100)	3-15	HADS (NR)	44.0 (60 mos)
Popovic et al. <sup>65</sup> 2004 Serbia Tertiary care center	67 (64.2)	3-13	ZDS (41.2)	46.3

**Table 9. Prevalence of depression by timing of assessment (continued)**

Author Year Country Setting	N with TBI, (% with Depression Measure)	GCS Score	Assessment Method (mean score)	Prevalence %
<b>&gt;12 months since injury</b>				
Seel et al. <sup>74,78</sup> 2003 U.S. Rehabilitation centers	666 (100)	8.6 (mean)	NFI-D (NR)	27.0
Sherman et al. <sup>93</sup> 2000 Canada Other	175 (100)	ACRM criteria	MMPI (NR)	33.0
Stalnacke <sup>38</sup> 2007 Sweden Tertiary care center	201 (81)	13-15	BDI (6.88) Mild to Mod Mod to Severe	25.0 15.0

No evidence suggests that study setting, country, or size of study population influences the observed prevalence. As expected, smaller studies report a wider range of prevalence and estimates from larger studies are closer to the mean estimates (Figure 3).

**Figure 3. Relationship of study size to observed prevalence of depression**



Data are sparse to assess whether severity of injury influences risk of depression. Using structured interviews, the overall prevalence of depression was 20.3 percent in those with mild or mild/moderate TBI compared to 32.5 percent in studies that enrolled or followed up populations of all severity. Too few studies isolate a sufficient number of those with mild TBI compared to those with moderate and/or severe injuries to make valid severity-based estimates of prevalence. In the sole model that assessed GCS scores, coma length, and duration of post-traumatic amnesia, none of the factors were associated with depression or its severity.<sup>131</sup> Another group using the Injury Severity Score also found no association between severity and prevalence of

depression.<sup>134</sup> Likewise, stratification of prevalence by explanatory factors such as age, gender, area of brain injured, or mechanism of injury is not possible within the current body of literature.

## **Risk Factors**

Fourteen studies in 13 distinct study populations report results from multivariate models to identify predictors or risk factors for depression after TBI.<sup>14-15,36,51,63,77,91,112,116,131-134,138</sup> Age was reported in a large United States cohort (n = 559), to be an independent risk factor for depression among both those without prior depression and those with prior episodes. In this study, which reflects the full spectrum of severity of TBI, risk decreased with increasing age, such that those age 60 and older were at lowest risk.<sup>138</sup> In another study aiming at predicting risk, when age was grouped with other factors, the combination of older age at injury, CT scan with documented intracranial lesion, and higher 1-week CES-D scores, were sensitive (93 percent) though not specific (62 percent) for identifying those with mild TBI who were depressed by 3 months after their injury.<sup>63</sup> One group has found that women have higher risk (relative risk [RR] = 1.27; 95 percent confidence interval [CI]: 1.07, 1.52) of new but not recurrent depression after TBI after adjusting for other risk factors.<sup>138</sup>

History of alcohol and substance abuse increase risk.<sup>15,77,138</sup> Pain, involvement in litigation related to the injury, and perceived stress have been reported as risk factors among those entering rehabilitation care and in prospective cohorts.<sup>36,134</sup> Psychosocial supports were often described in this literature, and data from caregivers, partners, and family members were common. However, few models incorporated social support items. One group reported that “availability of a confidant” reduced risk of depression,<sup>91</sup> and another that years married were inversely related to risk, while presence and degree of cognitive disability, motor disability, and social aggression elevated risk.<sup>112</sup> Concepts related to resilience or personality traits have not been widely investigated but scores on the Adult Hope Scale ( $p < 0.005$ ) and the Life Orientation Test-Revised ( $p < 0.05$ ), a measure of dispositional optimism, are both found contribute independently to predicting depression and its severity as measured by the BDI in a small Israeli study (n = 65).<sup>132</sup> History of depression has been documented as a substantive risk for having depression at followup (RR = 1.54; 95 percent CI: 1.31, 1.82), as was depression at the time of the injury (RR = 1.62; 95 percent CI: 1.37, 1.91).<sup>138</sup>

A cluster of reports were focused on investigating whether incorporating information about the area of the brain affected by the injury helped identify those at highest risk. Imaging research about the areas of the brain injured and the relationship to depression risk has inconsistent results. In aggregate for all those with TBI, onset of major depression within 3 months of injury has been reported to be sevenfold as common (95 percent CI: 1.36 to 43.48) among those with abnormal CT scan results after injury compared with normal imaging.<sup>63</sup> Focusing on locations of injury, Jorge and colleagues<sup>14,116</sup> have replicated their findings in several CT-based studies that left anterior lesions involving the left dorsolateral frontal cortex and/or left basal ganglia are associated with increased risk of acute depression ( $p = 0.006$ ) when injury location is assessed in multivariate regression models. They also note that frontal lesions, whether left, right, or bilateral, are associated with decreased risk of acute depression ( $p = 0.04$ ). In contrast delayed-onset major depression was not associated with lesion location. In a subanalysis of depression types, depression alone was related to left hemisphere injury ( $p = 0.003$ ), while depression associated with anxiety was more common among those with right hemisphere injury ( $p = 0.003$ ). A specific assessment of the presence or absence of contusions found the type of injury

was not predictive and that depression was somewhat more common among those with contusions (71 percent) than among those without (62 percent). Using MRI near the time of injury, the findings from CT studies are not supported and the only lesion type to emerge as a significant predictor was the protective effect of temporal lesions compared to other injury locations ( $p = 0.028$ ).<sup>51</sup> Study size and timing in relation make this literature more exploratory than conclusive in beginning to understand the relationship between pathophysiology related to the brain injury and risk and timing of onset of depression. In a study of political prisoners, up to 50 years after injury, TBI-associated cerebral cortical thinning in the left superior frontal and bilateral superior temporal cortex, as assessed by MRI, were associated with depression, and similar effects were not seen in prisoners without a history of TBI with respect to depression risk.<sup>131</sup>

Overall, the quality of studies that provided prevalence estimates was 13 good quality (11.6 percent), 72 fair quality (64.3 percent), and 27 poor quality (24.1 percent). Many of these studies were not explicitly designed to assess prevalence and are of higher quality for their intended aims. Overall, the strength of the evidence to estimate prevalence is moderate. Factors included in the assessment were varied methods for defining TBI and depression, small study populations, and predominance of populations such as those in tertiary care referral centers, trauma centers, and rehabilitation programs that cannot represent the entire denominator of individuals with head injury in the United States. Experts suggest this shortcoming relates to a lack of funding resources to identify and follow large cohorts of varied injury severity and mechanism over time. However, despite these limitations, no evidence suggests depression prevalence is not elevated in general TBI populations.

## KQ2. Screening for Depression After TBI

After answering the question of prevalence of depression in the patient with TBI, the next step is to identify the timing of screening for depression, which screening tools to utilize, and the optimal setting for screening.

In all timeframes and with all measures, depression is common (Table 10). No distinct trend is apparent to suggest a peak time of enhanced risk or a related priority window for screening. In general, the proportion of those diagnosed as depressed through structured clinical interviews is lower than standardized instruments. This would be expected, as the majority of tools are designed to be more sensitive than specific in order not to miss potential cases. Around 1 year and beyond, both categories of assessments converge around 33 percent.

This review cannot distinguish between whether this suggests that other tools “over-detect” depression relative to structured clinical interviews or whether differences in study design and population create the observed effect. We also cannot distinguish if features unique to a population with TBI make clinical diagnosis more challenging, or whether evaluators in clinical settings are less likely to classify a patient as depressed early after trauma, deferring definitive diagnosis until later in followup as other sequelae of injury subside or stabilize.

As presented in Table 10, prevalence of depression is higher in all timeframes than would be expected from population-based estimates. These estimates may center around 30 percent in all windows for several reasons. In one scenario, prevalence reaches this level quickly; depression is under-recognized or poorly responsive to treatment; and overall, the same individuals are affected over time and therefore available in each time window to be detected. In another scenario, there could be an initial wave of “reactive” depression that resolves in some individuals

such that later timeframes reflect continued symptoms in some and new onset of depression in others. In this scenario, individuals are moving in and out of the “case” group over time but the average proportion at any one time approaches one-third.

Overall, the quality of studies that provide information to assess when to screen was 13 good quality (11.5 percent), 73 fair quality (64.6 percent), and 27 poor quality (23.9 percent). The strength of the body of evidence is low for selecting time and setting for screening. Deficits relate to the high proportion of the literature that is cross-sectional so that natural history information cannot be provided, and the small proportion of studies that are prospective having, as a group, relatively few followup intervals. From an ethics perspective, this uncertainty suggests we are obligated to recognize that those with TBI likely have elevated risk of depression and to screen frequently until evidence becomes available to better target timing of evaluations or to confirm that risk is elevated and stays elevated relative to the general population.

Overall, the quality of studies that provide information comparing tools is poor. While many studies evaluate psychometric properties and validation of tools and subscales, few examine the diagnostic test characteristics of tools for clinical use in comparison to a gold standard such as the SCID. Given that TBI is relatively common and that psychiatric and psychological evaluation services can be challenging to access, there would be substantial value in understanding which tools perform best in selecting those individuals most likely to need treatment while still retaining a high negative predictive value so that cases are not missed. Thus, the strength of the body of evidence is insufficient for selecting method of screening.

**Table 10. Prevalence of depression by method of assessment, setting, and time from injury**

	Structured Clinical Interview Protocols					Other Validated Depression Assessment Tools				
	Time from Injury to Assessment					Time from Injury to Assessment				
	0-3 mos	3-6 mos	6-12 mos	12+ mos	All times	0-3 mos	3-6 mos	6-12 mos	12+ mos	All times
<b>All study settings and TBI severity</b>										
Studies with data (n)	9	7	6	17	39	4	3	13	34	54
Prevalence (%)	18.3	26.8	31.9	32.5	27.4	34.3	45.7	31.8	32.8	33.3
<b>Tertiary care populations</b>										
Studies with data (n)	2	1	3	8	14	2	2	2	11	17
Prevalence (%)	18.5	48.0	28.3	38.7	34.5	36.8	44.6	35.5	28.2	32.7
<b>Trauma center populations</b>										
Studies with data (n)	3	5	2	4	14	0	0	5	8	13
Prevalence (%)	19.8	22.4	31.8	18.5	20.1	0	0	30.1	38.3	34.5
<b>Rehabilitation centers</b>										
Studies with data (n)	2	0	0	3	5	2	0	6	6	14
Prevalence (%)	14.0	0	0	42.5	32.0	29.2	0	33.8	37.2	35.5
<b>All levels of TBI severity</b>										
Studies with data (n)	4	3	3	8	18	1	1	6	10	18
Prevalence (%)	23.9	33.3	35.9	35.9	32.5	31.9	48.9	29.9	28.9	30.9
<b>Populations with mild and/or mild/moderate TBI by Glasgow Coma Scale*</b>										
Studies with data (n)	4	4	2	2	12	1	0	1	4	6
Prevalence (%)	16.6	25.4	21.3	16.8	20.3	34.3	0	28.7	45.1	39.1
<b>Populations with moderate and/or severe TBI by Glasgow Coma Scale*</b>										
Studies with data (n)	0	0	0	0	0	0	1	2	5	8
Prevalence (%)	0	0	0	0	0	0	50.0	37.7	30.1	32.5

\* Number of studies reporting data for those with mild TBI alone is insufficient to report weighted means.

**Table 11. Validity of tools to diagnose depression after TBI**

Author, Year, Country Setting	Study Design N	Comparison and measures	Outcomes
Sliwinski et al. <sup>103</sup> 1998 US Other	Cross-sectional N=100	<ul style="list-style-type: none"> <li>BDI vs SCID</li> <li>Validity measures, including sensitivity and specificity</li> </ul>	<ul style="list-style-type: none"> <li>Correlation between the SCID and BDI was 0.30, p&lt;0.05</li> <li>With specificity set at 0.80, the BDI correctly identified 36% of individuals diagnosed with depression via the SCID</li> <li>With specificity set at 0.90, only 20% were correctly classified as depressed</li> <li>A modified (six item) BDI was more strongly correlated with DSM-IV diagnosis (r=0.40, p&lt;0.05), and sensitivity increased to 48% at 80% specificity and to 32% at 90% specificity</li> </ul>
Homaifar et al. <sup>128</sup> 2009 US Tertiary care center	Cross-sectional N=52	<ul style="list-style-type: none"> <li>BDI-II vs SCID</li> <li>Validity measures included sensitivity, specificity and ROC analysis</li> </ul>	<ul style="list-style-type: none"> <li>Maximum sensitivity (87%) and specificity (79%) were achieved using a BDI cutoff of 19 for those with mild TBI and 35 for those with moderate or severe TBI</li> <li>A BDI score of 6 or higher produced 100% sensitivity for those with mild TBI, while a score of 23 or higher produced 100% sensitivity for those with moderate or severe TBI</li> <li>At 100% sensitivity, specificity decreased to 59%</li> </ul>
Fann et al. <sup>139</sup> 2005 US Trauma center	Prospective cohort N=135	<ul style="list-style-type: none"> <li>PHQ-9 vs SCID</li> <li>Validity measures included sensitivity, specificity, PPV and NPV</li> <li>ROC analysis identified optimal scoring algorithm</li> </ul>	<ul style="list-style-type: none"> <li>Various scoring algorithms were used with the PHQ-9</li> <li>“Optimal” algorithm has sensitivity 0.93, specificity 0.89, PPV 0.63 and NPV 0.99.</li> </ul>
Whelan-Goodinson et al. <sup>130</sup> 2009 Australia Tertiary care center	Cross-sectional N=100	<ul style="list-style-type: none"> <li>HADS vs SCID</li> <li>Validity measures included sensitivity, specificity, PPV, NPV and ROC analysis</li> </ul>	<ul style="list-style-type: none"> <li>The manual-defined HADS cutoff of 7/8 produced a sensitivity of 62% and a specificity of 92% as compared with the SCID</li> <li>The PPV for depression given a cutoff of 7/8 was 81%, while a more conservative cutoff of 12/13 produces a PPV of 100%</li> <li>The NPV for depression given a cutoff of 7/8 was 82%</li> </ul>
Al-Adawi et al. <sup>41</sup> 2007 Oman Tertiary care center	Cross-sectional N=68	<ul style="list-style-type: none"> <li>HADS vs CIDI (structured clinical interview for ICD-10 diagnosis)</li> <li>Validity measures included sensitivity, specificity and ROC analysis</li> </ul>	<ul style="list-style-type: none"> <li>Sensitivity of the depression subscale of HADS to identify patients considered depressed by clinical interview was 33.3%. Specificity was 100% (i.e., no false positives).</li> <li>ROC analysis suggested that sensitivity can be increased with lower HADS cutoff</li> <li>An “optimal” cutoff off of 4 produced a sensitivity of 53.8% and specificity of 75.9%</li> </ul>

Five studies assessed the ability of various tools to screen for depression in individuals with TBI relative to a structured clinical interview, which is accepted as the gold standard for diagnosing depression. Three of the studies were conducted in the United States, one at a trauma center,<sup>139</sup> one in the community,<sup>103</sup> and one in a tertiary care center.<sup>128</sup> The community-based study was an analysis of individuals participating in a larger quality of life study focused on community integration of individuals with TBI. One study each was conducted in Oman<sup>140</sup> and

in Australia,<sup>130</sup> both at tertiary care centers. The U.S. and Australian studies used as their gold standard the SCID, based on DSM-IV criteria, while the Oman study used the Composite International Diagnostic Interview (also a structured clinical interview) that is based on ICD-10 criteria for diagnosis. Differences in the reference and index tools preclude synthesis so the studies are described separately below. In their study of the BDI's ability to correctly identify depressed individuals, Sliwinski and colleagues selected 100 individuals randomly from a larger pool of 433 participating in a quality of life study. All participants had a brain injury that had occurred at least 1 year prior, were between the ages of 18 and 65, and were able to engage in a three to four hour interview. All participants were given both a SCID and a BDI, and sensitivity and specificity calculations were used to assess the ability of the BDI to identify the depressed individuals. Setting specificity at either 80 percent or 90 percent (reflecting the proportion of nondepressed individuals correctly classified as nondepressed), they found low sensitivities (proportion of truly depressed individuals identified by the tool) of 36 percent and 20 percent, despite a statistically significant correlation (albeit low) between the tools of 0.30. After modifying the BDI to include six items that best discriminated between depressed and nondepressed individuals, sensitivity increased slightly but did not exceed 48 percent. Similarly, Homaifar and colleagues studied the validity of the BDI-II, again comparing it to the SCID, in 72 veterans. Of particular importance, this analysis identified different BDI-II cutoffs to maximize validity of the tool, depending on severity of the TBI. In a Receiver Operating Characteristic (ROC) analysis, maximum sensitivity of 87 percent and specificity of 79 percent were obtained with cutoffs of 19 for participants with mild TBI, and 35 for those with moderate or severe TBI.

Fann and colleagues recruited participants from a level one trauma center, with head injuries with a GCS score of less than or equal to 12. Participants were recruited prior to discharge and assessed every month for 6 months and then at 8, 10, and 12 months following injury. Participants were initially given the Patient Health Questionnaire-9 (PHQ-9) over the phone and invited to complete a SCID only if their PHQ-9 score met criteria for possible depression, thus restricting the analysis to a population with fairly high likelihood of depression. The investigators then assessed the ability of various algorithms for scoring the PHQ-9 to identify individuals with depression, using a ROC analysis to find the optimal criteria. The best algorithm, based on maximizing both sensitivity and specificity, resulted in a positive predictive value of 0.63 and a negative predictive value of 0.99. Sensitivity for this algorithm was 0.93 (0.74–1.00), and specificity was 0.89 (0.82–0.94).

Two studies assessed the HADS, both at tertiary care centers. Al-Adawi and colleagues studied 68 consecutive patients at a tertiary care center in Oman who had suffered TBIs, excluding individuals with a preinjury psychiatric condition or other neurological history. They used a structured clinical interview based on the ICD-10 criteria for diagnosis as the gold standard, and assessed the ability of the HADS to correctly identify depressed individuals. Depressive disorder was diagnosed with clinical interview in 57.4 percent of the participants. Using the HADS subscale as recommended resulted in a low sensitivity of 33.3 percent and 100 percent specificity. A lower cutoff of 4 was identified as optimal in a ROC analysis, providing a sensitivity and specificity of 53.8 percent and 75.9 percent, respectively. However, in a similar study conducted in Australia,<sup>130</sup> the manual defined cutoff (7/8) resulted in greater sensitivity (62 percent) and slightly lower specificity (92 percent). Nonetheless, this study also supported the use of a more conservative cutoff of 12/13 if the goal is to achieve higher positive predictive value.

Huang and colleagues conducted SCIDs and the Zung depression scale on 70 consecutive patients from a physical rehabilitation hospital but provide no diagnostic test characteristics by which to assess the results.<sup>59</sup>

With only five studies that included test characteristics available, each using a different screening tool, there is insufficient evidence to determine whether tools validated in other populations for screening depression appropriately identify individuals with depression after a TBI. Several additional studies were identified that compared various screening tools against one another, but none of these conducted a clinical interview to diagnose depression as a comparison.<sup>44,74,78,121</sup> In the absence of a clinical diagnosis, it is difficult to assess the utility of these tools for identifying correctly depressed individuals. However, Bay and colleagues did use an expert consensus process to select subscale domains of three screening tools (Neurobehavioral Functioning Index, Profile of Mood States-Depression, CES-D) that correspond to the DSM-IV criteria for major depressive episode, and then found that the three tools were highly correlated ( $r > 0.80$ ) in their identification of depressed individuals. Nonetheless, SCIDs were not actually done in the study.

This area of research represents a significant gap in the current literature. Given the wide range, and potentially high prevalence of depression after TBI, effective approaches to screening and diagnosis that can be deployed in large populations are needed. As studies are conducted to establish the prevalence of depression, substudies could be conducted focusing on establishing or comparing the validity and reliability of screening tools for this population.

### KQ3. Prevalence of Concomitant Psychiatric Conditions

This section presents the results of our literature search and findings about the prevalence of concomitant psychiatric conditions in patients who develop depression after incurring a traumatic brain injury. We reviewed seven papers from six studies, of which all seven were of fair quality.

Concomitant psychiatric conditions that we included for review included: post-traumatic stress disorder (PTSD), other anxiety disorders, substance abuse, irritability/aggression, and any other named Axis I or Axis II disorders.

#### Content of the Literature

We identified nine studies<sup>14,70,72,104,109,111,123,130,138</sup> from eight populations that reported prevalence of concomitant psychiatric conditions within the population of depressed TBI patients,<sup>14,109,111,130</sup> or compared rates of comorbid conditions in those with and without depression.<sup>70,72,104,123,138</sup> Papers that reported the overall prevalence of psychiatric conditions other than depression among the overall population of TBI patients with no data on their association with depression were excluded for this key question.

Study designs of the eight studies (one study was represented in two papers) included five prospective cohorts,<sup>14,70,72,111,123,138</sup> one retrospective cohort,<sup>104</sup> and two cross-sectional studies.<sup>109,130</sup> Seven studies were conducted in the United States. One was conducted in Australia.<sup>130</sup> One was conducted at an academic medical center;<sup>70</sup> one at a rehabilitation center;<sup>109</sup> one in the community;<sup>104</sup> one at two hospitals within the same state;<sup>72</sup> one at a tertiary care center;<sup>130</sup> and three at trauma centers.<sup>14,111,123-138</sup> The most common condition studied in combination with depression was anxiety, which was assessed in six studies.<sup>14,72,104,109,130,138</sup> Depression was diagnosed via clinical interview in most of the studies.<sup>14,70,72,104,109,111,130,138</sup>

## Summary of the Literature on Concomitant Psychiatric Conditions

The included studies reported relatively high rates of concomitant psychiatric conditions (8 to 93 percent of depressed participants had some concomitant condition), but because few presented these data separately for the depressed and nondepressed groups, few conclusions related specifically to this key question can be drawn. Nonetheless, anxiety appeared to be the most common comorbid condition. In the one study that compared rates of comorbid anxiety in patients with and without depression, it was significantly more common in the depressed group (76.7 percent versus 20.4 percent,  $p < 0.001$ ).<sup>72</sup>

The four studies that explicitly compare rates of concomitant psychiatric conditions in depressed and nondepressed patients are most useful for answering this key question.

The recruitment phase of a clinical trial for sertraline to treat major depressive disorder (MDD) was described in the largest study, and included 1-year followup of 599 participants, all of whom had GCS scores of  $\leq 12$ .<sup>138</sup> Participants were enrolled from among 1,000 potentially eligible patients in a U.S. trauma center and were contacted monthly for months 1 through 6, and then at 8, 10, and 12 months to obtain information on depression status and other psychiatric conditions. Depression was assessed with a structured interview based on the PHQ-9, and assessment for anxiety disorders also used modules of the PHQ. The 1-year cumulative incidence of MDD in this population was 53.1 percent. During this first year following injury, individuals with major depressive disorder had substantially higher rates of a concomitant anxiety disorder than did participants without MDD (60 percent vs. 7 percent: RR, 8.77; 95 percent CI, 5.56 – 13.83).

In the second study,<sup>123</sup> patients who were hospitalized with TBI of GCS severity  $\leq 12$  were assessed 1 to 6 months postinjury. Attempts were made to contact each patient monthly, but not all patients were reached every month. The overall cumulative incidence of both depression (per the PHQ-9) and PTSD (per the PTSD Checklist-Civilian [PCL-C]) were calculated. While the overall incidence of PTSD was 11.3 percent for the cohort, the rate was 37 percent among the 27 individuals who also experienced depression, compared with none among those who did not. No other studies directly compared the proportion of depressed patients with and without PTSD.

Anxiety and aggression were measured in patients participating in a second prospective cohort in which participants were consecutively admitted patients at two hospitals.<sup>72</sup> The study compared outcomes among patients with closed head injury to those with multiple trauma but no central nervous system involvement. Among the 91 TBI patients, 68 had sustained their injuries in a motor vehicle accident. Patients were followed up at 3, 6, and 12 months, at which time depression was assessed using a clinical interview and the HADS, and aggressive behavior was assessed with the Overt Aggression Scale. About one-third (33 percent) of patients had major depressive disorder (mood disorder with major depressive features). Over the course of followup, 23 of 30 (77 percent) of patients with major depressive disorder also had anxiety, compared with 9 of 44 (20.4 percent) of nondepressed patients (note: total N does not add up due to lack of complete data). Of note, PTSD was included with anxiety in this study and was the defining psychiatric feature for 7 of the 23 patients diagnosed with anxiety. Similarly, 17 of 30 (56.7 percent) depressed patients exhibited aggression, compared to 10 of 44 (22.7 percent) nondepressed patients.

A cohort of 188 individuals with TBI who were enrolled in a larger, third study of mood disorders and psychosocial functioning after TBI was assessed twice over 12 months for depression and other psychiatric comorbidities.<sup>70-71</sup> The participants were all living in the

community and had sustained their head injury within the past 5 years. They were recruited via telephone, and those who agreed to participate were assessed in person at study entry and 12 months later. In part, this study focused not only on the presence or absence of depression and other psychiatric conditions, but on the timing of the depression as it related to the presence of co-occurring psychiatric disorders. Therefore, individuals were subdivided into four groups for analysis: no depression at either time point, resolved depression (present at study entry but not at 12 months), late-onset depression (present at 12 months but not at study entry) and chronic depression (present at study entry and 12 months). At study entry, co-occurring psychiatric conditions were most frequent among those individuals who would have late-onset depression (74 percent of late onset patients) and lowest among those in the chronic depression group (26 percent). At reassessment, the presence of psychiatric conditions had increased in every group except those never diagnosed with depression, although in this group more than half of the individuals had depression at both time points. Among the psychiatric conditions examined, anxiety was most common at both study entry and 12 months (19 percent and 16 percent, respectively). Psychiatric diagnoses before the TBI itself were common across all groups (56 percent of the overall population) with no statistically significant differences between groups.

The other two papers<sup>14,111</sup> representing one study that used a prospective cohort design did not provide a measure of the incidence of psychiatric comorbidity in the nondepressed group. The authors report that 41 percent and 8 percent of depressed TBI patients had anxiety and bipolar disorder, respectively.<sup>14,111</sup>

In other study designs, a retrospective cohort of community-dwelling individuals with TBI at least 1 year prior to interview<sup>104</sup> found that among pairs of concomitant psychiatric conditions, depression and anxiety combined was most common (25 percent), and that individuals with a pre-TBI Axis I diagnosis were most likely to experience coexisting diagnoses post-TBI ( $p < 0.03$ ). Four of 13 individuals with major depressive episodes (MDE) in a cross-sectional study of 50 outpatients at a rehabilitation clinic also had anxiety disorder, as assessed by clinical interview. One cross-sectional study<sup>130</sup> intended as a validation study of the HADS to assess depression and anxiety in TBI. Among 34 percent of participants with a SCID-diagnosed depression, about one-third (36 percent) also had a concurrent anxiety disorder.<sup>130</sup>

All of the available studies reported a high rate of concomitant psychiatric conditions associated with depression after a TBI. Rates ranged from 8 percent to 93 percent depending on the particular psychiatric condition and the study population and design. Those studies that presented data on psychiatric conditions by depression status found higher rates among the depressed groups. None of the studies was able to ascertain directionality for the observed association. Anxiety disorders including generalized anxiety disorder, PTSD, panic disorder, obsessive-compulsive disorder, and specific phobias were the most commonly reported conditions. Most studies grouped these conditions together and reported the overall prevalence of any anxiety disorder.

When the conditions were reported individually, anxiety disorders were most prevalent and affected from 31 percent to 61 percent of study participants in four papers.<sup>14,72,109,138</sup> PTSD was observed in 37 percent of depressed patients and none of those without depression.<sup>123</sup> Panic disorder was seen in 15 percent of patients with MDE but not measured in those without depression.<sup>109</sup>

## KQ4. Outcomes of Interventions for Treatment for Depression After TBI

To understand the treatment options for patients with TBI and subsequent depression, we sought publications that clearly documented the intervention, duration, and response to treatment.

### **Treatment Outcomes in TBI**

Using this approach, we identified two publications<sup>141-142</sup> from two distinct study populations that specifically addressed a treatment intervention for individuals diagnosed with depression after a TBI. Detailed summaries for both studies are included in Appendix C.

One of the treatment studies was conducted in the United States,<sup>141</sup> and the second was in Canada.<sup>142</sup> Both were studies of medication, the first being a randomized controlled trial (RCT) of sertraline, while the second was an open-label case series of the effects of citalopram.

The study on sertraline was a double-blind placebo controlled trial, with block randomization, in which treatment was administered for 10 weeks.<sup>141</sup> Participants were at least 6 months post-TBI, and TBI included documented loss of consciousness or other evidence, such as pathology or imaging. Diagnosis of depression was established with DSM-IV criteria and a Hamilton Rating Scale for Depression (HAM-D) score higher than 18. Dosage of sertraline was not fixed and could be adjusted at 2-week intervals, with a maximum dosage of 200 mg/d. Of 91 individuals screened, 52 were eligible and agreed to participate; 41 completed the study and contributed data to the analysis. Eight of the 11 participants who discontinued were excluded because of noncompliance with the treatment protocol. Generally speaking, participants in this study were middle aged, male, and of lower socioeconomic status (predominantly  $\leq$  \$20,000 annually). Time since injury ranged up to 30 years, and reasons for the TBI included assault (46.3 percent), fall (14.6 percent), gunshot wounds (2.4 percent) being hit by a falling object (2.4 percent), and motor vehicle accidents or a pedestrian hit by a moving vehicle (34.2 percent). The primary outcome of interest was a change in depression status measured with the HAM-D. A positive response was considered to be a decrease of 50 percent or a drop below 10 on the HAM-D. Of those who completed the study, 59 percent of the treated group and 32 percent of the control group had a positive response; the difference in response rates between the two groups was not statistically significant ( $p = 0.08$ ).

Rapoport and colleagues<sup>142</sup> studied the effect of citalopram on depressive symptoms after TBI, using an open-label, single arm (case series) design. The study was limited to individuals with mild to moderate TBI. Mild TBI was defined as loss of consciousness at time of injury of 20 minutes or less, an initial GCS of 13–15 and post-traumatic amnesia (PTA) of less than 24 hours. Moderate to severe TBI had a GCS of less than 13, a PTA greater than 24 hours or an abnormal CT image. Fifty-four of 65 patients attending the mild-to-moderate TBI clinic were diagnosed with major depression due to TBI, with a major depressivelike episode, using the depression module of the SCID Axis I disorders. All 65 patients began the study; however, 54 completers provided data for analysis. Although the study was intended to evaluate the effects of a 6-week course of treatment, low response rates resulted in a study extension for some participants to 10 weeks. Therefore, although 6-week data were available for all 54 completers, 10-week data were available for 26 participants. Dosage of citalopram was titrated as deemed medically appropriate by the study physicians. The primary outcome measured was a change on the HAM-D score, with an improvement of 50 percent or more designated a positive response, and a score of less than 8 defined as remission. In the 6-week data ( $n = 54$ ), 27.7 percent were

classified as responders and 24.1 percent were in remission. Among participants with data at 10 weeks, 46.2 percent were responders and 26.9 percent were in remission. Results at both time points were significant ( $p < .0001$ ). Of the 11 individuals who dropped out of the study, 6 were in the intended 6-week group and 5 were in the intended 10-week group. Ten of the 11 experienced an adverse event.

## KQ5. Comparisons of Treatments

No studies addressed KQ5. It is discussed as a part of Future Research.

## KQ6. Modifiers of Outcomes of Treatment

No studies addressed KQ6. It is discussed as a part of Future Research.

# Grey Literature Results

## Publications Included in This Review

A relevant pool of 56 potentially useful items were located following a series of Internet and relevant grey literature searches of United States government and military sources, nonprofit organizations, United States and international clinical trials registries, meeting proceedings, and dissertation databases. Selected resources were identified from the United States (one government report, one nonprofit white paper, five clinical trial protocols, one funding/grant opportunity, one systematic review, six funded projects, eight conference proceedings, and nine dissertations), New Zealand (one guideline), Australia (two clinical trials), Europe (five conference proceedings, including one from Turkey), and Canada (three clinical trials, one conference proceeding, and one dissertation).

**Internet searches.** The relevant retrieval from different Google searches included one guideline, two reports, and one systematic review that in whole or in part focus on treatment or screening for depression associated with TBI. A guideline from the New Zealand Guidelines group, not indexed in MEDLINE, provided guidance on treatment of depression in TBI that was based solely on expert opinion, thus contributing little to the literature for this topic. The RAND Corporation and Institute of Medicine (IOM) reports give a review of the current prevalence of depression, PTSD, and TBI in military populations. Only the IOM report provided a review of the literature regarding prevalence or the relationship between TBI and depression, while the RAND report provides a comprehensive overview of the literature for TBI, PTSD, and depression independently. These reports do provide a foundation for future research in the treatment of depression in the context of TBI, but add very little to the published literature summarized in this review.

A systematic review that had not been picked up in the original search of the TBI published literature provided a critical review of literature regarding pharmacologic, other biologic, psychotherapeutic, or rehabilitation treatment of depression after TBI. After a review of 658 articles retrieved from various bibliographic databases, 27 (13 pharmacological, six other biological, and eight psychotherapeutic/rehabilitation intervention) articles were included in the review based on study inclusion/exclusion criteria and study abstract and full-text reviews. The study found a paucity of adequately powered and controlled studies in the literature to make conclusions on the best treatment modality for depression in TBI.

**Funding opportunities and ongoing research.** Nonpublished grey literature resources may indicate areas of future research for management of depression in TBI patients. Examples include a recent announcement regarding a military funding opportunity to support research in the treatment or prevention of depression or other mood disorders in TBI.<sup>143</sup> Also, 6 funded projects from the National Institutes of Health Research Portfolio Online Reporting Tools (RePORTER) and 10 clinical trials from various clinical trials registries report studies underway for treatment of depression in TBI patients. These projects will assess the impact of behavioral therapies;<sup>144-152</sup> supportive psychotherapy;<sup>153</sup> exercise;<sup>154</sup> transcranial magnetic stimulation;<sup>155</sup> and drug interventions (e.g. sertraline, venlafaxine, and citalopram).<sup>156-158</sup> Several projects also focus on identification of risk factors for depression in the context of TBI.<sup>159</sup>

**Meeting abstracts, proceedings, and dissertations.** A significant pool of meeting abstracts, proceedings, and dissertations were retrieved from the literature that focused on topics already covered in the published research. Overall, 14 conference proceedings and 10 dissertations were located that assessed treatment options for depression<sup>160-163</sup> and potential methods for characterizing or measuring development of depression in TBI.<sup>152,164-182</sup> Examples of therapy modalities include use of nontraditional approaches, such as neurologic music therapy<sup>160</sup> and written emotional expression technique,<sup>162</sup> and medical approaches with methylphenidate and sertraline drug therapy.<sup>161</sup> Lack of reported data makes it difficult to identify or assess any impact of these treatments on depression in TBI patients. Additionally, the papers focusing on patient characteristics or modifiers that may affect outcome,<sup>164-166,168-170,172-174,176-177,179,181</sup> disease progression,<sup>163,167,175,182</sup> or rating scales<sup>171,178,180</sup> of depression in TBI patients provide very little data to make accurate assumptions of reported conclusions.

**Summary and literature method critique.** A review of the grey literature, government/nonprofit reports, and other unpublished resources did not retrieve much additional information to what had been found in the published and peer-reviewed literature. The majority of the high quality, relevant data comes from two large-scale reports/white papers that mainly focus on the prevalence or the connection between depression and TBI. As was discovered from a review of published literature,<sup>183</sup> we noted very little data in the grey literature that assessed the impact of treatment for depression in TBI, although the pool of current clinical trial protocols and funded projects indicate growth in this area of the literature.

During the review of this material, we found some overlap between what was found in the published literature and the current search retrieval. Although we attempted to extract only unique or new data from the pool of grey literature sources, there may be some redundancy in this section of the report given the nature of how this material is reported and maintained in data repositories and online databases.

Citations for all grey literature identified are in Appendix F.

## Discussion

This chapter summarizes the strength of the evidence to address our key questions (KQs) and presents methodologic considerations and a discussion of the findings for each of our six key questions. We conclude with a discussion of the status of research, limitations of the current literature, and our recommendations for future research priorities.

### Strength of the Evidence

Strength of evidence is typically assigned to reviews of medical treatments after assessing four domains: risk of bias, consistency, directness, and precision.<sup>29</sup> Although these categories were developed for assessing the strength of treatment studies, the domains also apply to studies of prevalence and screening. Available evidence for each key question was assessed for each of these four domains; the domains were combined qualitatively to develop the strength of evidence for each key question.

We graded the body of literature for each key question and present those ratings as part of the discussion in Chapter 4. The possible grades were:

**I. High:** High confidence that the evidence reflects the true effect. Further research is unlikely to change estimates.

**II. Moderate:** Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of effect and may change the estimate.

**III. Low:** Low confidence that the evidence reflects the true effect. Further research is likely to change confidence in the estimate of effect and is also likely to change the estimate.

**IV. Insufficient:** Evidence is either unavailable or does not permit a conclusion.

As a global assessment of this literature, the evidence about prevalence and elevated risk of depression is moderate.

The strength of the evidence to inform when, with what tools, and in what settings screening for depression should occur after traumatic brain injury (TBI) is low. This assessment is based on lack of studies designed to specifically address these concerns that make explicit comparisons. The risk for bias is high since the data used was often cross-sectional, full populations were rarely delimited, and settings and populations may represent a biased portion of the spectrum of both the severity of TBI and of depression. As for prevalence, data are inconsistent across studies. Summary evidence is to a degree indirect. Though we included only studies for which the timing of administration of the screening or diagnostic tool was known and for which the tool was described, the studies overall were not designed for this use, and estimates are imprecise.

Likewise, understanding of psychiatric comorbidities is based on a small number of studies that do not provide consistency in conditions measured and are at risk of bias, resulting in low strength of evidence. Intervention studies included one randomized controlled trial (RCT) of good quality and one case series; therefore, risk of bias was high, consistency was unknown, and results lacked precision. The strength of evidence is insufficient for pharmacologic treatment of depression after TBI.

## Principal Findings and Considerations

### KQ1. Prevalence and Incidence of TBI and Depression

We identified 112 publications<sup>30,13-15,31-138</sup> from 79 distinct study populations in which prevalence could be estimated.

We considered the Structured Clinical Interview for DSM-IV (SCID) and other formal structured clinical interview protocols that map to the DSM and/or International Classification of Diseases (ICD) codes to be the measures of depression that are most relevant to clinical care. Among studies that used an SCID or other structured protocol to reach a formal diagnosis of depression, the prevalence of depression after TBI ranged from 12.2 percent<sup>66</sup> to 76.7 percent.<sup>13</sup> If we focus on the subset of studies with both clearly operationalized criteria for TBI and use of the SCID, the range was 12.2 percent<sup>66</sup> to 54.0 percent.<sup>109</sup>

Data are sparse to assess whether severity of injury influences risk of depression. Using structured interviews among those with mild or mild/moderate TBI populations, the overall prevalence of depression was 20.3 percent compared to 32.5 percent in studies that enrolled or followed up populations of all severities. Too few studies isolate a sufficient number of those with mild TBI compared to those with moderate and/or severe injuries to make valid severity-based estimates. Some multivariate models suggest severity of injury is not a strong predictor of risk.<sup>131,134</sup> Likewise, stratification of prevalence by explanatory factors such as age, gender, area of brain injured, or mechanism of injury is not possible within the current body of literature.

No strong predictors of risk are available to tailor guidance or screening of those with TBI.

### KQ2. Screening for Depression After TBI

We identified 113<sup>30,13-15,31-137,139</sup> publications in 79 distinct populations that provide information about timing of screening or comparison of tools.

Across all timeframes and using all depression measures, in studies with clear TBI definitions, the weighted average for prevalence of depression was 31.8 percent. Among those studies with repeated assessments and/or longer term followup, no clear pattern of expected natural history or peak prevalence emerged. Depression was more common among those with TBI than among normal comparison groups.

Five publications compared SCID to candidate tools for assessment of depression, the Beck Depression Inventory (BDI), Patient Health Questionnaire-9 (PHQ-9), and Hospital Anxiety and Depression Scale (HADS).<sup>41,103,128,130,139</sup> None of the tools reported simultaneous sensitivity and specificity above 90 percent. One study identified different optimal cutoffs of the BDI-II; maximum sensitivity of 87 percent and specificity of 79 percent were obtained with cutoffs of 19 for participants with mild TBI and 35 for those with moderate or severe TBI. With modification of the scoring algorithm as proposed by the authors, the PHQ-9 achieved a sensitivity of 93 percent, specificity of 89 percent, positive predictive value of 63 percent, and negative predictive value of 99 percent. The BDI had poor sensitivity of 48 percent and 32 percent at specificities of 80 and 90 percent, respectively. The HADS provided 54 percent sensitivity and 76 percent specificity.

Therefore, no evidence provides a basis for targeting screening to one timeframe over another. Likewise, the literature is insufficient to determine whether tools validated in other populations for detecting depression appropriately identify individuals with depression after a TBI, or to choose among available tools.

### **KQ3. Prevalence of Concomitant Psychiatric Conditions**

In general, the few papers that do specifically examine the prevalence of concomitant psychiatric conditions within the population of depressed TBI patients report high rates of such conditions within this population. When conditions were reported individually, anxiety disorders were most prevalent and affected 31 percent to 61 percent of study participants in four papers.<sup>14,72,109,138</sup> Post-traumatic stress disorder (PTSD), a major anxiety disorder, was observed in 37 percent of depressed patients and in no patients without depression,<sup>123</sup> and panic disorder was seen in 15 percent of patients with major depression but not measured in those without depression.<sup>109</sup> Consideration of potential for coexisting psychiatric conditions is warranted.

### **KQ4. Outcomes of Treatment for Depression After TBI**

Only two publications<sup>141-142</sup> addressed a treatment for individuals diagnosed with depression after TBI. One of the treatment studies was conducted in the United States,<sup>141</sup> and the second was in Canada.<sup>142</sup> Both were studies of medication, the first being an RCT of sertraline; the second, an open-label case series of the effects of citalopram. Of those that completed the sertraline study, 59 percent of the treated group and 32 percent of the control group had a positive response; the difference in response rates between the two groups was not statistically significant ( $p = 0.08$ ). In the 6-week data on citalopram ( $n = 54$ ), 27.7 percent were classified as responders and 24.1 percent were in remission. Among participants with data at 10 weeks, 46.2 percent were responders and 26.9 were in remission. Results at both time points were significant ( $p < .0001$ ). Of the 11 individuals who dropped out of this case series, 10 had experienced an adverse event.

### **KQ5. Comparisons of Treatments**

No studies were available to answer this key question.

### **KQ6. Modifiers of Outcomes of Treatment**

No studies were available to answer this key question.

# Future Research

## State of the Literature

The amount of literature about TBI is increasing rapidly, with the focus on the relationship between TBI and depression also growing. As is typical of advancing areas of research, early publications about TBI and depression have been predominantly cross-sectional, with little apparent consensus about measures or key covariates and a high degree of variability in quality of publications.

Prospective studies of sufficient size to enable multivariate modeling of predictors of outcome or analysis of outcome by factors such as severity are rare. Likewise, studies that are prospective in the sense that they include repeated measures of depression are few. Often studies meet criteria for prospective investigation by enumerating patients at the time of injury and counting time elapsed until followup as the prospective component. However, with a single measure of depression at one time of followup, this data is in essence cross-sectional and cannot contribute to understanding the natural history of the onset and course of depression after TBI.

Achieving representative study populations is challenging and rarely achieved because enumerating the entire population eligible for followup is hampered by the portion of the population who do not seek care for head injury. While studies in specialized settings like neuropsychiatric clinics or rehabilitation programs can be applicable to estimating risk in those settings, they cannot be generalized to base the population of all those with injuries.

Overall, the content of the current literature is fair to poor, with a preponderance of study designs that do not provide strong evidence. As a result, the strength of the literature is low for understanding the predictors, natural history, treatment options, and modifiers of outcomes of depression that follows TBI. Strength is moderate for establishing that depression is common and exceeds the prevalence expected in the general population.

**Concerning deficits in research methods.** As a body of literature a number of concerning deficits were recurring. Less than 12 percent of included studies met criteria for good quality. For example, many publications lacked one or more of the following:

- Operational definitions using standard approaches to diagnosing and categorizing severity of TBI.
- Description of the method of enumerating potentially eligible TBI participants.
- Timeframe in which participants were accrued.
- Report of the proportion of potentially eligible individuals who could be contacted and those who agreed to enroll.
- Analysis of any difference between those reached and enrolled and those not reached and/or who declined enrollment.
- Analysis of dropout and loss to followup.
- Uniform time from injury at followup.
- Non-TBI comparison groups.
- Description of the validity and reliability of methods used to measure depression.
- Sufficient detail about the cutoffs used to assign categories of depression severity from screening scales.

- Collection of crucial covariates that should be investigated as candidate predictors or direct risk factors for developing depression after TBI such as other psychiatric comorbidity, level of disability, cognitive function, and level of self-awareness.
- Collection of crucial covariates to assess potential confounding of the relationship between TBI and depression, such as litigation status.
- Stratification of findings to help understand how characteristics such as severity of injury or age contribute to depression risk
- Use of multivariate models in populations large enough to incorporate factors that confound and modify the relationship between TBI and depression risk.
- Masking of assessors to TBI status to prevent potential for overdiagnosing depression because TBI is thought to be associated with depression.
- Statement of hypotheses and power calculations.

**Gaps in knowledge.** Five of the six key questions for this report could not be adequately answered with existing literature, and the question about prevalence was only partially satisfied. The key questions were derived with expert and stakeholder input to define core knowledge for which we should have information. The questions themselves can serve as an outline for critical areas in which knowledge is insufficient. Lack of studies to assess how best to identify and treat depression after TBI is disconcerting. High-quality research is warranted across the spectrum of study designs and aims which includes:

- Collaborative studies in which multiple sites form networks to enumerate and followup large and more representative populations.
- Documentation of the natural history of onset and the course of depression after TBI.
- Investigation of the predictors of depression with emphasis on understanding etiology and better targeting of clinical resources.
- Direct comparison of screening tools and their yield in common clinical care settings for those with history of TBI including primary care practice.
- Intervention studies assessing the efficacy and effectiveness of the leading therapeutic modalities for depression.
- Head-to-head comparison of those found effective to assess comparative risks, benefits, and costs.
- Investigation of preventive interventions to decrease risk of onset of depression.
- Study of the value of educational interventions for those injured and their support networks to assist in detection of depression and in enhancing supports to mitigate negative effects on quality of life and function.

## Conclusions

Overall, the content of the current literature is fair to poor, with a preponderance of study designs that do not provide strong evidence. As a result, the strength of the literature is low for understanding the predictors, prevalence, natural history, treatment options, and modifiers of outcomes of depression that follows TBI. Nonetheless, considerable evidence suggests depression after all forms and severity of TBI is common.

We find a concerning lack of high-quality evidence to inform clinical decisionmaking for the 1 million to 2 million individuals in the United States who experience TBI each year. Lack of treatment studies focused on this populations is especially remarkable. Given how common, concerning, and debilitating the combination of TBI and depression can be, a priority on promoting high-quality research in the United States is imperative.

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## Acronyms/Abbreviations

[la]/LA	Language
[mh:noexp]	does not include MeSH terms found below this term in the MeSH tree
[mh]	Medical Subject Heading
[pt]/PT	Publication type
[tw]	Text word
ab.	Abstract word
ABI	Acquired Brain Injury
AES-S	Apathy Evaluation Scale-Self Rated
AUDIT	Alcohol Use Disorders Identification Test
BDI	Beck Depression Inventory
BHS	Becks Hopelessness Scale
BIS	Brain Injury Scale
BSI	Brief Symptom Inventory
CAQ	Clinical Analysis Questionnaire
CES-D	Center for Epidemiologic Studies Depression Scale
CHI	Closed head injury
CIDI	Composite International Diagnostic Interview
CiOP	Changes in Outlook Questionnaire
CIQ	Community Integration Questionnaire
CIRS	Cumulative Illness Rating Scale
CIS-R	Clinical Interview Schedule-Revised
CNS	Central nervous system
COF	Causes of Fatigue Questionnaire
COS	Community Outcome Scale
CPCS	Checklist of Postconcussion Symptoms
CT	Computed tomography
DASS	Depression Anxiety Stress Scales
DAST	Drug Abuse Screening Test
DE	Descriptors/Descriptors assigned to citations
DIS-III-A	The Diagnostic Interview Schedule Version A
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition
EBIQ	European Brain Injury Questionnaire
FAM	Functional Assessment Measure
FIM	Functional Independence Measure
FSS	Fatigue Severity Scale
GAF	Global Assessment of Functioning
GCS	Glasgow Coma Scale
GHQ	General Health Questionnaire
GOS	Glasgow Outcome Scale
GOS-E	Glasgow Outcome Scale Extended
GSW	Gunshot wound(s)
HADS	Hospital Anxiety and Depression Scale
HAM-D	Hamilton Rating Scale for Depression

HAS	Hamilton Anxiety Scale
HIBS	Head Injury Behavior Rating Scale
HSCL-25	Hopkins Symptom Checklist
HTQ	Harvard Trauma Questionnaire
ICD-10	International Classification of Diseases version 10
IDPESQ	Indice de detresse psychologique de l'Enquete Sante Quebec (French adaptation of the Psychiatric Symptom Index)
ISS	Injury Severity Scale
K-10	Kessler Psychological Distress Scale
kw/KW	Key words
Lg.	language
LOC	Loss of Consciousness
LSI-A	Life Satisfaction Index I-A
MADRS	Montgomery and Asberg Depression Rating Scale
MASQ	Mood and Anxiety Symptom Questionnaire—Short Form
MCMII-II/III	Millon Clinical Multi-Axial Inventory (version 2/3)
MDE	Major depressive episode(s)
MeSH	Medical Subject Heading
mg/dL	Milligram per deciliter
MMPI-2	Minnesota Multiphasic Personality Inventory version 2
MPAI	Mayo-Portland Adaptability Inventory
NEOPI-R	NEO Personality Inventory-Revised
NFI-Dep	Neurobehavioral Functioning Index Depression Subscale
NPI	Neuropsychiatric Inventory
NRS-R	Neurobehavioral Rating Scale-Revised
PAI	Personality Assessment Inventory
PCS	Postconcussion Syndrome
PHQ-9	Patient Health Questionnaire-9
PIM	Participation and Independence Measure
PO	population
POMS	Profile of Mood States
PRIME-MD	Primary Care Evaluation of Mental Disorders
PSE	Present State Examination
PSS	Perceived Stress Scale
PTA	Post-traumatic Amnesia
QoL	Quality of life
RDS	Referral Decision Scale
RPCQ	Rivermead Post-Concussion Disorder Questionnaire
SCAN	Schedules for Clinical Assessment in Neuropsychiatry
SCID	Structured Clinical Interview for DSM-IV
SCL 90	Symptom Checklist 90
SCL-20	Hopkins Symptom Checklist depression subscale
SF-12 v2	12-Item Short Form Health Survey-Version 2
SF-36	36-Item Short Form Survey Instrument
SIP	Sickness Impact Profile

TBI	Traumatic Brain Injury
ti.	Title word
VAS-D	Visual Analog Scale - Depression
VAS-F	Visual Analog Scale - Fatigue
WHOQOL-BREF	World Health Organization Quality of Life Questionnaire
WSRS	Wimbledon Self-Report Scale
ZDS	Zung Depression Scale
ZSDS	Zung Self-rating Depression Scale

## Appendix A. Exact Search Strings

### PubMed search strategies

Search #	Terms	Retrieval
#1	(Brain Concussion[mh] OR brain injuries[mh:noexp] OR Brain Hemorrhage, Traumatic[mh] OR Epilepsy, Post-Traumatic[mh] OR Head Injuries, Closed[mh] OR Head Injuries, Penetrating[mh] OR Intracranial Hemorrhage, Traumatic[mh] OR Craniocerebral Trauma[mh] OR TBI[tiab] OR head injuries[tiab] OR head injury[tiab] OR traumatic brain injury[tiab] OR traumatic brain injuries[tiab] OR neurotrauma[tiab] OR diffuse axonal injury[mh] OR diffuse axonal injury[tiab] OR brain trauma[tiab] OR head trauma[tiab])	109,710
#2	Depressive Disorder[mh] OR Depression[mh] OR depressive[tiab] OR depression[tiab] OR depressed[tiab] OR sadness[tiab] OR sad[tiab] OR hopelessness[tiab] OR suicidal[tiab] OR suicide[tiab] OR Mental Disorders[mh:noexp] OR mood[tiab]	396,835
#3	#1 AND #2 AND eng[la] AND humans[mh]	2,388
#4	#3 AND case reports[pt]	511
#5	#3 AND letter[pt]	38
#6	#3 AND comment[pt]	22
#7	#3 AND editorial[pt]	13
#8	#3 AND practice guideline[pt]	2
#9	#3 AND news[pt]	4
#10	#3 AND review[pt]	383
#11*	#3 NOT (#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10)	1,491*

\*Numbers do not total due to exclusions in more than one category (12 items were indexed as letter and comment; 2 were case reports, letters, and comments; 17 were case reports and letters; 36 were case reports and reviews; 4 were editorials and comments; 1 was a review and a comment; and 2 were editorials and reviews).

### PsycINFO search results

Search #	Terms	Retrieval*
#1	DE=("head injuries" or "brain concussion" or "traumatic brain injury") or KW=("head injury" or "head injuries" or "traumatic brain injury" or "traumatic brain injuries" OR "craniocerebral trauma" or neurotrauma or "brain trauma" OR "head trauma" OR TBI)	9,647
#2	DE=("depression emotion" or "major depression" or "hopelessness" or "sadness" or "suicidal ideation" or "suicide") or KW=(depressive or sad or hopeless or sadness)	107,224
#3	#1 AND #2 AND LA=(English) AND PO=(Human)	333*
#4	#3 AND PT=(letter)	6*
#5	#3 AND PT=(comment/reply)	6*
#6	#3 AND PT=(editorial)	2*
#10	#3 NOT (#4 OR #5 OR #6)	319*

\* Denotes number of citation retrieved from peer-reviewed journals

### Embase search results

Search #	Terms	Retrieval
#1	head injury/ or brain concussion/ or brain contusion/ or diffuse axonal injury/ or postconcussion syndrome/ or traumatic brain injury/ or ("craniocerebral trauma" or "brain trauma" or "head trauma" or TBI or "traumatic brain injury" or "traumatic head injury" or "traumatic brain injuries" or "traumatic head injuries").ab. or ("craniocerebral trauma" or "brain trauma" or "head trauma" or TBI or "traumatic brain injury" or "traumatic head injury" or "traumatic brain injuries" or "traumatic head injuries").ti.	12,018
#2	mental disease/ or mood disorder/ or depression/ or major depression/ or suicidal ideation/ or hopelessness/ or (depressive or sad or sadness or hopeless).ti. or (depressive or sad or sadness or hopeless).ab.	102,913
#3	1 and 2 and english.lg. and human/	505
#4	3 and conference paper.pt.	13
#5	3 and editorial.pt.	15
#6	3 and letter.pt.	13
#7	3 and note.pt.	16
#8	3 and review.pt.	221
#9	3 and short survey.pt.	14
#10	3 not (4 or 5 or 6 or 7 or 8 or 9)	213

### CINAHL search results

Search #	Terms	Retrieval
S1	("traumatic brain injury") or (MH "Brain Injuries+") OR "neurotrauma" OR "brain injuries" OR "TBI" OR "concussion" OR "head injuries" OR "head injury" OR "head trauma" OR "brain trauma"	14,021
S2	((MH "Depression+") OR "depressive disorder" OR "sadness" OR "depressed" OR (MH "Suicide") or (MH "Suicide, Attempted") or (MH "Suicidal Ideation") OR "suicide" OR "hopelessness" or (MH "Hopelessness") OR "mood")	45,193
S3	S1 AND S2 AND LA English	481
S4	S3 AND Exclude MEDLINE Records	145
S5	S4 and PT doctoral dissertation	18
S6	S4 and PT commentary	3
S7	S4 and PT letter	2
S8	S4 and PT systematic review	1
S9	S4 and PT review	11
S10	S4 and PT audiovisual	1
S11	S4 not (S5 OR S6 OR S7 OR S8 OR S9)	109

### PILOTS search results

Search #	Terms	Retrieval
#1	(DE="head injuries") or ("brain concussion" OR concussion OR "traumatic brain injury" OR "TBI" OR neurotrauma OR "traumatic brain injuries" OR "head trauma" OR "craniocerebral trauma" OR "brain injury" OR "brain injuries" )	667
#2	(DE="depressive disorders") or (depression OR depressed OR depressive OR suicidal OR suicide OR sadness OR hopelessness)	9,063
#3	#1 AND #2 AND LA=(English)	163
#4	#3, limited to peer-reviewed journals	116

## Search Strategies

### Search strategies for relevant white papers and reports

Resource	Date Searched	# of results	Search Strategy
Google search for .gov sites	2/2/2010	16,300 (examined the first15 pages of the search)	allintext: (depression OR depressive OR mood) AND ("acquired brain injury" OR "traumatic brain injury" OR TBI OR "head injury" OR neurotrauma OR "head trauma" OR "brain trauma") site:.gov excluded: press release, news, blog posts, PowerPoint, consumer health information
Google search for .mil sites	2/ 2/2010	1,1910 (examined the first15 pages of the search)	allintext: (depression OR depressive OR mood) AND ("acquired brain injury" OR "traumatic brain injury" OR TBI OR "head injury" OR neurotrauma OR "head trauma" OR "brain trauma") site:.mil excluded: press release, news, blog posts, PowerPoint, consumer health information
Google search for .edu sites	2/2/2010	18,100 (examined the first15 pages of the search)	allintext: (depression OR depressive OR mood) AND ("acquired brain injury" OR "traumatic brain injury" OR TBI OR "head injury" OR neurotrauma OR "head trauma" OR "brain trauma") site:.edu excluded: press release, news, blog posts, PowerPoint, consumer health information
Google search for .org sites	2/2/2010	119,000 (examined the first15 pages of the search)	allintext: (depression OR depressive OR mood) AND ("acquired brain injury" OR "traumatic brain injury" OR TBI OR "head injury" OR neurotrauma OR "head trauma" OR "brain trauma") site:.org excluded: press release, news, blog posts, PowerPoint, consumer health information

### Search strategies for relevant clinical trials and government funding

Resource	Date Searched	# of results	Search Strategy
Clinicaltrials.gov	2/2/2010	53	("traumatic brain injury" OR "traumatic head injury" OR "head injury" OR TBI OR "craniocerebral trauma" OR "brain trauma" OR neurotrauma OR "head trauma") AND (depressed OR depression OR depressive OR "Depressive Disorder" OR "mood disorder")
NIH RePORTER	2/2/2010	47	"traumatic brain injury" depression Limited: current projects
		13	"traumatic brain injury" mood Limited: current projects
		--	Other term combinations did not retrieve any unique results (tested terms include TBI, brain trauma, head trauma)
National Rehabilitation Information Center (NARIC)	2/2/2010	18	Search #1: "Brain injury" depression Limited to Ongoing projects Inclusion of mood, depressed, or depressive did not retrieve anymore relevant articles
International Clinical Registries (WHO)	2/2/2010	236	Traumatic AND brain AND injury Limited to results to registries other than Clinicaltrials.gov Inclusion of mood, depression, depressed, or depressive did not retrieve any unique articles
Grants.gov	2/2/2010	48	TBI depression
	2/2/2010	26	TBI psycholog* Inclusion of "traumatic brain injury", mood, depressed, or depressive did not retrieve any unique articles

### Search strategies for relevant conference proceedings

Resource	Date Searched	# of results	Search Strategy
BIOSIS	2/2/2010	117	TS=(depression OR depressive OR mood) AND TS=("acquired brain injury" OR "traumatic brain injury" OR TBI OR "head injury" OR neurotrauma OR "head trauma" OR "brain trauma"), Limits: Language=(English), Document Type=(Meeting OR Meeting Paper OR Technical Report OR Thesis Dissertation)
PsycInfo	2/2/2010	59	(DE=("head injuries" or "brain concussion" or "traumatic brain injury") or KW=("head injury" or "head injuries" or "traumatic brain injury" or "traumatic brain injuries" OR "craniocerebral trauma" or neurotrauma or "brain trauma" OR "head trauma" OR TBI)) and (DE=("depression emotion" or "major depression" or "hopelessness" or "sadness" or "suicidal ideation" or "suicide") or KW=(depressive or sad or hopeless or sadness)) AND (PT=(dissertation) or PT=(conference proceedings) or PT=(dissertation abstract))

### Resources that retrieved redundant information or did not retrieve relevant information

Resource	Date Searched
<ul style="list-style-type: none"> <li>• DeployMed Research Link (DoD-funded research)</li> <li>• Defense centers of excellence</li> <li>• Australian/New Zealand Clinical Trials Registry</li> <li>• PsiTri (Mental Health Registry)</li> <li>• Current Controlled Trials (UK)</li> <li>• PapersFirst</li> <li>• Sociological Abstracts</li> </ul>	February 2, 2010

# Appendix B. Sample Data Abstraction Forms

## Traumatic Brain Injury and Depression Systematic Evidence Review

### Abstract/Title Review Form

First Author, Year: \_\_\_\_\_

Reference # \_\_\_\_\_

Abstractor Initials: \_\_\_\_ \_\_\_\_ \_\_\_\_

<b>Primary Inclusion/Exclusion Criteria</b>			
1. Does study include traumatic brain injury as an exposure and depression as an outcome?	Yes	No	Cannot Determine
2. Original research (exclude editorials, commentaries, letters, reviews, etc.)	Yes	No	Cannot Determine
3. Adult study population ( $\geq 18$ years old)	Yes	No	Cannot Determine
4. Study published in English	Yes	No	Cannot Determine
5. Eligible study size Record N if < 50 relevant subjects enrolled: _____	Yes	No	Cannot Determine

# Traumatic Brain Injury and Depression Systematic Evidence Review

## Full-text Review Form

First Author, Year: \_\_\_\_\_

Reference # \_\_\_\_\_

Abstractor Initials: \_\_\_\_ \_\_\_\_ \_\_\_\_

<b>Primary Inclusion/Exclusion Criteria</b>		
1. Does study answer one or more of the following questions? (place an X next to the question(s) the study applies to)	Yes	No
<p>___KQ1. What is the prevalence of depression after traumatic brain injury (TBI), and do the area of the brain injured, the severity of the injury, the mechanism or context of injury, or time to recognition of the traumatic brain injury or other patient factors influence the probability of developing incident clinical depression?</p> <p>___KQ2. When should patients who suffer TBI be screened for depression, with what tools, and in what setting?</p> <p>___KQ3. Among individuals with TBI and depression, what is the prevalence of concomitant psychiatric/behavioral conditions, including anxiety disorders, PTSD, substance abuse, and major psychiatric disorders?</p> <p>___KQ4. What are the outcomes (short and long term, including harm) of treatment for depression among traumatic brain injury patients utilizing: a) psychotropic medications, b) individual/group psychotherapy, c) neuropsychological rehabilitation, d) community-based rehabilitation, e) CAM, f) neuromodulation therapies, and g) other?</p> <p>___KQ5. Where head-to-head comparisons are available, which treatment modalities are equivalent or superior with respect to benefits, short- and long-term risks, quality of life, or costs of care?</p> <p>___KQ6. Are the short- and long-term outcomes of treatment for depression after TBI modified by individual characteristics, such as age, pre-existing mental health status or medical conditions, functional status, and social support?</p>		
2. Original research (exclude editorials, commentaries, letters to editor, reviews, etc.)	Yes	No
3. Study published in English	Yes	No
4. Adult ( $\geq 16$ years old) study population If No, record % adult _____	Yes	No
5. Eligible study size ( $N \geq 50$ ) Record N if $< 50$ relevant subjects enrolled: _____	Yes	No

*EXCLUDE IF AN ITEM IN A GRAY BOX IS SELECTED*

**If EXCLUDED, retain for:**

- \_\_\_ **BACKGROUND/DISCUSSION**
- \_\_\_ **REVIEW OF REFERENCES**
- \_\_\_ **Other** \_\_\_\_\_

**COMMENTS:**

**Evidence Table (REF ID# )**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>	<b>Quality Rating</b>
<b>Author:</b> Author et al., YYYY <b>Country, Setting:</b> Country, setting <b>Enrollment Period:</b> <b>Design:</b> <b>Time from injury:</b> <b>Length of followup:</b> <b>Dep. Scale/Tool:</b>	<b>Inclusion criteria:</b> <ul style="list-style-type: none"> <li>• Inclusion #1</li> <li>• Inclusion #2</li> <li>• Inclusion #3</li> </ul> <b>Exclusion criteria:</b> <ul style="list-style-type: none"> <li>• Exclusion #1</li> <li>• Exclusion #2</li> <li>• Exclusion #3</li> </ul> <b>TBI Def:</b>	<b>Group(s):</b> <b>N screened:</b> <b>N eligible:</b> <b>N included:</b> <b>N at conclusion:</b> <b>Depression:</b> Prior to injury: At time of injury: <b>Other preexisting psychiatric conditions:</b> <b>N with prior TBI (%):</b> <b>Age, yrs ± SD:</b> <b>G1: XX ± ##</b> <b>Age ≥16, N (%):</b> <b>G1: XX (##)</b> <b>Global injury severity (ISS, RTS, etc.):</b> <b>Severity of TBI (GCS):</b> <b>Mechanism/type of injury:</b> <b>Area of brain injured:</b> <b>Concomitant injuries:</b>	<b>Depression:</b> (Starting with most severe) <b>Other co-morbidities:</b> PTSD: Other anxiety disorder: Irritability: Aggression: Suicidality: Substance use: Other psychiatric diagnoses (schizophrenia, psychosis, OCD, etc): <b>Health-related QoL or functional status:</b>	<b>Depression:</b> <b>Taking depression medications (%):</b> <b>Other co-morbidities:</b> PTSD: Other anxiety disorder: Irritability: Aggression: Suicidality: Substance use: Other psychiatric diagnoses: <b>Health-related QoL or functional status:</b>	

# Traumatic Brain Injury and Depression Systematic Evidence Review

## Criteria for KQ1 Includes

First Author, Year: \_\_\_\_\_

Reference # \_\_\_\_\_

Reviewer: \_\_\_\_\_

<b>1. Operational definition of traumatic brain injury:</b>	
<input type="checkbox"/> GCS Scores <input type="checkbox"/> Centers for Disease Control and Prevention <input type="checkbox"/> World Health Organization	<input type="checkbox"/> American Congress of Rehabilitation Medicine <input type="checkbox"/> National Brain Injury Foundation <input type="checkbox"/> National Athletic Trainers' Association
Other professional organization definition: _____	
<input type="checkbox"/> Self report <input type="checkbox"/> Ad hoc definition:  <input type="checkbox"/> Not defined	
<b>2. Operational definition of depression:</b>	
<input type="checkbox"/> SCID <input type="checkbox"/> HAM-D <input type="checkbox"/> BDI <input type="checkbox"/> HADS	<input type="checkbox"/> CES-D <input type="checkbox"/> NFI <input type="checkbox"/> SCL-90 <input type="checkbox"/> Clinical interview as part of study protocol
<input type="checkbox"/> Other validated instrument: _____	
<input type="checkbox"/> Self report <input type="checkbox"/> Ad hoc definition:  <input type="checkbox"/> Not defined	
<input type="checkbox"/> Chart Review	
<b>3. Proportion of study population with TBI for whom depression measure is obtained:</b>	
<p style="margin-left: 40px;">N with dep. measure = _____</p> <p style="margin-left: 80px;">Total N with TBI = _____</p> <p style="margin-left: 40px;">Percent evaluated = _____</p>	

COMMENTS:

# Traumatic Brain Injury and Depression Systematic Evidence Review

## Criteria for KQ2 Includes

First Author, Year: \_\_\_\_\_

Reference # \_\_\_\_\_

Reviewer: \_\_\_\_\_

4. Operational definition of traumatic brain injury:	
<input type="checkbox"/> GCS Scores	<input type="checkbox"/> American Congress of Rehabilitation Medicine
<input type="checkbox"/> Centers for Disease Control and Prevention	<input type="checkbox"/> National Brain Injury Foundation
<input type="checkbox"/> World Health Organization	<input type="checkbox"/> National Athletic Trainers' Association
Other professional organization definition: _____	
<input type="checkbox"/> Self report	
<input type="checkbox"/> Ad hoc definition:	
<input type="checkbox"/> Not defined	
5. Does the publication include:	
<input type="checkbox"/> Comparison of a tool with a gold standard (HAM-D to SCID, etc.) presenting diagnostic test characteristics (sensitivity, specificity, positive predictive value, negative predictive value, likelihood ratios)?	
<input type="checkbox"/> Test-retest reliability? (Administered and repeated)	
<input type="checkbox"/> Inter-rater reliability? (Comparison of two administrations by different people, or in different modes (written vs. phone, etc.))	

COMMENTS:

# Traumatic Brain Injury and Depression Systematic Evidence Review

## Criteria for KQ3 Includes

First Author, Year: \_\_\_\_\_

Reference # \_\_\_\_\_

Reviewer: \_\_\_\_\_

<b>1. Operational definition of traumatic brain injury:</b>	
<input type="checkbox"/> GCS Scores <input type="checkbox"/> Centers for Disease Control and Prevention <input type="checkbox"/> World Health Organization	<input type="checkbox"/> American Congress of Rehabilitation Medicine <input type="checkbox"/> National Brain Injury Foundation <input type="checkbox"/> National Athletic Trainers' Association
Other professional organization definition: _____	
<input type="checkbox"/> Self report <input type="checkbox"/> Ad hoc definition:  <input type="checkbox"/> Not defined	
<b>2. Operational definition of depression:</b>	
<input type="checkbox"/> SCID <input type="checkbox"/> HAM-D <input type="checkbox"/> BDI <input type="checkbox"/> HADS	<input type="checkbox"/> CES-D <input type="checkbox"/> NFI <input type="checkbox"/> SCL-90 <input type="checkbox"/> Clinical interview as part of study protocol
<input type="checkbox"/> Other validated instrument: _____	
<input type="checkbox"/> Self report <input type="checkbox"/> Ad hoc definition:	
<input type="checkbox"/> Not defined	
<b>3. Proportion of study population with TBI for whom depression measure is obtained:</b>	
N with dep. measure = _____  Total N with TBI = _____  Percent evaluated = _____	
<b>4. Are concomitant mental health conditions reported by depression status?</b>	
<input type="checkbox"/> Yes <input type="checkbox"/> No	

COMMENTS:

## **Appendix C. Evidence Tables**

Evidence Table 1. TBI and Depression

Evidence Table 2. Prevalence of Depression by Time of Assessment in Studies with Poorly Defined TBI

Evidence Table 3. Quality of Individual Nontreatment Studies

Evidence Table 4. Quality of Individual Treatment Studies

Evidence Table 5. Operational Definitions of TBI

Evidence Table 6. Depression and Quality of Life Assessment Tool

**Evidence Table 1. TBI and Depression**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Al-Adawi et al., 2007</p> <p><b>Country, Setting:</b> Oman, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, months± SD:</b> 18.2 ± 12.2</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS, CIDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• A score of 51 or higher on the 17-item Awareness Questionnaire</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Pre-injury psychiatric or neurological history other than TBI</li> <li>• Non-Omani</li> <li>• Sensory or cognitive impairments that would preclude completion of the protracted assessment</li> </ul> <p><b>TBI Def:</b> An injury to brain tissues caused by an external mechanical force as evidenced by LOC, post-traumatic cognitive and behavioral changes or objective neurological finding</p> <p>Mild TBI: GCS score of 13 to 15</p> <p>Moderate TBI: GCS score of 9 to 12</p> <p>Severe TBI: GCS score of 3 to 8</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 68</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: None (see exclusion criteria) At time of injury: None (see exclusion criteria)</p> <p><b>Other preexisting psychiatric conditions:</b> None (see exclusion criteria)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:*</b> 31.1 ± 7.6</p> <p><b>Age ≥16, n (%):</b> 68 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> Mild or moderate: majority of patients (exact number NR)</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured, n (%):</b> Diffuse: 21 (32.6) Focal: 14 (20.6) Frontal: 25 (36.8)</p>	<p><b>Depression:</b> HADS: score ≥ 8 indicated propensity for depression/ anxiety CIDI: clinical depression/ anxiety determined by clinical interview</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, HADS, n (%):</b> 13 (19.1)</p> <p><b>Depression, CIDI, n (%):</b> 39 (57.4)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Aloia et al., 1995</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> MMPI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Sample of private practice patients based on group criteria</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> HI and depression</p> <p><b>G2:</b> HI and no depression</p> <p><b>G3:</b> No HI and depression</p> <p><b>G4:</b> No HI and no depression</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b></p> <p><b>G1:</b> 277</p> <p><b>G2:</b> 471</p> <p><b>G3:</b> 220</p> <p><b>G4:</b> 214</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, mean yrs:</b></p> <p><b>G1:</b> 35.2</p> <p><b>G2:</b> 31.5</p> <p><b>G3:</b> 38.5</p> <p><b>G4:</b> 38.3</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> NR</p>	<p><b>Depression:</b> MMPI: T score of 70 or higher on the depression (D) scale</p> <p>Discriminate Functional analysis (DFA) and cross validation used to determine if characteristics of depression were the same for HI and no HI groups</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, MMPI, n:</b> 497 (42.0)</p> <p>MMPI depression (D) scale score, mean:</p> <p><b>G1:</b> 84.6</p> <p><b>G2:</b> 55.9</p> <p><b>G3:</b> 86.7</p> <p><b>G4:</b> 56.4</p> <p>Discriminate Functional analysis (DFA): Analysis for depression using entire HI population was successful (85.8%), cross validation with no HI group successful as well (85.6%, <math>X^2 = 0.0</math>, <math>P &gt; 0.10</math>)</p> <p>Analysis for no HI group was successful (92.4%) and cross validation was equally successful (77.4%, <math>X^2 = 2.4</math>, <math>P &gt; 0.10</math>)</p> <p>When MMPI variables removed, DFA not as successful in classifying HI patients as depressed or not depressed, cross validation only successful (48.3%, <math>X^2 = 13.2</math>, <math>P &gt; 0.001</math>)</p> <p>May imply that neuropsychological variables associated with depression are not the same in HI vs. no HI patients</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Ashman et al., 2009</p> <p><b>Country, Setting:</b> US, tertiary care hospital</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, yrs ± SD:</b> <b>G1:</b> 18.6 ± 13.8 <b>G2:</b> 16.6 ± 13.9</p> <p><b>Length of follow up:</b> 10 weeks</p> <p><b>Dep. Scale/Tool:</b> SCID, HAM-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• At least 18 yrs old</li> <li>• A history of TBI with a documented LOC or other evidence of a TBI (e.g., pathology on neuroimaging)</li> <li>• At least 6 mos postinjury</li> <li>• Meet DSM-IV diagnostic criteria for MDE</li> <li>• HAM-D score ≥ 18</li> <li>• Able to comprehend or answer verbal or written questionnaires</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Using antidepressant medication</li> <li>• Currently in psychotherapy</li> <li>• Active suicidal plans or depression severe enough to require hospitalization</li> <li>• Serious medical illness</li> <li>• Pregnant or breast-feeding</li> <li>• Mass brain lesions or other neurologic diagnoses other than TBI</li> <li>• A history of current or past psychosis or mania using DSM-IV criteria</li> </ul>	<p><b>Group(s):</b> <b>G1:</b> Sertraline group <b>G2:</b> Placebo group</p> <p><b>N screened:</b> 91</p> <p><b>N eligible:</b> 52</p> <p><b>N included:</b> <b>G1:</b> 22 <b>G2:</b> 19</p> <p><b>N at conclusion:</b> <b>G1:</b> 22 <b>G2:</b> 19</p> <p><b>Depression:</b> Prior to injury: See inclusion criteria At time of injury: See inclusion criteria</p> <p><b>Other preexisting psychiatric conditions:</b> See inclusion criteria</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 46.8 ± 12.8 <b>G2:</b> 51.5 ± 8.2</p> <p><b>Age ≥16, n (%):</b> 52 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Mild: <b>G1:</b> 20.0 <b>G2:</b> 50.0 Moderate: <b>G1:</b> 46.6 <b>G2:</b> 31.3 Severe: <b>G1:</b> 33.4 <b>G2:</b> 18.8</p>	<p><b>Depression:</b> SCID: DSM-IV criteria HAM-D ≥ 18</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: Beck Anxiety Inventory Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Life-3</p>	<p><b>Depression, SCID, n (%):</b> <b>G1:</b> 4 (18) <b>G2:</b> 7 (37)</p> <p>HAM-D score, mean ± SD: Baseline: <b>G1:</b> 27.5 ± 7.1 <b>G2:</b> 25.2 ± 8.0 End of treatment: <b>G1:</b> 13.7 ± 9.7 <b>G2:</b> 16.2 ± 9.6</p> <p><b>Taking depression medications:</b> None (see exclusion criteria)</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: BAI score, mean ± SD: Baseline <b>G1:</b> 23.2 ± 15.2 <b>G2:</b> 20.5 ± 14.9 End of treatment: <b>G1:</b> 11.1 ± 11.9 <b>G2:</b> 13.1 ± 11.6</p> <p>Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Life-3 score, mean ± SD: <b>G1:</b> 6.3 ± 8.0 <b>G2:</b> 4.9 ± 3.5</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Ashman et al., 2004 See Hibbard et al., 2004</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> March 1995 to December 2000</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> Initial assessment (T1) 3 months to 4 years post injury</p> <p><b>Length of follow up (years):</b> Second (T2) and third (T3) assessments 12 and 24 months after initial assessment</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Self-identified TBI</li> <li>• 3 months to 4 years postinjury</li> <li>• Between age 18 and 87</li> <li>• Residents of the United States living within the community</li> <li>• Capable of giving informed consent for participation and answering interviews independently</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• The presence of an acquired brain injury (e.g., cerebrovascular accident, aneurysm)</li> <li>• A preexisting neurocognitive disorder</li> <li>• Any preexisting psychotic disorder (e.g., schizophrenia, psychoses NOS, depression with psychotic features)</li> </ul> <p><b>TBI Def:</b> According to ACRM criteria</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 188</p> <p><b>N at conclusion:</b> 83</p> <p><b>Depression, %:</b> Prior to injury: 20</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, %:</b> PTSD: 10 Anxiety disorder: 16 Substance use: 32 Other psychiatric conditions: 5</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 40.4 ± 15.1</p> <p><b>Age ≥16, n (%):</b> 188 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Moderate to severe: 62 Mild : 29 LOC of unknown duration: 9</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: SCID</p> <p>Other anxiety disorder: SCID: OCD, GAD, panic, phobias</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: SCID: abuse and dependence</p> <p>Other psychiatric conditions: SCID: any axis I disorder other than above</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, %:</b> Initial assessment: 35 12 months: 24 24 months: 21</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: Initial assessment: 30 12 months: 18 24 months: 21</p> <p>Other anxiety disorder: Initial assessment: 27 12 months: 19 24 months: 9</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: Initial assessment: 14 12 months: 10 24 months: 17</p> <p>Other psychiatric conditions: Initial assessment: 9 12 months: 5 24 months: 0</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Bay and Donders, 2008</p> <p>See Bay et al. 2002 &amp; Bay et al. 2007</p> <p><b>Country, Setting:</b> US, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD (range):</b> 15.1 ± 11.3 (1-36)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> NFI-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 1 to 36 mos postinjury</li> <li>• Must have been hospitalized (ED or in-patient for the injury)</li> <li>• Must be English speaking and competent to sign informed consent as determined by the admitting neuropsychologist</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• History of neurological conditions known to affect cognition, such as Parkinson's or Alzheimer's disease</li> <li>• Severe TBI according to admitting ED (GCS ≥9)</li> </ul> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> <b>G1:</b> Borderline or clinically depressed patients with TBI <b>G2:</b> Not or minimally depressed patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 49 <b>G2:</b> 35</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> "Prior psychiatric history": 26 (31.0) Prior history of substance abuse, n (%): 14 (16.7)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 38.0 ± 11.3</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS, n (%):</b> 13-15: 65 (77.4) 9-12: 19 (22.6)</p>	<p><b>Depression:</b> NFI-D: 13-28: Minimally depressed 29-42: Borderline depressed 43-65: Clinically depressed</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> PSS IES-R MPQ-SF MFIS: 0: None 1: Mild 2: Moderate 3: Severe Reaction time: index of information processing speed</p>	<p><b>Depression, n (%):</b> Total: 49 (58.3)</p> <p>NFI-D score, mean ± SD: <b>G1:</b> 39.6 ± 6.1 <b>G2:</b> 20.7 ± 4.4 Total: 31.7 (10.8)</p> <p>NFI-D score, median (range): Total: 32 (13-56)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> PSS score, mean ± SD: <b>G1:</b> 27.4 ± 5.5 <b>G2:</b> 19.7 ± 4.3 IES-R score, mean ± SD: <b>G1:</b> 22.7 ± 8.8 <b>G2:</b> 12.1 ± 8.5 MPQ-SF score, mean ± SD: <b>G1:</b> 1.5 ± 1.0 <b>G2:</b> 0.6 ± 0.9</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Bay et al., 2002<sup>^</sup> Bay et al., 2007 See Bay and Donders, 2008</p> <p><b>Country, Setting:</b> US, rehabilitation centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD:</b> 9.57 ± 6.31</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> NFI-D, POMS-D, CES-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 65 years old</li> <li>• Mild or moderate brain injury</li> <li>• Hospitalization for the injury</li> <li>• Evaluation by a neuropsychologist with expertise in assessment of brain injury</li> <li>• Within two years of the injury</li> <li>• English-speaking</li> <li>• Not psychotic at the time of neuropsychological evaluation</li> <li>• No preinjury neurological impairment</li> <li>• A relative or significant other (R/SO) who agreed to participate</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Severe TBI</li> </ul> <p><b>TBI Def:</b> Mild TBI: According to ACRM criteria  Moderate TBI: LOC exceeding 30 minutes but less than 2 weeks, GCS score of 9-12 or 13-15 with an abnormal CT scan<sup>^</sup></p>	<p><b>Group(s):</b> Patients with mild or moderate TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 75</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Psychiatric disorders including depression: 15 (20) Suicidal thoughts in the year prior to injury: 6 (8)</p> <p><b>N with prior TBI, n (%):</b> 12 (16.0)</p> <p><b>Age, yrs ± SD:</b> 37.4 ± 12.1</p> <p><b>Age ≥16, n (%):</b> 75 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Mild: 50 Moderate: 50</p> <p>PTA duration, mean days ± SD: 7.7 ± 8.9</p>	<p><b>Depression:</b> NFI-D: 13-28: Minimally depressed 29-42: Borderline depressed 43-65: Clinically depressed  POMS-D: NR  CES-D: 16-20: Mild depression 21-26: Moderate 27-60: Severe</p> <p><b>Other co-morbidities:</b> PTSD:NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, NFI-D, n (%):</b> Clinical: 11 (14.7) Borderline: 30 (40.0) Minimal: 34 (45.3)</p> <p>NFI-D score, mean ± SD (range): 30.7 ± 10.7 (13-54)</p> <p>POMS-D score, mean ± SD (range): 15.0 ± 14.1 (0-59)</p> <p>Depression, CES-D, n: Probable MDD: 22 (29.4) Moderate: 16 (21.3) Mild: 10 (13.3) Not in depression range: 27 (36)<sup>^</sup> CES-D &gt; 30.5: 12 (20)<sup>^</sup></p> <p>CES-D score, mean ± SD (range): 20.5 ± 13.2 (0-57)</p> <p><b>Taking depression medications (%):</b> 40</p> <p><b>Other co-morbidities:</b> PTSD:NR  Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR  Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Bombardier et al., 2006</p> <p>See Fann et al., 2005; Fann et al., 2009; Bombardier et al., 2010</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> May 2001 to January 2003</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> Up to 6 months</p> <p><b>Length of follow up, mos:</b> 6</p> <p><b>Dep. Scale/Tool:</b> PHQ-9</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 18 yrs old</li> <li>English speaking</li> <li>Residing in King, Pierce, Kitsap, or Snohomish counties (WA)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Uncomplicated MTBI</li> <li>Homelessness,</li> <li>Incarceration</li> <li>A history of schizophrenia</li> <li>Participation in an investigational drug study</li> </ul> <p><b>TBI Def:</b> Radiological evidence of acute brain abnormality or lowest GCS score less than or equal to 12 within the first 24 hours since admission.</p> <p>Complicated mild TBI: GCS of &gt; 12 and abnormal CT</p> <p>Uncomplicated MTBI: GCS of 13 to 15 and no CT abnormality</p> <p>Moderate TBI: GCS of 9 to 12</p> <p>Severe TBI: GCS of ≤ 8</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>G1:</b> Patients with TBI and PTSD</p> <p><b>G2:</b> Patients with TBI and no PTSD</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 211</p> <p><b>N included:</b> 141</p> <p><b>N at conclusion:</b> <b>G1:</b> 14 <b>G2:</b> 110</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> History of anxiety or depression: 68 (54.8)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 43 ± 18.6</p> <p><b>Age ≥16, %:</b> 100</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Comp. Mild: 44 Moderate: 30 Severe: 27</p> <p><b>Mechanism/type of injury, %:</b> MVC: 49 Falls: 32 Assault: 7 Other: 12</p>	<p><b>Depression:</b> PHQ-9: NR</p> <p><b>Other co-morbidities:</b> PTSD: PCL-C Criteria F</p> <p>Other anxiety disorder: PHQ Self-history</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: Positive for Toxicology screening test for amphetamines/ Cocaine</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Cognistat</p> <p>GHS of SF-36</p>	<p><b>Depression, PHQ-9, n (%):</b> MDD: 27 (21.8)^</p> <p>MDD, %: <b>G1:</b> 71.4 <b>G2:</b> 15.5 <i>P</i> &lt; 0.001</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: 14 (11.3) PTSD + criteria F: 10 (8*) PTSD + all criteria (A2,B,C,D,F,PCL-C): 7/125 (5.6*)</p> <p>Other anxiety disorder: PHQ, %: <b>G1:</b> 21.4 <b>G2:</b> 4.5 <i>P</i> &lt; 0.046</p> <p>Other anxiety disorders, %: <b>G1:</b> 71.4 <b>G2:</b> 18.2 <i>P</i> &lt; 0.001</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: Positive toxicology test for amphetamine/ Cocaine, n (%): <b>G1:</b> 4 (3.2) <b>G2:</b> 8 (7.3)</p> <p>Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Bombardier et al., 2010</p> <p>See Fann et al., 2005; Bombardier et al., 2006; Fann et al., 2009</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> June 2001 to March 2005</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, mos, n:</b> 1: 289 2: 380 3: 408 4: 415 5: 423 6: 432 8: 385 10: 358 12: 365</p> <p><b>Length of follow up:</b> 12 mos</p> <p><b>Dep. Scale/Tool:</b> Structured interview based on PHQ-9</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 18 yrs old</li> <li>English speaking</li> <li>Admission to Harborview Medical Center (a level I trauma center in Seattle, Washington)</li> <li>TBI and radiological evidence of acute, traumatically induced brain abnormality or GCS score lower than 13 (based on the lowest score within 24 hours after admission or the first after paralytic agents were withdrawn)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Uncomplicated mild TBI (GCS 13-15 and no radiological abnormality)</li> <li>Homelessness (or no contact information available)</li> <li>Incarceration</li> <li>Schizophrenia</li> </ul>	<p><b>Group(s):</b> <b>G1:</b> Participants with MDD <b>G2:</b> Participants without MDD</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 1,080</p> <p><b>N included*:</b> 559 <b>G1:</b> 262 <b>G2:</b> 297</p> <p><b>N at conclusion:</b> 365</p> <p><b>Depression, n (%):</b> Prior to injury: 150 (26.7) At time of injury: 88 (15.7)</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Unspecified diagnosis: 61 (10.9) PTSD: 36 (6.4)</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age, yrs ± SD:</b> 42.5 ± 17.9</p> <p><b>Age ≥16, N (%):</b> 559 (100)</p> <p><b>Global injury severity<sup>†</sup>, n (%):</b> 0:153 (27.4) 1-2: 192 (34.4) 3-5: 212 (37.9)</p>	<p><b>Depression:</b> PHQ-9: MDD based on DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: CAGE Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> SF-36 EQoL</p>	<p><b>Depression, n (%):</b> 1 mo: 90/289 (31.1) 2 mos: 94/380 (24.7) 3 mos: 100/408 (24.5) 4 mos: 91/415 (21.9) 5 mos: 97/423 (22.9) 6 mos: 90/432 (20.8) 8 mos: 93/385 (24.2) 10 mos: 97/358 (27.1) 12 mos: 85/365 (23.3)</p> <p>Any time: 297 (53.1) ≥ 1 positive screening, %: 27.0 Positive screening in ≥ 6 mos, %: 36.0</p> <p><b>Taking depression medications (%):</b> <b>G1:</b> 41.0 <b>G2:</b> 18.0 RR=2.3 95% CI (1.7,3.1)</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: <b>G1:</b> 54.0 <b>G2:</b> 6.0 RR= 8.8 95% CI (5.4, 14.4) Irritability: NR Aggression: NR Suicidality: NR Substance use: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Brooks et al., 1987</p> <p><b>Country, Setting:</b> UK, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mean yrs (range):</b> 3.4 (2-8)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> Questionnaire by structured interview of patients and relatives</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Coma duration of at least 6 hrs</li> <li>• Intracranial hematoma requiring surgery</li> <li>• PTA of at least two days</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> Patients with severe closed- head injury</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 134</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, time of assessment, n (%):</b> 15-25: 34 (25.4) 26-35: 25 (18.7) 36-45: 23 (17.2) 46-55: 23 (17.2) 56-65: 21 (15.7) 65-70: 7 (5.2) Missing: 1 (0.7)</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, PTA, n (%):</b> 2-14 days: 34 (25.4) 15-28 days: 31 (23.1) 1-2 months: 32 (23.9) 3-6 months: 23 (17.2) &gt;6 months: 3 (2.2) Missing: 11 (8.2)</p>	<p><b>Depression:</b> Internally developed structured questionnaires administered to patient and to close family member, querying depression</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: Internally developed structured questionnaire administered to patient and to close family member, querying tension/anxiety/ worry Irritability: See Aggression</p> <p><b>Aggression:</b> Internally developed structured questionnaire administered to patient and to close family member, querying anger/ irritation/ impatience Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p>	<p><b>Depression, %:</b> Patient report: 49 Relative report: 63</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR Other anxiety disorder: Patient report: 35 Relative report: 65 Irritability: See Aggression Aggression: Patient report: 62 Relative report: 74 Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status, reported by relative, %:</b> Worrying that patient could not be left in charge of the household: 47 Patient still needed "looking after": 36 Relative worried about patient going out alone: 24 Washing difficulty: 20 Problems with personal hygiene: 27</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Brown et al., 2004</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> August 1999 to March 2001</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, wks ± SD:</b> 12 ± 2</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, CES-D, VAS-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Age 16 or older</li> <li>• Residence within Harris County, TX</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating missile injury of the brain</li> <li>• History of diagnosed schizophrenia</li> <li>• Mental deficiency</li> <li>• Hospitalization for prior TBI</li> <li>• History of treatment for recent substance abuse</li> <li>• Blood alcohol level &gt; 200 mg/dL when examined in ER</li> </ul> <p><b>TBI Def:</b> Mild TBI: A closed head injury producing a LOC ≤ 20 min, lowest postresuscitation GCS of 13 to 15, no extracranial injury that necessitated surgical repair under general anesthesia, and CT findings after 24 hours indicating normal intracranial findings or a brain lesion that did not require surgical evacuation</p> <p>Moderate TBI: Lowest post-resuscitation GCS of 9 to 12 with or without evidence of lesion on CT</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with TBI</p> <p><b>G2:</b> Patients with general trauma (GT)</p> <p><b>Ga:</b> European American patients</p> <p><b>Gb:</b> Hispanic American patients</p> <p><b>Gc:</b> African American patients</p> <p><b>N screened:</b></p> <p><b>G1:</b> 399</p> <p><b>G2:</b> 255</p> <p><b>N eligible:</b></p> <p><b>G1:</b> 399</p> <p><b>G2:</b> 255</p> <p><b>N included:</b></p> <p><b>G1:</b> 135</p> <p><b>G1a:</b> 28</p> <p><b>G1b:</b> 63</p> <p><b>G1c:</b> 44</p> <p><b>G2:</b> 83</p> <p><b>G2a:</b> 17</p> <p><b>G2b:</b> 46</p> <p><b>G2c:</b> 20</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b></p> <p><b>G1:</b> 33.9 ± 14.5</p> <p><b>G2:</b> 34.9 ± 12.7</p> <p><b>Age ≥16, n (%):</b> 218 (100)</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p>CES-D: NR</p> <p>VAS-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> SF-36 (PCS/ MCS)</p> <p>CIQ</p> <p>SSQ</p>	<p><b>Depression, SCID, %:</b></p> <p>MDE:</p> <p><b>G1:</b> 16</p> <p><b>G1a:</b> 11</p> <p><b>G2b:</b> 17</p> <p><b>G1c:</b> 18</p> <p>CES-D score, mean ± SD:</p> <p><b>G1:</b> 21.8 ± 14.8*</p> <p><b>G1a:</b> 17.9 ± 16.0</p> <p><b>G1b:</b> 21.3 ± 14.3</p> <p><b>G1c:</b> 24.9 ± 13.9</p> <p><b>G2:</b> 18.8 ± 14.6*</p> <p><b>G2a:</b> 17.5 ± 13.9</p> <p><b>G2b:</b> 18.9 ± 14.9</p> <p><b>G2c:</b> 19.7 ± 14.2</p> <p>VAS-D score, mean ± SD:</p> <p><b>G1:</b> 39.5 ± 34.8</p> <p><b>G1a:</b> 32.4 ± 35.7</p> <p><b>G1b:</b> 37.0 ± 32.8</p> <p><b>G1c:</b> 47.3 ± 36.5</p> <p><b>G2:</b> 26.7 ± 31.7</p> <p><b>G2a:</b> 21.2 ± 28.1</p> <p><b>G2b:</b> 30.1 ± 33.3</p> <p><b>G2c:</b> 23.5 ± 31.4</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Bryant et al., 2001</p> <p><b>Country, Setting:</b> Australia, rehabilitation center</p> <p><b>Enrollment Period:</b> July 1994 to July 1997</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD:</b> 6.4 ± 1.3</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Admission to major brain injury rehabilitation center after severe TBI</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Insufficient cognitive ability to understand or respond to the interview</li> <li>Inability to speak English without an interpreter</li> </ul> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI and PTSD <b>G2:</b> Patients with TBI and no PTSD</p> <p><b>N screened:</b> 161</p> <p><b>N eligible:</b> 96</p> <p><b>N included:</b> <b>G1:</b> 26 <b>G2:</b> 70</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 34.26 ± 12.82</p> <p><b>Age ≥16, n (%):</b> 96 (100)</p> <p><b>Global injury severity (ISS, RTS, etc.):</b> NR</p> <p><b>Severity of TBI, GCS score, mean ± SD:</b> Total: 8.0 ± 3.8 <b>G1:</b> 6.9 ± 3.5 <b>G2:</b> 8.4 ± 3.8</p> <p><b>Mechanism/type of injury, n:</b> MVC: 70 Assault: 12 Work: 14</p>	<p><b>Depression:</b> BDI: &gt; 30: Severe 25-29: Moderate 19-24: Mild 11-18: Minimal &lt; 10: None</p> <p><b>Other co-morbidities:</b> PTSD: PTSD-I Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: OAS, GHQ</p> <p><b>Health related QoL or functional status:</b> FAM CIQ SWLS</p>	<p><b>Depression, %:</b> Severe: 8 Moderate: 11 Mild: 0 Minimal: 27</p> <p>BDI score, mean ± SD: <b>G1:</b> 23.0 ± 13.9 <b>G2:</b> 9.9 ± 9.8</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD, n (%): 26 (27) Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: OAS total score, mean ± SD: <b>G1:</b> 4.5 ± 3.8 <b>G2:</b> 2.5 ± 3.0 <b>G1/G2:</b> P = 0.01</p> <p>GHQ score, mean ± SD: <b>G1:</b> 7.6 ± 3.4 <b>G2:</b> 3.5 ± 3.8</p> <p><b>Health related QoL or functional status:</b> FAM score, mean ± SD: <b>G1:</b> 198.8 ± 8.2 <b>G2:</b> 203.1 ± 6.8 <b>G1/G2:</b> P = 0.01</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Bryant et al., 2010</p> <p><b>Country, Setting:</b> Australia, trauma centers</p> <p><b>Enrollment Period:</b> April 2004 to February 2006</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, mos :</b> 3, 12</p> <p><b>Length of follow up:</b> 12 mos</p> <p><b>Dep. Scale/Tool:</b> MINI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 70 yrs old</li> <li>• Hospital admission of more than 24 hours following traumatic injury</li> <li>• Ability to understand and speak English proficiently</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Moderate or severe brain injury (LOC &gt; 30 mins or GCS score &lt; 13)</li> <li>• Currently psychotic or suicidal</li> <li>• Non-Australian visitor</li> <li>• Under police guard</li> </ul> <p><b>TBI Def:</b> Mild TBI: GCS score of 13-15; ICD-9 documented head injury, LOC&lt;30 min, no focal neurologic deficit or intracranial complications</p>	<p><b>Group(s):</b> <b>G1:</b> Participants with mild TBI randomly selected from trauma center admissions <b>G2:</b> Participants with no TBI randomly selected from trauma center admissions</p> <p><b>N screened:</b> 1,477</p> <p><b>N eligible:</b> <b>G1:</b> 437 <b>G2:</b> 647</p> <p><b>N included:</b> <b>G1:</b> 377 <b>G2:</b> 555</p> <p><b>N at conclusion:</b> <b>G1:</b> 321 <b>G2:</b> 496</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age, yrs ± SD:</b> 3 mos: 38.3 ± 13.6 12 mos: 38.9 ± 13.6</p> <p><b>Age ≥16, N (%):</b> 1,084 (100)</p>	<p><b>Depression:</b> MINI: MDD</p> <p><b>Other co-morbidities:</b> PTSD: Clinician Administered PTSD Scale-IV Other anxiety disorder: MINI Irritability: NR Aggression: NR Suicidality: NR Substance use: MINI Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> WHOQOL</p>	<p><b>Depression, n (%):</b> 3 mos: <b>G1:</b> 68 (18.0) <b>G2:</b> 93 (16.8)</p> <p>12 mos: <b>G1:</b> 56 (17.5) <b>G2:</b> 77 (15.5) 54.7% depressed at 12 mos also depressed at 3 mos</p> <p><b>Taking depression medications:</b> Receiving mental health treatment, %: 12 mos: 41.2</p> <p><b>Other co-morbidities, n (%):</b> PTSD: 3 mos: <b>G1:</b> 48 (12.7) <b>G2:</b> 42 (7.6)</p> <p>12 mos: <b>G1:</b> 43 (13.0) <b>G2:</b> 36 (7.2)</p> <p>Other anxiety disorder: GAD: 3 mos: <b>G1:</b> 37 (9.8) <b>G2:</b> 47 (8.5)</p> <p>12 mos: <b>G1:</b> 43 (13.4) <b>G2:</b> 48 (9.7)</p> <p>Other* 3 mos: <b>G1:</b> 119 (31.6) <b>G2:</b> 112 (20.2)</p> <p>12 mos: <b>G1:</b> 107 (33.3) <b>G2:</b> 105 (21.2) 59.9% with anxiety disorder at 12 mos also had disorder at 3 mos</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Chamelian and Feinstein, 2006 See Chamelian et al., 2004</p> <p><b>Country, Setting:</b> Canada, tertiary care hospital</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 6 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 60 yrs old</li> <li>• Mild to moderate TBI</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Mild TBI: GCS score of 13 to 15, LOC &lt; 20 minutes and PTA &lt; 24 hours Moderate TBI: GCS score of 9 to 12, PTA &gt; 24 hours but less than 1 week</p>	<p><b>Group(s):</b> <b>G1:</b> Participants with subjective cognitive complaints <b>G2:</b> Participants without subjective cognitive complaints</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 34 <b>G2:</b> 29</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> <b>G1:</b> 17 (20.6) <b>G2:</b> 3 (10.3)</p> <p><b>N with prior TBI (%):</b> <b>G1:</b> 7 (20.6) <b>G2:</b> 5 (17.2)</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 34.9 ± 12.8 <b>G2:</b> 31.3 ± 10.2</p> <p><b>Age ≥16, n (%):</b> 63 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS score, mean ± SD:</b> <b>G1:</b> 14.6 ± 0.7 <b>G2:</b> 13.7 ± 1.6</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: CAGE Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> <b>G1:</b> 5 (18.5) <b>G2:</b> 0</p> <p><b>Taking depression medications, %:*</b> Psychotropics and/or analgesics: <b>G1:</b> 61.8 <b>G2:</b> 37.9</p> <p><b>Other co-morbidities, %:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: Problem drinking: <b>G1:</b> 32.3 <b>G2:</b> 51.7 Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Chamelian et al., 2004 See Chamelian and Feinstein, 2006</p> <p><b>Country, Setting:</b> Canada, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 6 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 60 yrs old</li> <li>• Non-penetrating mild or moderate TBI</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Mild TBI: GCS score of 13 to 15; LOC &lt; 20 min; PTA &lt; 24 hrs Moderate TBI: GCS score of 9 to 12; PTA &gt; 24 hrs but less than 1 week</p>	<p><b>Group(s):</b> <b>G1:</b> Participants with TBI and positive for the APOE-ε4 allele <b>G2:</b> Participants with TBI and negative for the APOE-ε4 allele</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 19 <b>G2:</b> 71</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> <b>G1:</b> 4 (21.1) <b>G2:</b> 12 (17.0)</p> <p><b>N with prior TBI (%):</b> <b>G1:</b> 6 (31.6) <b>G2:</b> 16 (22.5)*</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 31.2 ± 13.3 <b>G2:</b> 34.1 ± 12.3</p> <p><b>Age ≥16, n (%):</b> 90 (100)</p> <p><b>Global injury severity, AISS, mean ± SD:</b> <b>G1:</b> 12.6 ± 9.5 <b>G2:</b> 13.5 ± 10.3</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: GHQ Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS RHFUQ RPQ GHQ Resumption of work or studies</p>	<p><b>Depression, n (%):</b> <b>G1:</b> 11 (18.2) <b>G2:</b> 51 (11.8)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: GHQ anxiety score, mean ± SD: <b>G1:</b> 2.2 ± 2.6 <b>G2:</b> 3.0 ± 2.7 Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS score, 6 months, mean ± SD: <b>G1:</b> 4.3 ± 0.5 <b>G2:</b> 4.3 ± 0.6 RHFUQ score, 6 months, mean ± SD: <b>G1:</b> 17.9 ± 14.0 <b>G2:</b> 18.7 ± 13.7 RPQ score, 6 months ± SD: <b>G1:</b> 19.6 ± 18.2 <b>G2:</b> 24.6 ± 18.1 GHQ total score, 6 months, mean ± SD: <b>G1:</b> 7 ± 9.0 <b>G2:</b> 9.6 ± 8.6</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Chiu et al., 2006</p> <p><b>Country, Setting:</b> Taiwan, tertiary care hospitals</p> <p><b>Enrollment Period:</b> January 2002 to June 2002</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 1.0 ± 0.7</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> CES-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Admission to one of 22 hospitals with diagnosis of TBI based on the ICD criteria</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Patient transferred from other hospital</li> </ul> <p><b>TBI Def:</b> Newly diagnosed TBI were identified by the presence among the discharge diagnoses of any of the following ICD-9 codes: 800-801.9, 803-804.9, and 850-854.9</p> <p>Mild TBI: GCS score of 14 to 15</p> <p>Moderate TBI: GCS score of 9 to 13</p> <p>Severe TBI: GCS score of 3 to 8</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 675</p> <p><b>N included:</b> 199</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>Depression status prior to TBI:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 45.4 ± 20.3</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Severe: 7.5 Moderate: 22.6 Mild: 66.9</p> <p>AIS-H score, %: 1-2: 52 3-4: 35.7 5: 12.2</p> <p><b>Mechanism/type of injury, %:</b> MVC: 58.1 Falls: 26.3 Violence: 7.1 Others: 8.6</p>	<p><b>Depression:</b> CES-D &gt; 16</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS: Severe, Moderate, Good</p> <p>Cognition TICS: &lt; 38: Impaired</p> <p>Functional Independence: Barthel Index (BI) 0-60: Severe dependence: 61-90: Moderate dependence 91-100: Mild/no dependence</p>	<p><b>Depression, %:</b> 23.9</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS, %: Severe: 5.4 Moderate: 9.7 Good: 84.9</p> <p>TICS, improvement, %: 25.6</p> <p>Functional independence, %: Moderate/severe independence: 40.6 Mild/no independence: 59.5</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Curran et al., 2000 See Parcell et al., 2006; Perlesz et al., 2000</p> <p><b>Country, Setting:</b> Australia, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 1 to 5 years</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b> • Received inpatient rehabilitation</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Severe concussion: Recovery of consciousness delayed; PTA 1-7 days*</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI <b>G2:</b> Patients with orthopedic injuries <b>Ga:</b> Male patients <b>Gb:</b> Female patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 88 <b>G1a:</b> 61 <b>G1b:</b> 27 <b>G2:</b> 40 <b>G2a:</b> 22 <b>G2b:</b> 18</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, time of injury, yrs ± SD:</b> <b>G1:</b> 33.7 ± 15.6 <b>G2:</b> 44.0 ± 18.0</p> <p><b>Age ≥16, n (%):</b> <b>G1:</b> NR <b>G2:</b> 40 (100)</p> <p><b>Global injury severity, days in inpatient and outpatient rehabilitation, mean ± SD:</b> <b>G1:</b> 199.0 ± 181.0 <b>G2:</b> 112.0 ± 112.0</p>	<p><b>Depression:</b> BDI: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: STAI Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Coping Scale for Adults (CSA) Craig Handicap Assessment and Reporting Technique (CHART): 0: maximum degree of handicap 100: no handicap Rosenberg's Self-Esteem Scale: 0-2: High 3-4: Medium 5-6: Low</p>	<p><b>Depression, %:</b> Extremely severe: <b>G1:</b> 14.0 <b>G2:</b> 5.0 Severe: <b>G1:</b> 18.0 <b>G2:</b> 18.0 Mild to moderate: <b>G1:</b> 25.0 <b>G2:</b> 33.0</p> <p><b>BDI score, mean ± SD:</b> <b>G1:</b> 14.4 ± 11.3 <b>G2:</b> 12.3 ± 9.1 <b>G1/G2:</b> <i>P</i> = 0.33 <b>G1a:</b> 14.0 ± 11.1 <b>G1b:</b> 15.3 ± 12.0 <b>G1a/G1b:</b> <i>P</i> = 0.62 <b>G2a:</b> 13.8 ± 9.5 <b>G2b:</b> 10.6 ± 9.5 <b>G2a/G2b:</b> <i>P</i> = 0.29</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: STAI-state score, mean ± SD: <b>G1:</b> 41.9 ± 16.2 <b>G2:</b> 39.8 ± 14.3 <b>G1a:</b> 41.3 ± 14.9 <b>G1b:</b> 43.4 ± 19.2 <b>G1a/G1b:</b> <i>P</i> = 0.58 <b>G2a:</b> 44.5 ± 13.5 <b>G2b:</b> 33.5 ± 13.3 <b>G2a/G2b:</b> <i>P</i> = 0.02</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Deb and Burns, 2007 See Deb et al., 1999 &amp; Deb et al., 1999</p> <p><b>Country, Setting:</b> UK, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 12 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCAN, behavioral checklist</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• A period of unconsciousness</li> <li>• Evidence of fracture on skull X-rays</li> <li>• Contusion or hemorrhage in CT or MRI brain scans</li> <li>• Focal neurological signs</li> <li>• A GCS score of less than 15</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> According to ICD-9 codes</p>	<p><b>Group(s):</b> <b>G1:</b>Patients with TBI aged 18 to 65 <b>G2:</b> Patients with TBI aged 65 and older</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 120 <b>G1:</b> 45</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, mean:</b> <b>G1:</b> 35.5 <b>G2:</b> 79.2</p> <p><b>Age ≥16, n (%):</b> 165 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Minor: <b>G1:</b> 97 (81) <b>G2:</b> 38 (85) Moderate: <b>G1:</b> 16 (13) <b>G2:</b> 6 (13) Severe: <b>G1:</b> 7 (6) <b>G2:</b> 1 (2)</p>	<p><b>Depression:</b> Reported as part of SCAN results; patients with ICD-10 code for depressive disorder</p> <p>Checklist of neurobehavioral symptoms, scored from 1 (most severe) to 6 (least severe); score of 1 to 4 indicates the presence of the symptom</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: Checklist of neurobehavioral symptoms Aggression: NR Suicidality: NR Substance use: NR</p> <p><b>Health related QoL or functional status:</b> GOS ERSS GHQ-28: score of 11 or more is significant</p>	<p><b>Depression, SCAN, n (%):</b> <b>G1:</b> 19 (16)* <b>G2:</b> 5 (11)*</p> <p>Depressed mood, checklist of neurobehavioral symptoms, n (%): <b>G1:</b> 27 (23) <b>G2:</b> 5 (11)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety disorder: NR Irritability: <b>G1:</b> 44 (37) <b>G2:</b> 14 (31) Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses, n (%): Mood swings: <b>G1:</b> 36 (30) <b>G2:</b> 10 (22) Sleep problems: <b>G1:</b> 44 (37) <b>G2:</b> 18(18) Slowness in thinking: <b>G1:</b> 15 (12) <b>G2:</b> 15 (33) Safety hazard: <b>G1:</b> 7 (6) <b>G2:</b> 8 (18) Fatigue: <b>G1:</b> 33 (27) <b>G2:</b> 6 (13)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Deb, Lyons, and Koutzoukis, 1999</p> <p>Deb, Lyons, Koutzoukis et al., 1999<sup>^</sup></p> <p>See Deb and Burns, 2007</p> <p><b>Country, Setting:</b> UK, tertiary care center</p> <p><b>Enrollment Period:</b> July 1994 to June 1995</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 1 year</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCAN, behavioral checklist</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• At least 17 yrs old</li> <li>• A period of unconsciousness</li> <li>• Evidence of fracture on skull X-rays</li> <li>• Contusion or hemorrhage in CT/magnetic resonance imaging scans</li> <li>• Focal neurological signs</li> <li>• A GCS score of less than 15</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Based on ICD-9 codes.</p> <p>Mild TBI: GCS of 13-15</p> <p>Moderate TBI: GCS of 9-12</p> <p>Severe TBI: GCS &lt; 9</p>	<p><b>Group(s):</b> Patients with HI</p> <p><b>N screened:</b> 346</p> <p><b>N eligible:</b> 196</p> <p><b>N included:</b> 164</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n:<sup>^</sup></b> History of psychiatric illness: 28</p> <p><b>N with prior TBI:<sup>^</sup></b> 42</p> <p><b>Age, median yrs (range):</b> 43.5 (18-94)</p> <p><b>Age ≥16, n (%):</b> 196 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n:</b> Mild: 134 Moderate/severe: 30</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> SCAN: NR</p> <p>Depressed mood: based on checklist of neurobehavioral symptoms, scored from 1 (most severe) to 6 (least severe); score of 1 to 4 indicates the presence of the symptom</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: SCAN Irritability: SCAN Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: SCAN</p> <p><b>Health related QoL or functional status:</b> Not reported by depression status Edinburgh Rehab Status Scale (based upon GOS)</p>	<p><b>Depression, n (%):</b> Severe/moderate: 15 (9) Moderate/mild: 17 (10.4) Depressive episode, n (%):<sup>^</sup> 21 (12.8) Depressed mood, n (%): Mild TBI: 22 (16.3) Moderate/Severe TBI: 10 (33.3)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety Disorder: GAD:<sup>^</sup> 3 (2.5) Irritability: Mild/Moderate: 35 (21.3) Severe/Moderate: 23 (14) Aggression: NR Suicidality: NR Substance use:<sup>^</sup> Alcohol: 6 (4.9) Other psychiatric diagnoses: Panic disorder associated with depressive episode: 5 (NR) Psychiatric cases (CIS-R and PSQ): 28 (17)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Dunlop et al., 1991</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> At least 2 months</p> <p><b>Dep. Scale/Tool:</b> Modified version of the NRS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Evidence of deterioration (G1) or improvement (G2) of emotional or cognitive function between the time interval from 2 to 6 months postinjury</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with emotional or cognitive deterioration (an increase of 2 or more points in the total NRS score)</p> <p><b>G2:</b> Patients with emotional improvement (a decrease of 2 or more points in the total NRS score)</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 193</p> <p><b>N included:</b> <b>G1:</b> 34 <b>G2:</b> 34</p> <p><b>N at conclusion:</b> <b>G1:</b> 34 <b>G2:</b> 34</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, %:</b> <b>G1:</b> 18 <b>G2:</b> 21</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 34.6 ± 10.9 <b>G2:</b> 34.6 ± 9.8</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> 10 item neurologic rating scale and 15 item neuropsychiatric rating scale, with scores ranging from 1-5: 5: Severe 1: No impairment</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: Neuropsychiatric rating scale Irritability: NR Aggression: Neuropsychiatric rating scale Suicidality: NR Substance use: Positive Prior History of alcohol abuse Other psychiatric diagnoses: Past history</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, %:</b> Moderate to severe symptoms at 2-6 mos: <b>G1:</b> 57 <b>G2:</b> 44 Showing deterioration after 6 mos: <b>G1:</b> 28 <b>G2:</b> 0</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR Other anxiety disorder: Anxiety: Moderate to severe symptoms at 2-6 mos: <b>G1:</b> 33 <b>G2:</b> 47 Showing deterioration after 6 mos: <b>G1:</b> 26 <b>G2:</b> 0 Irritability: NR Aggression: Agitation/hostility: Moderate to severe symptoms at 2-6 mos: <b>G1:</b> 3 <b>G2:</b> 44 Showing deterioration after 6 mos: <b>G1:</b> 41 <b>G2:</b> 6 Suicidality: NR Substance use: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Evans et al., 2005</p> <p><b>Country, Setting:</b> US, rehabilitation center</p> <p><b>Enrollment Period:</b> December 1998 to March 2002</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> CES-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Participation in the TBIMS research program funded by the National Institute for Disability and Rehabilitation Research</li> <li>• Inclusion criteria for the TBIMS program are medically documented TBI, admission to an affiliated trauma center within 24 hours of injury, admission to the system inpatient BI program within 72 hours of discharge from the trauma center, aged 16 years or older, and provision of informed consent by the participant or legal proxy as appropriate</li> <li>• Resolution of PTA prior to discharge from inpatient rehabilitation (to respond meaningfully to questionnaires)</li> <li>• Adequate language ability to respond to questionnaires</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p>	<p><b>Group(s):</b> Participants with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 96</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, median (IQR):</b> 32 (22, 44)</p> <p><b>Age ≥16, n (%):</b> 96 (100)</p> <p><b>Global injury severity, DRS, admission, mean (IQR):</b> 11 (8,15)</p> <p><b>Severity of TBI, n (%):</b> Severe: 55 (57) Moderate: 18 (19) Mild: 23 (24)</p> <p><b>Mechanism/type of injury, %:</b> Whites (n=69): MVC: 79 Assault: 6.6 African-American (n=27): MVC: 58 Assault: 27</p>	<p><b>Depression:</b> CES-D: 16-20: Mild 21-26: Moderate ≥ 27: Severe</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Satisfaction With Life Scale (SWLS) ranges from 5 to 35 Disability Rating Scale (DRS) ranges from 0-30 Awareness Questionnaire (AQ) scale ranges from 17-85</p>	<p><b>Depression, %:</b> Severe: 25 Moderate: 12 Mild: 17</p> <p>CES-D score, median (IQR): 17 (9,27)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> AQ score, median (IQR): Clinician: Total: 32 (27,37) Cognitive: 12 (9,12) Behavioral: 11 (9,13) Motor: 9 (8,10) Patient: Total: 47 (40,53) Cognitive: 19 (16,22) Behavioral: 17 (15,20) Motor: 11 (9,12) Family: Total: 37 (31,44) Cognitive: 15 (12,17) Behavioral: 14 (11,16) Motor: 10 (8,10)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Fann et al., 2009</p> <p>See Fann et al., 2005; Bombardier et al., 2006; Bombardier et al., 2010</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> July 2004 to October 2004</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mean mos ± SD:</b> 6.4 ± 3.7</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> PHQ-9</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• At least 18 yrs old</li> <li>• English speaking</li> <li>• Hospitalized patients who sustained a traumatic injury to the head, with either the lowest GCS score ≤ 12 or radiological evidence of acute brain abnormality</li> <li>• Resident of greater Puget Sound region (King, Pierce, Kitsap, Jefferson, Mason, Thurston, or Snohomish counties)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Homelessness (or no contact information available)</li> <li>• Incarceration</li> <li>• A history of schizophrenia</li> <li>• Participation in an investigational drug study</li> </ul> <p><b>TBI Def:</b> Complicated mild: GCS 13-15 and abnormal CT scan Moderate: GCS 9-12 Severe: GCS ≤ 8</p>	<p><b>Group(s):</b> Participants with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 145</p> <p><b>N included:</b> 145</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Lifetime history of antidepressants: 54 (37.4) Lifetime history of outpatient mental health services: 21 (14.5)</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age, yrs ± SD:</b> 42.4 ± 18.3</p> <p><b>Age ≥16, N (%):</b> 145 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Complicated mild: 89 (61.4) Moderate: 28 (19.3) Severe: 28 (19.3)</p>	<p><b>Depression:</b> PHQ-9: Major depression based on DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, PHQ-9, n (%):</b> 37 (25.5)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Fann et al., 2005</p> <p>See Bombardier et al., 2006; Fann et al., 2009; Bombardier et al., 2010</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> April 2001 to November 2004</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up, mos:</b> 12</p> <p><b>Dep. Scale/Tool:</b> PHQ-9, SCID, SCL-20, HAM-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• At least 18 yrs old</li> <li>• English speaking</li> <li>• Hospitalized patients who sustained a traumatic injury to the head, with either the lowest GCS score ≤ 12 or radiological evidence of acute brain abnormality</li> <li>• Resident of greater Puget Sound region (King, Pierce, Kitsap, Jefferson, Mason, Thurston, or Snohomish counties)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Homelessness (or no contact information available)</li> <li>• Incarceration</li> <li>• A history of schizophrenia</li> <li>• Participation in an investigational drug study</li> </ul> <p><b>TBI Def:</b> Complicated mild: GCS of 13 to 15 Moderate: GCS of 9 to 12 Severe: GCS of ≤ 8</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 478</p> <p><b>N at conclusion:</b> 135</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 42.0 ± 16.8 (n=135)</p> <p><b>Age ≥16, n (%):</b> 478 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Severe: 34 (25.2) Moderate: 25 (18.5) Complicated mild: 76 (56.3)</p> <p><b>Mechanism/type of injury, n (%):</b> MVC: 56 (41.5) Fall: 45 (33.3) Assault: 15 (11.1) Recreation/Sport: 7 (5.2) Other: 12 (8.9)</p> <p><b>Area of brain injured:</b> NR</p>	<p><b>Depression:</b> PHQ-9: ≥ 10, other criteria SCID:DSM-IV criteria; served as comparator for sensitivity/specificity analyses HAM-D SCL-20</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, PHQ criteria, %:</b> PHQ-9 score ≥ 10: 22.5 PHQ-9 score ≥ 10, at least one cardinal symptom scored ≥ 2: 16.3</p> <p>At least five symptoms scored ≥ 2, at least one cardinal symptom: 11.6</p> <p>At least five symptoms scored ≥ 1, at least one cardinal symptom: 24.1</p> <p>At least one cardinal symptom scored ≥ 2: 20.5</p> <p>Pearson's correlations: PHQ-9, SCL-20: 0.8 (<i>P</i> &lt; 0.001), n=39 0.9 (<i>P</i> &lt; 0.001), n=138 PHQ-9, HAM-D: 0.7 (<i>P</i> &lt; 0.001), n=39 0.8 (<i>P</i> &lt; 0.001), n=138</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Fann et al., 1995</p> <p><b>Country, Setting:</b> US, TBI rehabilitation center</p> <p><b>Enrollment Period:</b> September 1992 to December 1993</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD (range):</b> 32.5 ± 35.1 (1-128)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DIS Version III-A</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Mild or moderate/severe TBI</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Based on ACRM criteria for mild and moderate/ severe TBI</p> <p>Mild: 1) LOC &lt;30 mins 2) PTA &lt;24 hrs 3) Focal neurologic deficits when severity does not differ from the following – LOC&lt;30 mins, GCS 13-15 after 30 mins, PTA &lt;24 hrs</p> <p>Moderate/severe: 1) GCS &lt;13 2) LOC &gt;30 mins 3) PTA &gt;24 hrs</p> <p>Head Injury Symptom Checklist includes subscale for patient self perceptions of injury</p>	<p><b>Group(s):</b> <b>G1:</b> Current major depression <b>G2:</b> Current generalized anxiety disorder <b>G3:</b> Current non-depressed, non-anxious</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 50</p> <p><b>N included:</b> <b>G1:</b> 13 <b>G2:</b> 12 <b>G3:</b> 29</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression, n (%):</b> Major depression, prior to injury: 6 (12) At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Psychiatric disorder: 25 (50)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1+G2:</b> 40.8 ± 13.5 <b>G3:</b> 35.9 ± 12.5 <b>Total:</b> 38.0 ± 13.0</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity (ISS, RTS, etc.):</b> NR</p>	<p><b>Depression:</b> DIS: DSM-III-R criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: DSM-III-R</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: DSM-III-R</p> <p>Other psychiatric diagnoses: DSM-III-R</p> <p><b>Health related QoL or functional status:</b> Medical outcomes health survey: (scored 0-100) Physical functioning: degree to which health limits physical activities Role functioning (physical): degree to which physical health limits work/daily activities. Role functioning (emotional): extent to which mental health interferes with daily activities Social functioning Bodily pain: effect of pain on work</p>	<p><b>Depression, n (%):</b> Major depression: Current: 13 (26) After BI, resolved: 14 (28) Before BI: 6 (12) Lifetime: 33 (66)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR</p> <p>Other anxiety disorder: Current GAD: <b>G1:</b> 4/13 (30.8) <b>Total:</b> 12/50 (24.0)</p> <p>Current panic disorder: <b>G1:</b> 2/13 (15.4) <b>Total:</b> 2/50 (4.0)</p> <p>Current agoraphobia: <b>G1:</b> 0/13 <b>Total:</b> 1/50 (2.0)</p> <p>Irritability: NR Aggression: NR Suicidality: NR Current alcohol/drug use: <b>G1:</b> NR <b>Total:</b> 4/50 (8.0)</p> <p>Current dysthymia: <b>G1:</b> 5/13 (38.5) <b>Total:</b> 7/50 (14.0)</p> <p>Current bipolar disorder: <b>G1:</b> 0/13 <b>Total:</b> 0 /50</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Federoff et al., 1992<sup>^</sup> Jorge, Robinson, and Arndt, 1993* Jorge, Robinson, Arndt, Starkstein et al., 1993† See Jorge, Robinson, Arndt, Forrester et al., 1993; Jorge, Robinson, Starkstein, and Arndt, 1994 ; Jorge, Robinson, Starkstein, and Arndt, 1994</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> NA</p> <p><b>Length of follow up:</b> 12 mos</p> <p><b>Dep. Scale/Tool:</b> DSM-III-R, HAM-D, PSE</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Shock trauma admissions with acute closed head injury</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Penetrating head injuries or associated spinal cord injury</li> <li>Multiple system involvement such as fractures which would influence physical recovery or produce significant secondary brain damage as a result of hypovolemic shock or severe hypoxia (abdominal hemorrhages or lung collapse)</li> <li>Decreased level of consciousness (drowsy, stuporous, or comatose) or delirium</li> <li>Aphasic disorders (unable to follow a two-stage command) that interfered with comprehension of questions</li> </ul>	<p><b>Group(s):</b></p> <p><b>G1<sup>^*</sup>:</b> Patients with major depression</p> <p><b>G1<sup>†</sup>:</b> Patients with major or minor depression</p> <p><b>G2:</b> Nondepressed patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b></p> <p><b>G1<sup>^*</sup>:</b> 17</p> <p><b>G1<sup>†</sup>:</b> 19</p> <p><b>G2:</b> 47</p> <p><b>N at conclusion:</b></p> <p><b>G1<sup>^*</sup>:</b> 17</p> <p><b>G1<sup>†</sup>:</b> 19</p> <p><b>G2:</b> 47</p> <p><b>Depression, n:</b> Prior to injury: 0</p> <p>At time of injury: 0</p> <p><b>Other preexisting psychiatric conditions:</b> Personal history of psychiatric disorder, %:</p> <p><b>G1<sup>^*</sup>:</b> 71</p> <p><b>G1<sup>*</sup>:</b> 24</p> <p><b>G1<sup>†</sup>:</b> 68</p> <p><b>G2<sup>†^</sup>:</b> 37</p> <p><b>G2<sup>*</sup>:</b> 13</p> <p>Personal history of alcohol or drug abuse, n (%):*</p> <p><b>G1:</b> 8 (47)</p> <p><b>G2:</b> 11 (23)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, median yrs (IQR):†</b></p> <p><b>G1:</b> 25 (8.0)</p> <p><b>G2:</b> 27 (13.5)</p>	<p><b>Depression:</b> Patient self-report of depressed mood; structured initial psychiatric evaluation at 1 month post-TBI with assessment for DSM-III criteria for depression; Hamilton Depression Rating Scale (HAM-D); Present State Examination (PSE)</p> <p>5 DSM-III-R symptoms significantly different between depressed and non depressed patients and used for discriminatory analysis: suicidal ideation, inappropriate guilt, anergia, psychomotor agitation, weight loss/poor appetite</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: PSE, DSM-III-R Irritability: DSM-III-R Aggression: NR Suicidality: DSM-III-R Substance use: Patients queried regarding personal history of alcohol and other substance abuse</p>	<p><b>Depression, %:</b></p> <p>Initial evaluation: Mood:† 19 Major:<sup>^*</sup> 17 Minor:<sup>^*</sup> 2</p> <p>3 months: Mood:† 16 Major:<sup>^*</sup> 12 Minor:<sup>^*</sup> 4</p> <p>6 months: Mood:† 12 Major:<sup>^*</sup> 10 Minor:<sup>^*</sup> 1</p> <p>12 months: Mood:† 11 Major:<sup>^*</sup> 8 Minor:<sup>^*</sup> 3</p> <p>Depression, incidence, n (%):</p> <p>3 months: Major: 4/38 (10) Minor: 3/38 (8)</p> <p>6 months: Major: 4/27 (15) Minor: 0/27 (0)</p> <p>12 months: Major: 3/25 (12) Minor: 1/25 (4)</p> <p>DSM-III-R symptoms, median (IQR):<sup>^*</sup></p> <p>Initial evaluation: <b>G1:</b> 3 (3-3.25) <b>G2:</b> 0 (0-1)</p> <p>3 months: <b>G1:</b> 4 (3-5) <b>G2:</b> 0 (0-1)</p> <p>6 months: <b>G1:</b> 4 (3-4) <b>G2:</b> 0 (0-1)</p> <p>12 months: <b>G1:</b> 4 (3.5-4) <b>G2:</b> 0 (0-0)</p> <p>HAM-D score, initial evaluation, median (IQR):†</p> <p><b>G1:</b> 13 (5) <b>G2:</b> 7 (3)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Felde et al., 2006</p> <p><b>Country, Setting:</b> US, psychiatric/ specialty center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DSM III-R, BDI, HAM-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Voluntary, sequential adult patients enrolled in a university substance abuse program</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> A trained research associate at the master's level made an assessment regarding the presence or absence of TBI with unconsciousness during adulthood, asking "As an adult, have you ever been unconscious as the result of a head injury?"</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with prior TBI <b>G2:</b> Patients without prior TBI</p> <p><b>N screened:</b> 550</p> <p><b>N eligible:</b> 550</p> <p><b>N included:</b> <b>G1:</b> 218 <b>G2:</b> 332</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> <b>G1:</b> 218 <b>G2:</b> 0</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 30.2 ± 8.7 <b>G2:</b> 31.8 ± 11.1</p> <p><b>Age ≥16, n (%):</b> 550 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> NR</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p>	<p><b>Depression:</b> DSM III-R: NR BDI: NR HAM-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HAM-A Irritability: NR Aggression: NR Suicidality: BPRS</p> <p><b>Substance use:</b> MN-SAPS (clinician-rated scale) MAST/AD (self-rated scale) Other psychiatric diagnoses: BPRS</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> Depressive disorder: <b>G1:</b> 34 (16) <b>G2:</b> 55 (17) <b>G1/G2:</b> <i>P</i> = 0.854</p> <p>BDI score, mean ± SD: <b>G1:</b> 19.9 ± 11.8 <b>G2:</b> 18.1 ± 12.2 <b>G1/G2:</b> <i>P</i> = 0.106</p> <p>HAM-D score, mean ± SD: <b>G1:</b> 18.3 ± 11.2 <b>G2:</b> 15.8 ± 10.8 <b>G1/G2:</b> <i>P</i> = 0.009</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder, n (%): <b>G1:</b> 12 (6) <b>G2:</b> 20 (6) <b>G1/G2:</b> <i>P</i> = 0.954</p> <p>HAM-A score, mean ± SD: <b>G1:</b> 14.6 ± 9.2 <b>G2:</b> 12.9 ± 8.8 <b>G1/G2:</b> <i>P</i> = 0.032</p> <p>Irritability: NR Aggression: NR Suicidality: Suicide Attempt Ever: <b>G1:</b> 101 (48) <b>G2:</b> 120 (37) <b>G1/G2:</b> <i>P</i> = 0.019</p> <p>Substance abuse diagnosis, n (%): <b>G1:</b> 217 (100) <b>G2:</b> 331 (100)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Franulic et al., 2004</p> <p><b>Country, Setting:</b> Chile, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 2-10 years</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HAM-D</p>	<p><b>Inclusion criteria:</b> See exclusion criteria</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Concomitant pathologies (paraplegia after spinal cord injury, amputations, etc.)</li> <li>Living outside the hospital catchment area</li> </ul> <p><b>TBI Def:</b> NR<sup>^</sup></p>	<p><b>Group(s):</b> <b>G1:</b> TBI patients 2 years postinjury <b>G2:</b> TBI patients 5 years postinjury <b>G3:</b> TBI patients 10 years postinjury</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 71 <b>G2:</b> 73 <b>G3:</b> 58</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, mean*:</b> <b>G1:</b> 37.9 <b>G2:</b> 41.8 <b>G3:</b> 37.2</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Mild TBI: <b>G1:</b> 71.4 <b>G2:</b> 59.1 <b>G3:</b> NR</p>	<p><b>Depression:</b> HAM-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HAM-A Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Employed vs. unemployed NRS-R</p>	<p><b>Depression, HAM-D score, mean ± SD†:</b> <b>G1:</b> 12.0 ± 6.1 <b>G2:</b> 14.0 ± 7.5 <b>G3:</b> 14.6 ± 8.9</p> <p>Depressive symptoms, %: <b>G1:</b> 42.3 <b>G2:</b> NR <b>G3:</b> 59.3</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HAM-A score, mean ± SD†: <b>G1:</b> 19.7 ± 8.5 <b>G2:</b> 20.5 ± 9.2 <b>G3:</b> 18.1 ± 9.7 Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Employed, %: <b>G1:</b> 53.5 <b>G2:</b> 55.6 <b>G3:</b> 69 NRS-R score, mean ± SD: <b>G1:</b> 47.0 ± 9.1 <b>G2:</b> 25.3 ± 9.1 <b>G3:</b> 49.2 ± 11.6</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Frenisy et al., 2006</p> <p><b>Country, Setting:</b> France, tertiary care center</p> <p><b>Enrollment Period:</b> 1998 to 2000</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> G1: 1.02 ± 0.39 G2: 0.93 ± 0.41</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> NRS-R, SCL 90-R</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Admitted patients were selected in alphabetical order</li> <li>G1: Aged 18 to 40 years and a severe, isolated BI with a rated GCS score ≤ 8 and/or have undergone brain surgery within the first 6 hours without any serious associated lesions, or minor lesions associated without long-term extra cranial consequences</li> <li>G2: Aged between 18 and 50 years and had to exhibit a multiple trauma with no associated severe or moderate BI</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Patients with severe or incapacitating pathologies with psychiatric antecedents</li> <li>Patients whose injuries were self-inflicted</li> <li>Patients who exhibited medullar lesions</li> </ul> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> G1: Patients with severe brain injuries G2: Patients with multiple trauma</p> <p><b>N screened:</b> G1: 486 G2: 111</p> <p><b>N eligible:</b> G1: 486 G2: 111</p> <p><b>N included:</b> G1: 25 G2: 25</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> G1: 26.1 ± 9.6 G2: 33.8 ± 10.4</p> <p><b>Age ≥16, n (%):</b> 50 (100)</p> <p><b>Global injury severity, ISS score, mean ± SD:</b> G1: 25.4 ± 10.8 G2: 22.0 ± 10.1</p> <p><b>Severity of TBI, GCS score, mean ± SD:</b> G1: 6.6 ± 1.2 G2: 14.2 ± 2.2</p>	<p><b>Depression:</b> NRS-R: NR SCL 90-R: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NRS-R SCL 90-R Spielberger's State-Trait Anxiety Scale Irritability: NRS-R Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NRS-R SCL 90-R</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, NRS-R, n (%):</b> G1: 19 (76) G2: 19 (76)</p> <p>SCL 90-R, depression score, mean ± SD: G1: 9.7 ± 9.1 G2: 9.4 ± 7.8</p> <p><b>Taking depression medications, n (%):</b> G1: 2 (8) G2: 0</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: Anxiety NRS-R, n (%): G1: 17 (68) G2: 21 (84)</p> <p>SCL 90-R, anxiety score, mean ± SD: G1: 5.2 ± 7.4 G2: 4.7 ± 4.6</p> <p>Spielberger's State score, mean ± SD: G1: 39.4 ± 16.8 G2: 37.7 ± 13.2</p> <p>Spielberger's Trait score, mean ± SD: G1: 44.9 ± 15.4 G2: 41.8 ± 12.3</p> <p>Irritability, n (%): G1: 20 (80) G2: 13 (52)</p> <p>Aggression: NR Suicidality: NR Substance use: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Gagnon et al., 2006</p> <p><b>Country, Setting:</b> Canada, rehabilitation center</p> <p><b>Enrollment Period:</b> 1986 to 2000</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> G1: 3.3 ± 3.15 G2: NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>TBI occurring at or above the age of 16</li> <li>Younger than 60 yrs old at time of study</li> <li>Moderate or severe TBI diagnosis</li> <li>TBI occurred at least 1 year prior to the study in order to ensure that post-TBI behavioral changes were stable</li> <li>Subjects had to show sufficient motor, language, perceptual and memory skills to allow for valid testing</li> <li>Subjects had to be living in the community (none were hospitalized)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Pre-TBI neurological or psychiatric history of an axis II personality disorder in the medical records</li> </ul>	<p><b>Group(s):</b> G1: Participants with TBI G2: Participants matched by gender, age, and education</p> <p><b>N screened:</b> 169</p> <p><b>N eligible:</b> 83</p> <p><b>N included:</b> G1: 30 G2: 30</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: G1: 4 (13) G2: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> G1: 3 (10) G2: 4 (13)</p> <p><b>N with prior TBI:</b> G1: 0 G2: 0</p> <p><b>Age, yrs ± SD:</b> G1: 36.3 ± 13.1 G2: 36.3 ± 13.3</p> <p><b>Age ≥16, n (%):</b> 60 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Severe: G1: 17 (56.7) Moderate: G1: 14 (43.3)</p>	<p><b>Depression:</b> BDI: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: Diagnostic Interview for Borderlines (DIB)</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: DIB</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Interpersonal features: DIB</p>	<p><b>Depression, n (%):</b> Severe: G1: 1 (3) Moderate-severe: G1: 4 (13) Mild-moderate: G1: 2 (7) Minimal: G1: 6 (20)</p> <p>BDI score, mean ± SD: G1: 10.5 ± 8.0 G2: 2.7 ± 4.0 G1/G2: <i>P</i> &lt; 0.001</p> <p>DIB-R, chronic major depression, n (%): G1: 15 (50) G2: 1 (3.3) G1/G2: <i>P</i> &lt; 0.0001</p> <p>DIBR/BDI, correlation coefficient: DT: G1: 0.6 (<i>P</i> = 0.001) G2: 0.5 (<i>P</i> = 0.01) DA: G1: 0.5 (<i>P</i> = 0.01) G2: 0.1 (<i>P</i> = NS) DC: G1: 0.2 (<i>P</i> = NS) G2: 0.2 (<i>P</i> = NS) DI: G1: 0.4 (<i>P</i> = 0.05) G2: 0.7 (<i>P</i> = 0.001) DR: G1: 0.5 (<i>P</i> = 0.01) G2: 0.4 (<i>P</i> = 0.05)</p> <p><b>Taking depression medications during testing, n (%):</b> Anti-convulsive or anti-depressive: 19 (63.3)</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Gass et al., 1991</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 1.1 ± 1.3</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> MMPI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>No history of substance abuse or emotional disturbance</li> <li>Within 5 years of injury</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> Males with closed head trauma</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 58</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: None (see inclusion criteria) At time of injury: None (see inclusion criteria)</p> <p><b>Other preexisting psychiatric conditions:</b> None (see inclusion criteria)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 34.9 ± 13.7</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, LOC, %:</b> &gt; 1 week: 17 1-7 days: 11 &lt; 24 hrs: 72</p> <p><b>Mechanism/type of injury:</b> NR</p>	<p><b>Depression:</b> MMPI: depression (D) scale &gt; 69</p> <p>Harris-Lingoes subjective depression (D1) subscale &gt; 69</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: MMPI subscale</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, MMPI, %:</b> Original profile: 53 Adjusted profile: 36</p> <p>Depression, Harris-Lingoes (D1) subscale, %: 22</p> <p>MMPI depression (D) score, mean ± SD: Original profile: 70.8 ± 14.5 Adjusted profile: 63.8 ± 13.5</p> <p>Harris-Lingoes subjective depression (D1) score, mean ± SD: 59.1 ± 13.0</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: Schizophrenia, MMPI, %: Original profile: 43 Adjusted profile: 12</p> <p>MMPI schizophrenia score, mean ± SD: Original profile: 68.3 ± 15.0 Adjusted profile: 57.8 ± 10.3</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Ghaffar et al., 2006</p> <p><b>Country, Setting:</b> Canada, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 6 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> GHQ, RPCQ</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 60 yrs of age</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Major medical illness such as cardiac or cerebrovascular disease</li> </ul> <p><b>TBI Def:</b> According to ACRM criteria</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with mTBI randomly assigned for assessment and treatment 1 week post-injury</p> <p><b>G2:</b> Patients with TBI not offered follow up and treatment</p> <p><b>Ga:</b> Depressed patients (GHQ <math>\geq</math> 1)</p> <p><b>Gb:</b> Nondepressed patients (GHQ = 0)</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 86 <b>G2:</b> 84 <b>Ga:</b> 35 <b>Gb:</b> 87</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, %:</b> Psychiatric illness: 22.9</p> <p><b>N with prior TBI, n (%):</b> 52/170 (30.6)</p> <p><b>Age, yrs <math>\pm</math> SD:</b> <b>G1:</b> 30.7 <math>\pm</math> 10.9 (n=97) <b>G2:</b> 33.3 <math>\pm</math> 12.4 (n=94)</p>	<p><b>Depression:</b> GHQ: depression subscale <math>\geq</math> 1</p> <p>RPCQ: depression questions</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: GHQ Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Cognitive testing (Stroop Color-Word test, Symbol-Digit Modalities test, The Paced Visual Serial Addition Task, Simple Reaction time, Choice Reaction time, Hopkins Verbal-Learning test, The Vocabulary subset and Letter-Number Sequencing, The Matrix-Reasoning subset of the WAIS-III) RFQ GHQ: social dysfunction subscale and somatic concern subscale</p>	<p><b>Depression, GHQ, n (%):</b> 35/122 (28.7)</p> <p>GHQ total score*, mean <math>\pm</math> SD: <b>G1:</b> 6.6 <math>\pm</math> 7.6 <b>G2:</b> 6.8 <math>\pm</math> 7.9</p> <p>RPCQ total score*, mean <math>\pm</math> SD: <b>G1:</b> 17 <math>\pm</math> 18 <b>G2:</b> 16.3 <math>\pm</math> 15.9</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: GHQ: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> RFQ total score, mean <math>\pm</math> SD: <b>G1:</b> 10.9 <math>\pm</math> 11.5 <b>G2:</b> 10.6 <math>\pm</math> 12.0</p> <p>Stroop Symbol-Digit Modalities, seconds <math>\pm</math> SD: <b>Ga:</b> 12.4 <math>\pm</math> 3.5 <b>Gb:</b> 10.5 <math>\pm</math> 1.8 <b>Ga/Gb:</b> <math>P = 0.01</math></p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Gomez-Hernandez et al., 1997</p> <p><b>Country, Setting:</b> Spain, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury to first assesment, median days (IQR):</b> 31 (32)</p> <p><b>Length of follow up:</b> 12 months</p> <p><b>Dep. Scale/Tool:</b> DSM-IV</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Older than 18 years</li> <li>• Predominant injury involving head trauma</li> <li>• Closed head injury</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating head injuries</li> <li>• Associated spinal cord injury</li> <li>• Multiple non-CNS involvement which would have influenced the course of their recovery (e.g., multiple fractures) or would have led to significant secondary brain damage as a result of severe hypotension or hypoxia (e.g., intra-abdominal hemorrhages, collapsed lungs, etc)</li> <li>• A decreased level of consciousness, disorientation or deliriousness, or had aphasic disorders that would interfere with the psychiatric interview</li> </ul> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> <b>G1:</b> Depressed patients with TBI <b>G2:</b> Non-depressed patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 23 <b>G2:</b> 42</p> <p><b>N at conclusion:</b> <b>G1:</b> 10 <b>G2:</b> 27</p> <p><b>Depression, n:</b> Prior to injury: 0 At time of injury: 0</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> History of alcohol or drug abuse: 30 (46.1) History of psychiatric disorder without alcohol or drug abuse: 9 (13.8)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 27.3 ± 8.4 <b>G2:</b> 29.3 ± 10.3</p> <p><b>Age ≥16, n (%):</b> 65 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Social Functioning Exam (SFE): A semi-structured clinical interview that assesses the patient's satisfaction with his or her social functioning. It consists of 28-items that are rated at 0=normal functioning, 1=moderate impairment, 2=severe impairment.</p>	<p><b>Depression, initial evaluation, n (%):</b> Major depression: 19/65 (29) Minor depression: 4/65 (6)</p> <p>Depression, 3 months, n (%): Major depression: 10/48 (21) Minor depression: 8/48 (15)</p> <p>Depression, 6 months, n (%): Major depression: 12/42 (28) Minor depression: 4/42 (9)</p> <p>Depression, 9 months, n (%): Major depression: 5/43 (12) Minor depression: 9/43 (21)</p> <p>Depression, 1 year, n (%): Major depression: 8/37 (22) Minor depression: 2/37 (5)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Substance use: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Gordon, Brown et al., 1998</p> <p>See Sliwinski et al., 1998</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> 1993 to 1997</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> G1: 14.7 ± 9.3 G2: 7.9 ± 7.9 G3: 14.2 ± 11.8 G4: NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 65 yrs old</li> <li>• Reside in a noninstitutional community setting</li> <li>• At least 1 year postinjury</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Hidden TBI: A blow to the head that, at a minimum, resulted in a dazed and confused state, but is not used as an explanatory principle in an individual's life (i.e. the individual does not identify themselves as a person with TBI)</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Participants with hidden TBI</p> <p><b>G2:</b> Participants with mild TBI</p> <p><b>G3:</b> Participants with head trauma</p> <p><b>G4:</b> Participants with no disability</p> <p><b>N screened:</b> G1: 143 G2-G4: 430</p> <p><b>N eligible:</b> G1: 21 G2-G4: 430</p> <p><b>N included:</b> G1: 21 G2: 21 G3: 21 G4: 21</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> G1: 37.6 ± 11.8 G2: 38.3 ± 11.2 G3: 37.4 ± 12.1 G4: 37.9 ± 12.1</p> <p><b>Age ≥16, n (%):</b> 451 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> BDI &gt; 15</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: Subjective self reported feeling of anxiousness</p> <p>Irritability: Subjective self reported feeling of irritability</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: Bigelow Quality of Life Questionnaire: negative consumption of alcohol and drugs</p> <p>Reported use of Alcoholics Anonymous or other 12-step program</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Bigelow quality of life questionnaire</p> <p>Community Integration Questionnaire (CIQ)</p> <p>Craig Handicap Assessment Capacity Technique (CHART)</p>	<p><b>Depression, %:</b> G1: 23.8 G2: 28.6 G3: 4.8 G4: 0</p> <p>BDI score, mean ± SD: G1: 10.2 ± 6.1 G2: 11.5 ± 10.1 G3: 3.4 ± 5.1 G4: 2.2 ± 2.8 G2/G4: P &lt; 0.003</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> NR PTSD: NR</p> <p>Other anxiety disorder: G1: 57.1 G2: NR G3: NR G4: 0</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: Bigelow quality of life questionnaire, mean score ± SD: Negative consumption alcohol: G1: 53.1 ± 3.8 G2: 55.0 ± 0 G3: 54.4 ± 1.8 G4: 55.0 ± 0</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Gordon, Sliwinski et al., 1998 See Sliwinski et al., 1998</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> 1993 to 1997</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury (yrs):</b> G1: 11.2 G2: 9.1 G3: NA G4: NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 65 yrs old</li> <li>• Reside in non-institutional community setting</li> <li>• At least 1 year postinjury</li> <li>• Exercise (jogging, swimming, biking) for at least 30 mins three times a week for at least the preceding 6 months</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b></p> <p>G1: TBI exercise group G2: TBI non-exercise group G3: Non-TBI exercise group G4: Non-TBI non-exercise group</p> <p><b>N screened:</b> G1+G2: 430 G3+G4: 287</p> <p><b>N eligible:</b> G1: 64 G2: 176 G3: 66 G4: 73</p> <p><b>N included:</b> G1: 64 G2: 176 G3: 66 G4: 73</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> G1: 37.8 ± 10.3 G2: 37.1 ± 10.0 G3: 38.3 ± 12.7 G4: 39.0 ± 11.3</p> <p><b>Age ≥16, n (%):</b> 379 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> BDI &gt; 15</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> TIRR SF-36</p>	<p><b>Depression, %:</b> G1: 12.5 G2: 33.7 G3: 6.1 G4: 6.8 G1+G2/G3+G4: <i>P</i> &lt; 0.0001 G1+G3/G2+G4: <i>P</i> &lt; 0.01</p> <p>BDI score, mean ± SD: Total: G1: 7.8 ± 7.1 G2: 13.9 ± 10.6 G3: 4.1 ± 5.3 G4: 5.4 ± 5.6</p> <p>Somatic items: G1: 2.9 ± 2.7 G2: 5.0 ± 3.9 G3: 1.3 ± 2.2 G4: 2.0 ± 2.1</p> <p>Non-somatic items: G1: 5.4 ± 5.3 G2: 8.8 ± 7.21 G3: 2.7 ± 4.2 G4: 3.4 ± 4.3</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Hawley and Joseph, 2008</p> <p><b>Setting:</b> UK, rehabilitation centers</p> <p><b>Enrollment Period:</b> 1991 to 1997</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, months ± SD:</b> <b>G1:</b> 4.65 ± 4.63 <b>G2:</b> 13.67 ± 17.92 <b>G3:</b> 19.83 ± 26.22</p> <p><b>Length of follow up:</b> 10 years</p> <p><b>Dep. Scale/Tool:</b> HADS, structured questionnaire</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 65 yrs old</li> <li>• Traumatic brain injury</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Non-traumatic brain injury, including subarachnoid hemorrhage</li> </ul> <p><b>TBI Def:</b></p> <p>Mild BI: LOC for 15 minutes or less and/or a GCS of 13 to 15</p> <p>Moderate BI: LOC for more than 15 minutes but less than 6 hours or a PTA of less than 24 hours and/or GCS of 9 to 12</p> <p>Severe BI: LOC for 6 hours or more or a PTA of 24 hours or more and/or GCS of 6 to 8</p> <p>Very severe BI: LOC for 48 hours or more or a PTA of 7 days or more and/or GCS of 3 to 5</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with mild TBI</p> <p><b>G2:</b> Patients with moderate TBI</p> <p><b>G3:</b> Patients with severe TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 563</p> <p><b>N included:</b></p> <p><b>G1:</b> 38 <b>G2:</b> 24 <b>G3:</b> 103</p> <p><b>N at conclusion:</b></p> <p><b>G1:</b> 38 <b>G2:</b> 24 <b>G3:</b> 103</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, 10 year follow up, yrs ± SD (range):</b> 45.5 ± 13.57 (26-79)</p> <p><b>Age ≥16, n (%):</b> 165 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Mild: 23 Moderate: 14.5 Severe: 62.4</p>	<p><b>Depression:</b></p> <p>HADS: 11-21: cases 8-10: borderline 0-7: non-cases</p> <p>10 year questionnaire: Frequent Occasional None</p> <p><b>Other co-morbidities:</b></p> <p>PTSD: NR</p> <p>Other anxiety disorder: HADS</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOSE FIM + FAM COS CiOP</p>	<p><b>Depression, HADS, 6 months, n (%):</b></p> <p>Cases: <b>G1:</b> 3/8 (37.5) <b>G2:</b> 3/12 (25) <b>G3:</b> 10/58 (17.2)</p> <p>Borderline: <b>G1:</b> 0/8 (37.5) <b>G2:</b> 0/12 (25) <b>G3:</b> 17/58 (29.3)</p> <p>Depression, 10 years, n (%):</p> <p>Frequent: <b>G1:</b> 6/38 (15.8) <b>G2:</b> 10/24 (41.7) <b>G3:</b> 22/103 (21.4)</p> <p>Occasional: <b>G1:</b> 20/38 (52.6) <b>G2:</b> 9/24 (37.5) <b>G3:</b> 44/103 (42.7)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR</p> <p>Other anxiety disorder: Anxiety, HADS, 6 months: Cases: <b>G1:</b> 2/8 (25) <b>G2:</b> 4/12 (33.3) <b>G3:</b> 19/58 (32.8)</p> <p>Borderline: <b>G1:</b> 2/8 (25) <b>G2:</b> 1/12 (8.3) <b>G3:</b> 10/58 (17.2)</p> <p>Anxiety, HADS, 10 years: Frequent: <b>G1:</b> 8/38 (21.1) <b>G2:</b> 6/24 (25) <b>G3:</b> 21/99 (21.2)</p> <p>Occasional: <b>G1:</b> 17/38 (44.7) <b>G2:</b> 12/24 (50) <b>G3:</b> 38/99 (38.4)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Hawthorne et al., 2009</p> <p><b>Country, Setting:</b> Australia, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, median mos (range):</b> 32 (3-136)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS, PRIME-MD</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 15 yrs old at time of injury</li> <li>3 mos to 15 yrs since injury</li> <li>Available GCS 24 hr worst score</li> <li>Diagnosis of TBI according to ICD-10</li> <li>Able to consent</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>GOS-E <math>\leq</math>3</li> <li>Spinal cord injury</li> <li>Presence of significant current or pre-injury psychiatric conditions or ongoing severe addiction</li> <li>Inability to understand, cooperate, and answer questions in English</li> <li>Terminal illness</li> <li>Major trauma, including life-threatening accident, rape or other sexual molestation, assault with serious physical injury, torture or kidnap, or having suffered a serious illness</li> </ul>	<p><b>Group(s):</b> <b>G1:</b> Participants with TBI randomly selected from trauma registry <b>G2:</b> Matched participants without TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 203</p> <p><b>N included:</b> <b>G1:</b> 66 <b>G2:</b> 66</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age, yrs <math>\pm</math> SD:</b> 39 <math>\pm</math> 15</p> <p><b>Age <math>\geq</math>16, N (%):</b> NR</p> <p><b>Global injury severity, n (%):</b> General health: <b>G1:</b> Excellent: 3 (4.5) Very good: 25 (37.9) Good: 24 (36.4) Fair/poor: 14 (21.2) <b>G2:</b> Excellent: 15 (22.7) Very good: 24 (36.4) Good: 17 (25.8) Fair/poor: 10 (15.2)</p>	<p><b>Depression:</b> HADS (G1): &gt;8 indicates probable morbidity PRIME-MD (G2): Major depression</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HADS Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> SF-36</p>	<p><b>Depression, HADS, n (%):</b> <b>G1:</b> 15 (22.7)</p> <p>PRIME-MD, n (%): <b>G2:</b> 2 (3.0)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR Other anxiety disorder: <b>G1:</b> 36 Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> SF-36 summary scales, mean <math>\pm</math> SD:: Physical: <b>G1:</b> 48.0 <math>\pm</math> 9.7 <b>G2:</b> 52.3 <math>\pm</math> 9.0 <math>P &lt; .01</math> Mental: <b>G1:</b> 43.3 <math>\pm</math> 10.7 <b>G2:</b> 51.0 <math>\pm</math> 9.6 <math>P &lt; 0.01</math></p> <p><b>Multivariate model predictors:</b> Injury severity (GCS score, coma length, PTA duration) did not predict risk of depression</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Herrmann et al., 2009</p> <p><b>Country, Setting:</b> Canada, tertiary care center</p> <p><b>Enrollment Period:</b> October 2003 to April 2007</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, d ± SD :</b> 113.6 ± 92.7</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Mild-to-moderate TBI within 1 yr</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Prior TBI</li> <li>• A significant acute medical illness</li> <li>• Presence of premorbid psychiatric diagnosis of schizophrenia, dementia, or bipolar disorder</li> </ul> <p><b>TBI Def:</b> Based on ACRM criteria Mild: LOC &lt;30 mins, GCS score at the emergency room of 13-15, duration of PTA &lt;24h, and negative CT scan results Moderate: GCS score of 9-12 and PTA &lt;1 wk Patients with indices of GCS score and PTA in the mild range who had focal injuries coded on their head CT were also categorized as moderate Severe: NR</p>	<p><b>Group(s):</b> Participants with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 200</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> None, see exclusion criteria</p> <p><b>Age, yrs ± SD:</b> Depressed: 37.4 ± 16.3 Nondepressed: 37.5 ± 17.8</p> <p><b>Age ≥16, N (%):</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild: 90 (45.0) Moderate: 110 (55.0)</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> SCID: Based on DSM-IV criteria Major depression-like episode: 5/9 categories of depression module met Depressive features: Not meeting full criteria, but with a predominant mood of “depressed” or answering positively to being depressed or down most of the day nearly every day for at least 2 weeks in the last month</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: 91/96 (94.8) reporting mild to severe symptoms Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> 96 (48.0)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety disorder: NR Irritability: 91/96 (94.8) reporting mild to severe symptoms Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Hibbard et al., 2004 See Ashman et al., 2004</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> March 1995 to December 2000</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, yrs ± SD:</b> <b>G1:</b> 2.51 ± 1.3 <b>G2:</b> 2.63 ± 1.3 <b>G3:</b> 2.52 ± 1.2 <b>G4:</b> 2.16 ± 0.5</p> <p><b>Length of follow up:</b> 1 year</p> <p><b>Dep. Scale/Tool:</b> SCID, BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Between the ages of 18 and 87</li> <li>Self-identified TBI</li> <li>Between 3 months and 4 years postinjury</li> <li>Residents of the United States living within the community</li> <li>Capable of giving informed consent for participation and answering interviews independently</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>The presence of an acquired brain injury (e.g., cerebrovascular accident, aneurysm)</li> <li>A preexisting neurocognitive disorder</li> <li>Any preexisting psychotic disorder (e.g., schizophrenia, psychoses not otherwise specified, depression with psychotic features)</li> </ul> <p><b>TBI Def:</b> According to ACRM criteria<sup>^</sup></p>	<p><b>Group(s):</b> <b>G1:</b> Patients experiencing no depression after TBI <b>G2:</b> Patients with resolved depression after TBI <b>G3:</b> Patients with late-onset depression after TBI <b>G4:</b> Patients with chronic depression after TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 91 <b>G2:</b> 52* <b>G3:</b> 19 <b>G4:</b> 27</p> <p><b>N at conclusion:</b> <b>G1:</b> 91 <b>G2:</b> 52* <b>G3:</b> 19 <b>G4:</b> 27</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, %:</b> Mood disorders: 24 Substance abuse: 22 Anxiety: 9 Eating disorders: 1</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 43.8 ± 16.7 <b>G2:</b> 43.1 ± 14.7 <b>G3:</b> 38.5 ± 17.9 <b>G4:</b> 44.8 ± 10.0</p>	<p><b>Depression:</b> SCID: No depression: Did not meet DSM-IV criteria for major mood disorder at either T1 (time 1=initial screening) or T2 (time 2= 1 year following initial screening). Resolved depression: Diagnosed with major depression at T1 resolved by T2. Late-onset-depression: Not depressed at T1 but met the criteria for DSM-IV diagnoses of major depression at T2. Chronic depression: Met the DSM-IV criteria for major depression at both T1 and T2. BDI: used to measure depression severity at T1 and T2 <b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: DSM-IV Irritability: NR Aggression: NR Suicidality: NR Substance use: DSM-IV Other psychiatric diagnoses: DSM-IV</p>	<p><b>Depression, n:</b> Chronic depression: 27 Late onset depression: 19 Resolved depression: 52* No depression: 91</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety Disorder, %: Initial screening: 19 1 year follow-up: 16 Irritability: NR Aggression: NR Suicidality: NR Substance use, %: Initial screening: 4 1 year follow-up: 6 Other psychiatric diagnoses: Co-occurring psychiatric disorder, initial screening, n (%): <b>G1:</b> 47 (52) <b>G2:</b> 23 (44) <b>G3:</b> 14 (74) <b>G4:</b> 7 (26) Co-occurring psychiatric disorder, 1 year follow-up, n (%): <b>G1:</b> 48 (53) <b>G2:</b> 38 (73) <b>G3:</b> 16 (84) <b>G4:</b> 25 (93)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Hibbard et al., 1998 See Sliwinski et al., 1998</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, years:</b> 7.6</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 65 yrs old</li> <li>• At least 1 year post-TBI</li> <li>• Resident of New York state and living within the community</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Non-traumatic brain injuries (brain tumors, stroke, etc.)</li> </ul> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> Patients with TBI <b>G1:</b> Patients with pre-TBI Axis I diagnosis <b>G2:</b> Patients with no pre-TBI Axis I diagnosis</p> <p><b>N screened:</b> 431</p> <p><b>N eligible:</b> 100</p> <p><b>N included:</b> <b>G1:</b> 51 <b>G2:</b> 49</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury, n (%): 17 (17) At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Dysthymia: 1 (1) PTSD: 6 (6) OCD: 1 (1) Panic disorder: 4 (4) Phobias: 4 (4) Substance use disorder: 40 (40) One Axis 1 disorder: 34 (34) Two or more Axis 1 disorders: 17 (17)</p> <p><b>Depression status prior to TBI:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs:</b> 39.8 ± 10.2</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: SCID Other anxiety disorder: SCID Irritability: NR Aggression: NR Suicidality: NR Substance use: SCID Other psychiatric diagnoses: SCID</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, post-TBI, n (%):</b> MDD: 61 (61) MDD with psychotic features: 14 (14) Dysthymia: 3 (3)</p> <p>Depression, onset post-TBI, n (% resolved): MDD: <b>G1:</b> 16 (69) <b>G2:</b> 32 (59) Dysthymia: <b>G1:</b> 1 (0) <b>G2:</b> 1 (0)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, onset post-TBI, n (% resolved):</b> PTSD: <b>G1:</b> 8 (38) <b>G2:</b> 9 (44)</p> <p>Other anxiety disorder: MDD and anxiety: <b>G1:</b> 7 (43) <b>G2:</b> 18 (39) Panic disorder: <b>G1:</b> 4 (75) <b>G2:</b> 7 (57) GAD: <b>G1:</b> 4 (0) <b>G2:</b> 4 (0) Phobias: <b>G1:</b> 4 (25) <b>G2:</b> 3 (33)</p> <p>Irritability: NR Aggression: NR Suicidality: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Himanan et al., 2009</p> <p>See Koponen et al., 2002 &amp; Koponen et al., 2004; Koponen et al., 2005; Koponen et al., 2006</p> <p><b>Country, Setting:</b> Finland, tertiary care center</p> <p><b>Enrollment Period:</b> February 1998 to April 1999</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> G1: 31.0 ± 3.6 G2: NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI, SCAN</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• A head trauma severe enough to cause TBI and neurological symptoms (including headache and nausea) lasting at least 1 week</li> <li>• At least one of the following: LOC ≥ 1 min, PTA ≥ 30 min, neurological symptoms (excluding headache and nausea) during the first 3 days after injury, or neuroradiological findings suggesting TBI (e.g., skull fracture, intracerebral hemorrhage)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Neurological illness before TBI</li> <li>• Clinical symptoms of a non-traumatic neurological illness that developed after TBI (excluding dementia)</li> <li>• Insufficient cooperation</li> <li>• Unavailability of medical records</li> </ul>	<p><b>Group(s):</b> <b>G1:</b> Participants with TBI <b>G1a:</b> TBI with depressive symptoms <b>G1b:</b> TBI without depressive symptoms <b>G2:</b> Neurologically healthy comparison group</p> <p><b>N screened:</b> <b>G1:</b> 210 <b>G2:</b> NR</p> <p><b>N eligible:</b> <b>G1:</b> 78 <b>G2:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 61 <b>G1a:</b> 32 <b>G1b:</b> 29 <b>G2:</b> 31</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 60.1 ± 10.6 <b>G2:</b> 61.1 ± 7.9</p> <p><b>Age ≥16, N (%):</b> 92 (100)</p>	<p><b>Depression:</b> BDI: Short form version; score &gt;5 indicates depressive symptoms</p> <p>SCAN: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> MMSE: General cognitive impairment</p>	<p><b>Depressive symptoms, BDI, n (%):</b> <b>G1:</b> 32 (52.5) <b>G2:</b> NR</p> <p>BDI mean ± SD: <b>G1a:</b> 9.6 ± 4.3 <b>G1b:</b> 1.0 ± 1.1 <b>G2:</b> 2.7 ± 3.1</p> <p>Major depression, SCAN, n (%): <b>G1:</b> 6 (9.7) <b>G2:</b> NR</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> MMSE, mean ± SD: <b>G1a:</b> 25.6 ± 3.7 <b>G1b:</b> 27.7 ± 1.7 <b>G2:</b> 27.2 ± 2.3</p> <p>G1 vs G2: p=0.026 (NS)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Hoge et al., 2008</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> 2006</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> PHQ-9</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Soldiers from two U.S. Army combat infantry brigades returned from a yearlong deployment in Iraq were administered the questionnaire</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Incompletion of questionnaire</li> <li>Report of head injury without LOC or altered mental status</li> </ul> <p><b>TBI Def:</b> Mild TBI*: Concussion characterized by brief LOC or altered mental status. A soldier was considered to have had a mild traumatic brain injury if any of three questions – regarding “losing consciousness (knocked out),” “being dazed, confused, or ‘seeing stars,’” or “not remembering the injury” – elicited a positive response*</p>	<p><b>Group(s):</b> <b>G1:</b> TBI with LOC <b>G2:</b> TBI with altered mental status (AMS) <b>G3:</b> Other injury <b>G4:</b> No injury</p> <p><b>N screened:</b> 4,618</p> <p><b>N eligible:</b> 2,525</p> <p><b>N included:</b> <b>G1:</b> 124 <b>G2:</b> 260 <b>G3:</b> 435 <b>G4:</b> 1,706</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> NR</p> <p><b>Age ≥16, n (%):</b> 2,525 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> PHQ: subjects had to meet DSM-IV criteria and report impairment in work, home, or interpersonal functioning at the “very difficult” level</p> <p><b>Other co-morbidities:</b> PTSD: Subjects had to meet DSM-IV criteria (one intrusion symptom, three avoidance symptoms, and two hyperarousal symptoms) and had to have substantial distress, as measured by a total score of at least 50.</p> <p>Other anxiety disorder: NR</p> <p>Irritability: PHQ-9</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Measures of Physical Health: Measured by the Patient Health Questionnaire 15-item somatic symptom severity scale (PHQ-15)</p>	<p><b>Depression:</b> Major depression, n (%): <b>G1:</b> 27 (22.9) <b>G2:</b> 21 (8.4) <b>G3:</b> 28 (6.6) <b>G4:</b> 55 (3.3)</p> <p><b>Taking depression medication:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD, n (%): <b>G1:</b> 54 (43.9) <b>G2:</b> 71 (27.3)</p> <p>PTSD Checklist score, mean ± SD: <b>G1:</b> 46.8 ±19.0 <b>G2:</b> 39.8 ±16.3</p> <p>Other anxiety disorder: NR</p> <p>Substance use: NR</p> <p>Irritability: <b>G1:</b> 67 (56.8) <b>G2:</b> 118 (47.6)</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Patient Health Questionnaire score ≥15, n (%): <b>G1:</b> 30 (24.8) <b>G2:</b> 41 (16.1)</p> <p>Post-concussive memory problems, n (%): <b>G1:</b> 29/118 (24.6) <b>G2:</b> 41/253 (16.2) <b>G3:</b> 58/422 (13.7) <b>G4:</b> 124/1,680 (7.4)</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/ Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/ Prevalence & Co-morbidities
<p><b>Author:</b> Holsinger et al., 2002</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> 1996 to 1997</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> Approximately 50 years</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DSM-IV</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>World War II US Navy or Marine Corps male veterans who were on active duty during 1944-1945 and hospitalized during their military service with a diagnosis of head injury, pneumonia, or laceration, puncture, or incision wounds</li> <li>Head trauma that was documented in the military medical records, occurred during military service, and produced LOC, PTA, or nondepressed skull fracture</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Head trauma that penetrated the duramater or resulted in significant cognitive impairment or neurological sequelae (likely to cause substantial limitation in ADLs) more than 3 months after trauma</li> <li>Dementia</li> <li>Head injury prior to enlistment</li> </ul>	<p><b>Group(s):</b></p> <p><b>G1:</b> Veterans with recorded HI</p> <p><b>G2:</b> Veterans with no recorded HI</p> <p><b>N screened:</b> 5,444</p> <p><b>N eligible:</b></p> <p><b>G1:</b> 578</p> <p><b>G2:</b> 1,198</p> <p><b>N included:</b></p> <p><b>G1:</b> 528</p> <p><b>G2:</b> 1,198</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b></p> <p><b>G1:</b> 73.2 ± 3.4</p> <p><b>G2:</b> 72.5 ± 3.8</p> <p><b>Age ≥16, n (%):</b> 1,718 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> NR</p>	<p><b>Depression:</b></p> <p>Major depression: 5 symptoms which included depressed mood or loss of interest/ pleasure</p> <p>Minor depression: 2 symptoms, at least one of which had to be depressed mood or loss of interest/ pleasure</p> <p>Lifetime depression: 2 wks of any of the following:</p> <p>Depressed, sad, or blue mood</p> <p>Loss of interest/ pleasure</p> <p>Irritability</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: CAGE interview questionnaire ≥ 2 positive responses, indicative of possible alcohol abuse</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, lifetime, %:</b></p> <p>Major depression: <b>G1:</b> 18.5</p> <p><b>G2:</b> 13.4</p> <p>Minor depression: <b>G1:</b> 7.1</p> <p><b>G2:</b> 5.3</p> <p>Depression, life-time, HI severity, OR vs. no HI:</p> <p>Severe: 1.99</p> <p>Moderate: 1.40</p> <p>Mild: 1.49</p> <p>Major depression, current, %:</p> <p><b>G1:</b> 11.2</p> <p><b>G2:</b> 8.5</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use, n: <b>G1:</b> 409</p> <p><b>G2:</b> NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Homaifer et al., 2009</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, years ± SD range:</b> 23 ± 15 (1-51)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, BDI-II</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Veterans receiving outpatient and inpatient services for treatment related to TBI and/or PTSD</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• A history of neurologic disease other than TBI</li> <li>• Sleep apnea</li> <li>• Presence of the following psychiatric disorders: schizophrenia, psychosis, or bipolar I disorder</li> <li>• Scores on the BDI-II that were more than 2 SDs higher than a historical mean of scores obtained by persons participating in this VA facility's PTSD Residential Rehabilitation Program</li> <li>• A Computerized Assessment of Response Bias performance of type III (very poor effort) or IV (extreme exaggeration or response bias)</li> <li>• Active substance abuse responses on the SCID-IV that suggested abuse in the 7 days prior to participation</li> </ul>	<p><b>Group(s):</b> Participants with TBI</p> <p><b>N screened:</b> 107</p> <p><b>N eligible:</b> 59</p> <p><b>N included:</b> 52</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> 10 (19) with remote history of multiple TBIs</p> <p><b>Age, yrs ± SD (range):</b> 51.7 ± 10.3 (23-74)</p> <p><b>Age ≥16, N (%):</b> 52 (100)</p> <p><b>Global injury severity):</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild: 25 (48.1) Moderate: 9 (17.3) Severe: 18 (34.6)</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria for MDD</p> <p>BDI-II: Minimal: 0 to 13 Mild: 14 to 19 Moderate: 20 to 28 Severe: 29 to 63</p> <p><b>Other co-morbidities:</b> PTSD: SCID</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, SCID, n (%):</b> 23 (44.2)</p> <p>BDI-II, mean ± SD (range): 25.0 ±14.6 (0-53)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD, n (%): 18 (35)</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Hoofien et al., 2001</p> <p><b>Country, Setting:</b> Israel, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 14.1 ± 5.5</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCL-90-R</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Medically documented TBI occurring at least 5 yrs prior to the study</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Severe psychiatric problems</li> <li>Substance abuse</li> </ul> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> Patients with severe TBI</p> <p><b>N screened:</b> 321</p> <p><b>N eligible:</b> 198</p> <p><b>N included:</b> 76</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 24.9 ± 7.6</p> <p><b>Age ≥16, n (%):</b> 76 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, duration of coma, n (%):</b> No coma: 5 (6.6) &lt; 24 hrs: 9 (11.8) 1-7 days: 13 (17.1) 8-30 days: 26 (34.2) ≥ 30 days: 21 (27.6)</p> <p><b>Mechanism/type of injury, n (%):</b> MVC: 48 (64) Combat: 19 (25) Work accident: 9 (11)</p>	<p><b>Depression:</b> SCL-90-R &gt; 95<sup>th</sup> percentile of normative data</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: SCL-90-R &gt; 95<sup>th</sup> percentile Irritability: NR Aggression: SCL-90-R &gt; 95<sup>th</sup> percentile Suicidality: NR Substance use: NR Other psychiatric diagnoses: SCL-90-R &gt; 95<sup>th</sup> percentile</p> <p><b>Health related QoL or functional status:</b> GSI Acceptance of Disability Questionnaire Extended ADL: social activities, home activities, and independence in mobility subscales</p>	<p><b>Depression, %:</b> 45.3</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: Anxiety, %: 43.8 Irritability: NR Aggression: Elevated SCL-90-R hostility score, %: 51.6 Suicidality: NR Substance use: NR Other psychiatric diagnoses, %: Psychoticism: 35.6 Obsessive-compulsive: 29.7 Phobic-ideation: 27.7 Paranoid ideation: 7.9 Interpersonal: 6.5</p> <p><b>Health related QoL or functional status:</b> GSI score, mean ± SD: 5.5 ± 0.7 Correlation between acceptance of disability and GSI and SCL-90-R subscales: GSI score: -0.7 Somatization: -0.7 Obsessive-compulsive: -0.6 Interpersonal sensitivity: -0.5</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Huang et al., 2005</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 1 year</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, ZDS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>TBI patients with closed head injuries</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Open head injuries</li> <li>Penetrating head injuries (e.g., stab wounds and missile wounds)</li> <li>Non-traumatic brain injuries (e.g., stroke, malignancy and anoxic brain injuries)</li> <li>Past or present disabling injuries in addition to brain trauma (e.g., patients with spinal cord and brain injuries)</li> <li>Pre-existing or current DSM-IV Axis I and II psychiatric disorders as determined by a psychiatrist at the institution</li> </ul> <p><b>TBI Def:</b> Mild: GCS score of 13 to 15 Moderate: GCS score of 9 to 12 Severe: GCS score of 3 to 8</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with mild TBI <b>G2:</b> Patients with moderate TBI <b>G3:</b> Patients with severe TBI</p> <p><b>N screened:</b> 70</p> <p><b>N eligible:</b> 61</p> <p><b>N included:</b> <b>G1:</b> 22 <b>G2:</b> 20 <b>G3:</b> 17</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: None (see exclusion criteria) At time of injury: None (see exclusion criteria)</p> <p><b>Other preexisting psychiatric conditions:</b> None (see exclusion criteria)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 45.5 ± 8.2 <b>G2:</b> 45.9 ± 7.7 <b>G3:</b> 41.7 ± 6.7</p> <p><b>Age ≥16, n (%):</b> 59 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria ZDS cutoff: 55</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, SCID, n (%):</b> <b>G1:</b> 0 <b>G2:</b> 1 (5) <b>G3:</b> 7 (41)</p> <p>MDD, ZDS, n (%): <b>G1:</b> 0 <b>G2:</b> 0 <b>G3:</b> 10 (59)</p> <p>ZDS score, mean ± SD: <b>G1:</b> 24.9 ± 2.1 <b>G2:</b> 42.8 ± 3.5 <b>G3:</b> 54.7 ± 4.8</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Jorge, Robinson, Arndt, Forrester et al., 1993</p> <p>See Federoff et al., 1992 &amp; Jorge, Robinson, and Arndt, 1993 &amp; Jorge, Robinson, Arndt, Starkstein et al., 1993</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> NA</p> <p><b>Length of follow up:</b> 12 months</p> <p><b>Dep. Scale/Tool:</b>, DSM-III-R, HAM-D, PSE</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Shock trauma admissions with acute closed head injury</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Penetrating head injuries or associated spinal cord injury</li> <li>Multiple system involvement such as fractures which would influence physical recovery or produce significant secondary brain damage as a result of hypovolemic shock or severe hypoxia (abdominal hemorrhages or lung collapse)</li> <li>Decreased level of consciousness (drowsy, stuporous, or comatose) or delirium</li> <li>Aphasic disorders (unable to follow a two-stage command) that interfered with comprehension of questions</li> </ul> <p><b>TBI Def:</b> Injury that requires medical treatment</p> <p>Mild TBI: GCS 12 to 15</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with acute-onset major depression</p> <p><b>G2:</b> Patients with delayed-onset major depression</p> <p><b>G3:</b> Nondepressed patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 66</p> <p><b>N at conclusion:</b></p> <p><b>G1:</b> 17</p> <p><b>G2:</b> 11</p> <p><b>G3:</b> 32</p> <p><b>Depression, n:</b></p> <p>Prior to injury: 0</p> <p>At time of injury: 0</p> <p><b>Other preexisting psychiatric conditions, n (%):</b></p> <p>History of psychiatric disorder:</p> <p><b>G1:</b> 12 (70.6)</p> <p><b>G2:</b> 9 (81.8)</p> <p><b>G3:</b> 6 (19.3)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b></p> <p><b>G1:</b> 26.8 ± 5.8</p> <p><b>G2:</b> 28.9 ± 6.4</p> <p><b>G3:</b> 29.5 ± 11.7</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b></p> <p>Patient self-report of depressed mood; structured initial psychiatric evaluation with assessment for DSM-III criteria for depression; Hamilton Depression Rating Scale (HAM-D); Present State Examination (PSE)</p> <p><b>Other co-morbidities:</b></p> <p>PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b></p> <p>Johns Hopkins Functioning Inventory (JHFI)</p> <p>Social Functioning Exam (SFE)</p> <p>Social Ties Checklist (STC)</p>	<p><b>Depression, n (%):</b></p> <p>Initial evaluation: MDD: 17/66 (25.8)</p> <p>Minor depression: 2/66 (3.0)</p> <p>Delayed onset: MDD: 11/66 (16.7)</p> <p>Minor depression: 4/66 (6.1)</p> <p>HAM-D score, mean ± SD:</p> <p><b>G1:</b> 13.8 ± 3.2</p> <p><b>G2:</b> 11.0 ± 1.3</p> <p><b>G3:</b> 5.5 ± 2.4</p> <p><b>Taking depression medications, n:</b> ≥ 2</p> <p><b>Other co-morbidities:</b></p> <p>PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b></p> <p>JHFI score, mean ± SD:</p> <p><b>G1:</b> 2.2 ± 3.3</p> <p><b>G2:</b> 0.4 ± 0.8</p> <p><b>G3:</b> 1.0 ± 0.9</p> <p><b>G1/G2:</b> <i>P</i> &lt; 0.05</p> <p>STC score, mean ± SD:</p> <p><b>G1:</b> 4.2 ± 1.2</p> <p><b>G2:</b> 4.3 ± 1.6</p> <p><b>G3:</b> 3.6 ± 1.1</p> <p><b>G1/G3:</b> <i>P</i> &lt; 0.05</p> <p><b>G2/G3:</b> <i>P</i> &lt; 0.05</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Jorge et al., 2004  See Tateno et al., 2003; Tateno et al., 2004</p> <p><b>Country, Setting:</b> US, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> 12 months</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b> See exclusion criteria</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating head injuries</li> <li>• Clinical or radiological findings suggesting spinal cord injury</li> <li>• Patients with severe comprehension deficits (i.e., those who were unable to complete part II of the Token Test) that precluded a thorough neuropsychiatric evaluation</li> </ul> <p><b>TBI Def:</b> Mild TBI: GCS score between 13 and 15  Moderate TBI: GCS score between 9 and 12, or GCS score of 12 to 15 with intracranial surgical procedures or with focal lesions greater than 15 mL  Severe TBI: GCS score between 3 and 8</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI <b>G2:</b> Trauma patients without central nervous system damage</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 91 <b>G2:</b> 27</p> <p><b>N at conclusion:</b> <b>G1:</b> 74 <b>G2:</b> 27</p> <p><b>Depression, n (%):</b> Prior to injury: <b>G1:</b> 18 (19.8) <b>G2:</b> 4 (14.8)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 36.4 ± 15.7 <b>G2:</b> 35.7 ± 14.1</p> <p><b>Age ≥16, n (%):</b> NR</p> <p><b>Global injury severity, AIS score, mean:</b> 16.8</p> <p><b>Severity of TBI, %:</b> Mild: 44.3 Moderate: 32.5 Severe: 23.2</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: see below</p> <p>Other anxiety disorder: SCID: PTSD, GAD, panic</p> <p>Irritability: NR</p> <p>Aggression: Overt Aggression Scale (OAS)</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses:</p> <p><b>Health related QoL or functional status:</b> FIM RAVLT WCST Trail Making Test Stroop Color-Word Interference Test Multilingual Asphasia Examination</p>	<p><b>Depression, n (%):</b> <b>G1:</b> 30 (33) Initial evaluation: 15/30 (50) 3 months: 9/30 (30) 6 months: 6/30 (20)</p> <p><b>Taking depression medications, n (%):</b> 8 (33)</p> <p><b>Other co-morbidities, %:</b> PTSD: See below Other anxiety Disorder (includes PTSD): 43.2 Irritability: NR Aggression: 36.5 Suicidality: NR Substance use: Concurrent alcohol abuse, patients with TBI and major depression: 6.7 Concurrent other drug abuse, patients with TBI and major depression: 6.7 Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> FIM score, mean: 62.7 RAVLT score, mean ± SD: 8.3 ± 2.8 WCST Perseverative score, mean ± SD: 13.9 ± 11.1</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Jorge, Robinson, Starkstein, and Arndt, 1994</p> <p>See Federoff et al., 1992 &amp; Jorge, Robinson, and Arndt, 1993 &amp; Jorge, Robinson, Arndt, Starkstein et al., 1993</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, days, median (IQR):</b> 31 (32)</p> <p><b>Length of follow up:</b> 12 months</p> <p><b>Dep. Scale/Tool:</b> DSM-III-R, HAM-D, PSE</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Acute closed head injury</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating head injuries or associated spinal cord injury</li> <li>• Multiple system involvement such as fractures which would influence physical recovery or produce significant secondary brain damage as a result of hypovolemic shock or severe hypoxia (abdominal hemorrhages or lung collapse)</li> <li>• Decreased level of consciousness (drowsy, stuporous, or comatose) or delirium</li> <li>• Aphasic disorders (unable to follow a two-stage command) that interfered with comprehension of questions</li> </ul>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with major depression <b>G2:</b> Patients with major depression and anxiety <b>G3:</b> Nondepressed patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 66</p> <p><b>N at conclusion:</b> <b>G1:</b> 10 <b>G2:</b> 7 <b>G3:</b> 47</p> <p><b>Depression, n:</b> Prior to injury: 0 At time of injury: 0</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Psychiatric disorder: <b>G1:</b> 2 (20.0) <b>G2:</b> 2 (28.6) <b>G3:</b> 11 (23.4)</p> <p>Personal history of alcohol abuse, %: <b>G1:</b> 40 <b>G2:</b> 14 <b>G3:</b> 17</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 29.4 ± 6.2 <b>G2:</b> 25.0 ± 5.0 <b>G3:</b> 30.1 ± 10.8</p> <p><b>Age ≥16:</b> NR</p>	<p><b>Depression:</b> Patient self-report of depressed mood; structured initial psychiatric evaluation with assessment for DSM-III criteria for depression; Hamilton Depression Rating Scale (HAM-D-D); Present State Examination (PSE)</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: DSM-III R criteria for Anxiety &amp; depression PSE for mood &amp; anxiety disorders</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use:</p> <p>Other psychiatric diagnoses:</p> <p><b>Health related QoL or functional status:</b> Johns Hopkins Functioning Inventory (JHFI)</p>	<p><b>Depression, n (%):</b> MDD: 17/66 (25.8)</p> <p>HAM-D score, mean ± SD: <b>G1:</b> 12.6 ± 2.9 <b>G2:</b> 15.4 ± 2.9 <b>G3:</b> 6.7 ± 2.6</p> <p><b>Taking depression medications, n:</b> Benzodiazepines: <b>G1+G2:</b> 16 Antidepressants: <b>G1+G2:</b> 0</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: PSE score, mean ± SD: <b>G1:</b> 18.1 ± 3.7 <b>G2:</b> 21.8 ± 4.2 <b>G3:</b> 7.2 ± 4.6</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status, JHFI score, mean ± SD:</b> <b>G1:</b> 2.1 ± 2.0 <b>G2:</b> 0.9 ± 1.1 <b>G3:</b> 1.5 ± 2.8</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Jorge, Robinson, Starkstein, and Arndt, 1994</p> <p>See Federoff et al., 1992 &amp; Jorge, Robinson, and Arndt, 1993 &amp; Jorge, Robinson, Arndt, Starkstein et al., 1993</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, n:</b> 3 months: 52 6 months: 43 12 months: 43</p> <p><b>Length of follow up:</b> 12 months</p> <p><b>Dep. Scale/Tool:</b> Modified version of the PSE using DSM-III-R criteria</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Acute closed head injury</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating head injuries or associated spinal cord injury</li> <li>• Multiple system involvement such as fractures which would influence physical recovery or produce significant secondary brain damage as a result of hypovolemic shock or severe hypoxia (abdominal hemorrhages or lung collapse)</li> <li>• Decreased level of consciousness (drowsy, stuporous, or comatose) or delirium</li> <li>• Aphasic disorders (unable to follow a two-stage command) that interfered with comprehension of questions</li> </ul> <p><b>TBI Def:</b> Injury that requires medical treatment</p> <p>Mild TBI: GCS 12 to 15</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 66</p> <p><b>N at conclusion:</b> 52*</p> <p><b>Depression, n:</b> Prior to injury: 0 At time of injury: 0</p> <p><b>Other preexisting psychiatric conditions:</b> Unable to determine</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> NR</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Severe: 17 Moderate: 68 Mild: 15</p> <p>GCS score, median (IQR): 10 (6)</p> <p><b>Mechanism/type of injury:</b> MVA: "Most"</p> <p><b>Area of brain injured:</b> Reported but unable to determine from data presented</p>	<p><b>Depression:</b> DSM-III-R criteria</p> <p><b>Other co-morbidities:</b> PTSD:NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Johns Hopkins Functioning Inventory (JHFI) Social Functioning Exam (SFE) Social Ties Checklist (STC)</p>	<p><b>Depression, n (%):</b> MDD: 13 (25) Minor depression: 1 (2)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: Bipolar disorder: 1/52 Secondary mania (elevated mood): 5/52</p> <p><b>Health related QoL or functional status:</b> Poor psychosocial outcome, n: Long-lasting MDD: 4/6 No affective disorder: 3/19 <i>P</i> = 0.03 Poor ADL's outcome, n: Long-lasting MDD: 2/4 No affective disorder: 0/10 <i>P</i> = 0.03</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Kant et al., 1998</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DSM-III-R, BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Closed head injury (CHI)</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Mild TBI: GCS 13 to 15 and/or LOC &lt; 20 min Moderate TBI: GCS 9 to 12 and/or LOC &gt; 20 min but &lt; 24 hrs Severe TBI: GCS &lt; 8 and/or LOC &gt; 24 hrs</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> CHI with apathy and no depression <b>G2:</b> CHI with depression and no apathy <b>G3:</b> CHI with apathy and depression <b>G4:</b> CHI with neither apathy nor depression</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 9 <b>G2:</b> 9 <b>G3:</b> 50 <b>G4:</b> 15</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> History of psychiatric treatment: 10 (12)</p> <p><b>N with prior TBI (%):</b> 8 (9.6)</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 29.0 ± 11.9 <b>G2:</b> 41.8 ± 12.9 <b>G3:</b> 38.1 ± 11.5 <b>G4:</b> 42.1 ± 12.9</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> DSM-III-R criteria BDI &gt; 11</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: Apathy Evaluation Scale</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> 59 (71.1)</p> <p>BDI score, mean ± SD: <b>G1:</b> 7.3 ± 2.5 <b>G2:</b> 18.0 ± 5.3 <b>G3:</b> 23.5 ± 8.6 <b>G4:</b> 6.2 ± 2.4</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: Apathy, AES, n (%): 59 (71.1)</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Kashluba et al., 2006</p> <p><b>Country, Setting:</b> Canada, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury days ± SD:</b> G1: 12.1 ± 5.8</p> <p><b>Length of follow up:</b> 3 months</p> <p><b>Dep. Scale/Tool:</b> ICD-10</p>	<p><b>Inclusion criteria:</b> See exclusion criteria</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>History of inpatient treatment for any psychiatric disorder</li> <li>Diagnosis of mental retardation</li> <li>Inability to read fluently in English based on self-report</li> <li>History of TBI more severe than MTBI at any point in their life</li> <li>MTBI within 1 year prior to participation in the MTBI study</li> <li>Any ongoing central nervous system disorder</li> <li>Concurrent pregnancy</li> </ul> <p><b>TBI Def:</b> According to ACRM criteria</p>	<p><b>Group(s):</b> G1: Participants with TBI G2: Uninjured participants matched by age, sex, and years of education</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> G1: 110 G2: 118</p> <p><b>N at conclusion:</b> G1: 110 G2: 118</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> G1: 33.1 ± 12.0 G2: 30.4 ± 11.7</p> <p><b>Age ≥16, n (%):</b> 228 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> NR</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p>	<p><b>Depression:</b> Problem Checklist from the New York Head Injury Family Interview</p> <p>ICD-10 definition for PCS</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: Problem Checklist from the New York Head Injury Family Interview</p> <p>ICD-10 definition for PCS</p> <p>Irritability: ICD-10 definition for PCS</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> PCS symptoms using ICD-10 definition for PCS: fatiguing quickly, dizziness/vertigo, poor concentration, being forgetful, headaches, sleep disturbances, irritability</p>	<p><b>Depression, 1 month, %:</b> G1: 40 G2: 33 G1/G2: P = NS</p> <p><b>Depression, 3 months, %:</b> G1: 39 G2: 37 G1/G2: P = NS</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR</p> <p>Other anxiety disorder: Anxiety/tension, 1 month: G1: 63 G2: 60 G1/G2: P = NS</p> <p>Anxiety/tension, 3 months: G1: 51 G2: 58 G1/G2: P = NS</p> <p>Irritability, 1 month: G1: 61 G2: 47 G1/G2: P &lt; 0.05</p> <p>Irritability, 3 months: G1: 56 G2: 47 G1/G2: P = NS</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Keiski et al., 2007</p> <p><b>Country, Setting:</b> Canada, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, months ± SD:</b> 17.8 ± 16.8</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> PAI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 49 years of age</li> <li>• At least a mild TBI</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Injury received prior to age 15 years</li> <li>• Diagnosis of a condition unrelated to the brain injury (e.g., schizophrenia, developmental disability) that would grossly affect subject performance</li> <li>• Any deficits preventing a subject from completing a substantial portion of a comprehensive neuropsychological evaluation (e.g., aphasia, sensory impairment)</li> </ul> <p><b>TBI Def:</b> Mild TBI: Head injury resulting in any period of loss of consciousness, any loss of memory (whether retrograde or anterograde), any alteration in mental state, or focal neurological deficits (based on ACRM criteria)</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 53*</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression status prior to TBI:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 33.7 ± 10.1</p> <p><b>Age ≥16, n (%):</b> 53 (100)*</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Moderate: 16 (30.1) Mild: 37 (69.8)</p> <p><b>Mechanism/type of injury:</b> Most were MVA</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p> <p><b>Baseline depression status:</b> NR</p>	<p><b>Depression:</b> PAI &gt; 70</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> 24/43 (55.8)*</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

\* Study does not account for difference between group size and total N included

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Kennedy et al., 2005</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD:</b> 76 ± 94</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 18 yrs old</li> <li>At least 3 months postinjury</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Damage to brain tissue caused by an external mechanical force, as evidenced by LOC due to head trauma, PTA, skull fracture, or objective neurological findings</p> <p>Mild TBI: GCS score of 13 to 15</p> <p>Moderate TBI: GCS score of 9 to 12</p> <p>Severe TBI: GCS score of 3 to 8</p>	<p><b>Group(s):</b> Participants with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 78</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD (range):</b> 38.0 ± 12.2 (18-69)</p> <p><b>Age ≥16, n (%):</b> 78 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS score, %:*</b> Severe: 43 Moderate: 12 Mild: 45</p> <p>GCS score, mean ± SD: 9.3 ± 4.8</p> <p><b>Mechanism/type of injury, %:</b> MVC: 77 Assault: 12</p> <p><b>Area of brain injured:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria for MDD or depression due to general medical condition (GMC)</p> <p><b>Other co-morbidities:</b> PTSD: Other anxiety disorder: Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, SCID-I, %:</b> Total depressive disorder: 50 MDD: 14</p> <p>Current MDD with/without a GMC at evaluation, %: 30</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Kersel et al., 2001</p> <p>See Marsh and Kersel, 2006</p> <p><b>Country, Setting:</b> New Zealand, tertiary care center</p> <p><b>Enrollment Period:</b> April 1993 to August 1996</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, days ± SD (range):</b> 201 ± 23 (153-277); 387 ± 33 (345-497)</p> <p><b>Length of follow up:</b> 12 months</p> <p><b>Dep. Scale/Tool:</b> BDI short form, HIBS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 60 yrs old</li> <li>• Consent obtained from next-of-kin to participate in the study</li> <li>• Severe TBI as indicated by a GCS score of &lt; 9</li> <li>• The patient was required to be ventilated on clinical grounds for &gt; 24 hours, where the ventilation was, at least in part, required for the treatment of the TBI</li> <li>• English-speaking</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Previous psychiatric history</li> <li>• Prior significant TBI requiring hospitalization</li> </ul> <p><b>TBI Def:</b> Severe TBI: GCS score of &lt; 9</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> 123</p> <p><b>N eligible:</b> 123</p> <p><b>N included:</b> 123</p> <p><b>N at conclusion:</b> 58</p> <p><b>Depression:</b> Prior to injury: None, see inclusion criteria</p> <p>At time of injury: None, see inclusion criteria</p> <p><b>Other preexisting psychiatric conditions:</b> None, see inclusion criteria</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 28.0 ± 11.0</p> <p><b>Age ≥16, n (%):</b> 123 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Severe: 100</p> <p><b>Mechanism/type of injury, n (%):</b> Road traffic crash: 49 (75) Fall: 7 (11) Assault: 5 (8) Other causes (including sports injuries): 4 (6)</p>	<p><b>Depression:</b> BDI short form: NR</p> <p>HIBS, patient version: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: HIBS</p> <p>Aggression: HIBS</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> HIBS describes other characteristics in addition to depression and anxiety</p> <p>Glasgow outcome scale (GOS): Severely disabled, moderately disabled &amp; good recovery</p>	<p><b>Depression (BDI), 6 mos, n (%):</b> Severe depression: 9 (16) Mild depression: 5 (9) Total clinically depressed: 14 (24)</p> <p>BDI score, 6 mos, mean ± SD: 3.5 ± 4.4</p> <p>Depression (HIBS), 6 mos, n (%): 25 (42)</p> <p>Depression (BDI), 12 mos, n (%): Severe depression: 6 (10)* Mild depression: 8 (14)* Total clinically depressed: 14 (24)</p> <p>BDI score, 12 mos, mean ± SD: 3.6 ± 4.6.</p> <p>Depression (HIBS), 12 mos, n (%): 28 (47)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR</p> <p>Other anxiety disorder: 6 mos: 23 (39) 12 mos: 26 (44)</p> <p>Irritability: 6 mos: 29 (49) 12 mos: 26 (44)</p> <p>Aggression: 6 mos: 8 (14) 12 mos: 9 (15)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Kinsella et al., 1988</p> <p><b>Country, Setting:</b> Australia, rehabilitation centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury mos, n (%):</b> <b>G1:</b> &lt;6: 12 (30.7) 7-12: 11 (28.2) 13-18: 8 (20.5) 19-24: 8 (20.5) <b>G2:</b> NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> Leeds Scales for Anxiety and Depression, VAS-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 60 yrs old</li> <li>• Within 2 yrs of injury</li> <li>• “Close others” had frequent and personal contact with the head injured patients over a variety of situations during the last 2-3 months</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Premorbid history of serious brain impairment</li> </ul> <p><b>TBI Def:</b> Severe CHI: Brain damage without skull penetration, and had been unconscious and incurred a PTA of greater than 24 hrs</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with CHI <b>G2:</b> “Close others” to CHI patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 39 <b>G2:</b> 35</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, mean:</b> <b>G1:</b> 27.8 <b>G2:</b> NR</p> <p><b>Age ≥16, n (%):</b> <b>G1:</b> 39 (100) <b>G2:</b> NR</p> <p><b>Global injury severity (ISS, RTS, etc.):</b> NR</p> <p><b>Severity of TBI, n (%):</b> Duration of LOC: &lt;24 hours: 3 (7.7) 1-7 days: 9 (23.1) 1-4 weeks: 14 (35.9) &gt;4 weeks: 10 (25.6) Unknown: 3 (7.7)</p> <p>Duration of PTA: 1-7 days: 1 (2.6) 1-4 weeks: 9 (23.1) &gt;4 weeks: 29 (74.4)</p>	<p><b>Depression:</b> Leeds Scale for Depression: 15-items that describe common symptoms of depression and cut-off points used were the recommended 6/7</p> <p>Visual Analogue Scale for Depression: The distance (measured in mm), from the non-depressed ends of the scale to where the subjects mark the scale indicates the severity of depression</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: Leeds Scale for Anxiety, Visual Analogue Scale for Anxiety, Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: GHQ</p>	<p><b>Depression, n (%)*:</b> Leeds Scale for Depression: <b>G1:</b> 13 (33.3)</p> <p>VAS-D: <b>G1/G2:</b> <math>\rho=0.5090</math></p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%)*:</b> PTSD: NR</p> <p>Other anxiety disorder: Leeds: <b>G1:</b> 10 (25.6)</p> <p>VAS-A: <b>G1/G2:</b> <math>\rho=0.5265</math></p> <p>Irritability :NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: GHQ minor non-psychotic psychiatric disorders: <b>G1:</b> 23 (59.0)</p> <p><b>Health related QoL or functional status:</b> Physical Disability: A high score on the GHQ was best predicted by physical handicap (accounting for 12% of the variance)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Koponen et al., 2006  See Koponen et al., 2002 &amp; Koponen et al., 2004; Koponen et al., 2005; Himanen et al., 2009</p> <p><b>Country, Setting:</b> Finland, tertiary care center</p> <p><b>Enrollment Period:</b> January 1998 to April 1999</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 31.5 ± 4.5</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• A head trauma severe enough to cause TBI and neurological symptoms (including headache and nausea) lasting at least 1 week</li> <li>• At least one of the following: LOC ≥ 1 min, PTA ≥ 30 min, neurological symptoms (excluding headache and nausea) during the first 3 days after injury, or neuroradiological findings suggesting TBI (e.g., skull fracture, intracerebral hemorrhage)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Neurological illness before TBI</li> <li>• Clinical symptoms of a non-traumatic neurological illness that developed after TBI (excluding dementia)</li> <li>• Insufficient cooperation</li> <li>• Unavailability of medical records</li> </ul>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> 210</p> <p><b>N eligible:</b> 118</p> <p><b>N included:</b> 58</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: 0  At time of injury: 0</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Anxiety disorders: 6 (10.3)  Schizoaffective disorder: 1 (1.7)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 60.7 ± 10.2</p> <p><b>Age ≥16, n (%):</b> 58 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild: 15 (25.9) Moderate: 15 (25.9) Severe: 9 (15.5) Very severe: 19 (32.8)</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR  Other anxiety disorder: DSM-IV criteria  Irritability: NR  Aggression: NR  Suicidality: NR</p> <p><b>Substance use:</b> DSM-IV criteria</p> <p><b>Other psychiatric diagnoses:</b> DSM-IV criteria</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression:</b> Major depression, n (%): Total: 14 (24.1) Patients with contusions: 3/17 (17.6) Patients without contusions: 11/41 (26.8) <i>P</i> = 0.52</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR  Other anxiety disorder: Anxiety disorders: 10 (17.2)  Irritability: NR  Aggression: NR  Suicidality: NR</p> <p><b>Substance use:</b> Alcohol abuse or dependence: 7 (12.1)</p> <p><b>Other psychiatric diagnoses:</b> Any Axis I: 27 (46.6) Delusional: 3 (5.2) Psychotic: 1 (1.7) Bipolar II: 1 (1.7) Dissociative amnesia: 1 (1.7) Dementia: 3 (5.2)</p> <p><b>Any Axis II disorder, n (%):</b> 17 (29.3)</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Koponen et al., 2005</p> <p>See Koponen et al., 2002 &amp; Koponen et al., 2004; Koponen et al., 2006; Himanen et al., 2009</p> <p><b>Country, Setting:</b> Finland, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, median yrs (range):</b> 29.7 (26-47)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>A head trauma severe enough to cause TBI and neurological symptoms (including headache and nausea) lasting at least 1 week</li> <li>At least one of the following: LOC <math>\geq</math> 1 min, PTA <math>\geq</math> 30 min, neurological symptoms (excluding headache and nausea) during the first 3 days after injury, or neuroradiological findings suggesting TBI (e.g., skull fracture, intracerebral hemorrhage)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Neurological illness before TBI</li> <li>Clinical symptoms of a non-traumatic neurological illness that developed after TBI (excluding dementia)</li> <li>Insufficient cooperation</li> <li>Unavailability of medical records</li> </ul>	<p><b>Group(s):</b> <b>G1:</b> Patients referred for neuropsychological evaluation due to a recent TBI or with significant disability after an earlier TBI <b>G2:</b> Participants matched for gender, age, and severity of depression</p> <p><b>N screened:</b> 210</p> <p><b>N eligible:</b> 118</p> <p><b>N included:</b> <b>G1:</b> 54 <b>G2:</b> 54</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, median (range):</b> <b>G1:</b> 58.8 (44-80) <b>G2:</b> 59.0 (44-64)</p> <p><b>Age <math>\geq</math>16, n (%):</b> 108 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria BDI-13: <math>\geq</math> 16: Severe 8-15: Moderate 5-7: Mild 0-4: None/ minimal</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: SCID Irritability: NR Aggression: NR Suicidality: NR Substance use: SCID Other psychiatric diagnoses: SCID</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, SCID, n (%):</b> MDD: <b>G1:</b> 3/54 (5.6)</p> <p><b>Depression, BDI-13, n (%):</b> Severe: <b>G1:</b> 3/52 (5.8) <b>G2:</b> 3/54 (5.6) Moderate: <b>G1:</b> 14/52 (26.9) <b>G2:</b> 14/54 (25.9) Mild: <b>G1:</b> 8/52 (15.4) <b>G2:</b> 6/54 (14.8) None/minimal: <b>G1:</b> 27/52 (51.9) <b>G2:</b> 29/54 (53.7)</p> <p><b>BDI-13 score, median (range):</b> <b>G1:</b> 3.5 (0-26) <b>G2:</b> 4.0 (0-19)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety Disorder: <b>G1:</b> 10/54 (18.5) Irritability: NR Aggression: NR Suicidality: NR Substance use: Alcohol abuse/ dependence: <b>G1:</b> 4/54 (7.4) Other psychiatric diagnoses: Alexithymia: <b>G1:</b> 17/54 (31.5) <b>G2:</b> 8/54 (14.8)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Koponen et al., 2002*</p> <p>Koponen et al., 2004<sup>^</sup></p> <p>See Koponen et al., 2005; Koponen et al., 2006; Himanen et al., 2009</p> <p><b>Country, Setting:</b> Finland, tertiary center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 31.4 ± 4.4</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCAN</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Head trauma severe enough to cause TBI and neurological symptoms (including headache and nausea) lasting at least 1 week</li> <li>At least one of the following: LOC ≥ 1 minute, PTA ≥ t 30 minutes, neurological symptoms (excluding headache and nausea) during the first 3 days after the injury, or neuroradiological findings suggesting TBI (e.g., skull fracture, intracerebral hemorrhage)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Neurological illness before the brain injury</li> <li>Clinical symptoms of a nontraumatic neurological illness that developed after the TBI (excluding dementia)</li> <li>Insufficient cooperation</li> <li>Unavailability of medical records</li> </ul>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI and positive for the APOE-ε4 allele <b>G2:</b> Patients with TBI and negative for the APOE-ε4 allele</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 210</p> <p><b>N included:</b> Total*: 60 <b>G1<sup>^</sup>:</b> 19 <b>G2<sup>^</sup>:</b> 41</p> <p><b>N at conclusion:</b> Total*: 60 <b>G1<sup>^</sup>:</b> 19 <b>G2<sup>^</sup>:</b> 41</p> <p><b>Depression, n:</b> Prior to injury: 0</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Schizoaffective disorder: 1 (1.7) Delusional disorder: 0 Psychotic disorder not otherwise specified: 0 Bipolar II disorder: 0 Panic disorder: 0 Specific phobia: 5 (8.3) Social phobia: 3 (5) Generalized anxiety disorder: 0 Dissociative amnesia: 0</p>	<p><b>Depression:</b> SCAN: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: SCID: DSM-III-R criteria</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: SCID: DSM-III-R criteria</p> <p>Other psychiatric conditions: SCID: DSM-III-R criteria*</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, ever, n:</b> Total: 16 <b>G1:</b> 6 <b>G2:</b> 10</p> <p>Depression, onset post-TBI, n (%): &lt; 1 year: 6 (10) 1-10 years: 0 &gt; 10 years: 10 (16.7)</p> <p>Depression, current, n (%): 6 (10)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: Anxiety disorder, n:<sup>^</sup> Total: 11 <b>G1:</b> 3 <b>G2:</b> 8</p> <p>Generalized anxiety disorder, onset post-TBI, n (%):* &lt; 1 year: 0 1-10 years: 1 (1.7) &gt; 10 years: 0</p> <p>Generalized anxiety disorder, current: 1 (1.7)</p> <p>Substance use: Alcohol abuse or dependence, n:<sup>^</sup> Total: 7 <b>G1:</b> 2 <b>G2:</b> 5</p> <p>Alcohol dependence, onset post-TBI, n (%):* &lt; 1 year: 1 (1.7) 1-10 years: 0 &gt; 10 years: 0</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Kreuter, Sullivan et al., 1998</p> <p>Kreuter, Dahloff et al., 1998<sup>^</sup></p> <p><b>Country, Setting:</b> Sweden, tertiary care center</p> <p><b>Enrollment Period:</b> <b>G1:</b> 1971 to 1990 <b>G2:</b> November 1982 to July 1991 <b>G3:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, median yrs (range):</b> <b>G1:</b> 9 (1-20) <b>G2:</b> 5 (1-9) <b>G3:</b> NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 60 yrs old at time of injury (G1)</li> <li>• Over 18 yrs old at time of study</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Older than 70 at time of study, commotio cerebri injury, severe injuries precluding participation, or heavy alcohol abuse (G1)</li> <li>• Psychiatric illness (G2)</li> </ul> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with TBI</p> <p><b>G2:</b> Patients with spinal cord injuries</p> <p><b>G3:</b> Healthy participants</p> <p><b>N screened:</b></p> <p><b>G1:</b> 152 <b>G2:</b> 252 <b>G3:</b> 334</p> <p><b>N eligible:</b></p> <p><b>G1:</b> 116 <b>G2:</b> 167 <b>G3:</b> 334</p> <p><b>N included:</b></p> <p><b>G1:</b> 92 <b>G2:</b> 167 <b>G3:</b> 264</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b></p> <p><b>G1:</b> 40.5 ± 11.1 <b>G2:</b> 38.9 ± 15.7 <b>G3:</b> 36.9 ± 15.4</p> <p><b>Age ≥16, n (%):</b> 523 (100)</p> <p><b>Global injury severity:</b> Patients required an operation due to their intracranial injuries, %:<sup>^</sup> <b>G1:</b> 45</p>	<p><b>Depression:</b> Six items from the HADS scale</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: HADS Anxiety Irritability: NR Aggression: NR Suicidality: NR Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Global quality of life: recorded on a visual analogue scale (VAS) and endpoints were labeled 'very low' and 'very high'. For G2 and G3 participants, a 0-100 scale was applied while the TBI patients were examined with the aid of an earlier scale version linearly transformed to match the current scale. The higher score the better.</p> <p>Functional limitations: SIP GOS: Severe disability Moderate disability Good Recovery</p>	<p><b>Depression, %:<sup>^</sup></b></p> <p>Morbid depression: <b>G1:</b> 10</p> <p>Borderline depression: <b>G1:</b> 16</p> <p>HADS depression score, mean ± SD: <b>G1<sup>^</sup>:</b> 5.4 ± 4.3 <b>G1:</b> 4.7 ± 4.0 <b>G2:</b> 4.7 ± 3.8 <b>G3:</b> 2.7 ± 2.6 <b>G1/G2:</b> P = NS <b>G1/G3:</b> P &lt; 0.001 <b>G2/G3:</b> P &lt; 0.001</p> <p><b>Taking depression medications, %:</b> <b>G1<sup>^</sup>:</b> 10 <b>G2:</b> NR <b>G3:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder:<sup>^</sup> Morbid anxiety: <b>G1:</b> 12 Borderline anxiety: <b>G1:</b> 18</p> <p>HADS anxiety score, mean ± SD: <b>G1<sup>^</sup>:</b> 5.8 ± 4.9 <b>G2:</b> NR <b>G3:</b> NR</p> <p>Irritability: NR Aggression: NR Suicidality: NR Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Kreutzer et al., 2001</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 2.5 ± 3.5</p> <p><b>Length of follow up:</b> NR</p> <p><b>Dep. Scale/Tool:</b> SCID, NFI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Patients with brain injury referred for outpatient assessment</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> Outpatients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 722</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 36.0 ± 12.1</p> <p><b>Age ≥16, n (%):</b> 722 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, LOC, days ± SD (range):</b> 10.0 ± 27.6 (0-210)</p> <p><b>Mechanism/type of injury, %:</b> MVA: 76 Assault: 8 Falls: 7</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p>NFI scales grouped with DSM-IV symptom domains to examine the value of the NFI as a diagnostic instrument</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: DSM-IV</p> <p>Aggression: NR</p> <p>Suicidality: NFI</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, %:</b> MDD: 42</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: Jumpy or irritable: 25</p> <p>Aggression: NR</p> <p>Suicidality: Threaten to hurt themselves: Sometimes: 13 Often or always: 3</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Levin et al., 2005 See McCauley et al., 2005</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> August 2001 to April 2003</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> 12 weeks</p> <p><b>Dep. Scale/Tool:</b> SCID, CES-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Arrival to the hospital within 24 hours of injury</li> <li>• Blood alcohol level less than 200 mg/dL</li> <li>• Age 16 years and older</li> <li>• Fluent in English or Spanish</li> <li>• Residing in the hospital catchment area (Harris County, Texas)</li> <li>• Diagnosis of non-penetrating TBI</li> <li>• Lowest post-resuscitation GCS &gt; 8</li> <li>• CT scan of the brain performed within 24 hours of arrival</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Undocumented alien, incarcerated, homeless, or on active military service</li> <li>• Spinal cord injury</li> <li>• Previous TBI requiring hospitalization</li> </ul>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 239</p> <p><b>N at conclusion:</b> 129</p> <p><b>Depression:</b> Prior to injury: None (see exclusion criteria) At time of injury: None (see exclusion criteria)</p> <p><b>Other preexisting psychiatric conditions:</b> None (see exclusion criteria)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age at conclusion, yrs ± SD:</b> 31.5 ± 12.8</p> <p><b>Age ≥16, n (%):</b> 129 (100)</p> <p><b>Global injury severity, ISS score, mean ± SD:</b> 3.1 ± 4.1</p> <p>GCS score, mean ± SD: 14.8 ± 0.5</p> <p><b>Mechanism/type of injury, n (%):</b> Car accident: 87 (67.4) Assault: 27 (20.9) Fall/jump: 10 (7.8) Other: 5 (3.9)</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p>Predictors of MDE at 3 months determined by Odds Ratio (OR)</p> <p>Predictive model includes CES-D score, older age, and CT scan results*</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, 3 months, n (%):</b> MDE: 15 (11.6)</p> <p>MDE with abnormal CT scan (vs. no CT abnormality), OR (95% CI): 7.7 (1.4, 43.5)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p> <p><b>Multivariate model predictors, OR (95% CI):</b> Older age at injury: 1.1 (1.0, 1.1) Abnormal CT result: 7.7 (1.4, 43.5) Higher one-week CES-D scores: 1.1 (1.0, 1.2)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Levin et al., 2001 See McCauley et al., 2001</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD :</b> <b>G1:</b> 3.20 ± 1.45 <b>G2:</b> 3.25 ± 1.59</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, CES-D, VAS-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 years or older</li> <li>• Residence within Harris County (the catchment area for the trauma center)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating missile injury of the brain</li> <li>• History of diagnosed schizophrenia</li> <li>• Mental deficiency</li> <li>• Hospitalization for previous TBI</li> <li>• History of treatment for recent substance abuse</li> <li>• Blood alcohol level exceeding 200 mg/dL when examined in the EC</li> </ul> <p><b>TBI Def:</b> Mild TBI: A closed head injury producing a period of unconsciousness no longer than 20 min in duration, lowest postresuscitation GCS score of 13 to 15, no extracranial injury that necessitated surgical repair under general anesthesia, and CT findings within 24 hr after injury indicating normal intracranial findings or a brain lesion that did not require surgical evacuation</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with mild/moderate TBI <b>G1a:</b> Patients with mild TBI <b>G1b:</b> Patients with moderate TBI <b>G2:</b> Patients with general trauma</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 69 <b>G2:</b> 52</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 35.1 ± 14.7 <b>G2:</b> 36.3 ± 13.4</p> <p><b>Age ≥16, n (%):</b> 121 (100)</p> <p><b>Global injury severity (ISS), mean (range):</b> <b>G1:</b> 5.9 (0-26) <b>G2:</b> 4.2 (0-17)</p> <p><b>Severity of TBI, n:</b> Mild: <b>G1a:</b> 60 Moderate: <b>G1b:</b> 9</p>	<p><b>Depression:</b> SCID: DSM-IV criteria CES-D: NR VAS-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: PTSD Checklist Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Outcomes not reported separately for TBI (only for both groups combined) based on depression status</p>	<p><b>Depression, SCID, n :</b> <b>G1a:</b> 11 <b>G1b:</b> 1 MDD, n (%): <b>G1:</b> 12 (17) <b>G2:</b> 3 (6) <b>G1/G2:</b> <i>P</i> = 0.09</p> <p>CES-D score, mean ± SD: <b>G1:</b> 22.1 ± 15.2 <b>G2:</b> 17.2 ± 14.6</p> <p>VAS-D score, mean ± SD: <b>G1:</b> 40.8 ± 36.7 <b>G2:</b> 23.8 ± 32.8</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD, n (%): <b>G1a:</b> 8 (13) <b>G1b:</b> 0</p> <p>PTSD checklist, mean ± SD: <b>G1:</b> 25.5 ± 17.3 <b>G2:</b> 17.2 ± 15.5</p> <p>PTSD and MDD: <b>G1:</b> 4</p> <p>Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Lima et al., 2008</p> <p><b>Country, Setting:</b> Brazil, tertiary care center</p> <p><b>Enrollment Period:</b> September 2004 to October 2004</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> At least 18 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>GCS score between 13 and 15 with at least one of the following symptoms on hospital admission: headache, vertigo, amnesia, nausea, vomiting or LOC for less than 15 minutes</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Any history of head trauma (G2)</li> </ul> <p><b>TBI Def:</b> Mild head trauma (MHT): A transient neurological deficit after a trauma resulting from acceleration and deceleration forces that cause impairment or LOC lasting less than 15 min, short retrograde amnesia, change in the level of consciousness without focal neurological deficits and GCS score between 13 and 15 at hospital admission</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with MHT</p> <p><b>G2:</b> Participants living in the same household as G1 patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> <b>G1:</b> 41</p> <p><b>N included:</b> <b>G1:</b> 39 <b>G2:</b> 39</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI, %:</b> <b>G1:</b> NR <b>G2:</b> 0 (see exclusion criteria)</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 39 ± 2.87 <b>G2:</b> 40 ± 2.14</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS score:</b> <b>G1:</b> 13 to 15</p> <p>Injury on CT, n: <b>G1:</b> 6 No injury on CT, n: <b>G1:</b> 35</p>	<p><b>Depression:</b> HADS: 15-21: Abnormal 8-14: Borderline 0-7: Normal</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HADS, see depression cutoffs Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> SF-36</p>	<p><b>Depression, n (%):</b> Abnormal: <b>G1:</b> 9 (25.0) <b>G2:</b> 4 (11.1) Borderline: <b>G1:</b> 7 (19.4) <b>G2:</b> 6 (16.7)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety disorder: Abnormal: <b>G1:</b> 17 (47.2) <b>G2:</b> 8 (22.2) Borderline: <b>G1:</b> 9 (25.0) <b>G2:</b> 10 (27.8) Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status, SF36 domain scores, mean ± SD:</b> Functional capacity: <b>G1:</b> 77.4 ± 3.6 <b>G2:</b> 93.0 ± 2.2 Physical aspects: <b>G1:</b> 57.7 ± 6.9 <b>G2:</b> 71.6 ± 6.1 Pain: <b>G1:</b> 59.2 ± 4.9 <b>G2:</b> 73.9 ± 4.1 Overall health condition: <b>G1:</b> 58.1 ± 5.1 <b>G2:</b> 76.1 ± 4.1</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Linn et al., 1994</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD:</b> 70.3 ± 65.2</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCL-90-R</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 1 year postinjury</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> <b>G1:</b> TBI patients <b>G2:</b> Spouses</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 60 <b>G2:</b> 60</p> <p><b>N at conclusion:</b> <b>G1:</b> 60 <b>G2:</b> 60</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 40.8 ± 10.4 <b>G2:</b> 40.8 ± 9.9</p> <p><b>Age ≥16, n (%):</b> 120 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, PTA, n (%):</b> ≤ 1 week: 9 (15.0) 1-2 weeks: 7 (11.6) &gt; 2 weeks: 41 (68.3)</p> <p>LOC, days ± SD: 22.0 ± 41.2</p>	<p><b>Depression:</b> SCL-90 R depression subscale, T-scores: &lt; 60: no elevation 60-69: mild elevation 70-79: moderate elevation &gt; 79: severe elevation</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: SCL-90 R anxiety sub-scale, T-scores: see depression cutoffs Irritability: NR Aggression: Social aggression scale Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Health and Activity Limitations Survey (HALS), including motor disability and sensory disability subscores</p>	<p><b>Depression, %:</b> Severe: <b>G1:</b> 15.3 <b>G2:</b> 1.7 Moderate: <b>G1:</b> 13.6 <b>G2:</b> 26.7 Mild: <b>G1:</b> 40.7 <b>G2:</b> 45</p> <p>SCL-90 R depression subscale, T-score, mean ± SD: <b>G1:</b> 63.9 ± 13.3</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: Anxiety, %: Severe: <b>G1:</b> 8.9 <b>G2:</b> 1.7 Moderate: <b>G1:</b> 8.9 <b>G2:</b> 20 Mild: <b>G1:</b> 32.1 <b>G2:</b> 33.3</p> <p>SCL-90 R anxiety subscale, T-score, mean ± SD: <b>G1:</b> 62.1 ± 16.9</p> <p>Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> MacNiven and Finlayson, 1993</p> <p><b>Country, Setting:</b> Canada, NR</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> 1-2 years</p> <p><b>Dep. Scale/Tool:</b> MMPI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Diagnosis of CHI</li> <li>• Neurocognitive test results indicating competence to complete the MMPI</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> Patients with CHI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 59</p> <p><b>N at conclusion:</b> 14</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, mean yrs:</b> Men: 27 (n=42) Women: 22 (n=17)</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> NR</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> MMPI: elevated score in scale 2</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: Hypochondriasis: MMPI scale 1 Hysteria: MMPI scale 3 Psychopathic deviate: MMPI scale 4 Paranoia: MMPI scale 6 Psychasthenia: MMPI scale 7 Schizophrenia: MMPI scale 8 Hypomania: MMPI scale 9 Social introversion: MMPI scale 0</p> <p>T-score ≥ 70: elevated MMPI scale</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, elevated scale 2, (%):</b> Initial assessment: 40.68 1 year: 40.7 2 years: 42.9</p> <p>MMPI scale 2, T-score, mean ± SD: Initial assessment: 66.2 ± 14.3 1 year: 65.7 ± 15.4</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, T-score, mean ± SD:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: Hypochondriasis: Initial assessment: 60.3 ± 19.8 1 year: 60.4 ± 10.2</p> <p>Hysteria: Initial assessment: 61.8 ± 9.5 1 year: 61.4 ± 12.3</p> <p>Psychopathic deviate: Initial assessment: 63.2 ± 10.4 1 year: 67.5 ± 12.8</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Marsh and Kersel, 2006</p> <p>See Kersel et al., 2001</p> <p><b>Country, Setting:</b> New Zealand, tertiary care center</p> <p><b>Enrollment Period:</b> April 1993 to August 1996</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD:</b> 386 ± 31</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HIBS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Ventilation on clinical grounds was required for &gt; 24 hours, at least in part, for treatment of TBI</li> <li>• Between 16 and 70 years of age</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Non-English speaking</li> <li>• Previous hospital admission for TBI or psychiatric illness</li> </ul> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> Patients with TBI and caregivers nominated by family members</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 123</p> <p><b>N included:</b> 62</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 28 ± 11</p> <p><b>Age ≥16, n (%):</b> 62 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Severe: 50 (81) Moderate: 9 (15) Mild: 3 (5)</p> <p><b>Mechanism/type of injury, n (%):</b> Road traffic crash: 47 (76) Fall: 6 (10) Assault: 5 (8) Other: 4 (7)</p>	<p><b>Depression:</b> HIBS, self-report and caregiver versions: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: HIBS</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS: Severe disability, Moderate disability, Good recovery</p>	<p><b>Depression, n (%):</b> Self-report: 32 (52) Caregivers: 32 (52)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR</p> <p>Other anxiety disorder: Self-report: 28 (45) Caregivers: 32 (52)</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOSE, n (%): Severe disability: 15 (24) Moderate disability: 13 (21) Good recovery: 34 (55)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> McCauley et al., 2005 See Levin et al., 2005</p> <p><b>Country, Setting:</b> US, trauma center</p> <p><b>Enrollment Period:</b> January 1999 to April 2003</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD:</b> 86.4 ± 17.4</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, CES-D, VAS-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Arrival to hospital within 24 hours of injury</li> <li>• Blood alcohol level &lt; 200 mg/dL</li> <li>• Age 16 years or older</li> <li>• Fluent in English or Spanish</li> <li>• Residing in the hospital catchment area (Harris County, TX)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Undocumented alien, incarcerated, homeless, or on active military service</li> <li>• Spinal cord injury</li> <li>• Previous TBI requiring hospitalization</li> <li>• History of substance dependence, mental retardation, major psychiatric disorders, or other central nervous system disturbance</li> </ul>	<p><b>Group(s):</b></p> <p><b>G1:</b> Postconcussional disorder, DSM-IV criteria <b>G2:</b> No PCD <b>G3:</b> Postconcussional syndrome, ICD-10 criteria <b>G4:</b> No PCS</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 854</p> <p><b>N included:</b> Total: 340 <b>G1:</b> 59 <b>G2:</b> 281 <b>G3:</b> 183 <b>G4:</b> 157</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 32.3 ± 13.5*</p> <p><b>Age ≥16, n (%):</b> 340 (100)</p> <p><b>Global injury severity, ISS not including head region, mean ± SD:</b> <b>G1:</b> 3.0 ± 4.6 <b>G2:</b> 4.6 ± 5.6 <b>G3:</b> 4.0 ± 5.3 <b>G4:</b> 4.6 ± 5.6</p>	<p><b>Depression:</b> SCID: DSM-IV criteria CES-D: NR VAS-D: NR</p> <p><b>Other co-morbidities:</b> PTSD (PTSD Checklist-Civilian Form; SCID PTSD) and anxiety grouped together Other anxiety disorder: see PTSD Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS-E</p>	<p><b>Depression, SCID, current MDE, n (%):</b> <b>G1:</b> 28 (47.5) <b>G2:</b> 23 (8.2) <b>G3:</b> 48 (26.2) <b>G4:</b> 3 (1.9)</p> <p>CES-D score, mean ± SD: <b>G1:</b> 33.9 ± 1.7 <b>G2:</b> 17.5 ± 0.9 <b>G3:</b> 26.1 ± 1.0 <b>G4:</b> 11.2 ± 1.1</p> <p>VAS-D score, mean ± SD: <b>G1:</b> 57.5 ± 4.2 <b>G2:</b> 29.1 ± 2.4 <b>G3:</b> 45.8 ± 2.5 <b>G4:</b> 15.9 ± 2.8</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD/Anxiety: SCID-PTSD, n (%): <b>G1:</b> 21 (35.6) <b>G2:</b> 18 (6.4) <b>G3:</b> 33 (18.0) <b>G4:</b> 6 (3.8)</p> <p>PCL-C score, mean ± SD: <b>G1:</b> 38.2 ± 1.9 <b>G2:</b> 17.1 ± 1.1 <b>G3:</b> 29.1 ± 1.1 <b>G4:</b> 9.5 ± 1.2</p> <p>Other anxiety disorder: see PTSD Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> McCauley and Boake et al., 2001</p> <p>See Levin et al., 2001</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, days ± SD :</b> 31.4 ± 8.1; 87.7 ± 21.8</p> <p><b>Length of follow up:</b> 3 months</p> <p><b>Dep. Scale/Tool:</b> SCID, CES-D, VAS-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 16 years of age</li> <li>Non-penetrating head injury (G1)</li> <li>CT scan performed within 24 hrs of injury (G1)</li> <li>Fluency in English or Spanish</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Previous hospitalization for head trauma</li> <li>Preinjury major neuropsychiatric disorder</li> <li>Preinjury substance dependence (including alcohol)</li> <li>Pre-existing CNS disturbance (e.g., HIV/AIDS, seizure disorder, strokes, Parkinsonism, etc.)</li> <li>Associated spinal cord injury</li> <li>Undocumented resident status</li> <li>Blood alcohol level (BAL) ≥ 200 mg/dL when the GCS score was obtained without external signs of head trauma and in conjunction with a normal CT scan (G1)</li> <li>Surgery with general anesthesia for extracranial injuries</li> </ul>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with TBI</p> <p><b>G1a:</b> Patients with mild TBI</p> <p><b>G1b:</b> Patients with moderate TBI</p> <p><b>G2:</b> Patients with general trauma</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b></p> <p><b>G1:</b> 115</p> <p><b>G2:</b> 85</p> <p><b>N at conclusion:</b></p> <p><b>G1:</b> 115</p> <p><b>G2:</b> 85</p> <p><b>Depression, n (%):</b> Prior to injury:</p> <p><b>G1a:</b> 7 (7.9)</p> <p><b>G1b:</b> 3 (11.5)</p> <p><b>G2:</b> 7 (8.2)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age, time of injury, yrs ± SD:</b></p> <p><b>G1:</b> 33.4 ± 13.7</p> <p><b>G2:</b> 34.5 ± 12.5</p> <p><b>Age ≥16, n (%):</b> 200 (100)</p> <p><b>Global injury severity (ISS), mean ± SD:</b></p> <p><b>G1:</b> 4.9 ± 6.1</p> <p><b>G2:</b> 3.7 ± 4.4</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p>CES-D: NR</p> <p>VAS-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: SCID</p> <p>PCL-C</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Outcomes not reported by depression status</p>	<p><b>Depression, SCID, n (%):</b> Current MDD, n (%):</p> <p><b>G1a:</b> 19 (21.4)</p> <p><b>G1b:</b> 6 (23.1)</p> <p><b>G2:</b> 14 (16.5)</p> <p>CES-D score, mean ± SD:</p> <p><b>G1:</b> 22.5 ± 14.7</p> <p><b>G2:</b> 19.1 ± 14.1</p> <p>VAS-D score, mean ± SD:</p> <p><b>G1:</b> 40.1 ± 34.8</p> <p><b>G2:</b> 28.8 ± 32.1</p> <p>Dysthymia, n: Total: 2</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD, SCID, n (%):</p> <p><b>G1a:</b> 11 (12.4)</p> <p><b>G1b:</b> 4 (15.4)</p> <p><b>G2:</b> 12 (14.1)</p> <p>PCL-C score, mean ± SD:</p> <p><b>G1:</b> 24.3±16.7</p> <p><b>G2:</b> 20.9 ± 17.2</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: PCD, n (%):</p> <p><b>G1a:</b> 27 (33.0)</p> <p><b>G1b:</b> 8 (30.8)</p> <p><b>G2:</b> 13 (15.3)</p> <p>MDD among PCD patients, %: 47.9</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> McCauley and Levin et al., 2001</p> <p><b>Country, Setting:</b> US, trauma centers</p> <p><b>Enrollment Period:</b> October 1994 to November 1998</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, days ± SD:</b> 94.1 ± 10.2</p> <p><b>Length of follow up:</b> 6 months</p> <p><b>Dep. Scale/Tool:</b> NRS-R</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 15 to 65 yrs old</li> <li>• Abnormal CT within 24 hrs of injury</li> <li>• Postresuscitation GCS motor score of 1 to 5 (total GCS ≤ 8)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Evidence of hypotension (systolic BP &lt; 90 mm Hg for ≥ 30 mins after resuscitation)</li> <li>• Hypoxia (saturation &lt; 94%) for 30 minutes after resuscitation</li> <li>• Estimated AIS score of ≥ 4 for any organ system</li> <li>• GCS of 3 with uncreative pupils</li> <li>• Inability to randomize within 6 hours of injury</li> </ul> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with severe closed HI meeting inclusion criteria <b>G2:</b> Patients with severe closed HI not meeting inclusion criteria</p> <p><b>N screened:</b> 392</p> <p><b>N eligible:</b> 392</p> <p><b>N included:</b> <b>G1:</b> 315 <b>G2:</b> 77</p> <p><b>N at conclusion:</b> <b>G1:</b> 210 <b>G2:</b> 77</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 29.5 ± 11.0 <b>G2:</b> 35.4 ± 13.4</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS score, mean ± SD:</b> <b>G1:</b> 6.0 ± 1.2 <b>G2:</b> 5.4 ± 1.3</p>	<p><b>Depression:</b> NRS-R: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NRS-R Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NRS-R</p> <p><b>Health related QoL or functional status:</b> Cognitive battery: (Buschke verbal selective reminding test, immediate and delayed recall trials of the Rey-Osterrieth complex figure, trial making test B, symbol digit modalities, grooved peg board, controlled oral word association test)</p>	<p><b>Depression, 6 months, %:</b> Severe: 0.5 Moderate: 15.7 Mild: 34.8</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR Other anxiety disorder: Severe: 0 Moderate: 10.0 Mild: 36.7</p> <p>Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: Liability of mood: Severe: 0.5 Moderate: 3.3 Mild: 21.9 Unusual thought content: Severe: 0.5 Moderate: 1.0 Mild: 12.4 Disinhibition: Severe: 1.0 Moderate: 4.3 Mild: 12.9 Hyperactivity/ agitation: Severe: 0.5 Moderate: 1.0 Mild: 11.4</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> McCleary et al., 1998</p> <p>See Satz et al., 1998 &amp; Satz et al., 1998</p> <p><b>Country, Setting:</b> US, tertiary care centers</p> <p><b>Enrollment Period:</b> 1991 to 1995</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> 12 months</p> <p><b>Length of follow up:</b> 12 months</p> <p><b>Dep. Scale/Tool:</b> SCL-90-R, NRS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 16 yrs old</li> <li>Moderate to severe TBI (G1)</li> <li>GCS score of 12 or less, or GCS score of 13 or higher if abnormalities noted on the admission CT scan, or if the condition deteriorated to below 13 on the GCS prior to discharge (G1)</li> <li>Bodily injuries other than to the head (G2)</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI <b>G2:</b> Other injury patients matched by age, gender, and AIS score</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 105 <b>G2:</b> 40</p> <p><b>N at conclusion:</b> <b>G1:</b> 66 <b>G2:</b> 25</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 31.1 ± 13.1^ <b>G2:</b> 34.1 ± 11.7</p> <p><b>Age ≥16, n (%):</b> 145 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI (GCS):</b> All patients had moderate to severe injury</p> <p><b>Mechanism/type of injury:</b> NR</p>	<p><b>Depression:</b> SCL-90-R: &gt; 2 SD above the mean NRS: scores of 4-7 on item 13</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Based on GOS: ≥ 3 Severe disability Moderate disability Good recovery</p>	<p><b>Depression, n (%):</b> SCL-90-R and NRS, 6 mos: <b>G1:</b> 44/105 (41.9) <b>G2:</b> 8/40 (20)</p> <p>SCL-90-R and NRS, 12 mos: <b>G1:</b> 24/66 (36.3) <b>G2:</b> 8/26 (30.8)</p> <p>SCL-90-R, 6 mos: <b>G1:</b> 23/94 (24.4) <b>G2:</b> 5/33 (15.2)</p> <p>SCL-90-R, 12 mos: <b>G1:</b> 11/55 (20) <b>G2:</b> 3/21 (14.3)</p> <p>NRS, 6 mos: <b>G1:</b> 34/103 (33) <b>G2:</b> 4/40 (10)</p> <p>NRS, 12 mos: <b>G1:</b> 22/66 (33.3) <b>G2:</b> 7/26 (26.9)</p> <p>Depressed at both 6 and 12 months, n (%): <b>G1:</b> 17/24 (70.8)* <b>G2:</b> 3/6 (50)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Mobayed and Dinan, 1990</p> <p><b>Country, Setting:</b> Ireland, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 11 to 13 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DSM-III, Leeds Scales for Anxiety and Depression</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 65 yrs old</li> <li>• Negative neurological exam on admission and discharge</li> <li>• No medical complications</li> <li>• Closed mild head injury (MHI)</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> MHI: LOC for &lt; 20 mins, and hospitalization for &lt; 3 days</p>	<p><b>Group(s):</b> Patients with MHI</p> <p><b>N screened:</b> 70</p> <p><b>N eligible:</b> 55</p> <p><b>N included:</b> 55</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> History of affective disorder: 0 Family history of affective disorder, epilepsy, cognitive impairment, alcohol abuse or significant social stresses: 0</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> Patients with depression: 30.63 ± 2.39 (n=11) Patients without depression: 32.75 ± 2.27 (n=8)</p> <p><b>Age ≥16, n (%):</b> 55 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> MHI: 55 (100)</p>	<p><b>Depression:</b> DSM-III criteria</p> <p>Leeds self-rating questionnaire : Cutoff score of 6-7 for anxiety and depression</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, DSM-III, n (%):</b> MDD: 11/32 (34.4)</p> <p>Affective disorder, Leeds, n (%): 16/55 (29.1)</p> <p><b>Taking depression medications, n (%):</b> 1 (1.8)(diazepam, anti-anxiety)</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Mollica et al., 2009</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> May 2002 to June 2004</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, years :</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HSCL</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• South Vietnamese ex-political detainee who had been tortured in Vietnamese reeducation camps and resettled in the US</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Concussion associated traumatic head injury (THI): 1 or more occasions during which all 3 postconcussive symptoms (LOC, PTA, and any neurologic deficits) occurred</p>	<p><b>Group(s):</b> <b>G1:</b> Ex-political detained <b>G1a:</b> With THI <b>G1b:</b> Without THI <b>G2:</b> Non-reeducation camp, non-THI Vietnamese comparison group</p> <p><b>N screened:</b> <b>G1:</b> 337 <b>G2:</b> 82</p> <p><b>N eligible:</b> <b>G1:</b> 337 <b>G2:</b> 82</p> <p><b>N included:</b> <b>G1:</b> 42 <b>G1a:</b> 16 <b>G1b:</b> 26 <b>G2:</b> 16</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> NR Range of "trauma/torture" exposures: 5-40</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 62.9 ± 8.0 <b>G2:</b> 62.6 ± 9.6</p> <p><b>Age ≥16, N (%):</b> 58 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> Hopkins Symptom Checklist-25: 15 item scale for depression; cutoff of 1.75 for depression</p> <p><b>Other co-morbidities:</b> PTSD: Harvard Trauma Questionnaire Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, HSCL n (%):</b> <b>G1a:</b> 10/16 (62.5) <b>G1b:</b> 3/26 (11.5) <b>G2:</b> 6/16 (37.5)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: HTQ, n (%): <b>G1a:</b> 8/16 (50.0) <b>G1b:</b> 4/26 (15.4) <b>G2:</b> 0/16</p> <p>Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p> <p><b>Multivariate model predictors:</b> Right overall cerebral cortical thickness was negatively correlated with HSCL scores (<math>r = -0.6, P = 0.02</math>) Left overall cerebral cortical thickness was not correlated with HSCL scores (<math>r = -0.6, P = 0.05</math>)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Mooney et al., 2005 See Mooney and Speed, 2001</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, median:</b> 15 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DSM-IV, BDI-II</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Outpatient of mild TBI clinic of the tertiary care center</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> According to ACRM criteria</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 67</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression, n (%):</b> Prior to injury: 21 (34) At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Lifetime history of prior mental health problems: 36 (54) Anxiety disorder: 6 (9)</p> <p><b>N with prior TBI (%):</b> 17 (25)</p> <p><b>Age, yrs ± SD:</b> 41.4 ± 13.3</p> <p><b>Age ≥16, n (%):</b> 67 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> LOC: 4 (6) Amnesia: 47 (70) Dazed/confused at time of injury: 16 (24)</p>	<p><b>Depression:</b> DSM-IV criteria</p> <p>BDI-II; participant and/or family member interview used to determine depression status pre-TBI</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: participant and/or family member interview used to determine anxiety status pre-TBI Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: participant and/or family member interview used to determine mental health history pre-TBI</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, MDD, %:</b> 61</p> <p>BDI-II score, mean ± SD: Total: 22.0 ± 12.4 Disabled: 22.2 ± NR (n=47) Non-disabled: 16.6 (n=19) P = 0.03</p> <p>Correlation with BDI-II scores: Headache: 0.2 (P = 0.07) Non-cephalic pain: 0.3 (P = 0.05) PCS checklist scores: 0.6 (P &lt; 0.001)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety Disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses, moderate-severe, %: Headache: 72 Non-cephalic pain: 64 Dizziness: 32 Vertigo: 15</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Mooney and Speed, 2001 See Mooney et al., 2005</p> <p><b>Country, Setting:</b> US, TBI rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, weeks (median):</b> 24.50</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DSM-IV</p>	<p><b>Inclusion criteria:</b> • Mild TBI</p> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> According to ACRM criteria</p>	<p><b>Group(s):</b> Patients with actual or suspected mild TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 80</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression, n (%):</b> Prior to injury: 12 (15) At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Anxiety: 2 (3) Other psychiatric condition: 9 (11) Alcohol an injury related factor: (NR) 11</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 31.1 ± 13.4</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: Impact of event scale Other anxiety disorder: BSQ Fear survey Irritability: NR Aggression: NR Suicidality: NR</p> <p><b>Substance use:</b> Self-report / presence of positive blood alcohol levels noted in the clinical record</p> <p><b>Other psychiatric diagnoses:</b> MMPI DES</p> <p><b>Health related QoL or functional status:</b> POMS Post-concussion symptom check-list Complex partial seizure check list Cognitive function (WAIS-R, WMS-R, Auditory verbal learning test, Trail making test)</p>	<p><b>Depression, n (%):</b> 35 (44)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety Disorder, n (%): 19 (24) Irritability: NR Aggression: NR Suicidality: NR Substance use: Diagnosis, n (%): TBI only: 17 (21) Psychiatric condition only: 13 (16) TBI and psychiatric condition: 48 (60) No diagnosis: 2 (3) Other psychiatric diagnoses, n (%): MMPI: 6 (8) DES score, mean ± SD: 13.8 ± 12.6 DES score, poor recovery group, mean: 20.14</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Parcell et al., 2006 See Curran et al., 2000</p> <p><b>Country, Setting:</b> Australia, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mean:</b> <b>G1:</b> 230 days <b>G2:</b> NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 65 yrs old</li> <li>• Sufficient English language ability to complete the questionnaires</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Transmeridian travel across more than 1 time zone in the preceding 3 months and no shift work in the previous 12 months</li> <li>• Preinjury sleep disorder, as indicated by significant other's responses on a screening checklist for classic symptoms of periodic limb movement disorder, sleep apnea, or insomnia</li> <li>• Taking benzodiazepines or other sleeping medications</li> <li>• Previous head injury, neurologic disorder, or major psychiatric disorder</li> </ul> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> <b>G1:</b> Participants with TBI <b>G2:</b> Age and sex matched uninjured participants</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 63 <b>G2:</b> 63</p> <p><b>N at conclusion:</b> <b>G1:</b> 63 <b>G2:</b> 63</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> None (see exclusion criteria)</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 32.5 ± 1.7 <b>G2:</b> 30.5 ± 1.2</p> <p><b>Age ≥16, n (%):</b> 126 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> HADS: 15-21: Severe 11-14: Moderate 8-10: Mild</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HADS, see depression scale for cutoffs Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, %:</b> Severe: <b>G1:</b> 5 <b>G2:</b> 0 Moderate: <b>G1:</b> 6 <b>G2:</b> 0 Mild: <b>G1:</b> 27 <b>G2:</b> 2</p> <p>HADS score, mean ± SD: <b>G1:</b> 5.8 ± 0.5 <b>G2:</b> 2.1 ± 0.3 <b>G1/G2:</b> <i>P</i> &lt; 0.01</p> <p>Depression and GCS, correlation: 0.19 <i>P</i> = 0.15</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR Other anxiety disorder: Anxiety: Severe anxiety: <b>G1:</b> 3 <b>G2:</b> 3 Moderate anxiety: <b>G1:</b> 19 <b>G2:</b> 5 Mild anxiety: <b>G1:</b> 18 <b>G2:</b> 18</p> <p>HADS, anxiety score, mean ± SD: <b>G1:</b> 6.7 ± 0.6 <b>G2:</b> 5.7 ± 0.5 <b>G1/G2:</b> <i>P</i> = 0.17</p> <p>Irritability: NR Aggression: NR Suicidality: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Peleg et al., 2009</p> <p><b>Country, Setting:</b> Israel, rehabilitation centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 2.9 ± 2.3</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 to 60 yrs old</li> <li>• Medically documented TBI occurring at least 6 mos prior to the study</li> <li>• Able to give consent</li> <li>• Cognitively apt to answer different questionnaires</li> <li>• Non-psychotic</li> <li>• No report of depression prior to TBI onset</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> Participants with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 82</p> <p><b>N included:</b> 65</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: None, see inclusion criteria At time of injury: None, see inclusion criteria</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age, yrs ± SD:</b> 28.8 ± 9.0</p> <p><b>Age ≥16, N (%):</b> 65 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI†, %:</b> Mild: 31 Moderate: 8 Severe: 61</p> <p>GCS, mean ± SD (range): 8.7 ± 4.2 (3-15)</p> <p><b>Mechanism/type of injury, %:</b> Road accidents: 75.4 War accidents: 12.3 Falls: 12.3</p>	<p><b>Depression:</b> BDI: cutoffs NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, BDI, n (%):</b> Mild: 19 (29.2) Moderate: 15 (23.1) Severe: 14 (21.5)</p> <p>BDI score, mean ± SD: 19.3 ± 11.7</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p> <p><b>Multivariate model predictors:</b> Adult Hope Scale score: <i>P</i> &lt; 0.005 Life Orientation Test Revised score: <i>P</i> &lt; 0.05</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Perlesz et al., 2000 See Curran et al., 2000</p> <p><b>Country, Setting:</b> Australia, multicenter</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 1 to 5 years</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 16 yrs old</li> <li>1 to 5 years postinjury</li> <li>Discharged to home care following acute rehabilitation</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>No interest in participating (36, 22.4%)</li> <li>Minor head injury and discussion with researcher leading to decision that participation was not relevant (17, 10.6%)</li> <li>Anger with rehabilitation system and refusal to participate (5, 3.1%)</li> <li>Failure to return questionnaires (24, 14.9%)</li> </ul> <p><b>TBI Def:</b> Mild: PTA 5-59 minutes Moderate: PTA 1-23 hours Severe: PTA 1-6 days Very Severe: PTA 1-4 weeks Extremely severe: PTA 1-3 months Profoundly severe: PTA &gt; 3 months</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI <b>G2:</b> Relatives</p> <p><b>N screened:</b> 223 families of TBI patients</p> <p><b>N eligible:</b> 161 families</p> <p><b>N included:</b> <b>G1:</b> 65 <b>G2:</b> 147</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> <b>G1:</b> 7 (11) <b>G2:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 33.8 ± 15.0 <b>G2:</b> NR</p> <p><b>Age ≥16, n (%):</b> 212 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> BDI: score &gt; 10 indicates borderline or clinical depression</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: STAI &gt; 80<sup>th</sup> percentile Irritability: NR Aggression: NR Suicidality: NR Substance use: data gathered on Head Injury Family Interview (HI-FI) demo-graphic and pre-injury form Other psychiatric diagnoses: POMS: score ≥ 73 indicates a clinical level of mood disturbance</p> <p><b>Health related QoL or functional status:</b> Family Satisfaction Scale (FSS): midpoint of 32.5 indicates dissatisfaction with the family</p>	<p><b>Depression, n (%):</b> 37/62 (59.7)</p> <p><b>Taking depression medications:</b> NR*</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety disorder: 31/62 (50) Irritability: NR Aggression: NR Suicidality: NR Substance use: Alcohol: Severe: 0 (0) Moderate: 5 (7.7) Drugs : Severe: 0 (0) Moderate: 6 (9.2) Other psychiatric diagnoses: POMS: Anger: 35/61 (57.4) Fatigue: 35/61 (57.4)</p> <p><b>Health related QoL or functional status:</b> Family dissatisfaction, n (%): 10/41 (24.4)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Ponsford and Schönberger 2010</p> <p><b>Country, Setting:</b> Australia, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, years :</b> 2, 5</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Participants with TBI who had received rehabilitation in the context of a no-fault accident compensation system</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> Participants with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 2 yrs: 301 5 yrs: 266</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> NR</p> <p><b>Age at injury, yrs ± SD (range):</b> 2 yrs: 34.5 ± 15.9 (15-82) 5 yrs: 34.6 ± 16.7 (14-87)</p> <p><b>Age ≥16, N (%):</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> GCS, mean ± SD: 2 yrs: 7.9 ± 4.4 5 yrs: 7.4 ± 4.2 Range 3-15 at both time points</p>	<p><b>Depression:</b> HADS: clinically significant depression if score &gt;7</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: HADS: clinically significant anxiety if score &gt;7</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, %:</b> 2 yrs: 45 5 yrs: 44 p=NS</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR</p> <p>Other anxiety disorder: 2 yrs: 53 5 yrs: 49 p=NS</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Popovic et al., 2004</p> <p><b>Country, Setting:</b> Serbia, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 3.8 ± 0.7</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> ZDS, SCL-90-R</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Moderate-to-severe TBI</li> <li>At least 1 year after hospitalization</li> <li>Not treated with glucocorticoids while in the ICU</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Moderate TBI: GCS of 9 to 13 Severe TBI: GCS of &lt; 8</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with moderate-to-severe TBI <b>G2:</b> Healthy participants</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 67 <b>G2:</b> 78</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 37.5 ± 1.8 <b>G2:</b> 37.2 ± 1.4</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Moderate to severe: <b>G1:</b> 67 (100)</p> <p><b>Mechanism/type of injury:</b> NR</p>	<p><b>Depression:</b> ZDS &gt; 39 SCL-90-R: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: SCL-90-R Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, ZDS, n (%):</b> Total: 19/41 (46.3) Strong intensity of depression: 8/41 (19.5) Mild to moderate depression: 11/41 (26.8)</p> <p>ZDS score, mean: 41.2</p> <p>SCL-90-R, depression dimension, T-score: 0.51</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: SCL-90-R, phobic anxiety dimension, T-score: 0.57 SCL-90-R, psychoticism dimension, T-score: 0.53 Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Powell et al., 2002</p> <p><b>Country, Setting:</b> UK, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, yrs ± SD:</b> <b>G1:</b> 4.0 ± 4.9 <b>G2:</b> 2.7 ± 3.6</p> <p><b>Length of follow up:</b> 18 to 40 months</p> <p><b>Dep. Scale/Tool:</b> HADS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 65 yrs old</li> <li>• TBI as verified by hospital or general practitioner records</li> <li>• No concurrent neurological diagnoses</li> <li>• Living within 1 hour travel time of the hospital</li> <li>• Long term treatment goals agreed within the team as being amenable in principle to intervention</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b> <b>G1:</b> Outreach group <b>G2:</b> Information group</p> <p><b>N screened:</b> 166</p> <p><b>N eligible:</b> 110</p> <p><b>N included:</b> <b>G1:</b> 54 <b>G2:</b> 56</p> <p><b>N at conclusion:</b> <b>G1:</b> 48 <b>G2:</b> 46</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 34 ± 11 (n=48) <b>G2:</b> 35 ± 10 (n=46)</p> <p><b>Age ≥16, n (%):</b> 110 (100)</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> HADS &gt; 10</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: HADS &gt; 10</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> FIM+FAM</p> <p>Unmodified Barthel Index</p> <p>20: Physical independence</p> <p>Brain Injury Community Rehabilitation Outcome-39 scales (BICRO-39)</p>	<p><b>Depression, %:</b> Total: 35 HADS &gt; 13: 15</p> <p>HADS score, intake, mean ± SD: <b>G1:</b> 7.7 ± 4.2 <b>G2:</b> 8.5 ± 5.0</p> <p>HADS, follow-up, mean change ± SD: <b>G1:</b> 0 ± 4.2 <b>G2:</b> 0.4 ± 4.0</p> <p>HADS, improved at follow-up, n (%): <b>G1:</b> 10/20 (50) <b>G2:</b> 14/26 (53.8)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder, %: Total: 29 HADS &gt; 13: 15</p> <p>HADS score, intake, mean ± SD: <b>G1:</b> 8.7 ± 4.1 <b>G2:</b> 8.3 ± 4.8</p> <p>HADS, follow-up, mean change ± SD: <b>G1:</b> 0.5 ± 4.1 <b>G2:</b> -0.6 ± 3.8</p> <p>HADS, improved at follow-up, n (%): <b>G1:</b> 10/20 (50) <b>G2:</b> 9/26 (34.6)</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rao et al., 2009</p> <p>See Rao et al., 2008</p> <p><b>Country, Setting:</b> US, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos:</b> &lt;3</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 18 yrs old</li> <li>Ability to provide consent</li> <li>Admission to hospital for evaluation of head trauma</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Prior TBI</li> <li>Open-head injury</li> <li>History of any other type of brain illness</li> </ul> <p><b>TBI Def:</b> At least one of the following: clear history of LOC; GCS score less than 15; evidence of trauma on CT scan done as part of clinical workup</p> <p>Mild: GCS score of 13 to 15</p> <p>Moderate: GCS score of 9 to 12</p> <p>Severe: GSC score of 3 to 8</p> <p>Participants with mild TBI also met ACRM criteria</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 107</p> <p><b>N included:</b> 67</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury, n (%): 6 (9.0)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Any axis 1 diagnosis: 51 (76.1)</p> <p>Alcohol abuse/dependence: 35 (52.2)</p> <p>Substance abuse/dependence: 33 (49.3)</p> <p><b>N with prior TBI (%):</b> None, see exclusion criteria</p> <p><b>Age, yrs ± SD:</b> 42.6 ± 17.7</p> <p><b>Age ≥16, N (%):</b> 67 (100)</p> <p><b>Global injury severity:</b> General Medical Health Rating score, %</p> <p>Poor: 9 Fair: 21 Good: 40 Excellent: 30</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: SCID</p> <p>Irritability: NR</p> <p>Aggression: OAS</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: SCID</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> 8 (11.9)*</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR</p> <p>Other anxiety disorder: 12 (17.9)</p> <p>Irritability: NR</p> <p>Aggression: Total sample: 19 (28.4)</p> <p>5/8 (62.5) participants with depression and aggression</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: Postconcussion syndrome: 11 (16.4)</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rao et al., 2008</p> <p>See Rao et al., 2009</p> <p><b>Setting:</b> US, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, range:</b> 0 to 3 months</p> <p><b>Length of follow up:</b> 1 to 3 months</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 18 years of age</li> <li>Ability to provide consent</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Prior TBI</li> <li>Open-head injury</li> <li>History of brain illness</li> <li>No admission to hospital</li> <li>Absence of clear history of LOC</li> </ul> <p><b>TBI Def:</b> At least one of following: admitted to the hospital with clear history of loss of consciousness; GCS score of 15 or less; and/or evidence of trauma on computerized tomography (CT) scans done as part of clinical workup</p> <p>Mild: GCS score of 13 to 15</p> <p>Moderate: GCS score of 9 to 12</p> <p>Severe: GSC score of <math>\leq 8</math></p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> ~1,000</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 54</p> <p><b>N at conclusion:</b> 54</p> <p><b>Depression, n (%):</b> Prior to injury: 5 (9.3)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Anxiety disorder: 4 (7.4)</p> <p><b>N with prior TBI:</b> None, see exclusion criteria</p> <p><b>Age, yrs <math>\pm</math> SD:</b> 43.2 <math>\pm</math> 17.7</p> <p><b>Age <math>\geq 16</math>, n (%):</b> 54 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS, %:</b> Mild: 65.0 Moderate: 11.0 Severe: 19.0 Unknown: 5.5</p> <p><b>Mechanism / type of injury, %:</b> MVA: 52.0 Assault: 24.0 Falls: 22.0 UNK: 2.0</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: SCID</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> MOS</p>	<p><b>Depression, n (%):</b> Major depressive-like episode: 7 (13.0)</p> <p><b>Taking medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR</p> <p>Other anxiety disorder: General anxiety: 6 (11)</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status, MOS, mean <math>\pm</math> SD:</b> Sleep disturbance: Pre-TBI: 17.5 <math>\pm</math> 15.9 Post-TBI: 27.7 <math>\pm</math> 24.1 <math>P = 0.018</math></p> <p>Snoring: Pre-TBI: 18.4 <math>\pm</math> 30.2 Post-TBI: 14.5 <math>\pm</math> 26.9 <math>P = 0.4</math></p> <p>SOB/HA: Pre-TBI: 0.39 <math>\pm</math> 2.8 Post-TBI: 14.1 <math>\pm</math> 27.5 <math>P = 0.001</math></p> <p>Sleep adequacy: Pre-TBI: 26.7 <math>\pm</math> 28.2 Post-TBI: 38.6 <math>\pm</math> 31.1 <math>P = 0.023</math></p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rapoport et al., 2008</p> <p><b>Country, Setting:</b> Canada, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Case series</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> 10 weeks</p> <p><b>Dep. Scale/Tool:</b> SCID, HAM-D</p>	<p><b>Inclusion criteria:</b> See exclusion criteria</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Prior focal brain disease (e.g., stroke, tumor)</li> <li>• Significant acute medical illness</li> <li>• Alcohol abuse</li> <li>• CT abnormalities inconsistent with TBI</li> <li>• Current antidepressant treatment</li> <li>• Contraindications to citalopram</li> <li>• Premorbid diagnosis of schizophrenia, bipolar disorder or dementia</li> </ul> <p><b>TBI Def:</b> Mild TBI: LOC at the time of the injury of 20 min or less, an initial GCS of 13 to 15, PTA &lt; 24 hrs and a normal CT brain image.</p> <p>Moderate-to-severe TBI: GCS &lt; 13, PTA &gt; 24 hrs or an abnormal CT brain image</p>	<p><b>Group(s)*:</b> <b>G1:</b> 6 week citalopram trial, various doses <b>G2:</b> 10 week citalopram trial, various doses</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included*:</b> <b>G1:</b> 65 <b>G2:</b> 26</p> <p><b>N at conclusion*:</b> <b>G1:</b> 54 <b>G2:</b> 26</p> <p><b>Depression, n (%):</b> Prior to injury: 7/65 (10.8) At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 39.7 ± 19.0</p> <p><b>Age ≥16, n (%):</b> 65 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild: 33/65 (50.8) Mod-Severe: 32/65 (49.2)</p> <p><b>Mechanism/type of injury:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria; at least 5 out of 9 symptoms, one of which must be either depressed mood or anhedonia</p> <p>Response ≥ 50% in HAMD score</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression:</b> MDD, n (%): 54 (83.1)</p> <p>HAMD score, baseline, mean ± SD: 23.7 ± 6.6</p> <p>HAMD score, 6 weeks, mean ± SD: 16.3 ± 9.3 (n=59) p&lt;.0001</p> <p>Responded, 6 weeks, n (%): 15/54 (27.7)</p> <p>Remission, 6 weeks, n (%): 13/54 (24.1)</p> <p>HAMD score, 10 weeks, mean ± SD: 13.0 ± 7.9 (n=26) p&lt;.0001</p> <p>Responded, 10 weeks, n (%): 12/26 (46.2)</p> <p>Remission, 10 weeks, n (%): 7/26 (26.9)</p> <p><b>Taking depression medications, %:</b> Completed trial: 83.1</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rapoport, Herrmann et al., 2006 See Rapoport, Kiss et al., 2006</p> <p><b>Country, Setting:</b> Canada, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury:</b> 1 year</p> <p><b>Length of follow up:</b> 1 year</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Age 50 and over and within 2 months of injury (G1)</li> <li>Non-injured participants matched by age decade, education, and gender (G2)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>A pre-injury history of neurologic disease, serious acute medical illness, schizophrenia, or bipolar disorder</li> <li>Preexisting cognitive decline based on history and a score of &gt; 3.38 on the Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE)</li> <li>Lack of an informant to complete the IQCODE</li> </ul> <p><b>TBI Def:</b> Mild TBI: Loss or alteration of consciousness at the time of injury for ≤ 20 minutes, an initial GCS of 13 to 15, and PTA of &lt; 24 hour</p>	<p><b>Group(s):</b> <b>G1:</b> Participants with TBI <b>G2:</b> Participants without TBI</p> <p><b>N screened:</b> <b>G1:</b> 712 <b>G2:</b> 79</p> <p><b>N eligible:</b> <b>G1:</b> 248 <b>G2:</b> 79</p> <p><b>N included:</b> <b>G1:</b> 69 <b>G2:</b> 69</p> <p><b>N at conclusion:</b> <b>G1:</b> 49 <b>G2:</b> 69</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> None (see exclusion criteria)</p> <p><b>N with prior TBI (%):</b> Mild TBI: <b>G1:</b> 8 (11.8) <b>G2:</b> 5 (6.3)</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 67.0 ± 7.9 <b>G2:</b> 68.0 ± 8.5</p> <p><b>Age ≥16, n (%):</b> 138 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Moderate: 14 (20.1) Complicated Mild: 18 (26.1) Mild: 37 (53.6)</p>	<p><b>Depression:</b> SCID: DSM-IV Subsyndromal depression: minimum of three DSM-IV symptoms of a major depressive episode, at least one of which is persistent depressed mood or anhedonia, lasting for two weeks</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: Dementia: Mattis Dementia Rating Scale (DRS) and MMSE</p> <p><b>Health related QoL or functional status:</b> Psychologic distress: GHQ Informant ratings: FAQ</p>	<p><b>Depression, baseline, n (%):</b> Major Depression: <b>G1:</b> 11/69 (15.9) <b>G2:</b> 0 Subsyndromal depression: <b>G1:</b> 15/69 (21.7) <b>G2:</b> 3/79 (3.8 )</p> <p>Depression, 1 year, n (%): Major depression: <b>G1:</b> 6*/49 (12.2) <b>G2:</b> 1/68 (1.5) Subsyndromal depression: <b>G1:</b> 9 (18.8) <b>G2:</b> 2 (2.9)</p> <p><b>Taking depression medications, n (%):</b> <b>G1:</b> 10 (14.5) <b>G2:</b> 3 (4)</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: Dementia: DRS score, mean: <b>G1:</b> 135.4 ± 8.5 <b>G2:</b> 139.0 ± 3.7 MMSE, mean: <b>G1:</b> 28.2 ± 1.9 <b>G2:</b> 29.1 ± 1.2</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rapoport, Kiss et al., 2006</p> <p>See Rapoport, Herrmann et al., 2006</p> <p><b>Country, Setting:</b> Canada, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, days ± SD:</b> 46.9 ± 34</p> <p><b>Length of follow up:</b> 1 year</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 50 yrs old</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Pre-injury history of neurological disease</li> <li>Serious acute medical illness</li> <li>Schizophrenia or bipolar disorder</li> <li>Drug abuse</li> </ul> <p><b>TBI Def:</b> Mild TBI: According to ACRM criteria</p> <p>Moderate TBI: GCS score of 9 to 12 and PTA &lt; 1 week, or met criteria for mild TBI but had an intracranial complication of TBI (e.g., contusion)</p>	<p><b>Group(s):</b> Patients with mild to moderate TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 77</p> <p><b>N included:</b> 77</p> <p><b>N at conclusion:</b> 46</p> <p><b>Depression, n (%):</b> Prior to injury: 14 (18.2)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 67.12 ± 8.4</p> <p><b>Age ≥16, n (%):</b> 77 (100)</p> <p><b>Global injury severity (ISS, RTS, etc.):</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild: 44 (57.1) Moderate: 33 (42.9)</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Psychosocial functioning and psychological distress: RHFQ, GHQ</p> <p>Post-concussive symptoms: RPDQ</p> <p>Informant ratings: FAQ</p>	<p><b>Depression, n (%):</b> Baseline: 12 (15.6) 1-year*: 5/9 (55.6)</p> <p><b>Taking depression medications, 1 year, n (%):</b> Antidepressants: 4/5 (80%)</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> RHFQ, baseline, mean ± SD: MDD: 25.0 ± 7.9 (n=12) No MDD: 10.7 ± 10.9 (n=58)</p> <p>RHFQ, 6 months, mean ± SD: MDD: 26.2 ± 8.5 (n=6) No MDD: 9.9 ± 9.9 (n=38)</p> <p>RHFQ, 1 year, mean ± SD: MDD: 16.3 ± 13.0 (n=8) No MDD: 10.2 ± 11.3 (n=37)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rapoport et al., 2005</p> <p><b>Country, Setting:</b> Canada, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD:</b> <b>G1:</b> 214.7 ± 74.1 <b>G2:</b> 194.8 ± 34.8</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 65 or younger</li> <li>• Non-penetrating mild or moderate TBI</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Premorbid history of focal brain disease (e.g., stroke, tumor)</li> <li>• Serious medical illness (e.g., acute heart or renal failure, malignancy)</li> <li>• History of dementia, schizophrenia or bipolar disorder</li> </ul> <p><b>TBI Def:</b> Mild TBI: LOC ≤ 30 minutes; after 30 minutes, an initial GCS of 13-15; PTA ≤ 24 hrs (based on ACRM criteria)  Moderate TBI: GCS of 9-12 and PTA &lt; 1 week</p>	<p><b>Group(s):</b> Patients with TBI <b>G1:</b> Patients with major depression <b>G2:</b> Patients without major depression</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 21 <b>G2:</b> 53</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression, n (%):</b> Prior to injury: <b>G1:</b> 5 (23.8) <b>G2:</b> 3 (5.6)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, %:</b> Alcohol misuse: 13.5 Substance misuse: 16.2</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 41.4 ± 13.2 <b>G2:</b> 32.3 ± 12.2</p> <p><b>Age ≥16, n (%):</b> 74 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, PTA &gt; 24 hrs, n (%):</b> <b>G1:</b> 12 (60) <b>G2:</b> 35 (67.3)</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Cognitive Measures: Wechsler Adult Intelligence Scale: assessed attention/working memory and processing speed Wechsler Memory Scale: assessed logical memory Wisconsin Card Sorting Test: assessed executive functioning</p>	<p><b>Depression, n (%):</b> Major depression: 21 (28.4)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Wechsler Adult Intelligence Scale, mean ± SD: Working memory: <b>G1:</b> 22.6 ± 9.1 <b>G2:</b> 30.1 ± 6.4 Processing speed: <b>G1:</b> 14.4 ± 4.6 <b>G2:</b> 18.9 ± 4.9 Wechsler Memory Scale, mean ± SD: <b>G1:</b> 21.8 ± 8.6 <b>G2:</b> 29.8 ± 8.2 Wisconsin Card Sorting Test, mean ± SD: <b>G1:</b> 4.0 ± 2.2 <b>G2:</b> 5.3 ± 1.3</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rapoport et al., 2003</p> <p>See Rapoport et al., 2003</p> <p><b>Country, Setting:</b> Canada, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD:</b> 49.0 ± 30.0</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Non-penetrating, mild TBI</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Preinjury history of focal brain disease (e.g., stroke, tumor)</li> <li>• Serious acute medical illness (e.g., heart or renal failure, malignancy)</li> <li>• Previous diagnosis of schizophrenia, bipolar disorder, or dementia</li> </ul> <p><b>TBI Def:</b> Mild TBI: LOC ≤ 30 min; after 30 mins, an initial GCS of 13-15; PTA ≤ 24 hrs (based on ACRM criteria)</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI aged 16 to 59 <b>G2:</b> Patients with TBI aged 60 and older</p> <p><b>N screened:</b> 222</p> <p><b>N eligible:</b> 210</p> <p><b>N included:</b> <b>G1:</b> 146 <b>G2:</b> 64</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression, n (%):</b> Prior to injury: <b>G1:</b> 13 (8.9) <b>G2:</b> 16 (25.0)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> <b>G1:</b> 42 (28.8) <b>G2:</b> 18 (28.1)</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 36.4 ± 11.4 <b>G2:</b> 72.0 ± 8.6</p> <p><b>Age ≥16, n (%):</b> 210 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild: 210 (100)</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> Per MD records, no tests PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric conditions: NR</p> <p><b>Health related QoL or functional status:</b> MMSE</p>	<p><b>Depression, n (%):</b> Major Depression: <b>G1:</b> 31/146 (21.2) <b>G2:</b> 4/64 (6.3) <b>G1/G2:</b> <i>P</i> &lt; 0.01</p> <p>Depression, OR (95% CI): <b>G1/G2:</b> 4.04 (1.4, 12.0)</p> <p>Previous history of MD, patients with MD, n (%): 7/35 (20)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use, %: Drug: <b>G1:</b> 14.4 <b>G2:</b> 1.6 Alcohol: <b>G1:</b> 11.6 <b>G2:</b> 4.7</p> <p>Other psychiatric conditions: NR</p> <p><b>Health related QoL or functional status:</b> MMSE score, mean ± SD: Total: 28.9 ± 1.1 <b>G1:</b> 28.7 ± 1.2 <b>G2:</b> 29.0 ± 1.0 <b>G1/G2:</b> <i>P</i> = 0.069</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rapoport et al., 2003</p> <p>See Rapoport et al., 2003</p> <p><b>Country, Setting:</b> Canada, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days (range):</b> 48.4 ± 33.6 (1-227)</p> <p><b>Length of follow up:</b> NR</p> <p><b>Dep. Scale/Tool:</b> SCID</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Non-penetrating, mild TBI</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Preinjury history of focal brain disease (e.g., stroke, tumor)</li> <li>• Serious acute medical illness (e.g., heart or renal failure, malignancy)</li> <li>• Previous diagnosis of schizophrenia, bipolar disorder, dementia, or major depressive disorder</li> </ul> <p><b>TBI Def:</b> Mild TBI: LOC at time of injury of 30 min or less; after 30 mins, an initial GCS of 13-15; PTA less than 24 hrs (based on ACRM criteria)</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with depression post-TBI <b>G2:</b> Patients without depression post-TBI</p> <p><b>N screened:</b> 211</p> <p><b>N eligible:</b> 170</p> <p><b>N included:</b> <b>G1:</b> 26 <b>G2:</b> 144</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> History of significant alcohol misuse, n (%): <b>G1:</b> 3 (11.5) <b>G2:</b> 10(6.9)</p> <p>History of significant substance misuse, n (%): <b>G1:</b> 3 (11.5) <b>G2:</b> 13 (9)</p> <p><b>N with prior TBI (%):</b> <b>G1:</b> 6 (23.1) <b>G2:</b> 33 (22.9)</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 41.3 ± 17.8 <b>G2:</b> 44.8 ± 20.5 Total: 44.2 ± 20.1</p> <p><b>Age ≥16, n (%):</b> NR</p> <p><b>Global injury severity:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR</p> <p><b>Substance use:</b> Interview and clinician's judgment</p> <p><b>Other psychiatric diagnoses:</b> NR</p> <p><b>Health related QoL or functional status:</b> GHQ Riverhead Head Injury Follow-up Questionnaire NRS GOS</p>	<p><b>Depression, n (%):</b> Major depression: 26/170 (15.3)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: General Health Questionnaire, anxiety score, mean ± SD: <b>G1:</b> 5.5 ± 2.3 <b>G2:</b> 2.6 ± 2.6 <b>G1/G2:</b> <i>P</i> &lt; 0.0001</p> <p>Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: Rivermead Post Concussion Disorder Questionnaire score, mean ± SD: <b>G1:</b> 43.4 ± 17.2 <b>G2:</b> 19.9 ± 17.3 <b>G1/G2:</b> <i>P</i> &lt; 0.0001</p> <p><b>Health related QoL or functional status:</b> General Health Questionnaire, total score, mean ± SD: <b>G1:</b> 20.2 ± 6.6 <b>G2:</b> 9.6 ± 7.7 <b>G1/G2:</b> <i>P</i> &lt; 0.0001</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rapoport et al., 2002</p> <p><b>Country, Setting:</b> Canada, tertiary care centers</p> <p><b>Enrollment Period:</b> October 1994 to November 1998 (severe TBI); January 1998 to October 2000 (mild and moderate TBI)</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD:</b> G1: 77.95 ± 21.8 G2: 79.66 ± 24.4 G3: 93.80 ± 9.7</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> NRS-R</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Abnormal CT scan obtained within 24 hours of injury</li> <li>Postresuscitation GCS motor score of 1–5 (total GCS &lt;8)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Evidence of hypotension (systolic BP &lt; 90 mm Hg for &gt; 30 minutes after resuscitation)</li> <li>Hypoxia (saturation &lt; 94%) for 30 minutes after resuscitation</li> <li>Estimated AIS score &gt; 4 for any organ system</li> <li>GCS of 3 with unreactive pupils</li> <li>Inability to randomize within 6 hours of injury</li> <li>Prior admission for TBI</li> </ul> <p><b>TBI Def:</b> Mild TBI: LOC for less than 20 minutes, a GCS of 13 or above, and PTA for less than 24 hours (based on ACRM criteria) Moderate TBI: GCS of 9-12 or a GCS of ≥ 13 with intracerebral complication on CT scan Severe TBI: NR</p>	<p><b>Group(s):</b> G1: Patients with mild TBI G2: Patients with moderate TBI G3: Patients with severe TBI</p> <p><b>N screened:</b> 870</p> <p><b>N eligible:</b> 323</p> <p><b>N included:</b> G1: 102 G2: 41 G3: 139</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> G1: 32.3 ± 11.8 G2: 32.3 ± 12.5 G3: 31.9 ± 10.6</p> <p><b>Age ≥16, n (%):</b> NR</p> <p><b>Global injury severity, ISS score, mean ± SD:</b> G1: 15.4 ± 10.3 (n=83) G2: 17.4 ± 9.8 (n=34) G3: 25.6 ± 7.4</p>	<p><b>Depression:</b> NRS-R: classified as not present, mild, moderate, or severe</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NRS-R Irritability: NRS-R Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS: severe disability, moderate disability, good recovery</p>	<p><b>Depression, %:</b> Severe: G1: 0 G2: 0 G3: 0.7 Moderate: G1: 9.8 G2: 17.1 G3: 11.5 Mild: G1: 22.5 G2: 22.0 G3: 36.7 Not present: G1: 64.7 G2: 61.0 G3: 51.1</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, %:</b> PTSD: NR Other anxiety disorder: Severe G1: 2.0 G2: 0 G3: 0.7 Moderate G1: 9.8 G2: 22.0 G3: 10.1 Mild G1: 35.3 G2: 19.5 G3: 45.3 Not present G1: 52.9 G2: 58.5 G3: 43.9</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Rowland et al., 2005</p> <p><b>Country, Setting:</b> US, rehabilitation centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD (range):</b> 57.3 ± 37.8 (8-148)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI-II</p>	<p><b>Inclusion criteria:</b> See exclusion criteria</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Cognitive or motor abnormalities that precluded the ability to give informed consent or complete standard administrations of the neuropsychological tests</li> <li>Self-report of previous brain injury or documentation of previous TBI in medical records</li> </ul> <p><b>TBI Def:</b> Documented by neuroradiologic scans (e.g., MRI, CT) or indisputable independent evidence (e.g., paramedics at the scene or emergency room personnel observation and documentation of loss of consciousness due to traumatic impact)</p> <p>TBI Severity determined by several cut-offs: time to follow commands (24 hours), length of PTA (24 hours), and duration of coma (6 hours)</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 51</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> None (see exclusion criteria)</p> <p><b>Age, yrs ± SD (range):</b> 40.3 ± 16.0 (18-70)</p> <p><b>Age ≥16, n (%):</b> 51 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Severe: 26 (51) Mild-moderate: 25 (49)</p> <p><b>Mechanism/type of injury, n (%):</b> Car accident: 23 (45.1) Fall: 14 (27.5) Assault: 9 (17.6) Other: 5 (9.8)</p>	<p><b>Depression:</b> BDI-II ≥ 14 was classified as depressed (severity of depression not identified in this study)</p> <p>BDI-II analyzed to extract factors based on cumulative percent variance:</p> <p><b>Negative Self Evaluation:</b> measures level of person's perception and cognitive view of self</p> <p><b>Symptoms of Depression:</b> measures symptoms largely associated with DSMV-IV criteria for MDE</p> <p><b>Vegetative Symptoms of Depression:</b> symptoms associated with depression, but failed to load under same factor as depression</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR</p>	<p><b>Depression, BDI-II, n (%):</b> Depressed: 13 (25.5)*</p> <p>Total variance for each factor, %: Negative Self Evaluation: 20 Symptoms of Depression: 18* Vegetative Symptoms of Depression: 12</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: 13 (25.5) Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Ruocco et al., 2007</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> MCMI-III</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>At least 18 yrs of age</li> <li>Referred for neuropsychological evaluation in relation to head trauma</li> <li>Completion of the MCMI-III as part of a larger neuropsychological battery</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Suspected dementia (G2)</li> </ul> <p><b>TBI Def:</b> According to ACRM criteria</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with TBI</p> <p><b>G2:</b> Psychiatric patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b></p> <p><b>G1:</b> 231</p> <p><b>G2:</b> 231</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b></p> <p><b>G1:</b> 40.6 ± 12.4</p> <p><b>G2:</b> 40.9 ± 12.1</p> <p><b>Age ≥16, n (%):</b> 462 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b></p> <p>Mild: <b>G1:</b> 84.0</p> <p>Moderate: <b>G1:</b> 16.0</p> <p>Reported LOC: <b>G1:</b> 43.9</p>	<p><b>Depression:</b> MCMI-III: Base Rate (BR) scores ≥ 75 was used to demark scale elevations that are clinically significant and determine if there were any differences between the TBI sample and the matched group of psychiatric patients.</p> <p><b>Other co-morbidities:</b> PTSD: MCMI-III</p> <p>Other anxiety disorder: MCMI-III</p> <p>Irritability: NR</p> <p>Aggression: MCMI-III</p> <p>Suicidality: NR</p> <p>Substance use: MCMI-III</p> <p>Other psychiatric diagnoses: MCMI-III</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b></p> <p>Major depression: <b>G1:</b> 70 (30.3) <b>G2:</b> 68 (29.4)</p> <p>Depressive <b>G1:</b> 39 (16.9) <b>G2:</b> 96 (41.6)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b></p> <p>PTSD: <b>G1:</b> 52 (22.5)</p> <p>Other anxiety disorder: <b>G1:</b> 32 (57.1)</p> <p>Irritability: NR</p> <p>Aggression: Aggressive (sadistic): <b>G1:</b> 6 (2.6)</p> <p>Suicidality: NR</p> <p>Substance use: Alcohol dependence: <b>G1:</b> 3 (1.3) Drug dependence: <b>G1:</b> 5 (2.2)</p> <p>Other psychiatric diagnoses: Schizoid: <b>G1:</b> 57 (24.7) Avoidant: <b>G1:</b> 63 (27.3) Dependent: <b>G1:</b> 71 (39.7) Histrionic: <b>G1:</b> 37(16.0) Narcissistic: <b>G1:</b> 35 (15.2) Antisocial: <b>G1:</b> 10 (4.3) Compulsive: <b>G1:</b> 47 (29.3)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Satz, Zaucha et al., 1998</p> <p>Satz, Forney et al., 1998<sup>^</sup></p> <p>See McCleary et al., 1998</p> <p><b>Country, Setting:</b> US, academic medical centers</p> <p><b>Enrollment Period:</b> 1991 to 1995</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> Up to 6 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCL-90-R, NRS-13</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• At least 16 yrs of age</li> <li>• Initial GCS score ≤ 12, or initial GCS score of ≥ 13 with abnormalities on admission CT scan</li> <li>• Literate and able to understand either Spanish or English</li> <li>• Bodily injuries other than to the head, admitted to the hospital for 24 hours or more, and AIS severity level comparable to the TBI patients (G2)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Less than 6 mos postinjury</li> <li>• Too injured to complete neuropsychological assessments</li> <li>• Severe pre-existing comorbidity, such as chronic heart failure, stroke, chronic severe neurological disease (e.g., Parkinson's disease, AIDS dementia, presenile dementia), or previous severe diminished mental capacity</li> </ul> <p><b>TBI Def:</b> NR†</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> TBI patients with severe disability</p> <p><b>G2:</b> TBI patients with moderate disability</p> <p><b>G3:</b> TBI patients with good recovery</p> <p><b>G4:</b> Other injury comparison group</p> <p><b>Ga:</b> Depressed (SCL-90-R criteria) patients in G1+G2</p> <p><b>Gb:</b> Nondepressed patients in G1+G2</p> <p><b>Gc:</b> Nondepressed patients in G3+G4</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b></p> <p><b>G1:</b> 21</p> <p><b>G2:</b> 42</p> <p><b>G2<sup>^</sup>:</b> 43</p> <p><b>G3:</b> 37</p> <p><b>G3<sup>^</sup>:</b> 36</p> <p><b>G4:</b> 30</p> <p><b>Ga<sup>^</sup>:</b> 17</p> <p><b>Gb<sup>^</sup>:</b> 47</p> <p><b>Gc<sup>^</sup>:</b> 64</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p>	<p><b>Depression:</b> SCL-90-R: a deviation score of greater than 2 standard deviations adjusted for gender indicates major depression</p> <p>NRS-13: a score greater than 4 indicates moderate to severe depression</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> GOS: standard definitions</p>	<p><b>Depression, SCL-90-R, %</b></p> <p><b>G1:</b> 24</p> <p><b>G2:</b> 28</p> <p><b>G3:</b> 2.7</p> <p><b>G4:</b> 3.3</p> <p>Depression, NRS-13, %:</p> <p><b>G1:</b> 52</p> <p><b>G2:</b> 35</p> <p><b>G3:</b> 22</p> <p><b>G4:</b> 17</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:*</b> AIMS score, mean ± SD:</p> <p><b>Ga:</b> 59.1 ± 8.4</p> <p><b>Gb:</b> 42.5 ± 10.7</p> <p><b>Gc:</b> 39.2 ± 12.1</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Schofield et al., 2006</p> <p><b>Country, Setting:</b> Australia, other</p> <p><b>Enrollment Period:</b> September 2003 to June 2004</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NR</p> <p><b>Dep. Scale/Tool:</b> RDS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Inmates recruited consecutively or chosen randomly based on prison ID number on days with too many potential new participants to be interviewed</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Self-report of a blow to the head the causing the participant to become dazed and confused without LOC (TBI without LOC) or unconscious or blacked-out (TBI with LOC)</p> <p>Mild TBI: LOC &lt; 30 minutes</p>	<p><b>Group(s):</b> Inmates examined for TBI history</p> <p><b>G1:</b> No TBI's <b>G2:</b> 1 to 3 TBI's <b>G3:</b> ≥ 4 TBI's</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 36 <b>G2:</b> 79 <b>G3:</b> 85</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 30.6 ± 8.1</p> <p><b>Age ≥16, n (%):</b> 200 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n:</b> TBI with LOC ≥ 30 minutes: 53 TBI with LOC &lt;30 minutes: 77 TBI without LOC: 34</p> <p><b>Mechanism/type of injury:</b> NR</p>	<p><b>Depression:</b> RDS: score of one or more indicated positive result for lifetime history of major depressive disorder</p> <p><b>Other co-morbidities:</b> PTSD:NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: Suicide or self-harm – direct inquiry Substance use: AUDIT score of 8 or more Specific enquiry for illegal drug use in the past 4 weeks Other psychiatric diagnoses: Psychosis: screener from the Australian Low Prevalence Disorders Study: weighted scores of four or more = positive (current or past) ICD personality international personality disorder screener: 3 or more items from either scales for impulsive or dissocial personality</p>	<p><b>Depression:</b> Depression associated with TBI and increased as number of TBI's increased:</p> <p>Depression, n (%): <b>G1:</b> 3 (10) <b>G2:</b> 14 (19) <b>G3:</b> 26 (31)</p> <p>Depression, OR (95% CI): <b>G2+G3/G1:</b> 3.6 (1.0, 12.8) <b>G2/G1:</b> 2.5 (0.6,9.6) <b>G3/G1:</b> 4.7 (1.3, 17.5)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD:NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: Suicide or self-harm, n (%): <b>G1:</b> 4 (13) <b>G2:</b> 11 (14) <b>G3:</b> 21 (25) Suicide or self-harm, OR (95% CI): <b>G2+G3/G1:</b> 1.7 (0.6, 5.3) <b>G2/G1:</b> 1.1 (0.3, 4.0) <b>G3/G1:</b> 2.4 (0.7, 7.6)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Sebit et al., 1998</p> <p><b>Country, Setting:</b> Kenya, tertiary care center</p> <p><b>Enrollment Period:</b> 1991 to 1992</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 6 to 8 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> CIS-R, DSM-III-R</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 65 yrs old</li> <li>• Non-penetrating, closed head injury (CHI)</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Previous hospital admission due to LOC, associated fractures elsewhere in the body, or undergone major surgical interventions (i.e. elevation of depressed skull fracture) for the fractured lower limb injury group (G2)</li> </ul> <p><b>TBI Def*:</b> Mild CHI: Consciousness on admission and throughout the period of hospitalization and absence of neurologic deficits</p> <p>Moderate CHI: Comatose for not more than 24 hrs with possible neurologic deficits</p> <p>Severe CHI: Duration of coma exceeding 24 hours and may have manifested focal neurologic deficits.</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with CHI <b>G2:</b> Patients with FLLI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 100</p> <p><b>N included:</b> <b>G1:</b> 37 <b>G2:</b> 39</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 32.2 ± 9.1 <b>G2:</b> 30.5 ± 7.9</p> <p><b>Age ≥16, n (%):</b> 100 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, %:</b> Mild: <b>G1:</b> 59.5 Moderate: <b>G1:</b> 21.6 Severe: <b>G1:</b> 18.6</p>	<p><b>Depression:</b> CIS-R: cutoff for cases of 13 points then correlated with DSM-III-R criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: CIS-R cutoff for cases of 13 points then correlated with DSM-III-R criteria Irritability: NR Aggression: NR Suicidality: NR Substance use: WHO Audit Core and an 8 item procedure for alcohol abuse with a cutoff of 8 points Other psychiatric diagnoses: Psychiatric interview for delusional disorders using DSM-III-R criteria</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> <b>G1:</b> 20 (54.1) <b>G2:</b> 10 (25.6)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety disorder: <b>G1:</b> 8 (21.6) <b>G2:</b> 6 (15.4) Irritability: NR Aggression: NR Suicidality: NR Substance use: <b>G1:</b> 2 (5.4) <b>G2:</b> 1 (2.6) Other psychiatric diagnoses: Delusional disorder: <b>G1:</b> 0 <b>G2:</b> 3 (7.7)</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Seel and Kreutzer, 2003 See Seel et al., 2003</p> <p><b>Country, Setting:</b> US, rehabilitation center</p> <p><b>Enrollment Period:</b> 1996 to 2000</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD (range):</b> 27.8 ± 43.8 (1-323)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI, NFI-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Completion of comprehensive evaluations at an outpatient rehabilitation center between 1996 and 2000</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 172</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 36.5 ± 12.2</p> <p><b>Age ≥16, n (%):</b> 172 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS score, mean:</b> 10.51</p> <p><b>Mechanism/type of injury, %:</b> MVA: 68 Violence: 13 Falls: 12</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> BDI ≥ 21 NFI ≥ 43</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, BDI, %:</b> Extreme: 2 Severe: 12 Moderate: 24</p> <p>BDI score, mean ± SD: 16.9 ± 11.4</p> <p>Depression, NFI, %: 30</p> <p>NFI score, mean ± SD: 36.1 ± 11.6</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>

\*GCS scores recorded

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Seel et al., 2003 See Seel and Kreutzer, 2003</p> <p><b>Country, Setting:</b> US, rehabilitation centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mos ± SD:</b> 35.3 ± 26.9</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> NFI-R, DSM-IV</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Completion of a TBIMS outpatient follow-up evaluation between 1996 and 2000</li> <li>• Availability of demographic data</li> <li>• Completion of the NFI at annual follow-up intervals</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Damage to brain tissue caused by an external mechanical force as evidenced by medically documented LOC or PTA due to brain trauma or by objective neurological findings that can be reasonably attributed to TBI on physical examination or mental status examination</p>	<p><b>Group(s):</b> Patients with TBI <b>G1:</b> Depressed patients <b>G2:</b> Non-depressed patients</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> Total: 666 <b>G1:</b> NR <b>G2:</b> NR</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 38.0 ± 14.5</p> <p><b>Age ≥16, n (%):</b> 666 (100)</p> <p><b>Global injury severity:</b> Acute treatment, days ± SD: 21.2 ± 16.7 Inpatient rehabilitation, days ± SD: 33.7 ± 25.6</p>	<p><b>Depression:</b> Measured using NFI to screen for DSM-IV major depression symptoms. NFI comprised of 70 items measures neurobehavioral problems in TBI patients – contains 6 domains (depression, somatic, memory/attention, communication, aggression, &amp; motor) Respondents responses measured on 5 point Likert scale DSM-IV criteria used to classify depressive symptoms of NFI scale</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Substance use: NR</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, DSM-IV criteria, %:</b> MDE: 27</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: Threaten to hurt self, %: Total: 7 <b>G1:</b> 19 <b>G2:</b> 3 Substance use: NR Other psychiatric diagnoses:* NFI criteria, mood symptoms, always/often, % : Easily angered: 26 Frustrated: 25 Sad, blue: 18 Feel hopeless: Total:12 <b>G1:</b> 38 <b>G2:</b> 3 Argue: 16 Curse at others: 12 Scream or yell: 9 Hit or push others: 2 Bored: 22 Sit with nothing to do: 19 Lonely: 19 Loss of interest in sex: 16</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Sherer et al., 2007</p> <p><b>Country, Setting:</b> US, rehabilitation center</p> <p><b>Enrollment Period:</b> February 2003 to August 2005</p> <p><b>Design:</b> Prospective cohort</p> <p><b>Time from injury, days (range):</b> 82 (23-938)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> CES-D</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>All patients admitted to rehabilitation center and a family member/significant other</li> <li>Ability to provide informed consent</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> 94</p> <p><b>N eligible:</b> 94</p> <p><b>N included:</b> 69</p> <p><b>N at conclusion:</b> 49</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 29.3 ± 13.2</p> <p><b>Age ≥16, n (%):</b> NR</p> <p><b>Global injury severity, acute length of stay, mean ± SD:</b> 23.1 ± 16.2</p> <p><b>Severity of TBI, GCS score, mean ± SD:</b> 8.0 ± 3.7</p> <p><b>Mechanism/type of injury, n (%):</b> MVC: 54 (78.2) Fall: 6 (8.7) Assault: 5 (7.2) Other: 3 (4.3)</p> <p><b>Area of brain injured:</b> NR</p>	<p><b>Depression:</b> CES-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> California Psychotherapy Alliance Scale (CALPAS) Prigatano Alliance Scale (PAS) Awareness Questionnaire (AQ) Disability Rating Scale (DRS) Productivity Status</p>	<p><b>Depression, n (%):</b> Severe: 3 (4.3) Moderate: 6 (8.7) Mild: 13 (18.8)</p> <p>CES-D score, mean ± SD: 11.6 ± 8.0</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> CALPAS score, mean ± SD: 122.0 (16.5) CALPAS, family member, mean ± SD: 126.2 (10.3) CALPAS score, clinician, mean ± SD: clinician: 112.0(14.4) PAS score, mean ± SD: 11.3 ± (1.1) AQ score, mean ± SD: 49.4 ± 9.1</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Sherman et al., 2000</p> <p><b>Country, Setting:</b> Canada, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD:</b> 2.5 ± 2.0</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> MMPI-2</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Availability of information on head injury severity</li> <li>• Complete neuropsychological test data including MMPI-2</li> <li>• No evidence of symptom exaggeration (i.e. below-chance performance) on a forced-choice symptom validity measure (Victoria Symptom Validity Test)</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Mild HI: LOC of &lt; 1 hour and PTA of &lt; 24 hours (based on ACRM criteria)</p> <p>Moderate-to-severe HI: LOC &gt; 1 hour and PTA &gt; 24 hours</p>	<p><b>Group(s):</b> <b>G1:</b> Mild TBI <b>G2:</b> Moderate-to-severe TBI <b>Ga:</b> Low Dep score <b>Gb:</b> High Dep score</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> 175</p> <p><b>N included:</b> <b>G1:</b> 114 <b>G2:</b> 61 <b>Ga:</b> 117 <b>Gb:</b> 58</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 32.8 ± 12.7</p> <p><b>Age ≥16, n (%):</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild TBI: 114 (65) Moderate/Severe TBI: 61 (35)</p>	<p><b>Depression:</b> Measured by Depression content scale (Dep) of MMPI-2 High Dep score (T-score &gt; 65) includes all individuals with symptoms in the clinical range</p> <p>Low Dep score (T-score &lt; 65) includes all individuals with symptoms not in clinical range</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Other anxiety disorder: NR</p> <p>Suicidality: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Logical memory, test scores in impaired range, %: <b>Ga:</b> 19.2 <b>Gb:</b> 32.8 <b>Ga/Gb:</b> P = 0.04</p> <p>PASAT memory, test scores in impaired range, %: <b>Ga:</b> 25.5 <b>Gb:</b> 41.9 <b>Ga/Gb:</b> P = 0.10</p>	<p><b>Depression, high score, n (%)*:</b> Total: 58 (33) Mild TBI: 36 (32) Moderate/Severe TBI: 22 (36)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Logical memory, test scores in impaired range, %: <b>Ga:</b> 19.2 <b>Gb:</b> 32.8 <b>Ga/Gb:</b> P = 0.04</p> <p>PASAT memory, test scores in impaired range, %: <b>Ga:</b> 25.5 <b>Gb:</b> 41.9 <b>Ga/Gb:</b> P = 0.10</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Slaughter et al., 2003</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> PRIME-MD</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 years of age or older</li> <li>• English speaking</li> <li>• Completely sentenced on all current charges (no further pending legal charges)</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Mild TBI:* A head injury immediately followed by LOC ≤ 30 minutes, alteration of mental status at the time of the accident (e.g. feeling dazed, confused or disoriented), or loss of memory of the time around the injury (based on ACRM criteria)</p> <p>Moderate/severe TBI:* Any injury of greater severity than mild TBI</p>	<p><b>Group(s):</b> <b>G1:</b> Inmates with self-reported TBI <b>G2:</b> Inmates without self-reported TBI</p> <p><b>N screened:</b> 475</p> <p><b>N eligible:</b> 91</p> <p><b>N included:</b> <b>G1:</b> 25 <b>G2:</b> 25</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, n (%):</b> 18-29: 30 (43.5) 30-39: 20 (49.0) 40-49: 17 (24.6) 50-59: 2 (2.9)</p> <p><b>Age ≥16, N (%):</b> 69 (100)</p> <p><b>Global injury severity (ISS, RTS, etc.):</b> NR</p> <p><b>Severity of TBI, n:</b> Mild: <b>G1:</b> 20 Moderate/severe: <b>G1:</b> 5</p> <p><b>Mechanism/type of injury:</b> NR</p>	<p><b>Depression:</b> PRIME-MD: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: PRIME-MD</p> <p>Irritability: NR</p> <p>Aggression: Brief Anger and Aggression Questionnaire (BAAQ)</p> <p>Suicidality: NR</p> <p>Substance use: PRIME-MD</p> <p>Other psychiatric diagnoses: BAAQ, COWAT, WAIS-R Vocabulary, WAIS-R Picture Completion, Trail Making Test A and B, WMS-R</p> <p><b>Health related QoL or functional status:</b> BAAQ, COWAT, WAIS-R Vocabulary, WAIS-R Picture Completion, Trail Making Test A and B, WMS-R</p>	<p><b>Depression, n (%):</b> MDD: <b>G1:</b> 13 (52) <b>G2:</b> 9 (36) MDD in partial remission: <b>G1:</b> 1 (4) <b>G2:</b> 1 (4) Dysthymia: <b>G1:</b>10 (40) <b>G2:</b> 8 (32) Minor depressive disorder: <b>G1:</b> 2 (8) <b>G2:</b> 3 (12)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: Generalized anxiety disorder, n (%): <b>G1:</b> 10 (40) <b>G2:</b> 7 (28)</p> <p>Anxiety disorder NOS, n (%): <b>G1:</b> 3 (12) <b>G2:</b> 2 (8)</p> <p>Irritability: NR</p> <p>Aggression: BAAQ score, mean ± SD: <b>G1:</b> 11.6 <b>G2:</b> 7.8 <b>G1/G2:</b> P = 0.05</p> <p>Suicidality: NR</p> <p>Substance use: Probable alcohol abuse/dependence, n (%): <b>G1:</b> 14 (56) <b>G2:</b> 13 (52)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Sliwinski et al., 1998 See Hibbard et al., 1998; Gordon, Brown et al., 1998; Gordon, Sliwinski et al., 1998</p> <p><b>Country, Setting:</b> US, other</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mean yrs:</b> 7.6</p> <p><b>Length of follow up:</b> NR</p> <p><b>Dep. Scale/Tool:</b> SCID, BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 18 years of age or older at the time of injury</li> <li>• Brain injury of traumatic origin occurring at least 1 year prior to the study</li> <li>• Current age &lt; 65 years</li> <li>• Self-identified as having received a TBI and as having a disability</li> <li>• Able to engage in a 3 to 4-hour interview</li> <li>• Resident of New York state and living in non-institutional settings in the community</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Self-report</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> 433</p> <p><b>N eligible:</b> 100</p> <p><b>N included:</b> 100</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, assessment, yrs ± SD:*</b> 39.8 ± 10.2</p> <p>Age, time of injury, mean (range): 32 (18-59)</p> <p><b>Age ≥16, n (%):</b> 100 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, LOC, %:</b> Dazed/confused &lt; 20 minutes: 20 &gt; 20 min to &lt; 1 day: 9 &gt; 1 day to &lt; 1 week: 20 1-4 weeks: 17 &gt; 1 month: 24</p>	<p><b>Depression:</b> SICD: DSM-IV criteria BDI: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> TIRR</p>	<p><b>Depression, SCID, n (%):</b> MDD: 23 (23) Dysthymia: 2 (2)</p> <p>BDI score and SCID diagnosis of depression, correlation: 0.30 (<i>P</i> &lt; 0.05)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> BDI score and TIRR Symptom Checklist score, correlation: 0.67 (<i>P</i> &lt; 0.05)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Stalnacke, 2007</p> <p><b>Country, Setting:</b> Sweden, tertiary care center</p> <p><b>Enrollment Period:</b> 2001</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 3 years</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>Admitted to the ED within 24 hours after the trauma</li> <li>GCS 13 to 15 on arrival to the ED</li> <li>Diagnosis of concussion/ commotion cerebri/mild head injury/mild TBI resulting in hospitalization for observation</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> Mild TBI: GCS 13 to 15</p>	<p><b>Group(s):</b> Patients with mild TBI</p> <p><b>N screened:</b> 214</p> <p><b>N eligible:</b> 201</p> <p><b>N included:</b> 163</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression, n (%):</b> Prior to injury: 7 (4.3) At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI (%):</b> 68 (42)</p> <p><b>Age, yrs ± SD:</b> 30.6 ± 14.4</p> <p><b>Age ≥16, n (%):</b> 163 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Mild TBI: 163 (100)</p> <p>PTA, minutes ± SD (range): 41 ± 118 (0-720)</p> <p>LOC, minutes ± SD (range): 4.0 ± 7 (0-30)</p>	<p><b>Depression:</b> BDI: 0-9: Asymptomatic 10-18: Mild to moderate depression 19-29: Moderate to severe depression 30-63: Extremely severe depression</p> <p><b>Other co-morbidities:</b> PTSD: IES Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> CIQ LiSat-11 RPQ</p>	<p><b>Depression, %:</b> Mild to moderate depression: 25.0 Moderate to severe depression: 15.0</p> <p>BDI score, mean ± SD: 6.9 ± 8.1</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: IES score, mean ± SD: 9.6 ± 13.0 Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> CIQ score, mean ± SD: 20.2 ± 4.2 LiSat-11 score, mean ± SD: 46.4 ± 10.7 RPQ score, mean ± SD: 10.7 ± 13.2</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Tateno et al., 2004</p> <p>See Tateno et al., 2003; Jorge et al., 2004</p> <p><b>Country, Setting:</b> US, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, HAM-D</p>	<p><b>Inclusion criteria:</b> See exclusion criteria</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating head injury or spinal cord injury</li> <li>• Severe comprehension deficits that precluded thorough neuropsychiatric evaluation</li> </ul> <p><b>TBI Def:</b> Mild TBI: GCS score 13 to 15</p> <p>Moderate TBI: GCS score from 9 to 12, or a GCS score of 12 to 15 with intracranial surgical procedures or with focal lesions greater than 15 cc</p> <p>Severe TBI: GCS score from 4 to 8</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> 92</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Mood disorder: 23 (25.0)</p> <p>Anxiety disorder: 11 (11.9)</p> <p>Alcohol abuse: 18 (19.6)</p> <p>Drug abuse: 11 (11.9)</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> PLC: 30.4 ± 11.5 (n=10)</p> <p>No PLC: 36.9 ± 16.0 (n=82)</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p>51 (55.4)</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p>HAM-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: HAM-A</p> <p>Irritability: NR</p> <p>Aggression: Overt Aggression Scale (OAS)</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric conditions: Pathological Laughter and Crying (PLC) Scale</p> <p><b>Health related QoL or functional status:</b> FIM</p>	<p><b>Depression, SCID, %:</b> MDD: 21 (22.8)</p> <p>Minor depression: 8 (8.7)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder, n (%): 36 (39.1)</p> <p>GAD: 20 (21.7)</p> <p>Irritability: NR</p> <p>Aggression: OAS score, mean ± SD: 1.6 ± 3.0</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses n (%): PLC: 10 (10.9)</p> <p>Depression and PLC: 5 (5.4)*</p> <p><b>Health related QoL or functional status:</b> FIM, mean ± SD: 61.2 ± SD: 9.8</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Tateno et al., 2003</p> <p>See Jorge et al., 2004; Tateno et al., 2004</p> <p><b>Country, Setting:</b> US, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD:</b> <b>G1a:</b> 23.9 ± 17.7 <b>G1b:</b> 33.4 ± 26.5</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, HAM-D</p>	<p><b>Inclusion criteria:</b> See exclusion criteria</p> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Penetrating head injury or spinal cord injury</li> <li>• Severe comprehension deficits that precluded thorough neuropsychiatric evaluation</li> </ul> <p><b>TBI Def:</b> Closed head injury followed by PTA ≥ 30 mins</p> <p>Mild TBI: GCS score 13 to 15</p> <p>Moderate TBI: GCS score from 9 to 12, or a GCS score of 12 to 15 with intracranial surgical procedures or with focal lesions greater than 15 cc</p> <p>Severe TBI: GCS score from 4 to 8</p>	<p><b>Group(s):</b> <b>G1:</b> Patients with TBI <b>G1a:</b> Patients with TBI and significant aggression <b>G1b:</b> Patients with TBI but not significant aggression <b>G2:</b> Multiple trauma patients with no HI or spinal cord injury</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 89 <b>G1a:</b> 30 <b>G1b:</b> 59 <b>G2:</b> 26</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Mood disorder: <b>G1:</b> 23 (26.4) <b>G1a:</b> 13 (43.3) <b>G1b:</b> 10 (17.5) <b>G2:</b> 8 (34.8)</p> <p>Anxiety disorder: <b>G1:</b> 11 (12.6) <b>G1a:</b> 4 (13.3) <b>G1b:</b> 7 (12.3) <b>G2:</b> 2 (8.7)</p> <p>Aggressive behavior (post- traumatic): <b>G1:</b> 30 (33.7) <b>G2:</b> 3 (11.5)</p>	<p><b>Depression:</b> SCID: DSM-III-R criteria HAM-D: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: HAM-A Irritability: NR</p> <p>Aggression: Overt Aggression Scale (OAS) ≥ 3 and ≥ 4 episodes of aggressive behavior Suicidality: NR Substance use: NR Other psychiatric conditions: NR</p> <p><b>Health related QoL or functional status:</b> FIM</p>	<p><b>Depression, SCID, %:</b> MDD: <b>G1a:</b> 56.7 <b>G1b:</b> 28.8 Minor depression: <b>G1a:</b> 23.3 <b>G1b:</b> 27.1</p> <p>HAM-D score, mean ± SD: <b>G1a:</b> 12.2 ± 6.4 <b>G1b:</b> 7.6 ± 5.6 <b>G1a/G1b:</b> <i>P</i> &lt; 0.01</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HAM-A score, mean ± SD: <b>G1a:</b> 12.8 ± 6.6 <b>G1b:</b> 8.4 ± 5.4 <b>G1a/G1b:</b> <i>P</i> &lt; 0.01</p> <p>Irritability: NR</p> <p>Aggression, n (%): <b>G1:</b> 30/89 (34)</p> <p>Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> <b>G1:</b> 62.7 ± 10.1 <b>G1a:</b> 63.2 ± 9.7 <b>G1b:</b> 62.5 ± 10.4 <b>G2:</b> 59.4 ± 10.9</p>

Evidence Table 1. TBI and Depression (continued)

Study Description	Inclusion/Exclusion Criteria	Population and Baseline Characteristics	Study Definitions	Depression Incidence/Prevalence & Co-morbidities
<p><b>Author:</b> Varney et al., 1987</p> <p><b>Country, Setting:</b> US, tertiary care centers</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, mean yrs (range):</b> 3.4 (2-8)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> DSM-III</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>History of closed head injury</li> <li>Period of unconsciousness lasting from a few minutes to eight days</li> <li>At least two yrs postinjury</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>History of head injury (G2)</li> </ul> <p><b>TBI Def:</b> NR</p>	<p><b>Group(s):</b></p> <p><b>G1:</b> Patients with TBI</p> <p><b>G2:</b> Patients with back injury</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> NR</p> <p><b>N included:</b></p> <p><b>G1:</b> 120</p> <p><b>G2:</b> 60</p> <p><b>N at conclusion:</b></p> <p><b>G1:</b> 120</p> <p><b>G2:</b> 60</p> <p><b>Depression:</b> Prior to injury: NR</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b></p> <p><b>G1:</b> NR</p> <p><b>G2:</b> None (see exclusion criteria)</p> <p><b>Age:</b> NR</p> <p><b>Age ≥16:</b> NR</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI:</b> NR</p> <p><b>Mechanism/type of injury:</b> NR</p>	<p><b>Depression:</b> DSM-III criteria</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability: DSM-III</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses: DSM-III</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> MDD: <b>G1:</b> 92/120 (76.7) <b>G2:</b> 23/60 (38.3)</p> <p>MDD onset, n: Immediately or shortly after TBI: <b>G1:</b> 45/92 (48.9) At least six months post TBI: <b>G1:</b> 42/92 (45.7)</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: NR</p> <p>Irritability, n (%): Patient report: <b>G1:</b> 29/92 (31.5) <b>G2:</b> NR</p> <p>Relative report: <b>G1:</b> 80/92 (87.0) <b>G2:</b> NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: NR</p> <p>Other psychiatric diagnoses, n (%): Bipolar: <b>G1:</b> 4/120 (3.3) <b>G2:</b> 0</p> <p>Schizophrenic: <b>G1:</b> 1/120 (0.8) <b>G2:</b> 0</p> <p><b>Health related QoL or functional status:</b> NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Vasterling et al., 2000</p> <p><b>Country, Setting:</b> US, tertiary care center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> NR</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, BDI</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Military veterans with exposure to combat as verified by military records</li> <li>• Completion of the SCID, BDI, Mississippi Scale for Combat-related PTSD, CES, and self report measures of depression, PTSD symptomatology, and combat exposure</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> HI: Injuries to the head from blunt or penetrating force sufficient to cause intracranial injury</p>	<p><b>Group(s):</b> <b>G1:</b> Veterans with HI <b>G2:</b> Veterans with no HI</p> <p><b>N screened:</b> 260</p> <p><b>N eligible:</b> 171</p> <p><b>N included:</b> <b>G1:</b> 87 <b>G2:</b> 84</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> 48.3 ± 9.0</p> <p><b>Age ≥16, n (%):</b> 171 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n:</b> LOC: 56 Data missing: 5</p> <p><b>Mechanism/type of injury:</b> NR</p> <p><b>Area of brain injured:</b> NR</p> <p><b>Concomitant injuries:</b> NR</p>	<p><b>Depression:</b> SCID: DSM-IV criteria BDI: 0: None, 59: Severe</p> <p><b>Other co-morbidities:</b> PTSD: SCID Mississippi Scale score Other anxiety disorder: SCID Irritability: NR Aggression: NR Suicidality: NR Substance use: SCID Other psychiatric diagnoses: SCID</p> <p><b>Health related QoL or functional status:</b> NR</p>	<p><b>Depression, n (%):</b> Lifetime:* <b>G1:</b> 61 (70.0) <b>G2:</b> 61 (72.6) Current: <b>G1:</b> 58 (66.7) <b>G2:</b> 48 (57.1)</p> <p>BDI score, mean ± SD: <b>G1:</b> 31.8 ± 11.4 <b>G2:</b> 27.1 ± 12.3 <b>G1/G2:</b> <i>P</i> &lt; 0.05</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities:</b> PTSD, n (%): Lifetime:* <b>G1:</b> 78 (89.7) <b>G2:</b> 73 (86.9) Current: <b>G1:</b> 76 (87.4%) <b>G2:</b> 72 (85.7%)</p> <p>Mississippi Scale score (PTSD), mean ± SD: <b>G1:</b> 126.0 ± 22.3 <b>G2:</b> 120.2 ± 27.4</p> <p>Other anxiety disorder, n (%): Lifetime:* <b>G1:</b> 20 (23.0) <b>G2:</b> 18 (21.4) Current: <b>G1:</b> 22 (25.3) <b>G2:</b> 18 (21.4)</p> <p>Irritability: NR Aggression: NR Suicidality: NR</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Wade et al., 1998</p> <p><b>Country, Setting:</b> UK, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury:</b> 6 months</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Age 16-65 years</li> <li>• Reside in Oxfordshire</li> <li>• Admitted to hospital with head injury of any severity, with or without other injuries</li> </ul> <p><b>Exclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• Minor head injuries, not requiring admission</li> </ul> <p><b>TBI Def:</b> Head injury defined as "any blow to the head causing a clinical diagnosis of head injury to be made"</p> <p>Mild: PTA &lt; 1 hr</p> <p>Moderate: PTA ≥ 1 hr but &lt; 24 hrs</p> <p>Severe: PTA ≥ 24 hrs but ≤ 7 days</p> <p>Very severe: PTA &gt; 7 days</p>	<p><b>Group(s):</b> <b>G1:</b> OXHIS <b>G2:</b> Usual care</p> <p><b>N screened:</b> 321</p> <p><b>N eligible:</b> <b>G1:</b> 184 <b>G2:</b> 130</p> <p><b>N included:</b> <b>G1:</b> 181 <b>G2:</b> 122</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI:</b> NR</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 33.5 ± 14.0 <b>G2:</b> 32.5 ± 12.2</p> <p><b>Age ≥16, n (%):</b> 303 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, n (%):</b> Very severe: <b>G1:</b> 10 (8) <b>G2:</b> 7 (9) Severe: <b>G1:</b> 21 (18) <b>G2:</b> 17 (22)</p>	<p><b>Depression:</b> HADS: NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: NR Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> RHFUQ 0 1-10 11-20 21-30 31-40</p>	<p><b>Depression, n (%):</b> Feeling depressed: <b>G1:</b> 33 (25) <b>G2:</b> 29 (34)</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: NR Other anxiety disorder: NR Irritability: <b>G1:</b> 38 (29) <b>G2:</b> 36 (42) Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Some disability at follow up, %: 61 RHFUQ score, mean ± SD: <b>G1:</b> 5.4 ± 7.8 <b>G2:</b> 8.2 ± 8.8</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Whelan-Goodinson et al., 2008</p> <p>Whelan-Goodinson et al., 2009<sup>^</sup></p> <p><b>Country, Setting:</b> Australia, tertiary care center</p> <p><b>Enrollment Period:</b> July 2000 to July 2005</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, yrs ± SD (range):</b> 2.98 ± 1.47 (0.5-5.5)</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> SCID, HADS<sup>^</sup></p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 17 to 70 years of age at time of injury</li> <li>• Lowest recorded GCS score &lt; 15</li> <li>• Cognitive capacity for participation as determined by neuropsychologist</li> <li>• Proficient in English</li> <li>• No history of TBI or neurological disorders</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> Patients with TBI</p> <p><b>N screened:</b> 720</p> <p><b>N eligible:</b> 550</p> <p><b>N included:</b> 100</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression, n (%):</b> Prior to injury: 17 (17)</p> <p>At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions, n (%):</b> Anxiety disorder: 13 (13) Substance abuse disorder: 41 (41)</p> <p><b>N with prior TBI:</b> 0 (see inclusion criteria)</p> <p><b>Age, yrs ± SD:</b> 37.18 ± 14.19</p> <p><b>Age ≥16, n (%):</b> Total: 100 (100)</p> <p><b>Global injury severity :</b> Length inpatient stay, days: 41.59</p> <p><b>Severity of TBI<sup>^</sup>:</b> Lowest pre-intubation GCS score, mean ± SD: 9.1 ± 4.12</p> <p>GCS, %: 13-14: 35 9-12: 20 3-8: 45</p>	<p><b>Depression:</b> SCID: DSM-IV criteria</p> <p>HADS<sup>^</sup>: 7 item depression subscale, 4 pt scale per answer (0-3) 0-7: Normal 8-10: Mild 11-14: Moderate 15:21 Severe</p> <p><b>Other co-morbidities:</b> PTSD: NR</p> <p>Other anxiety disorder: SCID</p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: AUDIT, DAST</p> <p>Other psychiatric diagnoses: SCID</p> <p><b>Health related QoL or functional status:</b> SPRS</p>	<p><b>Depression, n (%):</b> Major depression: 32 (32) Non-major depression: 2 (2) Resolved post-TBI depression: 12 (12)</p> <p>Severity, n (%):<sup>^</sup> Mild: 9 (26.5) Moderate: 12 (35.3) Severe: 13 (38.2)</p> <p>13/34 (38.2) patients diagnosed with SCID depression were in the “normal” HADS range</p> <p>5/66 (7.6) patients without SCID diagnosed depression scored in the clinical range on the HADS; none scored above 12</p> <p><b>Taking depression medications:</b> NR</p> <p><b>Other co-morbidities, n (%):</b> PTSD: 11 (11)</p> <p>Other anxiety disorder: GAD: 14 (14)</p> <p>36 (36)<sup>^</sup> Depressed patients with comorbid anxiety, %: 73.5<sup>^</sup></p> <p>Irritability: NR</p> <p>Aggression: NR</p> <p>Suicidality: NR</p> <p>Substance use: Current use: 17 (17) Resolved use: 4 (4)</p>

**Evidence Table 1. TBI and Depression (continued)**

<b>Study Description</b>	<b>Inclusion/ Exclusion Criteria</b>	<b>Population and Baseline Characteristics</b>	<b>Study Definitions</b>	<b>Depression Incidence/ Prevalence &amp; Co-morbidities</b>
<p><b>Author:</b> Ziino and Ponsford, 2006</p> <p><b>Country, Setting:</b> Australia, rehabilitation center</p> <p><b>Enrollment Period:</b> NR</p> <p><b>Design:</b> Cross-sectional</p> <p><b>Time from injury, days ± SD (range):</b> <b>G1:</b> 240.3 ± 222.7 (21 to 1,153) <b>G2:</b> NA</p> <p><b>Length of follow up:</b> NA</p> <p><b>Dep. Scale/Tool:</b> HADS</p>	<p><b>Inclusion criteria:</b></p> <ul style="list-style-type: none"> <li>• 16 to 60 years old</li> <li>• Adequate physical and cognitive abilities and understanding of English to complete tasks</li> <li>• No history of previous neurological disturbance</li> <li>• Not using illicit drugs</li> <li>• Comparison group had no history of brain injury or neurological illness</li> </ul> <p><b>Exclusion criteria:</b> See inclusion criteria</p> <p><b>TBI Def:</b> NR*</p>	<p><b>Group(s):</b> <b>G1:</b> Participants with TBI <b>G2:</b> Comparison group (no TBI)</p> <p><b>N screened:</b> NR</p> <p><b>N eligible:</b> <b>G1:</b> 49 <b>G2:</b> NR</p> <p><b>N included:</b> <b>G1:</b> 46 <b>G2:</b> 46</p> <p><b>N at conclusion:</b> NA</p> <p><b>Depression:</b> Prior to injury: NR At time of injury: NR</p> <p><b>Other preexisting psychiatric conditions:</b> NR</p> <p><b>N with prior TBI, N:</b> <b>G1:</b> NR <b>G2:</b> 0</p> <p><b>Age, yrs ± SD:</b> <b>G1:</b> 35.3 ± 13.1 <b>G2:</b> 34.1 ± 10.4</p> <p><b>Age ≥16, N (%):</b> 92 (100)</p> <p><b>Global injury severity:</b> NR</p> <p><b>Severity of TBI, GCS mean ± SD (range):</b> 10.0 ± 4.0 (3 to 15)</p> <p>GCS score, %: 13 to 15: 36.4 9 to 12: 31.8 3 to 8: 31.8</p>	<p><b>Depression:</b> HADS cut-offs: 0 to 7: Normal &gt;7: Clinically significant</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HADS (see above) Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> Fatigue Severity Scale (FSS) Visual Analog Scale for Fatigue (VAS-F), Vigor and Fatigue subscales</p>	<p><b>Depression, HADS &gt;7, %:</b> <b>G1:</b> 39.1 <b>G2:</b> 6.5 P&lt;.001</p> <p><b>Taking depression medications (%):</b> NR</p> <p><b>Other co-morbidities:</b> PTSD: NR Other anxiety disorder: HADS &gt;7, %: <b>G1:</b> 45.7 <b>G2:</b> 34.8 P=.29 Irritability: NR Aggression: NR Suicidality: NR Substance use: NR Other psychiatric diagnoses: NR</p> <p><b>Health related QoL or functional status:</b> FSS mean ± SD: <b>G1:</b> 4.3 ± 1.6 <b>G2:</b> 3.4 ± 1.1 P≤.01 VAS-F Vigor mean ± SD: <b>G1:</b> 5.5 ± 2.1 <b>G2:</b> 5.9 ± 1.7 VAS-F Fatigue mean ± SD: <b>G1:</b> 3.2 ± 2.4 <b>G2:</b> 2.7 ± 2.0</p>

**Evidence Table 2. Prevalence of depression by time of assessment in studies with poorly defined TBI**

<b>Author, Year Country Setting</b>	<b>N with TBI* (% with Depression Measure)</b>	<b>GCS Score</b>	<b>Assessment Method (mean score)</b>	<b>Prevalence %</b>
<b>Unspecified timing from injury</b>				
Aloia et al. <sup>1</sup> 1995 U.S. Neuropsychology lab	748 (100)	NR	MMPI (66.5)	37.0
Kinsella et al. <sup>2</sup> 1988 Australia Rehabilitation center	39 (100)	NR	Leeds Scale (NR)	33.0
Schofield et al. <sup>3</sup> 2006 Australia Prison	164 (96.3)	NR	RDS (NR)	25.0
<b>&lt; 3 months since injury</b>				
Rowland et al. <sup>4</sup> 2005 U.S. Rehabilitation centers	51 (100)	NR	BDI-II (8.85)	25.5
<b>6 to 12 months since injury</b>				
Sebit et al. <sup>5</sup> 1998 Kenya Tertiary care center	37 (100)	NR	SCID	54.1
Slaughter et al. <sup>6</sup> 2003 U.S. Prison	25 (100)	NR	PRIME: Major Remission Minor Depression	52.0 4.0 8.0
Wade et al. <sup>7</sup> 1998 U.K. Rehabilitation center	307 (71.0)	NR	HADS (NR)	28.4
<b>&gt;12 months since injury</b>				
Brooks et al. <sup>8</sup> 1987 U.K. Rehabilitation center	134 (100)	NR	Interview	49.0
Holsinger et al. <sup>9</sup> 2002 U.S. Veterans database	520 (100)	NR	Telephone SCID	11.2
Koponen et al. <sup>10-13</sup> 2004 Finland Tertiary care center	60 (100)	NR	SCID	26.7
Kreutzer et al. <sup>14</sup> 2001 U.S. Trauma center	722 (100)	NR	SCID	42.0

**Evidence Table 2. Prevalence of depression by time of assessment in studies with poorly defined TBI (continued)**

Author, Year Country Setting	N with TBI* (% with Depression Measure)	GCS Score	Assessment Method (mean score)	Prevalence %
<b>&gt;12 months since injury</b>				
Mobayed et al. <sup>15</sup> 1990 Ireland Tertiary care center	70 (78.6)	NR	SCID	20.0
Sliwinski et al. <sup>16-19</sup> 1998 U.S. Community sample	100 (100)	NR	SCID	23.0
Varney et al. <sup>20</sup> 1987 U.S. Tertiary care centers	120 (100)	NR	SCID	76.7
Curran et al. <sup>21-23</sup> 2000 Australia Rehabilitation center	88 (100)	NR	BDI (14.35)	55.7*
Felde et al. <sup>24</sup> 2006 U.S. Psychiatric/specialty	218 (100)	NR	HAM-D (18.3) BDI (19.9)	15.6
Gass et al. <sup>25</sup> 1991 U.S. Neuropsychology lab	58 (100)	NR	MMPI (59.1)	22.4
Hoofien et al. <sup>26</sup> 2001 Israel Rehabilitation center	76 (100)	NR	SCL-90 (1.07)	45.3
Kreuter et al. <sup>27-28</sup> 1998 Sweden Tertiary care center	92 (100)	NR	HADS (5.4)	9.8
Linn et al. <sup>29</sup> 1994 U.S. Support group	60 (100)	NR	SCL-90-R (63.9)	70.0
MacNiven and Finlayson <sup>30</sup> 1993 Canada Neuropsychology lab	59 (100) Year 1 59 (23.7) Year 2	NR	MMPI (66.24) MMPI (65.66)	40.7 42.9
Powell et al. <sup>31</sup> 2002 U.K. Tertiary care center	110 (85.5)	NR	HADS (8.1)	35.0
Vasterling et al. <sup>32</sup> 2000 U.S. Tertiary care center	87 (100)	NR	SCID	66.7

\*calculated by reviewer

**Evidence Table 3. Quality rating of individual nontreatment studies**

Citation	Overall Quality Score	Definition of TBI	Severity of TBI	Depression Definition	Participant Selection Criteria	Sampling Method Composite Score	LTFU	Prior Hx of Psychological Conditions
Al-Adawi et al. <sup>33</sup> 2007	Fair	++	+	+	+	+	N/A	+
Aloia et al. <sup>1</sup> 1995	Poor	-	+	+	-	+	N/A	-
Ashman et al. <sup>34</sup> 2004	Fair	++	+	++	+	+	-	+
Bay & Donders <sup>35</sup> 2008	Fair	+	+	+	+	+	N/A	+
Bay et al. <sup>36</sup> 2007	Poor	++	+	+	-	-	N/A	+
Bay et al. <sup>37</sup> 2002	Fair	++	+	+	+	+	N/A	+
Bombardier et al. <sup>38</sup> 2006	Fair	++	+	+	+	++	++	+
Bowen et al. <sup>39</sup> 1998	Good	++	+	+	+	+++	++	+
Brooks et al. <sup>8</sup> 1987	Poor	-	-	+	+	+	N/A	-
Brown et al. <sup>40</sup> 2004	Fair	++	+	++	+	+	N/A	-
Bryant et al. <sup>41</sup> 2001	Poor	-	+	++	+	+++	-	-
Chamelian et al. <sup>42</sup> 2004	Fair	++	+	++	+	+	N/A	+
Chamelian & Feinstein <sup>43</sup> 2006	Fair	++	+	++	-	++	++	+
Chiu et al. <sup>44</sup> 2006	Poor	++	+	++	-	+++	++	-
Curran et al. <sup>21</sup> 2000	Fair	+	+	++	-	+	++	-
Deb & Burns <sup>45</sup> 2007	Fair	++	+	++	+	+++	N/A	-
Deb et al. <sup>46-47</sup> 1999	Fair	++	+	+	+	+++	N/A	-
Dunlop et al. <sup>48</sup> 1991	Fair	-	-	+	+	++	N/A	+
Evans et al. <sup>49</sup> 2005	Fair	++	+	+	+	++	N/A	-
Fann et al. <sup>50</sup> 2005	Fair	++	+	++	+	+	-	+
Fann et al. <sup>51</sup> 1995	Fair	++	+	++	-	++	N/A	+
Jorge et al. <sup>52-53</sup> 1993 Fedoroff et al. <sup>54</sup>	Fair	++	+	++	+	+	+	+
Felde et al. <sup>24</sup> 2006	Poor	-	-	+	+	+++	N/A	+
Franulic et al. <sup>55</sup> 2004	Poor	-	+	++	-	+	N/A	-
Frenisy et al. <sup>56</sup> 2006	Poor	-	+	++	+	+++	++	-
Gagnon et al. <sup>57</sup> 2006	Fair	-	+	++	+	+++	+	+
Gass & Russell <sup>25</sup> 1991	Fair	-	+	+	+	+	N/A	+
Ghaffar et al. <sup>58</sup> 2006	Poor	++	+	+	+	+	++	+
Gomez-Hernandez et al. <sup>59</sup> 1997	Fair	-	+	+	+	+	+	+

**Evidence Table 3. Quality rating of individual nontreatment studies (continued)**

Citation	Overall Quality Score	Definition of TBI	Severity of TBI	Depression Definition	Participant Selection Criteria	Sampling Method Composite Score	LTFU	Prior Hx of Psychological Conditions
Gordon et al. <sup>18</sup> 1998	Fair	-	+	++	+	+++	N/A	-
Gordon et al. <sup>19</sup> 1998	Poor	-	+	++	+	+++	N/A	-
Hawley & Joseph <sup>60</sup> 2008	Fair	++	+	+	+	+++	++	-
Hibbard et al. <sup>17</sup> 1998	Fair	-	+	++	+	+++	N/A	-
Hibbard et al. <sup>61</sup> 2004	Fair	++	+	++	+	+	++	+
Hoge et al. <sup>62</sup> 2008	Fair	+	+	+	+	+++	++	-
Holsinger et al. <sup>9</sup> 2002	Fair	+	+	++	+	+++	N/A	-
Hoofien et al. <sup>26</sup> 2001	Fair	-	+	++	+	+++	++	+
Huang et al. <sup>63</sup> 2005	Fair	++	+	++	+	+++	++	+
Jorge et al. <sup>64</sup> 2004	Fair	+	+	++	+	+	++	+
Jorge et al. <sup>65</sup> 1993	Fair	++	+	++	+	+	+	+
Jorge et al. <sup>66</sup> 1994	Fair	++	+	++	+	++	+	+
Jorge et al. <sup>67</sup> 1994	Fair	++	+	++	+	+	+	+
Kant et al. <sup>68</sup> 1998	Fair	++	+	+	-	+	N/A	+
Kashluba et al. <sup>69</sup> 2006	Fair	++	+	+	+	+	++	+
Keiski et al. <sup>70</sup> 2007	Poor	++	+	+	+	+	++	-
Kennedy et al. <sup>71</sup> 2005	Poor	++	+	++	-	+	N/A	-
Kersel et al. <sup>72</sup> 2001	Good	++	+	+	+	+++	+	+
Kinsella et al. <sup>2</sup> 1988	Fair	+	+	-	+	+	N/A	-
Koponen et al. <sup>13</sup> 2006	Good	+	+	++	+	+++	N/A	+
Koponen et al. <sup>12</sup> 2005	Good	+	+	+	+	+++	N/A	+
Koponen et al. <sup>10-11</sup> 2002, 2004	Good	+	+	++	+	+++	N/A	+
Kreutzer et al. <sup>14</sup> 2001	Poor	-	+	++	-	+	N/A	-
Kreuter et al. <sup>27</sup> 1998	Fair	-	+	++	+	+++	N/A	-
Kreuter et al. <sup>28</sup> 1998	Poor	-	-	++	+	+++	++	-
Levin et al. <sup>73</sup> 2005	Fair	++	+	++	+	+	+	+
Levin et al. <sup>74</sup> 2001	Fair	++	+	++	+	+	N/A	+
Lima et al. <sup>75</sup> 2008	Fair	++	+	+	+	+++	N/A	-
Linn et al. <sup>29</sup> 1994	Poor	-	+	++	-	+	N/A	-
MacNiven & Finlayson <sup>30</sup> 1993	Poor	-	-	+	-	+	-	-

**Evidence Table 3. Quality rating of individual nontreatment studies (continued)**

Citation	Overall Quality Score	Definition of TBI	Severity of TBI	Depression Definition	Participant Selection Criteria	Sampling Method Composite Score	LTFU	Prior Hx of Psychological Conditions
Marsh & Kersel <sup>76</sup> 2006	Poor	-	+	-	+	+++	+	-
McCauley et al. <sup>77</sup> 2005	Fair	++	+	++	+	++	N/A	+
McCauley et al. <sup>78</sup> 2001	Fair	++	+	+	+	+	++	+
McCauley et al. <sup>79</sup> 2001	Fair	++	+	+	+	+++	++	-
McCleary et al. <sup>80</sup> 1998	Fair	-	+	+	+	+	+	-
Mobayed & Dinan <sup>15</sup> 1990	Fair	++	+	++	+	++	N/A	-
Mooney et al. <sup>81</sup> 2005	Fair	++	+	++	-	+	N/A	+
Mooney & Speed <sup>82</sup> 2001	Fair	++	+	++	-	+	N/A	+
Parcell et al. <sup>22</sup> 2006	Fair	-	+	++	+	+++	++	+
Perlesz et al. <sup>23</sup> 2000	Fair	-	+	++	+	+++	++	-
Popovic et al. <sup>83</sup> 2004	Fair	++	+	++	+	+	++	-
Powell et al. <sup>31</sup> 2002	Fair	+	+	+	+	+++	++	-
Rao et al. <sup>84</sup> 2008	Fair	++	+	++	+	+	N/A	+
Rapoport et al. <sup>85</sup> 2008	Fair	++	+	++	+	+	++	+
Rapoport et al. <sup>86</sup> 2003	Good	++	+	++	+	+++	N/A	+
Rapoport et al. <sup>87</sup> 2006	Good	++	+	++	+	+++	++	+
Rapoport et al. <sup>88</sup> 2006	Good	++	+	++	+	+++	+	+
Rapoport et al. <sup>89</sup> 2002	Good	++	+	+	+	+++	N/A	-
Rapoport et al. <sup>90</sup> 2003	Fair	++	+	++	+	+++	N/A	-
Rapoport et al. <sup>91</sup> 2005	Fair	++	+	++	+	+	N/A	+
Rowland et al. <sup>4</sup> 2005	Fair	+	+	++	+	+	N/A	+
Ruocco et al. <sup>92</sup> 2007	Poor	++	+	+	+	+	++	-
Satz et al. <sup>93</sup> 1998	Fair	++	+	+	+	+++	N/A	-
Satz et al. <sup>94</sup> 1998	Fair	++	+	+	+	+++	N/A	-
Schofield et al. <sup>3</sup> 2006	Poor	-	+	++	-	+	++	+
Sebit et al. <sup>5</sup> 1998	Fair	++	+	++	+	+	++	+
Seel & Kreutzer <sup>95</sup> 2003	Poor	-	+	++	-	+	N/A	-
Seel et al. <sup>96</sup> 2003	Fair	+	+	++	+	+	++	-
Sherer et al. <sup>97</sup> 2007	Fair	-	+	+	+	+	+	-
Sherman et al. <sup>98</sup> 2000	Fair	++	+	+	+	++	N/A	-

**Evidence Table 3. Quality rating of individual nontreatment studies (continued)**

<b>Citation</b>	<b>Overall Quality Score</b>	<b>Definition of TBI</b>	<b>Severity of TBI</b>	<b>Depression Definition</b>	<b>Participant Selection Criteria</b>	<b>Sampling Method Composite Score</b>	<b>LTFU</b>	<b>Prior Hx of Psychological Conditions</b>
Slaughter et al. <sup>6</sup> 2003	Poor	-	+	+	+	+++	N/A	-
Sliwinski et al. <sup>16</sup> 1998	Poor	-	-	++	+	+++	N/A	-
Stalnacke <sup>99</sup> 2007	Good	++	+	+	+	+++	++	+
Tateno et al. <sup>100</sup> 2003	Fair	++	+	++	+	+	++	-
Varney et al. <sup>20</sup> 1987	Poor	-	-	++	+	+	N/A	-
Vasterling et al. <sup>32</sup> 2000	Poor	-	-	++	+	+++	N/A	+
Wade et al. <sup>7</sup> 1998	Fair	+	+	+	+	+++	N/A	-
Whelan-Goodinson et al. <sup>101</sup> 2008	Good	++	+	++	+	+++	N/A	+

**Evidence Table 4. Quality rating of individual treatment studies**

Citation	Overall Quality Score	Randomization	Method and Blinding	Pt Selection Criteria	LTFU	Dropout Rates	Power Calculation	Statistical Issues	TBI Severity	Time Since Injury
Rapoport et al. <sup>85</sup> 2008	Fair	-	-	+	++	-	-	+	+	NR
Ashman et al. <sup>102</sup> 2009	Good	+	+	+	+	+	+	+	+	+

**Evidence Table 5. Operational definitions of TBI**

Association/Tool	Operational Definition
American Congress of Rehabilitation Medicine (ACRM)	<p>A patient with mild traumatic brain injury (mTBI) is a person who has had a traumatically induced physiological disruption of brain function, as manifested by <b>at least</b> one of the following: 1. any period of loss of consciousness; 2. any loss of memory for events immediately before or after the accident; 3. any alteration in mental state at the time of the accident (e.g., feeling dazed, disoriented, or confused); and 4. focal neurological deficit(s) that may or may not be transient; but where the severity of the injury does not exceed the following:</p> <ul style="list-style-type: none"> <li>• Loss of consciousness of approximately 30 minutes or less</li> <li>• After 30 minutes, an initial GCS score of 13–15</li> <li>• Post-traumatic amnesia (PTA) not greater than 24 hours<sup>103</sup></li> </ul>
Centers for Disease Control and Prevention (CDC)	<p>Mild TBI: A case of mTBI is an occurrence of injury to the head resulting from blunt trauma or acceleration or deceleration forces with one or more of the following conditions attributable to the head injury during the surveillance period:</p> <ul style="list-style-type: none"> <li>• Any period of observed or self-reported transient confusion, disorientation, or impaired consciousness</li> <li>• Any period of observed or self-reported dysfunction of memory (amnesia) around the time of injury;</li> <li>• Observed signs of other neurological or neuropsychological dysfunction, such as: <ul style="list-style-type: none"> <li>- Seizures acutely following head injury;</li> <li>- Among infants and very young children: irritability, lethargy, or vomiting following head injury;</li> <li>- Symptoms among older children and adults such as headache, dizziness, irritability, fatigue, or poor concentration, when identified soon after injury, can be used to support the diagnosis of mild TBI, but cannot be used to make the diagnosis in the absence of loss of consciousness or altered consciousness. Further research may provide additional guidance in this area.</li> </ul> </li> <li>• Any period of observed or self-reported loss of consciousness lasting 30 minutes or less.</li> </ul> <p>More severe brain injuries can include one or more of the following conditions attributable to the injury: loss of consciousness lasting longer than 30 minutes; PTA lasting longer than 24 hours; penetrating craniocerebral injury.<sup>104</sup></p>
Glasgow Coma Scale (GCS)	<p>A clinical scale developed for assessing the depth and duration of impaired consciousness and coma that can be employed following a TBI event. Three aspects of behavior are independently measured: motor responsiveness, verbal performance, and eye opening. A cumulative score can be calculated to determine the overall severity of the head injury.<sup>105</sup> Conventional cutoffs are:  3–8: severe TBI  9–12: moderate TBI  13–15: mild TBI</p>

**Evidence Table 5. Operational definitions of TBI (continued)**

<b>Association/Tool</b>	<b>Operational Definition</b>
World Health Organization (WHO)	Two common criteria used to define severity of brain injury include: (i) length of time the patient is unconscious after the injury, often termed loss of consciousness and (ii) length of PTA, that is, the time period from when the patient regains consciousness until he or she regains the capacity for continuous memory. The most common way of assessing the patient's level of consciousness is the GCS. Mild brain injury is defined as a GCS score of 13–15. PTA is often assessed more informally, by asking the patient, the family or the attending medical personnel to estimate the PTA time period. The cutoff for PTA for mild brain injury is usually 24 hours. When the length of time the patient is unconscious is used as a criterion for severity, a mild brain injury is usually defined as less than 30 minutes of unconsciousness. If a patient has a skull fracture, focal neurological deficits or hemiparesis, the brain injury is not usually considered to be mild. <sup>106</sup>
Other	Ad hoc definitions of TBI events and severity commonly include: <ul data-bbox="625 678 1047 789" style="list-style-type: none"><li>• Duration of loss of consciousness</li><li>• Duration of post-traumatic amnesia</li><li>• Altered mental status</li><li>• CT or MRI scans</li></ul>

**Evidence Table 6. Depression and quality of life assessment tools**

<b>Tool/Scale</b>	<b>Description</b>	<b>Scoring/Diagnosis</b>
Beck Depression Inventory (BDI/BDI-II)	A 21-item self-report of depression that assesses symptoms over a 7-day period. There is a 4-point scale for each item ranging from 0–3 (with 3 indicating maximum distress). The total self-rated scores range from 0 to 63. <sup>99</sup>	Conventional cutoffs: <sup>99</sup> Asymptomatic: 0–9 Mild-to-moderate: 10–18 Moderate-to-severe: 9–29 Extremely severe: 30–63 Individual studies may variously interpret the severity cutoffs assigned to specific scores.
Centers for Epidemiologic Studies-Depression (CES-D)	The 20-item CES-D asks respondents to rate the number of days (0–7) during the past week they experienced depressed symptoms. Higher scores denote greater levels of depression. As a measure of depressive symptoms, it contains Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV_ related items of depressed mood, sleep disturbance, weight change, diminished concentration, worthlessness, anhedonia, and decreased energy. <sup>36</sup>	Conventional cutoffs: <sup>36</sup> Mild: 16–20 Moderate: 21–26 Severe: 27–60 Individual studies may variously interpret the severity cutoffs assigned to specific scores.
WHO Composite International Diagnostic Interview (CIDI)	A comprehensive, fully standardized diagnostic interview for the assessment of mental disorders according to the definitions and criteria of the International Classification of Diseases version 10 (ICD-10) Diagnostic Criteria for Research and the DSM-III, Revised. <sup>107</sup>	The instrument contains 276 symptom questions, many of which are coupled with probe questions to evaluate symptom severity Diagnoses based on ICD-10 criteria and derived from patient responses to the symptom and probe questions. <sup>107</sup>
Clinical Interview Schedule-Revised (CIS-R)	Often reported in British studies, this structured interview instrument is useful for large surveys that use trained (but not necessarily expert) interviewers, or it can be completed as a self-report in a computerized version. Depression is one of 14 areas of symptoms that are elicited. It can provide both ICD-10 diagnoses and also, separately, severity scores. It takes less time to administer than the CIDI. <sup>108</sup>	Can be used to generate a total score, as well as diagnostic categories according to ICD-10 criteria (similar to the CIDI). <sup>108</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

<b>Tool/Scale</b>	<b>Description</b>	<b>Scoring/Diagnosis</b>
National Institute of Mental Health Diagnostic Interview Schedule (DIS-III-A)	A highly structured interview designed to make diagnoses by the following three systems: (1) DSM-III, published in 1980, (2) the Feighner criteria, published in 1972, and (3) the Research Diagnostic Criteria, published in 1978. Diagnostic questions incorporate elements from the three included systems. This highly structured interview allows for lay interviewers to perform the many tasks involved in making an accurate diagnosis. <sup>109</sup>	All diagnoses are made on a lifetime basis first, and then the interview inquires as to how recently the last symptom was experienced. On the basis of these answers it decides whether the disorder is current, defined for four time periods: the last 2 weeks, the last month, the last 6 months, and the last year. It also ascertains the age at the last symptom; the age at which the first symptom appeared; and, in the upcoming version 3, it will ascertain whether medical care was ever sought for symptoms of that disorder. In addition to diagnostic results, the DIS also provides a total symptom count across diagnoses for each of the three systems and a count of the number of criteria met for each diagnosis, whether or not that diagnosis is positive. <sup>109</sup>
Diagnostic and Statistical Manual of Mental Disorders (DSM-IV-TR, DSM-IV, DSM-III-R)	Standard manual for diagnosis published by the American Psychiatric Association and accepted nationally and increasingly worldwide. Provides diagnostic criteria with operationalized categorical thresholds. <sup>110</sup>	Depression is diagnosed as an episode, and then as a major depressive disorder (MDD) if depression is present without manic episodes. Specifiers allow depiction of severity, psychotic features, degrees of remission, chronicity, catatonic features, melancholic features, atypical features, and postpartum onsets. The diagnostician needs considerable training for use, and may also note Longitudinal Course Specifiers (With and Without Interepisode Recovery) or Seasonal Pattern. <sup>110</sup>
European Brain Injury Questionnaire (EBIQ)	63 questions regarding diverse "problems or difficulties that people sometimes experience in their lives" and it is requested that answers should concern the preceding month. The final question concerns "problems in general." <sup>111</sup>	The response alternatives are "not at all," "a little" or "a lot," are subsequently coded numerically as 1, 2, and 3 respectively. <sup>111</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

Tool/Scale	Description	Scoring/Diagnosis
Functional Independence/ Assessment Measures (FIM+FAM)	The Functional Assessment Measure (FAM) was developed for use in brain-injured individuals. FAM consists of 12 items intended to be added to the 18 items of the Functional Independence Measure (FIM). The FAM items emphasize the cognitive and psychosocial aspects of the disability. They total 30 items, each assessed on seven levels which, when summed, may be used to estimate a person's need for assistance (burden of care). The lower the score, the more severe the indicated dysfunction. The 18 FIM items concerning self-care, bladder and bowel control, mobility, and locomotion are indicators of motor disability. The 12 FAM items covering comprehension, expression, social interaction, emotional state, adaptation to limitations, ability to work, problem solving, memory, powers of concentration, and ability to form an opinion on safety are indicators of communication and psychosocial and cognitive functioning. <sup>27</sup>	An interviewer administered questionnaire. A score of 7 represents complete independence for a given item and a score of 1 represents complete dependence. <sup>60</sup>
General Health Questionnaire (GHQ)	A self-administered screening questionnaire designed for use in consulting settings aimed at directing those with a diagnosable psychiatric disorder. It concerns itself with two major classes of phenomena: inability to carry out one's normal "healthy" functions, and the appearance of new phenomena of a distressing nature. <sup>112</sup>	The GHQ may be thought of as comprising a set of questions that form a "lowest common multiple" of symptoms which will be encountered in the various differentiated syndromes of mental disorder, consisting of symptoms which best differentiate psychiatric patients from those who consider themselves to be well. The full-length version requires any 12 symptoms from a set of 60 total in order to identify probable cases. Scaled versions of the GHQ exist. <sup>112</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

<b>Tool/Scale</b>	<b>Description</b>	<b>Scoring/Diagnosis</b>
Hospitality Anxiety and Depression Scale (HADS)	A self-assessment questionnaire with subscales for anxiety and depression. Each subscale contains 7 items, with four possible answers for each, graded 0–3. <sup>75</sup>	Conventional cutoffs, individual subscales: Normal: 0–7 Borderline: 8–14 Abnormal: 15–21 The total score is obtained by adding two subscales and considering normal (0–14), borderline (15–28), and abnormal (29–42). <sup>75</sup> Individual studies may variously interpret the severity cutoffs assigned to specific scores.
Hamilton Depression Rating Scale (HAM-D)	This 17-item scale has often been used in expanded versions with 21 or 25 items. Consistently accepted since publication in 1960 as a standard severity measure for antidepressant medication outcome trials, its value derives from relatively balanced coverage of both somatic (sleep, appetite, energy) and psychological (sadness, guilt, suicidal thinking, insight) symptoms that are characteristic of depression. <sup>113</sup>	About half of the items are scored from 0 to 4; the others are measured from 0 to 2. Scores of 8 to 17 indicate subthreshold depression or dysthymic mood, 18 to 21 reflects a mild form of depression that will generally reach threshold for diagnosis, 22 to 24 is considered moderate, and 25 or more is often considered severe. <sup>113</sup>
Head Injury Behavior Rating Scale (HIBS)	A questionnaire containing 20 items describing behavioral problems often associated with traumatic brain injury (TBI). The patient is asked to indicate whether the identified behavior has become a problem for them since their TBI, and if so, how much distress this causes for them. The relatives' version of this measure contains the same 20 items as those in the TBI patients' version. The primary difference is that the caregiver is asked to rate the presence/absence of the problem behaviors in the TBI patient, and then rate how much distress it causes for them. <sup>76</sup>	In both the patient and caregiver versions, behavioral problems assessed as either yes/no, while distress is rated on a 4-point scale from 1 (no distress) to 4 (severe distress). <sup>114</sup>
Leeds Scales for Anxiety and Depression	15-item self assessment that describes common symptoms of anxiety and depression. The scales can be separated or administered together, and are derived from the HAM-D and the Hamilton Anxiety Scale. <sup>115</sup>	Conventional cutoffs: A score of 6-7 for both the depression and anxiety scores provides the most satisfactory division between healthy and sick populations. <sup>115</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

Tool/Scale	Description	Scoring/Diagnosis
Millon Clinical Multiaxial Inventory-III (MCMI-III)	The MCMI-III is a 175-item self-report true-false inventory. It was designed to measure the DSM-IV personality disorders in addition to depressive, sadistic/aggressive and masochistic/self-defeating personality disorders. The instrument distinguishes the severe personality disorders of schizotypal, borderline, and paranoid from the other personality patterns. It contains scales measuring clinical symptoms and conditions, including anxiety, somatoform disorder, mania, dysthymia, alcohol and drug dependence, post-traumatic stress disorder, thought disorder, major depression, and delusional disorder. <sup>92</sup>	The instrument uses base rate (BR) scores, which attempt to anchor scales to the base rate of psychiatric conditions in the population. The inventory also possesses four measures of response style. The validity index is sensitive to a random response set. The disclosure, desirability, and debasement scales, called the modifier indices, are measures of response style and dissimulation. The disclosure index is a measure of the overall number of symptoms reported on the inventory; elevations on this scale indicate a possible fake-bad response set, while very low scores may be indicative of a fake-good or defensive response set. The debasement index provides an indication of exaggerated psychopathology, while the desirability index gauges the tendency to present oneself in an overly positive light. <sup>92</sup>
Minnesota Multiphasic Personality Inventory (MMPI, MMPI-2)	Both the MMPI and MMPI-2 are subdivided into the same 10 clinical scales designed to assess an individual's perceived emotional, social, and behavioral functioning, as well as three validity scales, designated L, F, and K, designed to detect deviant test-taking attitudes. <sup>116</sup>	Scales: 1. Hypochondriasis 2. Depression 3. Hysteria 4. Psychotic deviate 5. Masculinity-femininity 6. Paranoia 7. Psychasthenia 8. Schizophrenia 9. Hypomania 10. Social introversion Mean subscale scores can be compared with a normative population to determine elevations. <sup>25</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

<b>Tool/Scale</b>	<b>Description</b>	<b>Scoring/Diagnosis</b>
Neurobehavioral Functioning Index-Depression (NFI-D)	The NFI is a factor-analytically derived and validated assessment tool. It consists of 6 scales—depression, somatic, memory/attention, communication, aggression, and motor—dealing with category-specific problems and symptoms characteristically experienced by people with recent onset of neurological and behavioral impairment. Seventy items are rated on a 5-point Likert-type scale and measure the frequency of behaviors and symptoms demonstrated by the identified participant (1 = never; 2 = rarely; 3 = sometimes; 4 = often; 5 = always). Higher scores indicate greater neurobehavioral problems. <sup>117</sup>	< 28: Not likely to be depressed 29–42: Borderline > 43: Highly correlated with clinical depression <sup>117</sup>
Neurobehavioral Rating Scale (NRS)	It contains 29 items subdivided into five factor categories and one nonfactor category. Factor I is memory difficulties, self-appraisal difficulties, reduction in affection, difficulties in flexible thinking, conceptual disorganization, disorientation, planning capacity problems, decline in initiative, and motivation. Factor II is anxiety, depressive moods, withdrawal. Factor III is hyperactivity—agitation, unusual thought content, mood swings, irritability, disinhibition, excitation, hostility, and suspiciousness. Factor IV is attention difficulties, loss of vigilance, motor slowing, and susceptibility to mental fatigue. Factor V is articulatory disorders, difficulties in oral expression, and difficulties in oral comprehension. <sup>56</sup>	Based on a 4-point scale (absent, mild, moderate, and severe). The ratings for each item are defined on the basis of the potential impact of the behavior on social and occupational independence. <sup>79</sup>
Personality Assessment Inventory (PAI)	Self-administered, objective inventory of adult personality. 344 items comprising 22 nonoverlapping full scales: 4 validity scales, 11 clinical scales, 5 treatment consideration scales, and 2 interpersonal scales. 27 critical items that act as indicators of potential crisis situations and have very low endorsement in normal sample. Responses to critical items facilitate followup questioning. <sup>118</sup>	Depression diagnosed if PAI score >70. <sup>70</sup> Individual studies may variously interpret the severity cutoffs assigned to specific scores.

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

Tool/Scale	Description	Scoring/Diagnosis
Patient Health Questionnaire-9 (PHQ-9)	The PHQ-9 parallels the 9 diagnostic symptom criteria that define DSM-IV MDD. The format and temporal framework of the items also correspond to the DSM-IV criteria and will facilitate the follow-up review of symptoms and diagnostic process. Unlike most other measures of depression, the PHQ-9 was developed, tested, and refined for use with medical patients. <sup>50</sup>	<p>The PHQ-9 is a self-report measure that asks if the subject had been bothered by the following problems in the past 2 weeks: (a) little pleasure or interest in doing things, (b) feeling down, depressed, or hopeless, (c) sleeping too little or too much, (d) feeling tired or having little energy, (e) poor appetite or overeating, (f) feelings of worthlessness or guilt, (g) concentration problems, (h) psychomotor retardation or agitation, and (i) thoughts of suicide.</p> <p>Subjects are asked to rate how often each symptom occurred: 0 (not at all), 1 (several days), 2 (more than half the days), or 3 (nearly every day). Several methods of depression screening using the PHQ-9. It can be scored on the basis of at least 5 symptom endorsed "more than half the days" (suicidal ideation could be "several days"), with at least one being a "cardinal symptom," that is, either (a) anhedonia or (b) depressed mood.<sup>38,50</sup></p> <p>Suggested cutoffs:<sup>50</sup>  Mild: 5–9  Moderate: 10–14  Moderately severe: 15–19  Severe: ≥20 depression</p> <p>Individual studies may variously interpret the severity cutoffs assigned to specific scores.</p>
Profile of Mood States (POMS)	A standardized list of 65 adjectives (happy, sad, angry, etc.) rated by the subject to measures six affective states, including a 15-item depressed mood. It uses a 0–5 Likert-type scale (0 = not at all; 5 = extremely). <sup>36</sup>	Range 0–60; higher scores indicate more severe depression. <sup>36</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

Tool/Scale	Description	Scoring/Diagnosis
Primary Care Evaluation of Mental Disorders (PRIME-MD)	A standardized, clinician-administered instrument that was developed to assess psychiatric disorders in primary care settings. It has been shown to be a psychometrically useful tool in identifying mental disorders in the medical setting as well as in research. (#461 Slaughter) Two components: a one-page patient questionnaire (PQ) that is completed by the patient before seeing the physician, and a 12-page clinician evaluation guide (CEG), a structured interview form that the physician uses to follow up on positive responses on the PQ. <sup>119</sup>	PQ: 26 yes/no questions about symptoms and signs present during the past month, divided into five diagnostic areas (mood, anxiety, somatoform, alcohol, and eating disorders). Patient responses to the PQ indicate to the physician which, if any, of the five diagnostic modules in the CEG should be used. CEG: Using the CEG, the clinician determines the presence or absence of 18 possible current mental disorders in the five broad diagnostic categories by asking specific questions based on the diagnostic criteria (often simplified for primary care use) contained in DSM-III-R. <sup>119</sup>
Referral Decision Scale (RDS)	Intended to provide researchers and trained correctional staff with a quick, easily administered/scored tool for screening jail detainees for serious mental illnesses (i.e., schizophrenia and the major affective disorders). Although offered as three subscales for identifying individuals with schizophrenia, bipolar, or depressive disorders, the RDS has not yet been demonstrated capable of distinguishing among these three major diagnostic categories. <sup>120</sup>	14 yes/no questions divided into three subscales and administered by trained individuals. <sup>120</sup>
Rivermead Post-Concussion Disorder Questionnaire (RPCQ)	It contains 18 questions probing symptoms of: headache, dizziness, nausea, noise sensitivity, sleep disturbance, fatigue, irritability, depression, frustration, forgetfulness, poor concentration, taking longer to think, blurred vision, light sensitivity, double vision, and restlessness. <sup>58</sup>	Self-report checklist in which patients rate Post-Concussion Syndrome symptoms according to whether they are no more of a problem, a mild problem, a moderate problem, or a severe problem in comparison with how they were functioning prior to their injury. <sup>121</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

Tool/Scale	Description	Scoring/Diagnosis
Schedule for Clinical Assessment in Neuropsychiatry (SCAN)	Developed with the aim of providing a comprehensive procedure for clinical examination that is also capable of generating many of the categories of the ICD-10 and DSM-III. <sup>122</sup>	It includes the Present State Examination 10th edition, the Item Group Checklist (IGCLIST), in which 59 item groups, each defined in terms of PSE-10 items, are rated directly; and the Clinical Information Schedule (CLINFO), containing summary items on intellectual level, personality disorders, social disablement, and clinical diagnosis. Information is obtained from the same sources as IGCLIST (case records, clinicians, and other informants). <sup>122</sup>
Structured Clinical Interview for the DSM-IV (SCID)	A structured interview assessment approach that operationalizes scoring elements of DSM criteria. It has been developed through the work of clinicians and researchers alike over the past 5 decades and is currently in its fourth revision (DSM-IV-TR). <sup>71</sup>	MDD: Five (or more) of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms is either item 1 or item 2: 1. Depressed mood most of the day, nearly every day 2. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day 3. Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite nearly every day 4. Insomnia or hypersomnia nearly every day 5. Psychomotor agitation or retardation nearly every day 6. Fatigue or loss of energy nearly every day 7. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick) 8. Diminished ability to think or concentrate, or indecisiveness, nearly every day (as indicated by either subjective account or observation made by others) 9. Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide. <sup>71</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

<b>Tool/Scale</b>	<b>Description</b>	<b>Scoring/Diagnosis</b>
Symptom Checklist (SCL-90-R, SCL-90, SCL-20)	A psychiatric checklist that produces psychopathology scores and a Global Severity Index (GSI), which reflects the clinical severity of all symptoms. The scale allows for the comparison of participants' scores to a U.S. normative sample. <sup>26</sup>	Can be administered as the full-length, 90-item version or a scaled version. The full-length version produces nine psychopathology scales. Results are compared with percentiles of the normative sample to determine elevations. <sup>26</sup>
Short Form Health Survey (SF-36, SF-12)	Self-report questionnaire designed to measure health and quality of life from the respondent's point of view. Available in full-length or scaled versions. <sup>19</sup>	1 (excellent) to 5 (poor) scoring on eight scales (full length): physical functioning (extent to which health limits physical activities), role functioning-physical (extent to which physical health interferes with work or other daily activities), bodily pain (intensity of pain and its effect on normal work), general health (personal evaluation of health), vitality (feeling energetic versus feeling tired), social functioning (extent to which physical health or emotional problems interfere with normal social activities), role functioning-emotional (extent to which emotional problems interfere with work or other daily activities), and mental health (general mental health, including depression, anxiety, behavioral-emotional control, and general positive affect). <sup>19</sup>
Visual Analog Scale for Depression (VAS-D)	Visual method for assessing depression. The distance in millimeters from the nondepressed side is the dependent measure. <sup>78</sup> Scoring is not usually applied to severity measures, but items can be compared within subjects for change in scoring with repeated measures.	Depressed mood is measured by asking the patient to make a mark on a 100 mm line between the statements "I am not depressed" to "I have never been more depressed." <sup>78</sup>

**Evidence Table 6. Depression and quality of life assessment tools (continued)**

<b>Tool/Scale</b>	<b>Description</b>	<b>Scoring/Diagnosis</b>
Short form of the WHO Quality of Life questionnaire (WHOQOL-BREF)	26 items or "facets" assessed. Facet defined as a behavior (e.g., walking), a state of being (e.g., vitality), a capacity or potential (e.g., the ability to move around), or a subjective perception or experience (e.g., feeling pain). 26 items include 2 items from the overall quality of life and general health facet and 24 facets further categorized into four domains: physical capacity (7 items), psychological well-being (6 items), social relationships (3 items), and environment (8 items). <sup>44</sup>	Each item uses a scale from 1 to 5, with a higher score indicating a higher quality of life. Domain scores are calculated by multiplying the mean of all facet scores included in each domain by a factor of 4, and potential scores for each domain vary from 4 to 20. <sup>44</sup>
Zung Depression Scale (ZDS)	A 20 item self-reported questionnaire descriptive of somatic and affective characteristics of depression. <sup>63</sup>	Each item rated from 1 to 4 to determine severity. Different cutoffs have been used for measuring depression: 55; $\geq 39$ . <sup>63,83</sup>

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## Appendix D. Excluded Studies

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## **Appendix E. Peer Reviewers**

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## Appendix F. Grey Literature Results

### Government and Nonprofit Publications

1. New Zealand Guidelines Group (NZGG). Traumatic brain injury: diagnosis, acute management and rehabilitation. Wellington (NZ): New Zealand Guidelines Group (NZGG); 2006 Jul. 240 p.  
[http://www.guideline.gov/summary/summary.aspx?doc\\_id=10281&nbr=5397&ss=6&x1=999#s24](http://www.guideline.gov/summary/summary.aspx?doc_id=10281&nbr=5397&ss=6&x1=999#s24)
2. Invisible Wounds of War. Psychological and Cognitive Injuries, Their Consequences, and Services to Assist Recovery (RAND Report) <http://www.dtic.mil/cgi-bin/GetTRDoc?AD=ADA494242&Location=U2&doc=GetTRDoc.pdf>
3. Gulf War and Health – IOM Report  
[http://www.nap.edu/catalog.php?record\\_id=12436#toc](http://www.nap.edu/catalog.php?record_id=12436#toc)
4. Fann JR, Hart T, Schomer KG. Treatment for Depression Following Traumatic Brain Injury: A Systematic Review. J Neurotrauma August 2009; ePub(ePub): ePub.  
<http://dx.doi.org/10.1089/neu.2009.1091>

### Nonpublished Research Opportunities and Current Projects

1. Psychological Health and Traumatic Brain Injury Advanced Technology/Therapeutic Development Award  
<http://www.grants.gov/search/search.do;jsessionid=bhWpKXcVBKCT217LKyv1Bjxz2QW4T8GXpWKn6rS8rg5dzVgXQdhH!-1757398871?oppId=48392&mode=VIEW>
2. Treatment strategy to prevent mood disorders following traumatic brain injury. PI: Ricardo Estiban Jorge. ICD: National Institute of Neurological Disorders & Stroke. Grant Number: 5R01NS055827-02  
[http://projectreporter.nih.gov/project\\_info\\_description.cfm?aid=7596417](http://projectreporter.nih.gov/project_info_description.cfm?aid=7596417)  
Project start date: 2008-04-01  
Project end date: 2013-03-31
3. Telephone and In-Person Cognitive Behavioral Therapy for Depression After Traumatic Brain Injury. PI: Jesse R. Fann, MD, MPH. Grant Number: H133G070016  
<http://www.naric.com/research/record.cfm?search=1&type=all&criteria=braininjuriesdepression&phrase=no&rec=1751>  
Start Date: October 1, 2007  
End Date: October 1, 2010
4. Effectiveness of a Group Cognitive-Behavioral Intervention for Depression after TBI and Factors that Affect Response to Treatment. PI: Allison Clark. Grant Number: H133G070222  
<http://www.naric.com/research/record.cfm?search=1&type=all&criteria=braininjuriesdepression&phrase=no&rec=1772>  
Start Date: October 1, 2007  
End Date: October 1, 2010

5. Post Traumatic Brain Injury (TBI) Depression, PI Information: Rao, VA. ICD: National Institute of Mental Health. Grant Number: 5K23MH066894-05  
Project Start: 01-AUG-2004  
Project End: 31-JUL-2009
6. Phone Cognitive Behavioral Therapy for Depression after Traumatic Brain Injury, PI Information: Fann, JR. ICD: Eunice Kennedy Shriver National Institute of Child Health and Human Development. Grant Number: 5R21HD053736-02  
Project Start: 15-SEP-2007  
Project End: 31-AUG-2009
7. Neuropsychiatry of Traumatic Brain Injury, PI Information: Kraus, MF. ICD: University of Illinois at Chicago. Grant Number: 5K23MH068787-05  
Project Start Date: 1-APR-2008  
Project End Date: 31-MAR-2010

## Clinical Trial Protocols

1. Mindfulness-Based Cognitive Therapy Intervention to Treat Depression in Individuals with a Traumatic Brain Injury Conditions: Depression; Traumatic Brain Injury Intervention: Behavioral: Mindfulness-Based Cognitive Therapy NCT ID: NCT00745940 Start Date: March 2009
2. Treatment Strategy to Prevent Mood Disorders Following Traumatic Brain Injury Condition: Traumatic Brain Injury Interventions: Drug: Placebo; Drug: Sertraline NCT ID: NCT00704379 Start Date: June 2008
3. Treatment of Post-TBI Depression Conditions: Traumatic Brain Injury; Depression Interventions: Behavioral: Cognitive behavioral therapy; Behavioral: Supportive psychotherapy NCT ID: NCT00211835 Start Date: November 2005
4. The Effect of Exercise on Mood After Traumatic Brain Injury Conditions: Traumatic Brain Injury Depression Interventions: Behavioral: Aerobic exercise Behavioral: No exercise NCT ID: NCT00571545
5. Pharmacological Intervention in Depression After Traumatic Brain Injury Conditions: TBI (Traumatic Brain Injury) Interventions: Drug: Venlafaxine NCT ID: NCT00205491
6. Depression and Traumatic Brain Injury Conditions: Depression Traumatic Brain Injury Interventions: Drug: citalopram (celexa) NCT ID: NCT00254007
7. TMS in the Treatment of the Sequelae of Closed Brain Injury Conditions: Depression; Closed Head Injury, Interventions: Device: rTMS; Device: Sham rTMS Start Date: October 2007 NCT ID: NCT00531258
8. Behavioral Activation for Posttraumatic Stress Disorder (PTSD)/ Depression Treatment in Operations Iraqi Freedom and Enduring Freedom (OIF/OEF) Veterans, Conditions: Posttraumatic Stress Disorder; Depression, Interventions: Behavioral Activation treatment; Other: Usual VA Treatment for PTSD, Start Date: May 2009 NCT ID: NCT00805532

9. Improving Psychological Wellness After Acquired Brain Injury Conditions: Depression;Anxiety;Brain Injury, Intervention: Cognitive Behavioural Therapy Start Date: June 2008, NCT ID: NCT00866632
10. The use of Motivational Interviewing and cognitive behavioural therapy to treat anxiety and/or depression following traumatic brain injury, Conditions: Traumatic Brain Injury, Depression, Anxiety, Intervention: Cognitive Behavioural Therapy (CBT), Start Date: June 2008, Registry Number: ACTRN12609000456257

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