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Prevalence of depression after moderate to severe traumatic brain injury among adolescents and young adults: A systematic review

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To review the prevalence of depression among adolescents and young adults after moderate to severe TBI. A systematic literature search was conducted on literature published up to December 2018 in PubMed, EMBASE, Cochrane and PsychInfo. A systematic review of the identified literature was based on PRISMA guidelines. Risk of Bias was evaluated based on the aspects of Risk of Bias assessment described by the Agency of Health Research and Quality. Seven studies were deemed eligible and information on the prevalence of depression among adolescents and young adults (age 13–35) after moderate to severe TBI was extracted. Depression was assessed at 12 months (n = 2), >12 months (n = 2) or at varying times (n = 3) after TBI. The identified studies reported a prevalence proportion of depression from 1.6% to 60%. The Risk of Bias assessment showed a range of study quality with the selection of subjects and analysis of attrition being problematic. Although literature is sparse and of varying quality, depression was found to be common among adolescents and young adults with moderate to severe TBI which implies a need to focus on depression in the rehabilitation process and calls for further research.

Key words: Adolescent, depression, prevalence, systematic review, traumatic brain injury, young adult.

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INTRODUCTION

Adolescence and young adulthood are life periods with many transitions that are characterized by increasing demands for independency (Meeus, 2016). The challenges of these life periods are unique to this age group as children live in a parent-protected environment while older adults have established themselves in relation to work and family. This means that teenagers and young adults with TBI struggle with expectations from both society and relatives on becoming independent while they are going through the rehabilitation process. This struggle might result in increased vulnerability for the development of depressive disorder that prevent proper rehabilitation as well as impairing psychosocial functioning (Hibbard, Ashman, Spielman, Chun, Charatz & Melvin, 2004) and quality of life (Di Battista, Godfrey, Soo, Catroppa & Anderson, 2014; Juengst, Kumar & Wagner, 2017). It is therefore vital to recognize the prevalence proportion of depression among adolescents and young adults after they have suffered a moderate to severe TBI.

Although most patients with TBI are adolescents and young adults, studies on depression after TBI focus primarily on adults (Guillamondegui, Montgomery, Phibbs et al., 2011; Osborn, Mathias & Fairweather-Schmidt, 2014; van Reekum, Cohen & Wong, 2000; Sasse, Gibbons, Wilson et al., 2014). To our knowledge, no reviews or meta-analyses on depression among adolescents and young adults age 13–35 years with moderate to severe TBI can be found in the literature. When looking at the studies of the adult population of patients with TBI, depression varies substantially from approximately 5.3% (Koponen, Taiminen, Hiekkanen & Tenovuo, 2011) to 76.6% (Varney, Martzke & Roberts, 1987); moreover, pooled prevalence estimates of depression among adults with TBI vary from 17% in the first year after TBI to 43% in the long-term (Scholten, Haagsma, Cnossen, Olff, van Beeck & Polinder, 2016). It is interesting to note that Guillamondegui et al. (2011) found a weighted average for prevalence of depression on 31% for adults regardless of time-since-injury and depression measures. Estimates of depression prevalence have been reported to be between 5.3% and 36% (Laliberté Durish, Pereverseff & Yeates, 2017) when looking at children and adolescents aged 0–18 years. The lower variance in the prevalence proportion of depression among children and adolescents aged 0–18 years with TBI compared to adults with TBI could reflect a general lower risk of developing a depression after TBI or be the result of fewer studies conducted among children and adolescents. It might, however, also reflect that this younger age group live in parent protected environments.

The displayed variation discussed above could reflect the use of different diagnostic tools, inconsistencies in depression diagnosis or pooling of brain injury severities (i.e., the population consisted of mild, moderate and severe TBI) (Guillamondegui et al., 2011; Osborn et al., 2014; Scholten et al., 2016). Thus, studies on depression after mild TBI report a prevalence of depression around 10–15% (Meares, Shores, Taylor et al., 2011; Ponsford, Cameron, Fitzgerald, Grant & Mikocka-Walus, 2011; Rao, Bertrand,

Rosenberg et al., 2010). The displayed variation might also depend on the timing of the occurrence of depression, for example, some studies investigate post-TBI depression, which is defined as depression that has developed after TBI, while other studies investigate depression in the TBI population regardless of whether the depression was present before the TBI. This distinction is particularly important because inclusion of participants with pre-TBI depression may elevate the prevalence proportion of depression after TBI as having depression before the TBI might increase the risk for depression after injury (Bombardier, Fann, Temkin, Esselman, Barber & Dikmen, 2010). The displayed variation might equally well be dependent on the definition of depression. Thus, to ensure that all relevant studies were included, this review used a broad definition of depression that included both depression diagnosed by the *Diagnostic and statistical manual of mental disorders* – 4ed (DSM-IV) (American Psychiatric Association, 1995) and the International statistical classification of diseases and related health problems – 10th edition (ICD-10) (World Health Organization, 2016), as well as depression described by clinically significant depressive symptoms.

In 2012, the Danish Ministry of Health and Elderly allocated money to investigate the need of rehabilitation among 15–30 year old survivors of an acquired brain injury. This, along with the fact that adolescence and young adulthood are life periods with many transitions and increasing demands for independency, are the reasons why this specific age group was chosen for the review aiming to identify existing knowledge about the prevalence of depression after moderate to severe TBI among adolescents and young adults age 15–30 years.

METHODS

The review was conducted according to the PRISMA (Preferred Reporting Items for Systematic reviews and meta-analyses) (Moher, Liberati, Tetzlaff & Altman, 2009) guidelines, and a protocol was developed before the search was conducted (cf. Data S1).

Search strategy

Relevant studies were identified through systematic literature searches in PubMed, EMBASE, PsychINFO and Cochrane. To ensure that all relevant studies were identified, the search was conducted without any specific time limits. The searches were imported in RefWorks and duplicate material was removed.

Search strategies were developed in consultation with a librarian and search specialist (please see Acknowledgement), and the search included a combination of subheadings and text words which are shown in the Appendix A and B.

PsychINFO subheadings differed from those in PubMed, EMBASE and Cochrane and were included because prevalence of depression was the focus of this review. Reference lists for included articles and relevant reviews were analyzed to identify additional relevant citations.

Study selection

Inclusion criteria. A study was evaluated as eligible if it fulfilled the inclusion criteria listed below concerning study design, participants and outcome measure.

Study design. Retrospective and prospective cohort, case-control and cross-sectional studies.

Participants. Our target group was those who were 15–30 years old at time of injury and had moderate to severe TBI. As none of the identified studies had a study cohort in the exact age range we were looking for (15–30 years), we decided to include studies with an age range of 13–35 years; thus, studies with either a wider or more narrow age-range were included if a prevalence of depression could be extracted for the included age group.

Within our definition of moderate to severe TBI, all patients with (1) an acute Glasgow Coma Scale (GCS) below 13 (Andriessen, Jacobs & Vos, 2010; Teasdale & Jennett, 1974), and those who had (2) an acute GCS above 12 and an abnormal computed tomography (CT) scan of cerebrum were included. The literature refers to the latter as complicated mild TBI and is included as studies have shown that sequelae after GCS > 12 and an abnormal CT-scan of the cerebrum more closely resembles the sequelae from moderate TBI rather than mild TBI (Kashluba, Hanks, Casey & Millis, 2008). A study was included if it was stated that the participants had moderate to severe TBI even if the definition of injury severity was either not reported or deviated from the above mentioned definition (cf. Risk of Bias assessment). This ensured that all relevant studies were included.

Outcome measure. We looked for a prevalence proportion of depression that could be extracted for the included participants regardless of assessment instrument/method.

According to DSM-IV and ICD-10, depression is defined as a major depressive episode (DSM-IV), minor depressive episode (DSM-IV) or depressive episode (ICD-10) (American Psychiatric Association, 1995; World Health Organization, 2016). It is general practice that depression is diagnosed through a diagnostic interview. Many international studies use a self-report questionnaire to identify the degree of depressive symptoms patients experience. Most self-report questionnaires use a cut-off score to identify cases of depression which are described as clinically significant depressive symptoms in the literature. Although participants with clinically significant depressive symptoms may not fulfil the diagnostic criteria for depression, significant knowledge would have been lost if studies that use this method were excluded.

Exclusion criteria. Reviews, case reports, editorials, conference abstracts and intervention studies were excluded. Intervention studies were excluded due to a high risk of selection bias. Articles written in languages other than English were also excluded.

Multiple publications. The included articles were evaluated to see if the same study population was used in more than one study. This was done to avoid counting prevalence rates multiple times. If it was found that the same population was used, the primary publication was included.

Data extraction

The first author (TOR) screened all titles and abstracts. Irrelevant citations were excluded. After the initial screening, the remaining citations were evaluated based on title, abstract and full-text, and citations were included according to the inclusion criteria. All citations evaluated as eligible and studies deemed by the first author to have uncertain inclusion criteria were discussed with the fifth author (CRB).

A data extraction form was developed to ensure that all relevant data were extracted. Data on the following variables were sought in the included articles: study design, country, study location, definition of TBI severity, size of the study population, distribution of gender, age (mean, SD and range), time-since-injury (mean, SD and range), inclusion and exclusion criteria for the study, assessment tool for evaluating depression or depressive symptoms and prevalence proportion of depression/clinically significant depressive symptoms. The first author made the data extraction which was then confirmed by the second author (SPJ). No authors of the identified studies were contacted to evaluate whether the results presented in the articles were correct or whether additional information was available.

Table 1. *Risk of Bias Assessment -description of the assessment criteria*

	Low risk	Unclear risk	High risk
Setting (selection bias)	Multi-center study	Unclear whether it is a single-center or multi-center study	Single-center study
Inclusion criteria (selection bias)	Inclusion and exclusion criteria are well-described	Either inclusion or exclusion criteria is not described	Inclusion and exclusion criteria are not described
Recruitment process (selection bias)	The recruitment process is well-described	The recruitment process is described but unclear	The recruitment process is not described or there has been a selection of contacted subjects
Completeness (attrition bias)	Attrition is reported and it is analyzed whether the included subjects differ from non-participants	There is uncertainty about the reported attrition and the analysis of participants and non-participants	Attrition is not reported and/or not analyzed
Definition of TBI severity (detection bias)	The definition of TBI severity is well-described	TBI severity is not defined, but data on GCS, PTA, coma length orCT-/MR-scan are available in the text	The definition of TBI severity is not described
Method to evaluate depression/ depressive symptoms (detection bias)	Structured interview with description of diagnostic method	Structured interview without description of diagnostic method	Self-report questionnaire
Report of outcome (reporting bias)	The relevant results are reported	The relevant results are reported, but descriptive data or attrition analysis is missing	The relevant results are not reported

Risk of Bias assessment

No specific Risk of Bias (RoB) assessment tool was identified as suitable as the included studies primarily consisted of cross-sectional observational studies. Instead, criteria for the RoB assessment were developed based on the aspects described by Agency of Health Research and Quality (Viswanathan, Ansari, Berkman et al., 2014) which is based on Cochrane Handbook of Systematic Reviews (Higgins & Green, 2011).

RoB was evaluated according to setting (selection bias), inclusion criteria (selection bias), recruitment process (selection bias), completeness (attrition bias), definition of TBI severity (detection bias), method to evaluate depression (detection bias) and report of outcome (reporting bias) and evaluated as "Low risk," "Unclear risk" and "High risk." A description of the evaluation criteria is presented in Table 1. The RoB assessment was conducted by the first author and evaluated by the co-authors.

RESULTS

Literature search

The systematic literature search was conducted on 16 January 2018. The search identified 1,208 potentially relevant, unique titles and was updated 14 December 2018. This search led to identification of 107 new potentially relevant, unique titles. Twenty additional articles were identified through references in the included articles and relevant reviews. Figure 1 shows the PRISMA-flowchart (Moher et al., 2009).

A total of 1,067 articles were excluded after title and abstract screening. Of the remaining 268 articles, 261 were excluded after full text reading. The main reasons for exclusion were: (1) results for patients with moderate to severe TBI could not be identified as they were pooled with patients with mild TBI; (2) results for adolescents and younger adults could not be identified because the younger participants were pooled with participants who were older; and (3) prevalence of depression was not reported. The remaining seven studies identified are the basis of this review.

Study characteristics

Table 2 shows the characteristics of the included studies. Three studies reported a prevalence of depression among adolescents and young adults with moderate to severe TBI (Garske & Thomas, 1992; Tyerman & Humphrey, 1984; Willmott, Spitz & Ponsford, 2015). Two studies had a population study group with a wider age range than our inclusion criteria. Even so, prevalence of depression for participants age 19–30 and age 18–29, respectively, could be extracted (Bombardier et al., 2010; van Reekum, Bolago, Finlayson, Garner & Links, 1996). Two studies reported a prevalence of depression on a more narrow age range – age 14–17 and age 14–18 respectively (O'Connor, Zatzick, Wang et al., 2012; Poggi, Liscio, Adduci et al., 2003).

The studies were conducted in five different countries: the United States (US) (n = 3) (Bombardier et al., 2010; Garske & Thomas, 1992; O'Connor et al., 2012), Canada (n = 1) (van Reekum et al., 1996), the United Kingdom (UK) (n = 1) (Tyerman & Humphrey, 1984), Italy (n = 1) (Poggi et al., 2003) and Australia (n = 1) (Willmott et al., 2015). Five studies were cross-sectional studies with only one assessment of depression (Garske & Thomas, 1992; Poggi et al., 2003; van Reekum et al., 1996; Tyerman & Humphrey, 1984; Willmott et al., 2015). Two studies were prospective studies with consecutive examinations in the same population (Bombardier et al., 2010; O'Connor et al., 2012). Participants were recruited from an acute trauma center (n = 1) (Bombardier et al., 2010), different hospitals (n = 1) (O'Connor et al., 2012) and a rehabilitation center/program (n = 5) (Garske & Thomas, 1992; Poggi et al., 2003; van Reekum et al., 1996; Tyerman & Humphrey, 1984; Willmott et al., 2015).

The sample size varied from 10 to 175. Demographics were available in six of the seven studies, but O'Connor et al. (2012) did not report data on age for the defined trauma groups. Bombardier et al. (2010) reported demographic information for

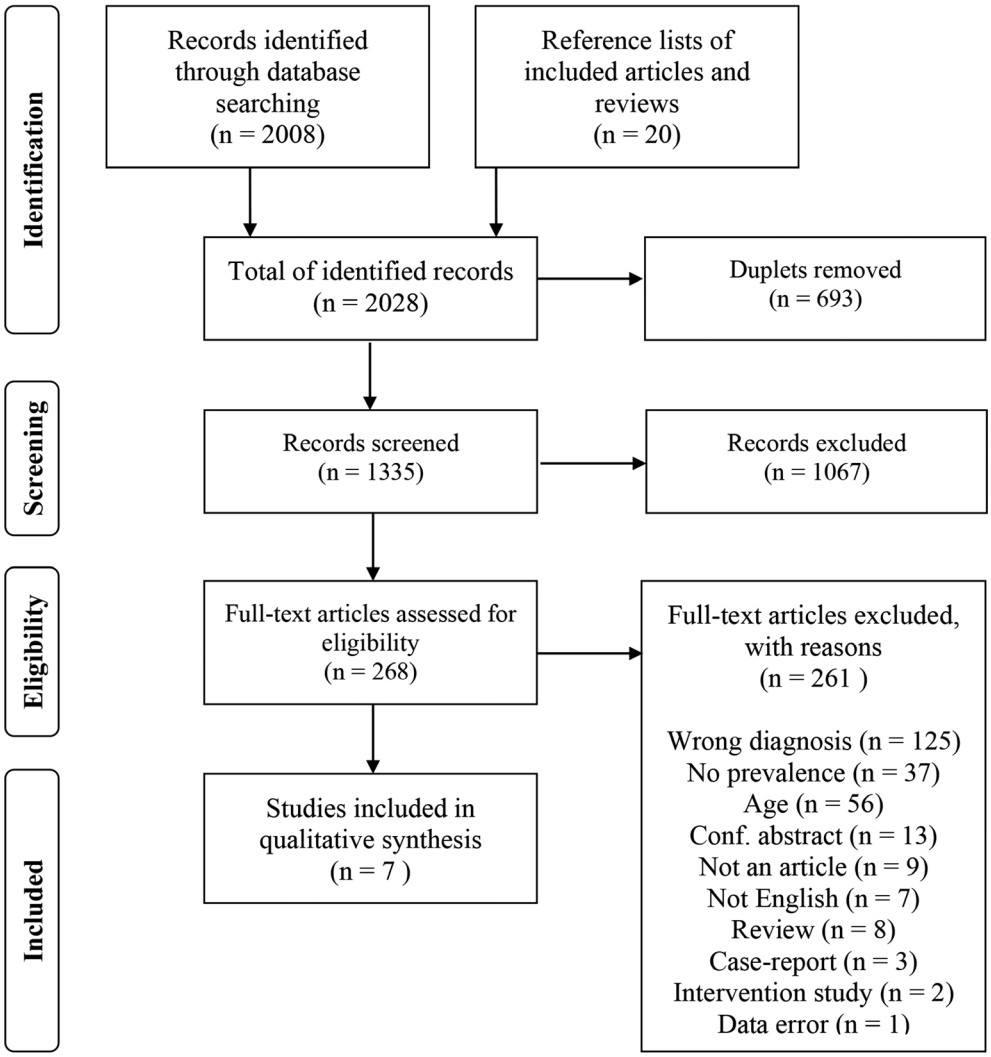

Fig. 1. Prisma flow diagram – study selection.

the whole study population and not according to the defined age groups. In the five studies reporting on age, the mean age varied from 15.8 to 23.4 years, and the ages ranged from 13 to 35 (Garske & Thomas, 1992; Poggi et al., 2003; van Reekum et al., 1996; Tyerman & Humphrey, 1984; Willmott et al., 2015). The majority of the participants were male and were 60–93% of the populations studied (Garske & Thomas, 1992; O'Connor et al., 2012; Poggi et al., 2003; Tyerman & Humphrey, 1984; van Reekum et al., 1996; Willmott et al., 2015). TBI severity was defined by either GCS and/or abnormal CT-scan of cerebrum (Bombardier et al., 2010; O'Connor et al., 2012; Poggi et al., 2003) or length of post traumatic amnesia (PTA) (Tyerman & Humphrey, 1984; Willmott et al., 2015). In two studies, the definition of TBI severity was not reported. In accordance with time-since-injury, two studies reported 12 months post-injury prevalence (Poggi et al., 2003; Willmott et al., 2015) while one study reported prevalences of 3, 12 and 24 months post-injury (O'Connor et al., 2012). Another study used five consecutive measurements to calculate how many participants developed MDD during the first 12 months after injury (Bombardier et al., 2010). One study included participants who were 2–15 months post-injury (Tyerman & Humphrey, 1984), and two studies were long-term follow-up (>12 months) (Garske & Thomas, 1992; van Reekum et al., 1996).

The studies used different assessments methods to screen for depression. Specifically, one study used a semi-structured interview made by an experienced psychiatric nurse (van Reekum et al., 1996), and another study used a structured interview based in PHQ-9 (Bombardier et al., 2010).The remaining studies used five different self-report questionnaires in which only the PHQ-9 and the Test of Anxiety and Depression in childhood and adolescence (TAD) were based on the diagnostic criteria for depression (Garske & Thomas, 1992; O'Connor et al., 2012; Poggi et al., 2003; Tyerman & Humphrey, 1984; Willmott et al., 2015).

Risk of Bias (RoB)

Figure 2 shows the RoB assessment. The RoB assessment showed that the identified studies had from one high risk assessment (Willmott et al., 2015) up to as many as five high risk assessments (Poggi et al., 2003). The main problem with the seven studies is knowing to what extend the results can be generalized to the whole population of adolescents and young adults with moderate to severe TBI. Willmott et al. (2015) was evaluated as having the

Table 2. *Characteristics of the seven-included studies*

Author, year, country, design	Study population	Inclusion (I)/exclusion (Ex)	Sample	Assessment
Bombardier et al., 2010, US, Prospective	Compl. mild to severe TBI, Level 1 trauma center (n = 175)	I: >18 y Ex: Uncompl. mTBI (GCS: 13–15 & no radio 1. abnorm)	18–29 y Demographics not available for the age group 18–29 y	Structured interview based on PHQ-9
Garske & Thomas, 1992, US, Cross-sectional	Severe TBI, Acute rehab. center, (n = 47)		22.9 y (5.5), 16–35; male 68%	BDI
Poggi et al., 2003, Italy, Cross-sectional	Moderate to severe TBI Rehab, center (n = 64)	I: 0–18 y, admission at max. 1 y from trauma E: positive history of previous brain injury, behavioural and psychological disorders, previous brain lesions, preexisting acute and chronic serious illness, vegetative state	15.8 y (1.48), 14–18; Male 77%	The first scale of the TAD
O'Connor et al., 2012 US, Prospective	Compl. mild (Mild II) to severe TBI, Nine hospitals (n = 64)	I: 14–17 y, discharged alive between March 1, 2007 and September 30, 2008	Age is not available for the two incl. groups male 72%	PHQ-9
Tyerman & Humphrey, 1984, UK, Cross-sectional	Severe TBI Rehab, center, (n = 22)	Ex: severe communication disorder	22, 17–34; male 93%	The Leeds scale of depression
van Reekum et al., 1996 Canada, Cross-sectional	Mild to severe TBI (only pts with moderate to severe TBI incL in current review) Rehab. program, (n = 10)	I: TBI secondary to MVA >2 y prior to study; Age <50 y; Suff. language, motor & perceptual skills to permit test; Lack of pre-TBI psychiatric history; Living in the community	23.4, 19–30; male 60%	Semi- structured interview SADS-L
Willmott et al., 2015, Australia, Cross-sectional	Compl. mild to severe TBI, Rehab, center, (n = 145)	I: students prior to injury	18.6 y (3.29), 13–34; male 64.1%	The Struct. outcome question

Notes: TAD, test of anxiety and depression in childhood and adolescence; PHQ-9, patient 60health questionnaire-9; BDI, beck depression inventory; SADS-L, schedule of affective disorder and schizophrenia-L; y, year.
[a]Age at assessment.

lowest RoB; however, the study focuses solely on individuals who were students prior to the injury and may therefore not be generalized to similarly aged TBI patients with different socioeconomic backgrounds. O'Connor et al. (2012) and Tyerman and Humphrey (1984) are the only multi-center studies among the included studies. In both studies, the recruitment process is unclear and attrition analyses were not reported. Thus, the results of the seven identified studies must be evaluated as a prevalence of depression for their specific sample and not the general population of adolescents and young adults with moderate to severe TBI (Bombardier et al., 2010; Garske & Thomas, 1992; O'Connor et al., 2012; Poggi et al., 2003; Tyerman & Humphrey, 1984; van Reekum et al., 1996; Willmott et al., 2015).

Prevalence proportion of depression

Table 3 reports the prevalence of depression and calculated 95% CI according to study and time-since-injury. The seven studies reported a prevalence of depression from 1.6% to 60% with assessment ranging from 3-month post-injury up to nine years after injury. At twelve months post-injury, the prevalence of depression varied from 13% to 39.3% (Poggi et al., 2003; Willmott et al., 2015). Long-term prevalence varied from 55.3% to 60% (Garske & Thomas, 1992; van Reekum et al., 1996). Tyerman and Humphrey (1984) found a prevalence of 60% two-fifteen months post-injury; and Bombardier et al. (2010) reported that during the first year after TBI, 52.6% of patients met criteria for MDD. O'Connor et al. (2012) found a stable and very low prevalence proportion of 1.6% among 14–17-year old adolescents at 3, 12 and 24 months post-injury.

A pooled prevalence proportion of depression has not been made due to the limitations of the individual studies on the generalizability of the results.

DISCUSSION

As no more than seven relevant studies were identified, this systematic literature review revealed limited existing knowledge on depression after moderate to severe TBI among adolescents and young adults. The primary reasons for exclusion of studies were due to pooling of severity and age as most studies included patients with mild, moderate and severe TBI and older life periods than our specified age group of 13–35 years. The included studies showed a high variation as O'Connor et al. (2012) found a very low prevalence of depression among patients (1.6%) while Tyerman and Humphrey (1984) and van Reekum et al. (1996) found prevalence proportions of 60%. A similar variation-span is seen in reviews on adults with TBI

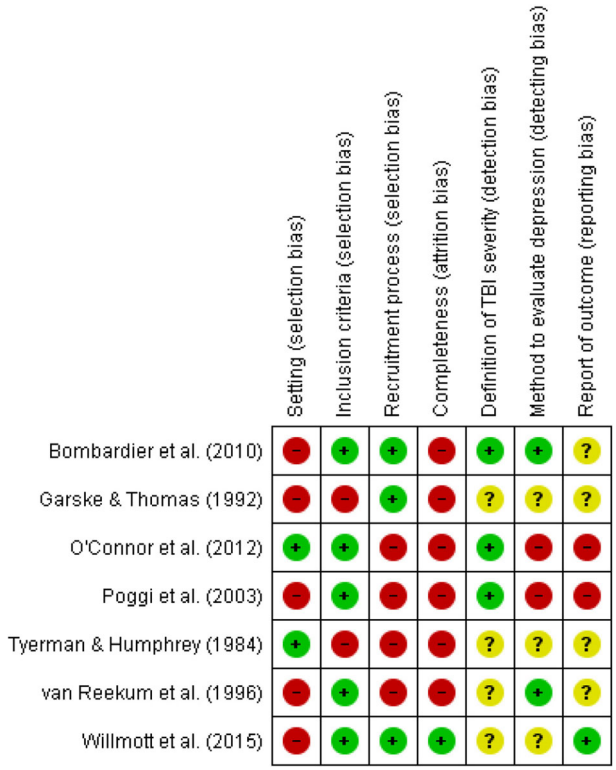

Fig. 2. Overview risk of bias assessment. "+" = "Low risk," "?" = "Unclear risk," "-" = "High risk." [Colour figure can be viewed at wileyonlinelibrary.com]

(Guillamondegui et al., 2011; Osborn, Mathias, Fairweather-Schmidt & Anstey, 2017; Scholten et al., 2016).

A pooled prevalence estimate was not calculated because the RoB assessment showed several limitations in the identified studies and their results may not, consequently, describe the general population of adolescents and young adults with a moderate to severe TBI. The primary limitations of the included studies were about selection of the study population and data completeness. An obscure recruitment process that is caused by selection of the participants or missing inclusion criteria can result in a questionable low or high prevalence of depression. Likewise, a missing attrition analysis can make it impossible to evaluate whether a difference between the non-attendees and the study population could have influenced the results. Accordingly, the generalizability of the results can also be affected by small study populations as this can result in questionable prevalence proportions of depression (Tyerman & Humphrey, 1984; van Reekum et al., 1996).

The limitations of the included studies can be one of the reasons for the high variation in the prevalence of depression as the studies reporting low and high prevalence proportions had the highest risk of biases. The variation could furthermore be the result of the application of different methods to evaluate the prevalence of depression. Hence, five of the studies used a self-report questionnaire which rated the amount of depressive symptoms instead of using the diagnostic criteria for depression (Garske & Thomas, 1992; O'Connor et al., 2012; Poggi et al., 2003; Tyerman & Humphrey, 1984; Willmott et al., 2015). This tendency was also observed in studies of the adult population (Osborn et al., 2014). The use of a cut-off score may elevate the prevalence proportion of depression because a patient can be evaluated as having depression without fulfilling the diagnostic criteria. In the same way, five consecutive assessments in the first year post-injury may also elevate the prevalence proportion of depression (Bombardier et al., 2010). Finally, the variation could illustrate a difference in the prevalence of depression among adolescents and young adults with the included studies indicating that young adults have higher prevalence of depression (Bombardier et al., 2010; Garske & Thomas, 1992; Tyerman & Humphrey, 1984; van Reekum et al., 1996; Willmott et al., 2015) than adolescents do (O'Connor et al., 2012; Poggi et al., 2003). Such a difference can be related to the demands of independency which increase from adolescence to young adulthood as part of psychosocial development (Erikson, 1950). The transition from childhood to adulthood and demands on independency is contextually and culturally dependent (Pao, 2017), and the prevalence of depression may increase at the same pace as the transition from a parent protected life to adult independency.

Overall, this review finds that there is a tendency among young survivors of a moderate to severe TBI of having increased risk of depression compared to the general population of adolescents and young adults. This is supported by the fact that six of the seven studies explored in this review found a higher prevalence proportion of depression than reported in studies of the general population. The EU-WMH project, which is based on data from 10 European countries, found a prevalence of depression of 5.2% among the 18–34-year old participants (Bruffaerts, Vilagut, Demyttebaere et al., 2009) which corresponds to the Global Health Estimates of depression of 3–6.5% within the 15–29-year old general population (World Health Organization, 2017).

Table 3. *Prevalence (%) of depression and time to follow-up. m = month; y = year*

Study	Severity	Prevalence (%) according to time of follow-up				95% CI	Follow-up mean (SD), *range*
		<1 year	1 year	>1 year	Varies		
Bombardier et al. (2010)	Compl. mild to severe				52.6[a]	44.9–60.2	1 m, 6 m, 8 m, 10 m, 1 y
Garske & Thomas (1992)	Severe			55.3		40.1–69.8	49.9 m (22.2), *16–97 m*
Poggi et al. (2003)	Moderate to severe		13			5.6–23.2	1 y
O'Connor et al. (2012)	Compl. mild to severe	1.6	1.6	1.6		0.0–8.4	3 m, 1 y, 2 y
Tyerman & Humphrey (1984)	Severe				60	36.4–79.3	7 m, *2–15 m*
van Reekum et al. (1996)	Moderate to severe			60		26.2–87.8	4.9 y, *2–9 y*
Willmott et al. (2015)	Compl. mild to severe		39.3			31.3–47.8	1 y

Note: Met MDD criteria in minimum one of 5 assessments during the first year after injury.

An increased risk of depression after a moderate to severe TBI in this group when compared to the general population may be related to a delay in the transition from adolescence into young adulthood as the sequelae from the TBI can limit the opportunity to gain independency, education and attachment to the labor market (Tibæk, Kammersgaard, Johnsen, Dehlendorff & Forchhammer, 2019). Moreover, an increased risk of depression could also be the result of peer victimization (Hung, Cassedy, Schultz et al., 2017) which appears to be related to psychosocial maladjustment and depression in adolescents without TBI (Hawker & Boulton, 2000). Taken together, it appears to be vital to focus on the significance of depression among adolescents and young adults with moderate to severe TBI as depression may complicate or delay the rehabilitation process (Bombardier et al., 2010; Hudak, Hynan, Harper & Diaz-Arrastia, 2012).

Strengths and limitations

The review was based on a thorough and systematic literature search. A limitation of the study is that one author had the primary responsibility for the selection process. Additionally, only the included studies and studies with doubt about inclusion were screened by a second author. This could have increased the risk of subjective assessment and affected the result of the study selection process.

Our choice to only include studies with adolescents and young adults approximately age 15–30 had both strengths and limitations. An opportunity to obtain knowledge about the existing literature on prevalence of depression in the defined age group was provided which has a special relevance as the proportion of TBI is relative high in this age group. The primary limitation of the limited age range is the fact that we identified very few studies and based on the Risk of Bias assessment, we did not calculate a pooled prevalence proportion.

Complicated mild TBI was included in the definition of moderate to severe TBI, as studies have shown that the sequelae of complicated mild TBI resembles the sequelae from moderate TBI rather than mild TBI (cf. Methods). This could both be a strength and a limitation, as it increased the number of identified studies but could have had an impact on the overall findings. The studies, which included patients with complicated mild TBI are the most recent studies and may illustrate a future definition of moderate to severe TBI. Finally, the fact that pre-TBI depression was not an exclusion criterion could be a study limitation, as inclusion of patients with pre-TBI depression may elevate the prevalence proportion of depression (see, for example the Introduction).

Implications for future research and clinical practice

Our work revealed a need of further studies on depression among adolescent and young adult survivors of moderate to severe TBI. Prospective multi-center studies on depression after moderate to severe TBI in well-defined cohorts is warranted to ensure knowledge about which patients are at risk of developing depression, the time-perspective for the development of a depression and to ensure that treatment of depressive symptoms is part of the rehabilitation programs. Although it is more time-consuming than using self-report questionnaires, a clinical diagnostic interview is the gold standard for diagnosing depression and is recommended for future studies. Further studies are also needed to evaluate whether adolescents and young adults differentiate from other age groups when it comes to depression after moderate to severe TBI.

Although, the review revealed limited data on depression among adolescents and young adults with moderate to severe TBI the results of the review demonstrate a need to allocate attention to and identify symptoms of depression among young survivors of moderate to severe TBI. If such symptoms are found, pharmacological and/or non-pharmacological interventions should be initiated to support the rehabilitation process.

CONCLUSIONS

Seven primary studies were identified from which a prevalence of depression among adolescents and young adult with moderate to severe TBI could be extracted. The individual prevalence proportions varied from 1.6% to 60%, however, the Risk of Bias assessment showed varying quality and the generalizability of the studies was questionable; consequently, a pooled prevalence estimate was not calculated. Overall, there is need for further studies to determine to what degree young survivors of moderate to severe TBI struggle with depression which can compromise the rehabilitation process.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article:

Data S1. Systematic review protocol.

APPENDIX A: LITERATURE SEARCH STRATEGIES

PubMed

("Brain Injuries"[Mesh] OR traumatic brain injur*[Text Word] OR brain contus*[Text Word] OR traumatic brain hemorrhag*[Text Word] OR diffuse axonal[Text Word] OR diffuse brain injur*[Text Word]) AND ("Depressive Disorder"[Mesh] OR "Depression"[Mesh] OR depressi*[Text Word]) AND (''Adolescent''[Mesh] OR "Young Adult"[Mesh] OR adolescen*[Text Word] OR young adult*[Text Word] OR youngster*[Text Word])

Embase

(traumatic brain injury/exp OR traumatic brain injur* (ti.ab.kw) OR brain contus* OR traumatic brain hemorrha* OR diffuse axonal OR diffuse brain injur*) AND (depression/exp OR depressi*) AND (adolescent/exp OR young adult/exp OR (adolescen* OR young adult* OR youngster))

Cochrane

(Brain Injuries [MeSH] OR traumatic brain injur* (ti,ab,kw) OR brain contus* (ti,ab,kw) OR traumatic brain hemorrhag* (ti,ab,kw) OR diffuse axonal (ti,ab,kw) OR diffuse brain injur* (ti,ab,

kw)) AND (Depressive Disorder [MeSH] OR Depression [MeSH] OR depressi* (ti,ab,kw)) AND (Adolescent [MeSH] OR Young Adult [MeSH] OR adolescen* (ti,ab,kw) OR young adult* (ti,ab, kw) OR youngster* (ti,ab,kw))

PsychInfo

(((**IndexTermsFilt**: (“Depression (Emotion))” *OR(***IndexTerms Filt**: (“Major Depression”)) *OR (***IndexTermsFilt**: (“Anaclitic Depression”)) *OR (***IndexTermsFilt**: (“Dysthymic Disorder”)) *OR (***IndexTermsFilt**: (“Endogenous Depression”)) *OR (***IndexTerms Filt**: (“Late Life Depression”)) *OR (***IndexTermsFilt**: (“Postpartum Depression”)) *OR (***IndexTermsFilt**: (“Reactive Depression”)) *OR (***IndexTermsFilt**: (“Recurrent Depression”)) *OR (***IndexTermsFilt**: (“Treatment Resistant Depression”)) *OR* (**title**: (depressi*)) *OR (***abstract**: (depressi*)) *OR* (**Keywords**: (depressi*))) *AND* ((**IndexTermsFilt**: (“Traumatic Brain Injury”)) *OR* (**IndexTerms Filt**: (“Head Injuries”)) *OR* ((**title**: (traumatic brain injur*)) *OR* (**abstract**: (traumatic brain injur*)) *OR* (**Keywords**: (traumatic brain injur*)) *OR* (**Any Field**: (“diffuse brain injur*”)) *OR* (**Any Field**: (“brain contus*”)) *OR* (**Any Field**: (“traumatic brain hemorrhag*”)) *OR* (**Any Field**: (“diffuse axonal”)) *AND* (**AgeGroupFilt**: “Young Adulthood (18-29 yrs)”)) *OR* (((**Index TermsFilt**: (“Depression (Emotion))” *OR(***IndexTermsFilt**: (“Major Depression”)) *OR (***IndexTermsFilt**: (“Anaclitic Depression”)) *OR (***IndexTermsFilt**: (“Dysthymic Disorder”)) *OR (***IndexTermsFilt**: (“Endogenous Depression”)) *OR (***IndexTerms Filt**: (“Late Life Depression”)) *OR (***IndexTermsFilt**: (“Postpartum Depression”)) *OR (***IndexTermsFilt**: (“Reactive Depression”)) *OR (***IndexTermsFilt**: (“Recurrent Depression”)) *OR (***IndexTermsFilt**: (“Treatment Resistant Depression”)) *OR* (**title**: (depressi*)) *OR (***abstract**: (depressi*)) *OR* (**Keywords**: (depressi*))) *AND* ((**IndexTermsFilt**: (“Traumatic Brain Injury”)) *OR* (**IndexTerms Filt**: (“Head Injuries”)) *OR* ((**title**: (traumatic brain injur*)) *OR* (**abstract**: (traumatic brain injur*)) *OR* (**Keywords**: (traumatic brain injur*)) *OR* (**Any Field**: (“diffuse brain injur*”)) *OR* (**Any Field**: (“brain contus*”)) *OR* (**Any Field**: (“traumatic brain hemorrhag*”)) *OR* (**Any Field**: (“diffuse axonal”)) *AND* (**AgeGroupFilt**: “Adolescence (13-17 yrs)”)) *OR* (((**IndexTerms Filt**: (“Depression (Emotion))” *OR(***IndexTermsFilt**: (“Major Depression”)) *OR (***IndexTermsFilt**: (“Anaclitic Depression”)) *OR (***IndexTermsFilt**: (“Dysthymic Disorder”)) *OR (***IndexTermsFilt**: (“Endogenous Depression”)) *OR (***IndexTermsFilt**: (“Late Life Depression”)) *OR (***IndexTermsFilt**: (“Postpartum Depression”)) *OR (***IndexTermsFilt**: (“Reactive Depression”)) *OR (***IndexTerms Filt**: (“Recurrent Depression”)) *OR (***IndexTermsFilt**: (“Treatment Resistant Depression”)) *OR* (**title**: (depressi*)) *OR (***abstract**: (depressi*)) *OR* (**Keywords**: (depressi*))) *AND* ((**IndexTermsFilt**: (“Traumatic Brain Injury”)) *OR* (**IndexTermsFilt**: (“Head Injuries”)) *OR* ((**title**: (traumatic brain injur*)) *OR* (**abstract**: (traumatic brain injur*)) *OR* (**Keywords**: (traumatic brain injur*)) *OR* (**Any Field**: (“diffuse brain injur*”)) *OR* (**Any Field**: (“brain contus*”)) *OR* (**Any Field**: (“traumatic brain hemorrhag*”)) *OR* (**Any Field**: (“diffuse axonal”)) *AND* ((**title**: (adolescen*)) *OR* (**abstract**: (adolescen*)) *OR* (**Keywords**: (adolescen*)) *OR* (**title**: (“young adult*”)) *OR* (**abstract**: (“young adult*”)) *OR* (**Keywords**: (“young adult*”)) *OR* (**title**: (youngster*)) *OR* (**abstract**: (youngster*)) *OR* (**Keywords**: (youngster*))))

APPENDIX B: KEYWORDS LITERATURE SEARCH FOR THE ORIGINAL SEARCH CONDUCTED 16 JANUARY 2018

#	Search	PubMed	Embase	Cochrane	PsychInfo
1	Brain Injuries [Mesh]/traumatic brain injury [exp]/Traumatic Brain Injury OR Head Injury	60,019	36,887	1,459	19,575
2	traumatic brain injur*	29,512	43,022	2,312	19,048
3	brain contus*	574	3,564	106	52
4	traumatic brain hemorrhag*	212	25	247	35
5	diffuse axonal	1,479	2,334	51	403
6	diffuse brain injur*	367	565	108	114
7	#1 OR #2 OR #3 OR #4 OR #5 OR #6	69,582	54,502	3,041	22,360
8	Depressive Disorder [Mesh]/Major Depression [Index Terms]	97,072		9,173	117,279
9	Depression [Mesh/exp/Index Terms]	98,419	416,405	7,550	24,274
10	depressi*	398,839	598,481	51,315	266,564
11	#8 OR #9 OR #10 #9 OR #10	399,487	632,417	51,360	266,815
12	#7 AND #11	2,520	4,220	254	1,803
13	Adolescent [MESH] OR Young Adult [MESH]	2,121,344			*
14	young adult [MESH/exp]		211,969	93,491	
15	Adolescent [MESH/exp]		1,466,172	275	
16	adolescen* OR young adult OR youngster	2,217,562	1,787,177		279,792
17	Adolescen*			119,862	
18	Young adult*			74,453	
19	Youngster*			105	
20	#13 OR #16/#14 OR #15 OR #16/#14 OR #15 OR #16 OR #17 OR #18 OR #19	2,217,562	1,787,177	163,126	279,792*
21	#12 AND #20	692	522	53	607

Note: *Index terms on age are not available in PsychInfo. Age filters are used in the final search