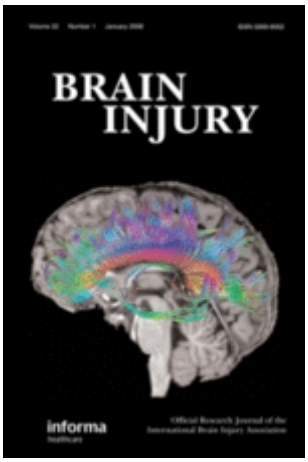

Cognitive and psychological interventions that might have changed postconcussion symptoms in patients with mild traumatic brain injury: a systematic review

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Title: Cognitive and psychological interventions that might have changed postconcussion symptoms in patients with mild traumatic brain injury: a systematic review

ABSTRACT

Objective: To evaluate the effects of cognitive and psychological interventions that might have changed postconcussion symptoms (PCS) in patients with mild traumatic brain injury (MTBI).

Data sources: The databases of CINAHL, Medline, PubMed, PsycINFO, Web of Science, and Cochrane Database of Systematic Reviews.

Review methods: Meta-analysis was conducted for randomized controlled trials that have included an assessment of PCS using the Rivermead Postconcussion Symptoms Questionnaire as primary outcomes by calculating the mean difference/ standardized mean difference using fixed/random effect models as appropriate.

Results: Systematic review with the date of the last search in Mar 2018 yielded 16080 articles, 17 articles with 3,081 participants were included in the final review. Interventions included psychoeducation (n=8), telephone problem-solving treatment (n=4), individual-based cognitive behavioural therapy (n=4), and cognitive training (n=1). No interventions is effective in reducing PCS at 3 to 6 months follow-up, however, an overall small effect size was found in pooled functional outcomes at 6 months.

Conclusions: There was no effect on symptom reduction at 3 to 6 months for interventions that might have changed PCS but improved functional outcomes were shown for patients with MTBI at 6 months. Long-lasting effects of interventions at 12 months or after were not studied.

(Word count: 200)

Keywords: mild traumatic brain injury, postconcussion symptoms, Rivermead Postconcussion Symptoms Questionnaire, cognitive and psychological interventions

INTRODUCTION

A large majority (75%) of head injuries results in a mild traumatic brain injury (MTBI) (1). The criteria of MTBI has been clearly defined (2, 3). Patients with MTBI typically have a favorable prognosis, generally expecting to recover within a few weeks to months post injury. However, about 5-20% of patients with MTBI continue to experience persistent post-traumatic complaints more than three months, or even years, postinjury (4). This is often termed postconcussion syndrome which is defined as "persistence of the symptoms beyond the expected time for recovery", i.e. >10–14 days in adults and >4 weeks in children, which has been suggested from 2 weeks to 3 months (3). Common symptoms arising from postconcussion syndrome may include, for example, headache, difficulty concentrating, anxiety, irritability, dizziness, imbalance, vertigo, photophobia, and phonophobia, etc. and these symptoms can cause postinjury posttraumatic stress disorder, stress, poor sleep, and somatic discomforts which may lead to significant problems in regard to resuming life roles, performing daily activities, or even returning to productive work, thus greatly impairing the psychological well-being, regardless of whether postconcussion symptoms are unique to a direct result of brain injury or traumatic injury itself (5).

There has been a paucity of research on non-pharmacological interventions targeted at the management of patients with postconcussion symptoms (PCS), and it would be difficult to conclude an early education and provision of information might be useful interventions for PCS (6, 7). Similarly, a previous systematic review which found only three randomized controlled trial studies outlining, psychoeducation and the provision of coping techniques, support, and reassurance as common management strategies for PCS, also did not find enough evidence to support the effectiveness of those suggested strategies because of great variety in sample selection, diagnostic criteria, methodology, and outcome measures (8). Effective interventions targeted at patients with MTBI and PCS have yielded mixed evidence to date, mainly because studies vary greatly in terms of sample selection, diagnostic criteria for traumatic brain injury, sample size, methodology, and choice of outcome measures used (4, 9), hence, the purpose of this

systematic review was to find out "what cognitive and psychological interventions that might have changed PCS in patients with MTBI where the frequency of PCS have been measured as an outcome, and what effect did they have?"

METHODS

Search strategy

The literature search, recruitment and selection process is summarized in Figure 1. A systematic search of quantitative articles for inclusion in this systematic review was conducted through an electronic search of six databases: CINAHL, Medline, PubMed, PsycINFO, Web of Science, and the Cochrane Database of Systematic Reviews. The keywords used in the search can be found in Figure 2. The inclusion criteria were as follows: 1) Randomized controlled trials with interventions that might have changed postconcussion symptoms (PCS); 2) interventions performed on patients with mild traumatic brain injury (MTBI) (age ≥ 18 year); 3) studies that have included an assessment of PCS using the Rivermead Postconcussion Symptoms Questionnaire (10) as primary functional outcomes at 3 to 6 months, and 4) full text English articles from Jan, 1998 to Dec, 2017. Exclusion criteria were interventions which were not of cognitive and/or psychological in nature, such as visual rehabilitation, vestibular rehabilitation, transcranial magnetic/electrical stimulation, exercise, etc.

Assessment of methodological quality

The selected articles that met the inclusion criteria were classified on the basis of the Oxford Centre for Evidence-Based Medicine levels of evidence (11), and were appraised for methodological quality using the Physiotherapy Evidence Database (PEDro) scale (12), as shown in Table 1, with scores of more than six classified as high quality, scores of four and five as fair quality, and scores below three as poor quality.

Meta-analysis

The outcome measures that were of primary focus in the review were identified in each

study and were considered for meta-analysis if the mean scores and standard deviation of the relevant outcome measures were available. Either mean difference (MD) or standardized mean difference (SMD) was reported to quantify the extent of treatment effectiveness. If the studies within the same meta-analysis used the same assessment tool with exactly the same unit of measurement, the mean difference was reported. If the studies within the same meta-analysis used different assessment tools or the same assessment tools with different units of measurement, the standardized mean difference was reported. The 95% confidence interval was also used to assess whether a significant treatment effect existed. If the 95% confidence interval covered the value of zero, this indicated that no significant treatment effect existed; if the 95% confidence interval did not cover the value of zero, this indicated the existence of a significant treatment effect. The I-square value of heterogeneity was computed for each meta-analysis, and it indicated a high level of heterogeneity across studies if the value approached the value of 1 or 100%. Moreover, the test of heterogeneity was used to determine whether the fixed-effect or random-effect model would be used for meta-analyses. If high heterogeneity with a significant result on the test of heterogeneity existed, the random-effect model was used, and if low heterogeneity with an insignificant result on the test of heterogeneity existed, the fixed-effect model was used. The software used for the meta-analysis was Review Manager 5.3.

RESULTS

Study selection

Systematic search with the date of the last search on 31th Mar, 2018 yielded a total of 16080 articles on interventions for patients with MTBI. After screening through the titles and abstracts, 16063 articles were excluded. The reasons for the exclusion of articles included duplicates, studies not focusing on related issues of PCS, non-traumatic brain injury population, non-intervention related studies, medical or pharmacological interventions, and not of cognitive and/or psychological interventions in nature.

Characteristics of study

A total of seventeen articles met the inclusion criteria and were included in the final review. Details of the characteristics and results of these studies are summarized in Table 2 and Table 3 respectively. According to the Oxford Centre for Evidence-Based Medicine levels of evidence criteria (11), 11 studies had 1b level of evidence and 6 had 2b level of evidence. Twelve studies were rated as high-quality controlled trials and five studies as fair-quality controlled trials according to the PEDro scale (Table 1) (12). In this systematic review, there were two groups of studies (four studies in total) with the same group of participants but measuring different outcome measures (13-16). There were also three articles which included a range of patients with mild to moderate traumatic brain injury that patients with MTBI could not be singled out (17-19).

The total number of subjects in this review was 3,081, with samples ranging from 28 to 395. The mean age of subjects ranged from 29.4 years to 41.4 years. The average length of time since injury reported in six studies was 2.44 years. In the 17 studies, the mechanisms of the injury resulting in traumatic brain injury were as follows: road traffic accident (47.1%), blast/combat (23.5%), falls (17.6%), not mentioned (11.8%). Only seven studies adopted the American Congress of Rehabilitation Medicine's definition of MTBI in their inclusion criteria (Table 2).

Outcome measures

Details of the outcome measures used in each study are summarized in Table 4; more than one primary outcome may be reported in each study. Thirteen studies had primary outcomes focused on symptom reduction, five studies focused on functional outcome, and four studies focused on health-related quality of life and life satisfaction. The majority of the studies used short follow-up periods, assessing patients 3 or 6 months post intervention, with only five studies assessing at 1-year follow-up (13, 16, 20-22). Only three studies provided outcome measure scores at post-intervention (17, 23, 24).

i) Symptom reduction

Among the seventeen studies, thirteen reported symptom reduction as primary outcome

measures (13, 14, 17-20, 23-29). Five studies (38.5%) reported a significant reduction in PCS, with four reporting symptom reduction at follow-up periods and one at post-intervention.

ii) Functional outcomes

Of the five studies that focused on functional outcomes, three reported on return-to-work (18, 21, 22) and two on daily activity and participation (15, 25). None of the five studies showed statistical differences in functional outcomes at follow-up periods.

iii) Health-related quality of life and life satisfaction

Of the four studies that focused on health-related quality of life and life satisfaction, three reported on quality of life as a primary outcome measure (15, 17, 27); only one reported on life satisfaction (20). None of these studies showed any statistical differences in quality of life and life satisfaction at post-intervention or follow-up period.

Interventions

The interventions in the 17 studies used in this systematic review can be categorized into psychoeducation (n=8), psychotherapy (n=8), and cognitive training (n=1). The results of each study are presented in Table 3.

The eight studies on psychoeducation evaluated the effectiveness of the provision of information, support, and reassurance for patients with MTBI and postconcussion symptoms, and the results can be compared in terms of minimal education model versus more intensive education model.

Matuseviciene et al. compared the effectiveness of an early intervention visit to a specialist (14), with an intervention including a standard examination of somatic symptoms, psychoeducation about symptoms, and referral to another specialist if required (intensive education model), to usual care, which includes receiving written

information about MTBI symptoms and outcomes, for patients who are at risk of developing postconcussion syndrome (≥3 symptoms) according to the Rivermead Postconcussion Symptoms Questionnaire] (minimal education model). No significant differences were found on the Rivermead Postconcussion Symptoms Questionnaire at 3-month follow-up. However, compared to the high risk groups, patients in the low risk groups (<3 symptoms according to the Rivermead Postconcussion Symptoms Questionnaire) were reported to face lesser problems in daily life and to have a better quality of life at 3-month follow-up (15).

Despite yielding no significant results on the Rivermead Postconcussion Symptoms Questionnaire, Ghaffar et al. found significant differences on depression outcome between the experimental and control group at 6 months (16). A similar result was also noted in the study by Belanger et al., in which the subgroup analysis showed that patients receiving concurrent mental health treatment benefited from the web-based education intervention ($p<0.05$) at 6-month follow-up, although no reduction in PCS was found.

Altogether, six out of the eight studies (75%) which provided psychoeducation as the intervention did not demonstrate significant differences on the Rivermead Postconcussion Symptoms Questionnaire at the 1-month (29), 3-month (14, 15), 6-month (23, 26), and 1-year follow-up (20). This suggests that early intervention, whether consisting of a single session of psychoeducation or more "intensive" psychoeducation with more follow-up appointments post discharge, has minimal impact on the reduction of PCS at various follow-up periods.

Only two studies showed positive outcomes on the Rivermead Postconcussion Symptoms Questionnaire at follow-up (19, 22). Wade et al. compared the effectiveness of an additional service by a specialist team for 6 months to existing standard services for patients suffering from a head injury of any severity (19). The experimental group was reported to have less social disability and less severe PCS at 6-month follow-up.

Vikane et al. investigated the efficacy of a multidisciplinary outpatient follow-up programme, consisting of a psychoeducation group intervention over a consecutive four-week period and individual contacts throughout the first year, on the return-to-work outcome for patients with MTBI (22). The multidisciplinary programme did not improve the return-to-work outcome; however, it was found to be helpful in reducing PCS at 1-year follow-up.

Only one of the selected studies used other interventions to evaluate the use of a 12-week compensatory cognitive training intervention, in addition to supported employment, on veterans with mild-to-moderate traumatic brain injury (18). The results from the study showed that the experimental group showed a significant improvement in PCS and prospective memory functioning at 3-month follow-up; however, no significant differences were found in return-to-work outcomes (50% versus 26% in the experimental and control group, respectively) (18).

The psychotherapy interventions (n=8) can be further classified into telephone problem-solving treatment (n=4) (13, 16, 21, 25), individual-based cognitive behavioural therapy (n=3) (17, 27, 28), and acceptance and commitment therapy (n=1) (23), with one study making a comparison between two interventions - cognitive behavioural therapy and telephone problem-solving treatment (20). Seven out of the eight studies showed that psychotherapy was effective in improving psychological distress (such as depression, anxiety, sleep quality) (13, 16, 17, 21, 24, 25, 28). However, only four studies, which were all conducted on civilians, demonstrated a significant reduction in PCS either at post-intervention (16) or at follow-up period (21, 25, 28) and the remaining three studies, which were all conducted on veterans, did not show a similar effect. None of the studies demonstrated any significant improvement in general health outcomes. Among the four studies which demonstrated a significant reduction in PCS, the interventions used were individual-based cognitive behavioural therapy (n=2) (17, 28) and telephone problem-solving treatment (n=2) (21, 25).

Meta-analysis results

A meta-analysis was conducted on the Rivermead Postconcussion Symptoms Questionnaire outcomes at 3 to 6 months (Figure 3). A total of five studies were included in the meta-analysis on the Rivermead Postconcussion Symptoms Questionnaire outcomes at 3 to 6 months using the random-effect model (I^2=67%, p=0.02). The results of the meta-analysis showed that there were no significant differences in the Rivermead Postconcussion Symptoms Questionnaire outcomes at 3 to 6 months (overall effect size of MD, -1.38, 95% confidence interval (-5.40, 2.64), p=0.50) (Figure 3).

Functional outcome measures, including the Rivermead Head Injury Follow-up Questionnaire (30), the Community Integration Questionnaire (31), and the Sheehan Disability Scale (32), which assess functional impairments in the area of productive work, social, and family life, were pooled together to conduct the meta-analysis at 6-month follow-up (Figure 4). A total of three studies were included in the meta-analysis at 6-month follow-up, using fixed-effect models (I^2=24%, p=0.27). The results of the meta-analysis showed that there were significant differences in pooled functional outcomes at 6 months (overall effect size of SMD, -0.20, 95% confidence interval (-0.36, -0.04), p=0.01) (Figure 4).

DISCUSSION

The strengths of this systematic review are that all the studies were randomized controlled trials and the majorities were high-quality controlled trials, and that only the Rivermead Postconcussion Symptoms Questionnaire was chosen to be the primary outcome. The meta-analysis also added rigor to our synthesis to evaluate the effectiveness of interventions in reducing PCS and improving functional outcomes. The results of the meta-analysis showed that there is no significant improvement in the Rivermead Postconcussion Symptoms Questionnaire outcomes at 3 to 6 months follow-up, indicating that there are no particular interventions which are effective in symptom reduction in PCS and that no intervention is more superior to others in reducing PCS.

In Figure 3, it can be seen that there is actually a mix of positive and negative results, which may indicate that interventions targeted at the reduction of PCS may have to be judged on a case by case, intervention by intervention basis until more robust evidence on the interventions that are effective in reducing PCS is available.

In our study, it can be derived from the results of our systematic review that tweaking the intensity of psychoeducation given to patients at-risk-of developing or with PCS, has a minimal impact on reducing PCS. The results could probably have been diluted by the inclusion of patients who made a very good spontaneous and functional recovery and thus did not need any interventions (33). Therefore, studies have recommended adopting more stringent criteria to identify patients who would benefit from further treatment, such as identifying those who are at high risk of developing postconcussion syndrome by having ≥3 symptoms according to the Rivermead Postconcussion Symptoms Questionnaire during the early phase post injury (15). In addition, several studies have also recommended the screening of patients at-risk-of developing specific mental health conditions, such as depression and anxiety as significant reductions in mental health related symptoms have been reported as a result of early interventions (23, 26).

Although the studies favoring the use of psychotherapy treatments, such as telephone problem-solving treatment and individual-based cognitive behavioural therapy, to reduce PCS in civilians, no positive evidence was found from our meta-analysis result. The same effect has been observed in veterans, particularly in terms of the reduction of PCS (24). Studies have postulated several explanations, with some attributing the reason to the participant's belief about whether the source of the postconcussion syndrome complaint could inflict permanent damage to the brain and some attributing it to biases in the participant's retrospective recall of their pre-traumatic brain injury functioning, which may have led to stable or minimal changes to the Rivermead Postconcussion Symptoms Questionnaire scores over time (34). Telephone-delivered problem-solving treatment, with an emphasis on overcoming barriers to participating

in everyday activities by managing patients' symptoms, can be a valuable intervention method as it is relatively cheap and easy to implement by a group of care providers (13). However, studies have also cautioned that telephone problem-solving treatment cannot replace cognitive behavioural therapy, particularly for patients at a high risk of developing, or with existing, mental health disorders (21).

Interestingly, positive outcomes were noted for the pooled functional outcomes (p=0.01) at 6-month follow-up, yielding an overall small effect size of 0.20. Interventions which contributed to the positive outcomes included: 1) an early intervention by a specialist team with continual follow-up till 6 months postinjury and advice on gradual return to everyday activities (effect size of 0.35) (19), and 2) the telephone problem-solving treatment, which focused on facilitating patients to develop strategies to manage their symptoms in order to achieve an early return to everyday activities (effect size of 0.19) (25). It is postulated that interventions which focus on improving functional outcomes and have follow-up till at least 6 months postinjury tend to yield better results.

Limitations of the review

There are a few limitations in this systematic review. First, as there is a paucity of research on PCS, it was impossible to conduct a meta-analysis on any particular interventions which could potentially emerge as specific cognitive and/or psychological interventions to reduce PCS. Second, it has only included studies from the year Jan 1998 to Dec 2017, interventions before 1998 and after Dec 2017 have not been reviewed. We also excluded other interventions for PCS in this review, which might potentially affect the outcome of concussion recovery. Third, 3 studies included both patients with mild or moderate traumatic brain injuries that patients with MTBI could not be singled out. Fourth, most of the selected studies only had short-term follow-up, up to 1 year, for patients with MTBI and PCS, and long-lasting effects of interventions were not studied; in particular, we found only two studies that included functional outcomes at 12-month follow-up, therefore, we could not conduct an analysis on the pooled functional outcomes at 12-month follow-up which violates the rule that at least

three studies are required for a meta-analysis. More randomized controlled trials on MTBI patients with PCS are necessary in future to evaluate the effectiveness of interventions for this group of patients.

CONCLUSIONS

Current cognitive and psychological interventions for PCS showed small effect size in functional outcomes for patients with MTBI at 6 months but there was no effect on symptom reduction. Long-lasting effects of interventions for PCS at 12 months or after were not studied.

(3,185 words)

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None

Disclosure of Interest Statement:

The authors report no conflict of interest.

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Figure 1. PRISMA flow diagram of the selection process

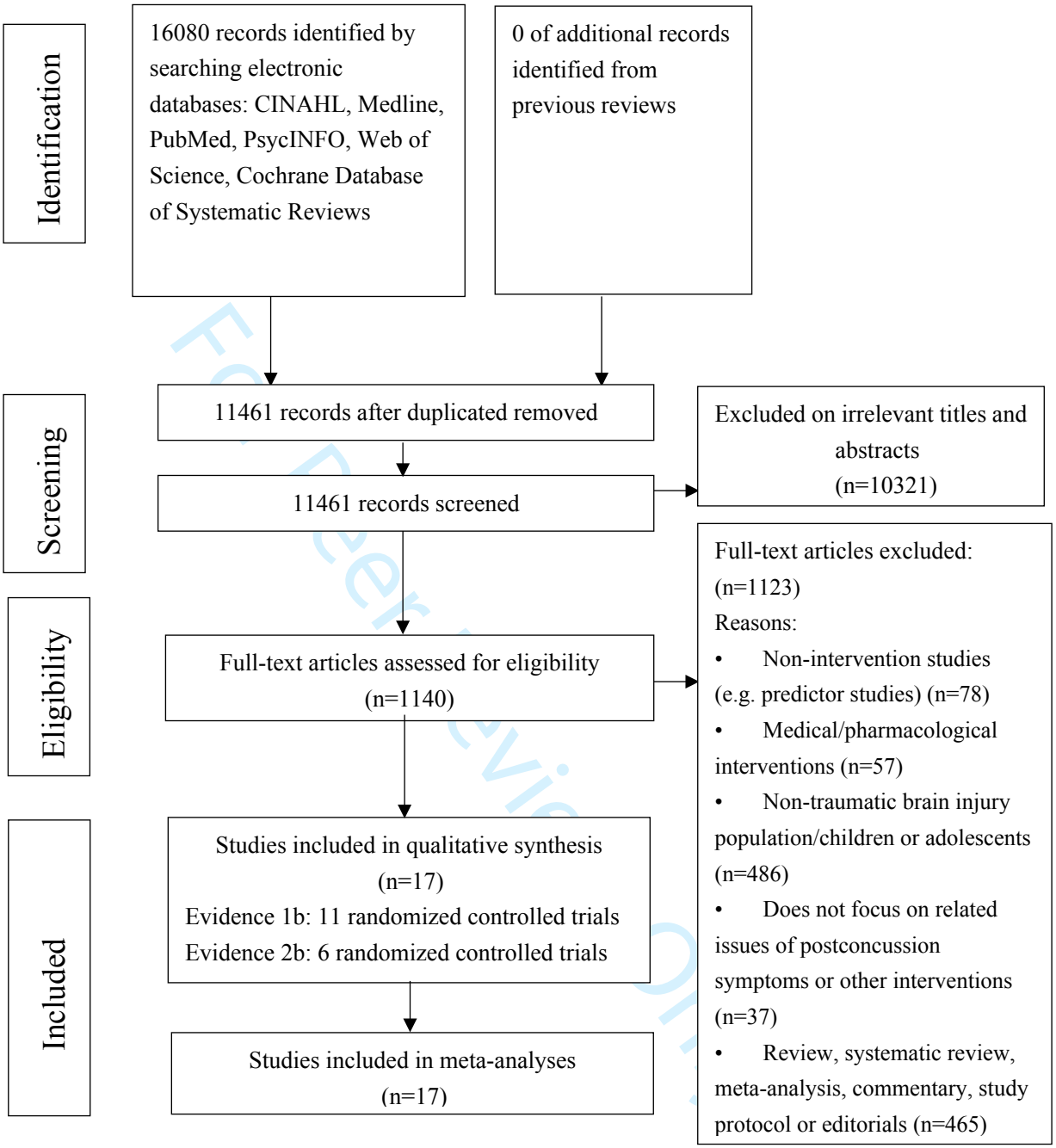

Figure 2: Number of articles searched in each database

1. Database: CINAHL

No	Keywords used	Articles yielded
1	Mild traumatic brain injury OR Mild head injury OR Closed head injury OR Postconcussion symptoms **AND**	794
2	Treatment OR Intervention OR Therapy OR Rehabilitation	
Total	**229**	

2. Database: Medline

No	Keywords used	Articles yielded
1	Mild traumatic brain injury OR Mild head injury OR Closed head injury OR Postconcussion symptoms **AND**	528
2	Treatment OR Intervention OR Therapy OR Rehabilitation	
Total	**318**	

3. Database: PubMed

No	Keywords used	Articles yielded
1	Mild traumatic brain injury OR Mild head injury OR Closed head injury OR Postconcussion symptoms **AND**	7679
2	Treatment OR Intervention OR Therapy OR Rehabilitation	
Total	**290**	

4. Database: PsycINFO

No	Keywords used	Articles yielded
1	Mild traumatic brain injury OR Mild head injury OR Closed head injury OR Postconcussion symptoms **AND**	2100
2	Treatment OR Intervention OR Therapy OR Rehabilitation	
Total	**448**	

5. Database: Web of Science

No	Keywords used	Articles yielded
1	Mild traumatic brain injury OR Mild head injury OR Closed head injury OR Postconcussion symptoms **AND**	4979
2	Treatment OR Intervention OR Therapy OR Rehabilitation	
Total	**1159**	

6. Database: Cochrane Database of Systematic Reviews

No	Keywords used	Articles yielded
1	Mild traumatic brain injury OR Mild head injury OR Closed head injury OR Postconcussion symptoms **AND**	0
2	Treatment OR Intervention OR Therapy OR Rehabilitation	
Total	**0**	

Table 1: PEDro scale

	Eligibility Criteria	1.Random Allocation	2.Concealed Allocation	3.Baseline Comparability	4.Blind Participants	5.Blind Therapists	6.Blind Assessors	7.Adequate follow-up	8.Intention-to-treat Analysis	9.Between-group Comparisons	10.Point Estimates and Variability	Total score	Type of RCT quality
(Bell et al., 2017)[12]	Yes	1	0	1	0	0	1	1	1	1	1	7	High
(Matuseviciene et al., 2013)[13]	Yes	1	0	1	0	0	1	0	1	1	1	6	High
(Matuseviciene et al., 2016)[14]	Yes	1	0	1	0	0	1	0	1	1	1	6	High
(Vuletic et al., 2016)[15]	Yes	1	0	1	0	0	1	1	0	1	1	6	High
(Potter et al., 2016)[16]	Yes	1	0	1	0	0	0	1	1	1	1	6	High
(Twamley et al., 2014)[17]	Yes	1	0	0	0	0	0	1	0	1	1	4	Fair
(Wade et al., 1998)[18]	Yes	1	0	1	0	0	1	0	1	1	1	6	High
(Elgmark Andersson et al., 2007)[19]	Yes	1	0	1	0	0	1	1	1	1	1	7	High
(Scheenen et al., 2017)[20]	Yes	1	0	1	0	0	1	0	0	1	1	5	Fair
(Vikane et al., 2017)[21]	Yes	1	1	1	0	0	1	1	1	1	1	8	High
(Belanger et al., 2015)[22]	Yes	1	0	1	0	0	1	1	0	1	1	6	High
(Bomyea et al., 2017)[23]	Yes	1	0	0	0	0	0	1	1	1	1	5	Fair
(Bell et al., 2008)[24]	Yes	1	1	0	0	0	1	1	1	1	1	7	High
(Ghaffar et al., 2006)[25]	Yes	1	0	1	0	0	0	0	0	1	1	4	Fair
(Kjeldgaard et al., 2014)[26]	Yes	1	1	1	0	0	0	1	0	1	1	6	High
(Silverberg et al., 2013)[27]	Yes	1	1	1	0	0	1	1	0	1	1	7	High
(Varner et al., 2017)[28]	Yes	1	1	0	0	0	1	0	0	1	1	5	Fair

Table 2: Characteristics of study (n=17)

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Authors	**No of participants (N), Age (y), Mean ±SD (range)**	**Country**	**Time since injury (months) & main cause of injury (%)**	**Inclusion criteria**	**Exclusion criteria**
(Potter et al., 2016)[16]	Total participants: n=46, Age=41.4±11.6 Experimental group: n=26, Age=40.1±10.3 Control group: n=20, Age=43.1±13.1	London, United Kingdom	Total participants: T=39±39 Experimental group: T=42±39 Control group: T=34±38 Main cause of injury: RTA (62%)	- Aged between 18-65 years old - Suffered MTBI (according to the definition from ACRM) for at least 6 months before	- MMSE < 20 - FAB < 10 - BI < 15 - Previous recipient of 4 or more sessions of CBT after TBI - Other neurological disorders independent of TBI - Drug/alcohol misuse - Clinically assessed risk of self-harm or severe psychiatric illness
(Vikane et al., 2017)[21]	Total participants: n=151, Age[a]=32[16,55] Experimental group: n=81, Age[a]=31[16,55] Control group: n=70, Age[a]=35[16.55]	Norway	Not mentioned Main causes of injury: Fall (37%); RTA (29%)	- Aged between 16-55 years old - MTBI (according to definition of Task Force on MTBI) - Had to be hospitalized for 5 hours or longer	- Patients with a major psychiatric disease or other disease (previous head trauma; substance abuse) that impacted their working skills and who were unemployed in last 6 months
(Kjeldgaard et al., 2014)[26]	Total participants: n=90, Age=34±11.3 Experimental group: n=45	Denmark	Total participants: T=27 Main cause of injury: RTA (45%)	- Aged between 18-65 years old - Diagnosed with CPTH attributed to MTBI	- Patients with other neurological or psychiatric disorders - Patients who developed CPTH due to whiplash injury

	Control group: n=45				- Patients whose neuroimaging scan showed signs of contusions or other traumatic brain lesions
(Silverberg et al., 2013)[27]	Total participants: n=28 Experimental group: n=13, Age=37.5±10 Control group: n=15, Age=40.4±13.5	Canada	Total participants: T=7 to 14 days Experimental group: T=25.4±9.1 days Control group: T=23.13±7 days Main cause of injury: RTA (42.9%)	- Aged between 18-65 years old - Incurred head trauma within 6 weeks of study entry - Met ACRM criteria for MTBI - Been considered at risk of chronic PCS on the basis of study-specific guidelines - Subjectively reported at least 1 symptom attributable to head trauma	- Medical documentation of intra-cranial abnormality on neuroimaging, consistent with "mild complicated TBI" - History of neurological disorder
(Belanger et al., 2015)[22]	Total participants: n=158 Experimental group: n=79 Control group: n=79	Florida, United States	Total participants: < 1 month: 36.7% 1 month up to 1 year: 31.6% >1 year: 31.6% Main cause of injury: Not mentioned	- Aged between 18-55 years old - History of self-reported MTBI within the past 2 years which met ACRM criteria - Currently symptomatic with at least 1 PCS symptom - Regular access to a computer and the internet - Able to read and understand English	- Patients with other neurological or psychiatric disorders
(Bomyea et al., 2017)[23]	Total participants: n=129 Experimental group:	United States	Not mentioned	- Met ACRM criteria for mild-to-moderate TBI	- Patients with other neurological or psychiatric disorders

	TBI+: n=41, Age=35.27±8.8 TBI-: 34.1±7.7 Control group: TBI+:n=42, Age=34.2±9.1 TBI-: n=25, Age=35±7.4		Main cause of injury: Combat (90.7%)	- Had at least 1 anxiety or depressive disorder	- Patients receiving concurrent psychotherapy for the presenting complaint
(Bell et al., 2017)[12]	Total participants: n=356, Age=29.4±7.2 Experimental group: n=178, Age=29.3±7.2 Control group: n=178, Age=29.4±7.2	United States	Total participants: T=2.4±1.8 years Experimental group: T=2.5±1.9 years Control group: T=2.4±1.7 years Main cause of injury: Blast (85%)	- Met MTBI criteria as diagnosed by the military hospital's TBI clinic	- Patients with moderate to severe TBI or psychiatric disorders
(Vuletic et al., 2016)[15]	Total participants: n=356, Age=29.4±7.2 Experimental group: n=178, Age=29.3±7.2 Control group: n=178, Age=29.4±7.2	United States	Total participants: T=2.4±1.8 years Experimental group: T=2.5±1.9 years Control group: T=2.4±1.7 years Main cause of injury: Blast (85%)	- Met MTBI criteria as diagnosed by the military hospital's TBI clinic	- Patients with moderate to severe TBI or psychiatric disorders
(Bell et al., 2008)[24]	Total participants: n=Ranges from 334-361 Experimental group: n=Ranges from 159-168, Age=33±13	United States	Not mentioned Main cause of injury: RTA (55.4%)	- 16 years old and above - Admission to ED within 48 hours of injury - Met MTBI criteria according to CDC	- Requiring admission to Intensive Care Unit - Intracranial abnormality on CT scan

	Control group: n=Ranges from 175-193, Age=32±13				- Evidence of major psychiatric illness, alcohol abuse, drug abuse, or other progressive neurological disease
(Scheenen et al., 2017)[20]	Total participants: n=84 Experimental group: CBT group: n=39, Age=38.8±14.9 TC group: n=45, Age=43.7±14.9	Netherlands	Not mentioned Main cause of injury: Not mentioned	- 16 years old and above - Met ACRM criteria for MTBI - Must have paid work or be studying at the time of injury - Had to be at risk for persistent post-traumatic complaints - Understand Dutch language	- Evidence of major psychiatric illness, alcohol abuse, drug abuse, or other progressive neurological disease
(Matuseviciene et al., 2013)[13]	Total participants: n=97 Experimental group: EIV group: n=48, Age=41 Control group: TAU group: n=49, Age=37.5	Sweden	Not mentioned Main cause of injury: Fall (40.2%)	- Aged between 16-70 years old - Seen in ED within 24 hours after closed head trauma - Met criteria for MTBI - Understand Swedish language	- Evidence of major psychiatric illness, alcohol abuse, drug abuse, or other progressive neurological disease
(Matuseviciene et al., 2016)[14]	Total participants: n=173 Experimental group: EIV group: n=48, Age=41 Control group: TAU group (High risk): n=49, Age=37.5	Sweden	Not mentioned Main cause of injury: Fall (41.6%)	- Aged between 16-70 years old - Seen in ED within 24 hours after closed head trauma - Met criteria for MTBI - Understand Swedish language	- Evidence of major psychiatric illness, alcohol abuse, drug abuse, or other progressive neurological disease

	TAU group (Low risk): n=76, Age=39.6				
(Varner et al., 2017)[28]	Total participants: n=118, Age=35.2±13.7 Experimental group: n=60, Age=34.3±13.4 Control group: n=58, Age=36.1±14.2	Canada	Not mentioned Main cause of injury: Fall (40.7%)	- Aged 18 years old and above - Seen in ED within 24 hours - Diagnosed with head injury, concussion, or MTBI by physician - Understand English	- GCS< 15 - Had acute intracranial injury identified on head CT scan - Cognitively impaired - Did not have a telephone
(Twamley et al., 2014)[17]	Total participants: n=34 Experimental group: n=16, Age=29.4±6.2 Control group: n=18, Age=34.3±7.4	United States	Experimental group: T=3.6±2.7 years Control group: T=5.1±5.3 years Main cause of injury: Blast (82%)	- OIF/OEF Veteran - History of mild-to-moderate TBI according to Clinical Practice Guideline - Impairment in at least one neuropsychological domain - Unemployed but stating a goal of willing to work	- Evidence of alcohol abuse or drug abuse - Those who were also participating in other intervention studies
(Ghaffar et al., 2006)[15]	Total participants n=191 Experimental group: n=97, Age=30.7±10.9 Control group: n=94, Age=33.3±12.4	Canada	Not mentioned Main cause of injury: RTA (50.8%)	- Aged between 16-60 years old - Met ACRM criteria for MTBI	- Major medical illness, such as cardiac or cardiovascular disease
(Wade et al., 1998)[18]	Total participants: n=314 Experimental group: n=184, Age=33.5±14	United Kingdom	Not mentioned Main cause of injury: RTA (41.3%)	- Aged between 16-65 years old - Admitted to hospital with a head injury of any severity	NA

	Control group: n=130, Age=32.5±12.2				
(Elgmark Andersson et al., 2007)[19]	Total participants: n=395 Experimental group: n=264, Age=32±12.6 Control group: n=131, Age=34±12.5	Sweden	Not mentioned Main causes of injury: Blow (25.1%); RTA (24.3%)	- Aged between 16-60 years old - Met ACRM criteria for MTBI - Understand Swedish language	- Evidence of major psychiatric illness, alcohol abuse, drug abuse, or other progressive neurological disease

[a]Median [min, max]

Note: ACRM=American Congress of Rehabilitation Medicine; MMSE=Mini-Mental State Exam; FAB=Frontal Assessment Battery; BI=Barthel Index; MTBI=Mild Traumatic Brain Injury; CBT=Cognitive behavioural therapy; GCS=Glasgow Coma Scale; PTA=Post-traumatic amnesia; RTA=Road Traffic Accident; CPTH=Chronic post-traumatic headache; CDC=Centers for Disease Control; ED=Emergency Department; EIV=Early intervention group; TAU=Treatment as usual; OIF=Operation Iraqi Freedom; OEF=Operation Enduring Freedom;

Table 3: Details of Intervention Studies (N=17)

Table 3: Details of Intervention Studies (N=17)				
Authors	**Objectives**	**Primary outcome**	**Study design and dosage of intervention**	**Results**
(Potter et al., 2016)[16]	To evaluate the effectiveness of a 12-session, individualized, formulation-based CBT	QOL	Experimental group: 12 weekly 1-hour sessions of CBT Control group: No intervention provided	Significant improvement associated with CBT found in QOLAS (p=0.020) at post-intervention. Treatment effects were also found for PCS (p=0.038), measures of anxiety (p=0.007), and fatigue (p=0.025) after covarying for treatment duration at post-intervention.
(Vikane et al., 2017)[21]	To evaluate the efficacy of a multidisciplinary outpatient follow-up programme by comparing with follow-up by GP	RTW	Experimental group: Psycho-education education group intervention once a week over 4 weeks and individual follow-ups throughout the first year (varied according to individual needs) Control group: Followed up by GP	The multidisciplinary outpatient follow-up programme did not improve RTW but may have reduced the development of PCS at 12 months (p=0.041).
(Kjeldgaard et al., 2014)[26]	To evaluate the effect of a group-based CBT intervention on patients with CPTH	Symptom reduction and QOL	Experimental group: 9 weekly 2-hour sessions of CBT in group format Control group: Did not receive any active treatment	Group-based CBT intervention was not successful in reducing symptoms or increasing QoL to a significant and clinically relevant level at 26 weeks. CBT intervention might be effective in an earlier stage of CPTH.
(Silverberg et al., 2013)[27]	To examine the tolerability and estimate the treatment effect of CBT delivered soon after TBI to patients at risk of chronic PCS	Symptom reduction	Experimental group: Received treatment as usual (TAU), which consisted of a single 3-hour session with a coordinator + 6 individual 50-minute sessions of CBT. Control group:	Treatment effect sizes were moderate for PCS (Cohen d=0.74, p=0.085) at 3-month follow-up, suggesting that CBT delivered soon after MTBI is well tolerated and may facilitate recovery in patients who are at risk of PCS

			Received TAU (education, reassurance, symptom management strategies)	
(Belanger et al., 2015)[22]	To investigate the effectiveness of a web-based educational intervention for reducing PCS	Symptom reduction	Experimental group: Received a web-based intervention based on a modified version of an existing empirically supported early education curriculum, "Recovering from head injury: A guide for patients" Control group: Did not receive any intervention beyond standard of care	No effect of intervention on symptom severity or attributions at 6-month follow-up. Subgroup analysis suggested benefit of the web-based intervention in those receiving concurrent mental health treatment and in those participants with the greatest time since injury (>1 year after MTBI).
(Bomyea et al., 2017)[23]	To describe psychotherapy response in veterans with and without TBI	Symptom reduction	Experimental group: Received 12 1-hour sessions of individual treatment on ACT Control group: Received 12 1-hour sessions of individual treatment on PCT, which was selected to be a credible control for nonspecific aspects of psychotherapy	Regardless of intervention, treatment response in those with and without TBI did not differ on the outcome measures at post-intervention. Modest improvements in psychological symptoms, functional impairment, and mental health-related functioning were noted over time; however, the impact of treatment on PCS was minimal.
(Bell et al., 2017)[12]	To evaluate the efficacy of delivered PST on psychological and physical symptoms in 365 post-deployment active duty service members with MTBI	Symptom reduction	Experimental group: Received 12 scheduled biweekly calls + educational brochures addressing problems common to MTBI Control group: Received educational brochures addressing problems common to MTBI	At 6 months, the PST group showed significant improvements on psychological distress (p=0.005), sleep (p=0.01), depression (p=0.03), PTSD (p=0.04), and physical functioning (p=0.03) but not on PCS (p=0.19). These effects did not persist at 12-month follow-up.
(Vuletic et al., 2016)[15]	To assess the longitudinal impact of PST on sleep quality	Symptom reduction	Experimental group: Received 12 scheduled biweekly calls + educational brochures addressing problems common to MTBI Control group:	Overall sleep quality was significantly different between the PST and EO groups at 6 months (p=0.003) but not at 12 months. Low sleep quality was associated with concussion

			Received educational brochures addressing problems common to MTBI	symptoms, pain, depression, and PTSD at all time points ($p < 0.001$).
(Bell et al., 2008)[24]	To evaluate if focused, scheduled TC during the first 3 months after MTBI decreases symptoms and improves functioning at 6 months	Symptom reduction and daily functioning	Experimental group: Received scheduled TC over the first 3 months after injury (within 2 days of injury, 4 follow-up calls at 2, 4, 8 and 12 weeks after injury) + receive standard patient instruction handout, study's toll-free contact number, and CDC booklet. Control group: Receive standard patient instruction handout and standard outpatient treatment, if prescribed.	The TC group had a significantly better outcome for symptoms ($p=0.016$, 95% CI: 1.2-12) but no difference in general health outcome ($p= 0.417$, 95% CI: 2.2-5.2) at 6-month follow-up.
(Scheenen et al., 2017)[20]	To examine the effectiveness of a newly developed CBT intervention compared to TC for at-risk MTBI patients	RTW	Experimental group: 1) CBT group: 5 sessions of 1-hour CBT treatment conducted in small groups of 2-4 patients at 4-6 weeks post-trauma. 2) TC group: 5 sessions of TC comprising information and reassurance, lasting for a few minutes to an hour, depending on patients' needs at 4-6 weeks post trauma	No significant differences were found with regard to RTW at 6- and 12-month follow-up, with 65% of patients in CBT group and 67% of patients in TC group reporting RTW at previous level. TC patients reported fewer complaints at 3 months ($p=0.01$) and 12 months ($p=0.006$), and more TC patients showed a full recovery 23 months post injury as compared to CBT group (62% vs 39%).
(Matuseviciene et al., 2013)[13]	To compare the effect of an early diagnostic and intervention visit to a specialist physician in neurorehabilitation after MTBI, with TAU.	Symptom reduction	Experimental group: Follow-up visit by a specialist physician in neurorehabilitation which included screening for anxiety and depression, providing psychoeducation, recommendations about gradual return to ordinary activities, and referral to other specialists as needed + received written information about MTBI at discharge Control group:	PRQ symptoms decreased significantly in both randomized groups ($p<0.001$) but were not significantly different in the groups at 3 months ($p=0.790$). Anxiety and depression scores did not differ between groups at 3 months.

			Received written information about MTBI at discharge + local routine which could comprise contact with a general practitioner at the patient's discretion but no routine follow-up.	
(Matuseviciene et al., 2016)[14]	To evaluate measures of activity, participation, and QoL 3 months after MTBI and the effect of an EI for patients with an estimated high risk of problems after MTBI.	Activity and participation QoL	Experimental group EIV group: Follow-up visit by a specialist physician in neurorehabilitation, which included screening for anxiety and depression, providing psychoeducation, recommendations about gradual return to ordinary activities, and referral to other specialists as needed, + received written information about MTBI at discharge Control group: TAU group (high risk) + TAU group (low risk): Received written information about MTBI at discharge + local routine which could comprise contact with a general practitioner at the patient's discretion but no routine follow-up.	At 3 months post injury, low-risk patients reported good QoL and significantly few problems in everyday life ($p<0.001$) as compared with high-risk patients. The intervention had no effect on activity, participation, or QoL.
(Varner et al., 2017)[28]	To determine if patients randomized to receive discharge instructions with an emphasis on gradual return to usual activities and on cognitive test showed differences in their symptom resolution 2 weeks after	Symptom reduction	Experimental group: Received discharge instructions with emphasis on a gradual return to usual activities plan based on head injury symptoms and on cognitive test Control group: Received discharge instructions including a description of common symptoms following MTBI and warning signs for missed intracranial injury.	No differences between the two groups with respect to change in PCSS at 2 weeks (95% CI:-11.7-7.0) and at 4 weeks (95% CI: -6.9-12.7).

	MTBI compared to patients who received usual care discharge instructions.			
(Twamley et al., 2014)[17]	To evaluate the effectiveness of CogSMART for veterans with TBI	Symptom reduction and RTW	Experimental group: Received CogSMART for 1hour/week for 12 weeks in addition to standard supported employment (2 visits/week) Control group: Received enhanced supported employment (2 visits/week) for 12 weeks	Significant reductions in PCS (Cohen's d=0.97, p=0.01) and improvements in prospective memory functioning (Cohen's d=0.72, p=0.05) in experimental group as compared to control group. Effect sizes favouring CogSMART for PTSD severity, depressive symptoms, and attainment of competitive work within 14 weeks were in the small to medium range (Cohen's d=0.35-0.49).
(Ghaffar et al., 2006)[25]	To determine if multidisciplinary treatment of MTBI improves neurobehavioural outcome at 6 months post injury.	Symptom reduction	Experimental group: Followed up in a multidisciplinary TBI clinic by an occupational therapist, physician, and neuropsychiatrist. Follow-up visits varied in frequency from weekly to monthly depending on clinical needs Control group: Were not offered follow-up visits or treatment	No significant differences noted between the two groups on any outcome measures at 6-month follow-up. However, in individuals with preinjury psychiatric difficulties (22.9% of the entire sample), subjects in the treatment group had significantly fewer depressive symptoms at 6 months post injury as compared to control group (p=0.01).
(Wade et al., 1998)[18]	To investigate whether a routine specialist follow-up service provided to patients with non-trivial head injury affected outcome at 6 months	Symptom reduction	Experimental group: Received routine follow-up by a senior nurse therapist or a senior clinical psychologist, either through face-to-face meeting or telephone follow-up Control group: Did not receive any intervention	The experimental group had significantly less social disability (p=0.01) and significantly less severe PCS (p=0.02) at 6 months follow-up as compared to the control group.
(Elgmark Andersson et al., 2007)[19]	To investigate if a programme of early and active management of	Symptom reduction,	Experimental group: Received routine examination by rehabilitation specialist and referral to other specialists as needed. Patients had	No significant differences found between the experimental and control group in terms of PCS and life satisfaction at 1-year follow-up.

	patients presenting to hospital services with an uncomplicated MTBI would reduce late sequelae at 1-year follow-up	life satisfaction	repeated outpatient appointments (mean 10, range 1-20) every week for the first weeks and telephone contacts (mean 10, range 1-20) thereafter. Control group: Received usual care and had access to existing hospital services, but these services did not include routine follow-up.	

Note: CBT=Cognitive behavioural therapy; RCT=Randomized controlled trial; QOLAS=Quality of Life Assessment Schedule; QOL=Quality of Life, RTW=Return to work; GP=General Practitioners; PCS=Postconcussion syndrome; ACT=Acceptance and Commitment Therapy; PCT=Present-centered Therapy; PST=Problem-solving treatment; EO=Education only; PTSD=Post traumatic stress disorder; CI=Confidence Interval; TC=Telephone Counselling; EI=Early Intervention; RPQ=Rivermead Post-Concussion Symptoms Questionnaire; PCSS=Postconcussion Symptom Score questionnaire; CogSMART=Cognitive Symptom Management and Rehabilitation Therapy.

Table 4: Outcome assessments used

Table 4: Outcome assessments used				
Study	**Assessment Time Points**	**Outcome assessed**		
		Impairment	**Activity & Participation**	**Others**
(Potter et al., 2016)[16]	Baseline (T1), post-intervention (intervention arm) or after 4 months (control arm) (T2)	RPQ, HADS, IES-R, CIS20R, MPQ, STAXI-2, VAS EQ-5D; QOLAS	BICRO-39, ,	
(Vikane et al., 2017)[21]	Baseline and 1-year follow-up	PRQ, HAD	GOSE, RTW measured by days to sustainable RTW at 12 months	PGIC
(Kjeldgaard et al., 2014)[26]	Baseline and after 26 weeks	PRQ, SCL-90-R, Danish version of SF-36, Pressure pain threshold, headache assessment via basic headache diary		
(Silverberg et al., 2013)[27]	Baseline and at 3-month follow-up	PRQ, IPQ-R, HADS	M2PI	
(Belanger et al., 2015)[22]	Baseline, 7 days and 6 months post intervention	NSI, BSI-18, SEsx, PCL-C		17-item quiz assessing basic knowledge of MTBI
(Bomyea et al., 2017)[23]	Pre-treatment, mid-treatment, and post-treatment	BSI-18, SFMCS-12, SFPCS-12, PRQ	SDS	I-TBI to screen for TBI history
(Bell et al., 2017)[12]	Baseline and at 6- and 12-month follow-up	BSI-18, PRQ, EuroQoL, PCL-M, PSQI, PHQ-9, CDRISC, AUDIT, SF-12	B-IFE, SDS	Client satisfaction scale

(Vuletic et al., 2016)[15]	Baseline and at 6- and 12-month follow-up	PSQI, PRQ, BSI-18, PCL-M, EuroQoL, NRS-11, PHQ-9, SF-12, AUDIT	SDS	
(Bell et al., 2008)[24]	Baseline and at 6-month follow-up	HISC, SF-12, PQOL, PHQ-Depression and Panic/Anxiety	Questions on change in major role performance and participation in community activities	
(Scheenen et al., 2017)[20]	Baseline and at 3-,6- and 12-month follow-up	HISC, PRQ, UCL, HADS	GOSE, RTW (or study),	
(Matuseviciene et al., 2013)[13]	Baseline and at 3-month follow-up	PRQ, HADS		
(Matuseviciene et al., 2016)[14]	Baseline and at 3-month follow-up	PRQ, SF 36	RHFUQ, OGQ	Data on sick leave and disability pension
(Varner et al., 2017)[28]	At 2 weeks and 4 weeks post ED discharge	PCSS		Number of missed days of school or work, number of repeat visits to a healthcare provider
(Twamley et al., 2014)[17]	At baseline and at 3-month follow-up	WRAT-3, MIST, WAIS-3 DSSS, CVLT II, D-KEFS, NSI, CAPS, HAM-D, QoL-B	Join attainment (competitive work)	Hours worked, wages earned
(Ghaffar et al., 2006)[25]	At baseline and at 6-month follow-up	PRQ, GHQ, SC-WT, S-DMT, PVSAT, SRT, CRT, HVLT-R, VS-WAIS-III, LNSS-WAIS-III, MRS-WAIS-III	RHFUQ	
(Wade et al., 1998)[18]	At baseline and at 6-month follow-up	PRQ	RHFUQ	Data on demographic details, details of injury were collected at 6-month follow-up
(Elgmark Andersson et al., 2007)[19]	At 1-year follow-up	PRQ, SF-36,	CIQ , SV-RC	LiSat-11, JSC, SV-IC

Note: CBT=Cognitive behavioural therapy; RCT=Randomized controlled trial; QOLAS=Quality of Life Assessment Schedule; RPQ=Rivermead Postconcussion Symptoms Questionnaire; BICRO-39=Brain Injury Community Rehabilitation Outcome Scale (BICRO-39); HADS=Hospital Anxiety and Depression Scale; IES-R=Impact of Event Scale-Revised; CIS20R=Checklist of Individual Strength; MPQ=McGill Pain Questionnaire; STAXI-2=State-Trait Anger Expression Inventory-2; VAS EQ-5D=Visual Analogue Scale of EuroQoL; GOSE=Glasgow Outcome Scale-Extended; PGIC=Patient's Global Impression of Change; HAD=Hospital Anxiety and Depression Scale; RTW=Return to work; SCL-90-R=The Symptom Checklist; M2PI=Mayo-Portland Participation Index; IPQ-R=Illness Perception Questionnaire-Revised; MTBI=Mild Traumatic Brain Injury; NSI=Neurobehavioural Symptom Inventory; BSI-18=Brief Symptom Inventory-18; SEsx=Self Efficacy for Symptom Management Scale; PCL-C=PTSD Checklist, Civilian Version; SDS=Sheehan Disability Scale; SFMCS-12=Short form 12 Mental health subscale; SFPCS=Short form 12 Physical health subscale; I-TBI=Injury and Traumatic Stress clinical consortium TBI screen; PCL-M=PTSD Checklist- Military Version; PSQI=Pittsburgh Sleep Quality Index; PHQ-9=Patient Health Questionnaire-9; CDRISC=Connor-Davidson Resilience Scale-10; B-IFE=Brief Inventory for Functioning Evaluation; AUDIT=Alcohol Use Disorders Identification Test; SF 12=12 item Short Form Health Survey; NRS-11=11-point Numerical Rating Scale; HISC=Head injury symptom checklist; PQOL=Perceived Quality of Life; UCL=Utrechtse Coping List; RHFUQ=Rivermead Head Injury Follow-up Questionnaire; OGQ=Occupational Gaps Questionnaire; ED=Emergency Department; PCSS=Postconcussion Symptom Score questionnaire; WRAT-3=Wide Range Achievement-3rd edition; MIST=Memory for Intentions Screening Test; WAIS-3 DSSS=Wechsler Adult Intelligence Scale-3rd Edition Digit Span scaled score; CVLT-II=California Verbal Learning Test-2nd Edition; D-KEFS=Delis-Kaplan Executive Function System; CAPS=Clinician-Administered PTSD Scale; HAM-D=Hamilton Depression Rating Scale; QoL-B=Quality of Life-Brief Version; GHQ=General Health Questionnaire; SC-WT=Stroop Color-Word Test; S-DMT=Symbol-Digit Modalities Test; PVSAT=Paced Visual Serial Addition Task; SRT=Simple Reaction Time; CRT=Choice Reaction Time; HVLT-R=Hopkins Verbal Learning Test-Revised; VS-WAIS-III=Vocabulary subtest of Wechsler Adult Intelligence Scale-3rd Edition; LNSS-WAIS-III=Letter-Number Sequencing subtest of Wechsler Adult Intelligence Scale-3rd Edition; MRS-WAIS-III=Matrix-Reasoning subtest of Wechsler Adult Intelligence Scale-3rd Edition; CIQ=Community Integration Questionnaire; LiSat-11=Life Satisfaction Questionnaire; SV-IC=Swedish version Interest Checklist; SV-RC=Swedish Version-Role Checklist; JSC=Job Satisfaction Checklist

Figure 3 Results of meta-analysis on RPQ outcomes

(A) RPQ at 3-6 months

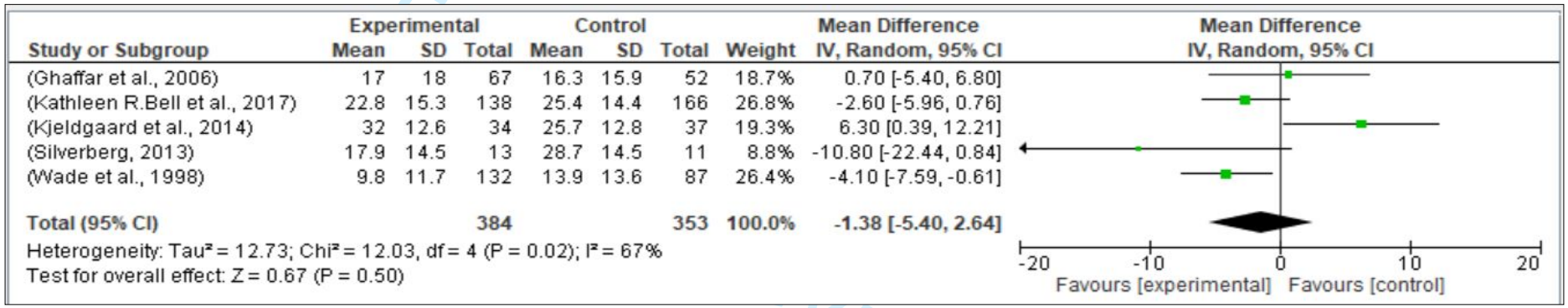

Figure 4 Results of meta-analysis on pooled functional outcomes

(A) Pooled functional outcomes at 6 months

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Fixed, 95% CI
(Ghaffar et al., 2006)	10.9	11.5	67	10.6	12	52	19.5%	0.03 [-0.34, 0.39]
(Kathleen R.Bell et al., 2017)	8	7.6	126	9.4	7.4	158	46.4%	-0.19 [-0.42, 0.05]
(Wade et al., 1998)	5.36	7.8	132	8.23	8.8	86	34.1%	-0.35 [-0.62, -0.07]
Total (95% CI)			**325**			**296**	**100.0%**	**-0.20 [-0.36, -0.04]**

Heterogeneity: Chi² = 2.63, df = 2 (P = 0.27); I² = 24%
Test for overall effect: Z = 2.46 (P = 0.01)