Effects of cognitive behavior therapy on patients with chronic whiplash-associated disorders: a systematic review and meta-analysis

Takahiro Miki (tkhr.mk@gmail.com)
Sapporo Maruyama Orthopedic Hospital https://orcid.org/0000-0002-0648-2675
Yu Kondo
Sapporo Maruyama Orthopedic Hospital
Hiroshi Kurakata
Yumenomachi Home Nursing care and rehabilitation service
Tsuneo Takebayashi
Sapporo Maruayama Orthopedic Hospital
Hiroshi Takasaki
Saitama prefectural University

Research Article

Keywords: whiplash-associated disorders, cognitive behavior therapy, systematic review

Posted Date: February 18th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1360019/v1

Abstract

Background: To determine the effectiveness of cognitive behavioral therapy (CBT) alone and a combination of physical interventions and CBT on pain, disability, quality of life, and psychological parameters in patients with chronic whiplash-associated disorders (WADs).

Methods: Several databases were systematically searched for randomized controlled trials (RCTs). Pooled effects were analyzed as standardized mean differences (SMD) and 95% confidence intervals (CI). We assessed the quality of the evidence using the Grading of Recommendations, Assessment, Development, and Evaluation approach.

Results: In total, 2,287 RCTs were found; among them, eight were included. Two RCTs, we found low evidence that CBT was better than the wait-and-see control group in improving disability (SMD, −0.61; 95% CI, −1.21 to −0.01) and psychological status, such as fear of physical activity (SMD, −1.04; 95% CI, −1.67 to −0.41), in the short-term. In addition, two RCTs, we found moderate evidence that CBT combined with physical interventions was better than what was advised in improving disability (SMD, −0.29; 95% CI, −0.53 to −0.06) in the long-term.

Conclusion: The study found moderately favorable evidence of the combined effect of physical interventions and CBT against advice alone in long-term disability.

Introduction

Chronic whiplash-associated disorders (WADs) often include not only physical but also diverse psychological and cognitive impairments (M. Sterling, 2014), whose characteristics are different from those of chronic idiopathic neck pain (Coppieters et al., 2017; Ris et al., 2017). Therefore, clinical practice guidelines suggest providing a Bio-Psycho-Social model of care to individuals with chronic WADs by including psychological interventions (Scholten-Peeters et al., 2002).

One intervention commonly suggested by clinical practice guidelines is cognitive behavior therapy (CBT). CBT helps in cognitive reconditioning and behavioral modifications of specific activities (Butler, Chapman, Forman, & Beck, 2006; Flor & Turk, 1984; Morley, 2011). In 2015, Monticone et al. (Monticone et al., 2015) have conducted a meta-analysis to investigate the effects of CBT alone on chronic neck pain. In their meta-analysis, patients with nonspecific neck pain and those with WADs were combined, limiting the clinical implications due to different characteristics of chronic WADs and idiopathic neck pain. Therefore, performing a new analysis by limiting participants to those with chronic WADs is necessary.

Investigating the effects of CBT alone on chronic WADs by performing a meta-analysis is an important step in considering the advantages of including CBT in the Bio-Psycho-Social model of care. However, note that CBT is a psychological intervention, not a Bio-Psycho-Social intervention (Urits et al., 2019). Therefore, understanding the effects of combining physical interventions and CBT on chronic WADs is clinically useful. In 2016, Shearer et al. (Shearer et al., 2016) have investigated the effects of a combination of physical interventions and CBT on chronic WADs in a systematic review involving the literature from 1990 to 2015. However, data synthesis was not undertaken due to the absence of multiple studies. We found multiple randomized controlled trials (RCTs) to be included in a meta-analysis (Michaleff et al., 2014; M. J. Stewart et al., 2007), and we found another eligible RCT in 2020 (Andersen et al., 2020). Therefore, an updated systematic review was necessary to understand the effects of the combination of physical interventions and CBT on chronic WADs.

This systematic review with meta-analysis has two purposes. First is to investigate the effects of CBT alone on pain, disability, quality of life (QoL), and psychological parameters in patients with chronic WADs. Second is to investigate the effects of the combination of physical interventions and CBT compared with those of CBT alone on pain, disability, QoL, and psychological parameters on patients with chronic WADs.

Methods

Protocol Registration and Search Strategy

This review was preregistered in PROSPERO (CRD42020193904) and conducted according to the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (Moher, Liberati, Tetzlaff, Altman, & Group, 2009). The following items were modified after the initial registration in PROSPERO: 1) Review questions were added to investigate the effects of the combination of physical interventions and CBT; 2) the definition of chronic WADs were defined as symptoms lasting for ≥ 3 months, which was revised from symptoms lasting for ≥ 6 months; 3) studies with one author were also included; and 4) the PsycINFO database was excluded due to limited access to the database.

An author (HK) systematically searched the following databases from inception to January 2021: CINAHL, Web of Science, MEDLINE, Embase, EMCare, and Physiotherapy Evidence Database (PEDro). The search strategies are presented in Appendix 1.

Study Selection

Screening and full-text inspection were performed by two authors (YK and TM) independently. Any disagreements on eligibility were resolved by discussion. Cross-referencing was performed with hand searches of the reference lists of studies included in the full-text screening.

Eligibility Criteria

All RCTs published as full-text articles were eligible for inclusion in this systematic review. No restrictions on language were employed.

Eligible participants were as follows: 1) adult individuals (≥ 18 years of age) with WADs with a whiplash injury grade of I, II, or III in the Quebec Task Force Classification (Spitzer et al., 1995), 2) patients from primary, secondary, or tertiary care institutions, and 3) patients with any persistent symptoms, such as musculoskeletal pain, sensorimotor control disturbances, and psychological problems, for more than 3 months after the accident. Studies with the following

participants were excluded from this systematic review: 1) patients with a cervical fracture or dislocation, 2) patients with injuries in other body areas other than the neck during the accident causing WAD, and 3) patients with previous WADs, preexisting neck pain, or previous neck surgery.

Eligible interventions were CBT with and without physical interventions. No consensus was made for a specific definition of CBT (Lamb et al., 2010); thus, CBT was identified in this study when the following criteria reported by Richmond et al. (Richmond et al., 2015) were satisfied: 1) treatments based on cognitive–behavioral principles that were explicitly or implicitly stated (Fisher et al., 2018; Gatchel, Peng, Peters, Fuchs, & Turk, 2007; Turk & Flor, 1984); 2) interventions using both cognitive and behavioral strategies were used in the same treatment package; 3) CBT was provided by an experienced healthcare professional; and 4) when multimodal treatments were provided, the intervention was assumed to be based on a CBT principle. Any disagreements in selecting CBT techniques were resolved through a discussion between the authors by contacting the corresponding authors of the study for additional information or by finding a process paper associated with the study that provided further information.

Eligible comparisons included any type of a single intervention or a wait-and-see control.

Eligible primary outcomes included pain intensity, disability, QoL, and

eligible secondary outcomes included psychological status. In addition, adverse events were recorded where mentioned. For pain intensity, when more than one patient-reported outcome measure (PROM) was reported, a numerical rating scale was used in the analysis, followed by a visual analog scale. For disability, when more than one PROM was reported, the Neck Disability Index (NDI) was used in the analysis. For QoL, when more than one PROM was reported, the 36-Item Short Form Health Survey (SF-36) was used in the analysis, followed by the 12-Item Short Form Health Survey (SF-12) and the EuroQol-5 Dimensions. For the SF-36 and SF-12, physical and mental component scores were used in the analysis.

Risk of Bias Assessment

The risk of bias was assessed using the PEDro scores (Maher, Sherrington, Herbert, Moseley, & Elkins, 2003). We used the scores reported in the PEDro (www.pedro.org.au). When no scores were available in the database, two authors (YK and TM) independently assessed the PEDro scores.

Disagreements were resolved by a third author (HK). Moderate to high quality studies were defined as studies with a PEDro score of ≥ 6 (Maher et al., 2003).

Data Extraction

Two authors (YK and TM) independently extracted data, and disagreements were resolved by discussion, moderated by a third author (HK). Extracted data were 1) country where data collection was performed, study design, setting and duration of the intervention, profession providing the intervention, and number of sessions of the intervention; 2) participants' diagnosis, age, and gender, number of participants, and pain duration; 3) intervention type and comparison; 4) adverse events and dropouts, including reasons, and the means and standard deviations of the PROM scores for pain, disability, QoL, and psychological status at short-, intermediate-, and long-term follow-ups. The definitions of short, intermediate, and long terms were according to previous studies.(Gross et al., 2015; Monticone et al., 2015) Short term was defined as less than 3 months after the start of the intervention. The time point closest to 4 weeks was used when multiple eligible follow-up points were available. Intermediate term was defined as ≥ 3 months and less than 12 months after the start of the intervention. The time point closest to 6 months was chosen when multiple eligible follow-up points were available. Long term was defined as ≥ 12 months after the start of the intervention. The time point closest to 1 year was chosen if multiple eligible time points were available. When such data were lacking in the published study, we contacted the corresponding author via email to request for the missing data. A reminder email was sent 2 weeks after the first contact. When no response was received after the second reminder, we considered it uncontactable.

Data Synthesis and Analysis

When multiple datasets of similar outcomes were available, a meta-analysis was performed using Review Manager 5 (The Nordic Cochrane Centre, København Ø, Denmark). First, the meta-analysis was attempted using change values from the baseline to each follow-up point. When the change values were unavailable, the values at each follow-up point were used for the meta-analysis.

The standardized mean difference (SMD) with 95% confidence intervals (CI) was calculated using the random-effects model. If necessary, the scores were reversed to show that high scores indicate a healthy status. The I^2 statistic was assessed for heterogeneity among trials, whose interpretations were as follows: 0%–40%, insignificant heterogeneity; 30%–60%, moderate heterogeneity; 50%–90%, substantial heterogeneity; and 75%–100%, considerable heterogeneity (Deeks JJ HJ, 2019).

The overall quality of evidence was evaluated in each meta-analysis using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach (Furlan et al., 2015; Pollock et al., 2016). The GRADE approach has five domains. Our review included RCTs only; thus, the starting GRADE score was high in each domain. The scores were downgraded by one or two levels in each domain as follows: 1) the risk of bias was downgraded one level when more than 25% of the participants are from studies conducted in low-quality methods (e.g. PEDro score of less than 6); 2) the inconsistency was downgraded one level when the I^2 value was more than 75%; 3) the indirectness was downgraded one level when the available evidence for population, interventions, comparisons, and outcomes differs from what was defined in the inclusion criteria of the review; 4) the imprecision was downgraded two levels when the number of participants within the pooled analysis was less than 100 and one level when the number of participants within the pooled analysis was less than 200 (Pollock et al., 2016); and 5) the publication bias was downgraded one level when a funnel plot comparing at least 10 studies suggested publication bias. Two authors (YK and TM) independently rated the GRADE scores and disagreements were resolved by discussion.

Results

Study Selection

Figure 1 presents the flow of the study selection. Two studies by Söderlund and Lindberg (Söderlund & Lindberg, 2001, 2007) and two studies by Wicksell et al. (Wicksell, Ahlqvist, Bring, Melin, & Olsson, 2008; Wicksell, Olsson, & Hayes, 2010) were from the same study project and, therefore, were treated as one, respectively. The risk of bias was assessed in eight studies (Andersen et al., 2020; Dunne, Kenardy, & Sterling, 2012; Ehrenborg & Archenholtz, 2010; Michaleff et al., 2014; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007; Wicksell et al., 2008; Wicksell et al., 2010). Table 1 demonstrates the results of the risk of bias assessment. One study (Andersen et al., 2020) did not have PEDro scores in the database, and the PEDro scores were determined by the two authors, where there was no disagreement. Six studies (Andersen et al., 2020; Dunne et al., 2012; Michaleff et al., 2014; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007; Wicksell et al., 2008; Wicksell et al., 2010) had a low risk of bias, and two studies (Ehrenborg & Archenholtz, 2010; Pato et al., 2010) had a high risk of bias.

Study Characteristics

The summary of the eight studies is presented in Table 2. Two studies have compared CBT with the wait-and-see control group (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010), where pain, disability, fear of physical activity, anxiety, depression, and posttraumatic stress in the short term were considered eligible for inclusion in the meta-analysis to investigate the effects of CBT alone. Two studies have compared CBT in addition to a comprehensive exercise program with advice alone (Michaleff et al., 2014; M. J. Stewart et al., 2007), where pain, disability, and QoL with SF-36's physical and mental component summary scores in the long term were considered eligible for inclusion in the meta-analysis to investigate the combined effects of CBT and physical interventions.

Other studies were deemed ineligible for the meta-analysis due to the lack of multiple studies with similar interventions. Andersen et al. (Andersen et al., 2020) have compared trauma-focused CBT in addition to exercise with exercise only. Söderlund and Lindberg (Söderlund & Lindberg, 2001, 2007) have compared CBT in addition to physical therapy with physical therapy alone. Pato et al. (Pato et al., 2010) have compared CBT in addition to other treatments (physical therapy, infiltration, or medication) with other treatments alone. Ehrenborg and Archenholtz (Ehrenborg & Archenholtz, 2010) have compared CBT in addition to surface electromyography biofeedback training with CBT alone. In the eight studies, CBT was provided by psychologists in four studies (Andersen et al., 2020; Dunne et al., 2012; Pato et al., 2010; Wicksell et al., 2008; Wicksell et al., 2010) and by physical therapists in four studies (Ehrenborg & Archenholtz, 2010; Michaleff et al., 2014; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007). The corresponding authors were never contacted to resolve doubts about the types and treatment characteristics of CBT. Three studies (Andersen et al., 2020; Michaleff et al., 2014; M. J. Stewart et al., 2007) have evaluated the adverse events of CBT, where no serious adverse events were observed. Minor adverse events, including muscle soreness, stiffness, headaches, and/or exacerbation of existing symptoms, were reported in the CBT group (Table 2).

Meta-analysis

Only one study has reported changes in values from baseline to each follow-up point (Wicksell et al., 2010). In the other studies, no additional data were available, and the values at each follow-up point were used for the meta-analysis. No disagreement was found in any rating of the GRADE scores between the two authors.

CBT versus wait-and-see control

For short-term pain, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose forest plot is presented in Figure 2. No statistically significant overall effect was observed (p = 0.11), indicating that CBT was not more effective than the wait-and-see control in reducing pain at the short-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low (Table 3).

For short-term disability, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose plot is presented in Figure 3. CBT had a statistically significant overall effect (p = 0.05), indicating that CBT was more effective than the wait-and-see control in terms of disability reduction at the short-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low (Table 3).

For fear of physical activity in the short term, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose forest plot is presented in Figure 4. CBT had a statistically significant overall effect (p = 0.001), indicating that CBT was more effective than the wait-and-see control in reducing the fear of physical activity at the short-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low (Table 3).

For short-term anxiety, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose forest plot is presented in Figure 5. CBT had a statistically significant overall effect (p = 0.002), indicating that CBT was more effective than the wait-and-see control in reducing anxiety at the short-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with two levels being downgraded from the GRADE score, the quality evidence was considered low (Table 3).

For short-term depression, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose forest plot is presented in Figure 6. CBT had a statistically significant overall effect (p = 0.001), indicating that CBT was more effective than the wait-and-see control in reducing depression at the short-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with two levels downgraded from the GRADE score, the quality evidence was deemed low (Table 3).

For posttraumatic stress in the short term, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose forest plot is presented in Figure 7. CBT had no statistically significant overall effect (p = 0.34), indicating that CBT was not more effective than the wait-and-see control in reducing posttraumatic stress at the short-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with two levels downgraded from the GRADE score, the quality evidence was deemed low (Table 3).

CBT in addition to physical interventions versus advice only

For long-term pain, 282 patients with chronic WADs from two studies (Michaleff et al., 2014; M. J. Stewart et al., 2007) were included in the meta-analysis, whose forest plot is presented in Figure 8. CBT in addition to physical interventions had no statistically significant overall effect (p = 0.09), indicating that CBT in addition to physical interventions was not more effective than advice in reducing pain at the long-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with one level downgraded from the GRADE score, the quality evidence was deemed moderate (Table 3).

For long-term disability, 282 patients with chronic WADs from two studies (Michaleff et al., 2014; M. J. Stewart et al., 2007) were included in the meta-analysis, whose forest plot is presented in Figure 9. CBT in addition to physical interventions had a statistically significant overall effect (p = 0.01), indicating that CBT in addition to physical interventions was more effective than advice only in reducing disability at the long-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with one level downgraded from the GRADE score, the quality evidence was considered moderate (Table 3).

For QoL in the long term, 282 patients with chronic WADs from two studies (Michaleff et al., 2014; M. J. Stewart et al., 2007) were included in the meta-analysis with the SF-36 scores. The forest plot of the physical component summary score in the SF-36 is presented in Figure 10, and that of the mental component summary score is presented in Figure 11. CBT in addition to physical interventions had no statistically significant overall effect (p = 0.09 for the physical component summary score; p = 0.32 for the mental component summary score), indicating that CBT in addition to physical interventions was not more effective than advice only in improving the QoL at the long-term follow-up. The I^2 value was 0%, indicating insignificant heterogeneity. Due to a serious impression with one level downgraded from the GRADE score, the quality evidence was considered moderate (Table 3).

Discussion

As far as the authors know, this is the first meta-analysis investigating the effects of CBT alone and those of the combination of CBT and physical interventions on patients with chronic WADs. Regarding the effects of CBT alone, data synthesis was possible only for the short term with two RCTs (Dunne et al., 2012; Wicksell et al., 2008; Wicksell et al., 2010), resulting in the low quality of evidence of all findings. Regarding the effects of the combination of CBT and physical interventions, data synthesis was possible in the comparison between CBT with exercises and advice only for the long term with two RCTs (Michaleff et al., 2014; M. J. Stewart et al., 2007), resulting in the moderate quality of evidence of all findings.

The meta-analysis for the effects of CBT alone compared with those of the wait-and-see control

At the short-term follow-up, statistically significant reductions in disability, fear of physical activity, anxiety, and depression were found in favor of CBT, although no difference in pain and posttraumatic stress was observed. Relatively, the effect size of the fear of physical activity, anxiety, and depression seems to be larger than that of disability, indicating the characteristics of CBT as a psychological intervention. In addition, no additional RCTs were included in the meta-analysis after the previous meta-analysis in 2016 (Anstey, Kongsted, Kamper, & Hancock, 2016). The lack of additional RCTs may indicate that interest in recent research has shifted to the investigation of the combined effects of CBT and other treatments, such as exercise (Andersen et al., 2020; Michaleff et al., 2014; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007).

The meta-analysis of the combined effects of physical interventions and CBT compared with those of advice only

A statistically significant reduction in disability was found in favor of CBT. The moderate quality of evidence of the long-term effects of CBT with physical interventions on disability would be an important finding to better guide management strategies for chronic WADs from a Bio-Psycho-Social perspective. However, further investigations are needed to implement this finding in clinical practice. First, the effect size of 0.29 is small; thus, further investigations are required to determine the most effective form of CBT, dose, optimal combination with other therapeutic modalities, and ways to deliver these approaches. Second, the usefulness of the inclusion of CBT components in physical interventions is recognized and provided as a management strategy for patients with chronic low-back pain, such as cognitive functional therapy (O'Sullivan et al., 2018). However, Beissner et al. (Beissner et al., 2009) have reported that physical therapists lack CBT implementation in clinical practice primarily due to limited knowledge about CBT techniques. Evidence has been increasing that educational/training level, not work experience, can be associated with the implementation of the Bio-Psycho-Social model of care with the identification of patients' psychological status (Miki, Kondo, Takebayashi, & Takasaki, 2020; Suzuki & Takasaki, 2020; Takasaki, Saiki, & Iwasada, 2014). Establishing a global educational/training system will be a challenge for physical therapists to be able to implement the Bio-Psycho-Social model of care not only using CBT

techniques but also other behavioral techniques, such as communication to increase patient's autonomy (Murray et al., 2019) and motivational interviews (Alperstein & Sharpe, 2016).

Evidence on the long-term effects of the combination of CBT and physical interventions compared with those of advice only is lacking, which is not surprising because the reduction of pain intensity is no longer the primary focus in patients with chronic WADs (Scholten-Peeters et al., 2002). However, evidence is lacking on the long-term effects of the combination of CBT and physical interventions compared with those of advice only on QoL measures, which were subscales of the SF-36, although a statistically significant effect on disability was observed measured by the NDI. The discrepancy may reflect the lower responsiveness of the SF-36 than that of the NDI in patients with chronic WADs (Stewart, Maher, Refshauge, Bogduk, & Nicholas, 2007). In this systematic review, all PROMs had the structure of pre-determined items. Such a structured PROM reduces responsiveness from individuals with neck pain (Cleland, Fritz, Whitman, & Palmer, 2006; M. Stewart et al., 2007) because each item has the same weight of importance among all participants, resulting in the lack of validity for measuring the intended health construct (Walton, Macdermid, & Nielson, 2010). The recently developed Satisfaction and Recovery Index is an importance-weighted health-related satisfaction tool that captures both the process and status of recovery following musculoskeletal trauma and is shown to be more responsive than SF-12 and region-specific disability measures (Modarresi & Walton, 2020; Walton, MacDermid, Pulickal, Rollack, & Veitch, 2014). Therefore, further studies are required to include such an importance-weighted PROM for outcome measures to clarify the effects of an intervention for those with musculoskeletal trauma.

In the two RCTs included in the meta-analysis, CBT was provided by physical therapists. Psychologically informed physical therapy would be recommended for managing patients with acute WADs who have a higher risk of a shift to chronic WADs (Ritchie, Hendrikz, Kenardy, & Sterling, 2013; Michele Sterling, 2014) to minimize the number of chronic WADs. However, it has been unknown which is better in terms of treatment effect and cost-effectiveness between multidisciplinary approach with separate roles of CBT for psychologists and physical interventions for physical therapists and physical therapist's delivering CBT with physical interventions. A solo approach performed by a physical therapist may not be sufficient in terms of the Bio-Psycho-Social model of care (Michele Sterling, 2014), but further investigations are required.

Limitations

Our meta-analysis had some limitations. The analysis was performed with a limited number of participants. Therefore, studies with a larger sample size should be performed in the future. Furthermore, we were unable to compare the advantages of combination of physical interventions and CBT with other treatments other than advice because of an insufficient number of RCTs pertaining to this topic. Finally, we did not actively seek unpublished studies. However, we believe it is unlikely to have had an important impact on the overall results.

Conclusion

This systematic review with meta-analysis involving patients with chronic WADs found a low level of evidence on the favorable effects of CBT alone compared with those of the wait-and-see control on disability, the fear of physical activity, anxiety, and depression in the short term. In addition, this study found a moderate favorable evidence on the effects of the combination of physical interventions and CBT compared with those of advice only on disability in the long term.

Declarations

Acknowledgments:

None.

Sources of funding:

No funding.

Conflict of Interest:

The authors declare that they have no conflict of interest.

Author contributions:

Conceptualization: Yu Kondo, Takahiro Miki, Hiroshi Takasaki.

Data curation: Yu Kondo, Takahiro Miki, Hiroshi Kurakata.

Formal analysis: Yu Kondo, Takahiro Miki, Hiroshi Kurakata.

Investigation: Yu Kondo, Takahiro Miki, Hiroshi Kurakata.

Methodology: Yu Kondo, Takahiro Miki, Hiroshi Kurakata, Hiroshi Takasaki.

Project administration: Miki Takahiro, Tsuneo Takebayashi, Hiroshi Takasaki. Supervision: Tsuneo Takebayashi, Hiroshi Takasaki.

Visualization: Tsuneo Takebayashi.

Writing – original draft: Yu Kondo, Takahiro Miki, Hiroshi Takasaki.

References

1. Alperstein, D., & Sharpe, L. (2016). The Efficacy of Motivational Interviewing in Adults With Chronic Pain: A Meta-Analysis and Systematic Review. *J Pain, 17*, 393-403.
2. Andersen, T. E., Ravn, S. L., Armfield, N., Maujean, A., Requena, S. S., & Sterling, M. (2020). Trauma-focused cognitive behavioural therapy and exercise for chronic whiplash with comorbid posttraumatic stress disorder: a randomised controlled trial. *Pain, 162*, 1221-1232.
3. Anstey, R., Kongsted, A., Kamper, S., & Hancock, M. J. (2016). Are People With Whiplash-Associated Neck Pain Different From People With Nonspecific Neck Pain? *J Orthop Sports Phys Ther, 46*, 894-901.
4. Beissner, K., Henderson, C. R., Jr., Papaleontiou, M., Olkhovskaya, Y., Wigglesworth, J., & Reid, M. C. (2009). Physical therapists' use of cognitive-behavioral therapy for older adults with chronic pain: a nationwide survey. *Phys Ther, 89*, 456-469.
5. Butler, A. C., Chapman, J. E., Forman, E. M., & Beck, A. T. (2006). The empirical status of cognitive-behavioral therapy: a review of meta-analyses. *Clin Psychol Rev, 26*, 17-31.
6. Cleland, J. A., Fritz, J. M., Whitman, J. M., & Palmer, J. A. (2006). The reliability and construct validity of the neck disability index and patient specific functional scale in patients with cervical radiculopathy. *Spine (Phila Pa 1976), 31*, 598-602.
7. Coppieters, I., De Pauw, R., Kregel, J., Malfliet, A., Goubert, D., Lenoir, D., Meeus, M. (2017). Differences Between Women With Traumatic and Idiopathic Chronic Neck Pain and Women Without Neck Pain: Interrelationships Among Disability, Cognitive Deficits, and Central Sensitization. *Phys Ther, 97*, 338-353.
8. Deeks JJ HJ, A. D. (2019). Analysing data and undertaking meta-analyses. *Cochrane Hand- book for Systematic Reviews of Interventions, 10*. https://training.cochrane.org/handbook/current/chapter-10.
9. Dunne, R. L., Kenardy, J., & Sterling, M. (2012). A randomized controlled trial of cognitive-behavioral therapy for the treatment of PTSD in the context of chronic whiplash. *Clin J Pain, 28*, 755-765.
10. Ehrenborg, C., & Archenholtz, B. (2010). Is surface EMG biofeedback an effective training method for persons with neck and shoulder complaints after whiplash-associated disorders concerning activities of daily living and pain – a randomized controlled trial. *Clin Rehabil, 24*, 715-726.
11. Fisher, E., Law, E., Dudeney, J., Palermo, T. M., Stewart, G., & Eccleston, C. (2018). Psychological therapies for the management of chronic and recurrent pain in children and adolescents. *Cochrane Database Syst Rev, 9*(9), Cd003968.
12. Flor, H., & Turk, D. C. (1984). Etiological theories and treatments for chronic back pain. I. Somatic models and interventions. *Pain, 19*, 105-121.
13. Furlan, A. D., Malmivaara, A., Chou, R., Maher, C. G., Deyo, R. A., Schoene, M., . . . Editorial Board of the Cochrane Back, N. G. (2015). 2015 Updated Method Guideline for Systematic Reviews in the Cochrane Back and Neck Group. *Spine (Phila Pa 1976), 40*, 1660-1673.
14. Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: scientific advances and future directions. *Psychol Bull, 133*, 581-624.
15. Gross, A., Kay, T. M., Paquin, J. P., Blanchette, S., Lalonde, P., Christie, T., . . . Cervical Overview, G. (2015). Exercises for mechanical neck disorders. *Cochrane Database Syst Rev, 1*, CD004250.
16. Lamb, S. E., Hansen, Z., Lall, R., Castelnuovo, E., Withers, E. J., Nichols, V., . . . Underwood, M. R. (2010). Group cognitive behavioural treatment for low-back pain in primary care: a randomised controlled trial and cost-effectiveness analysis. *The Lancet, 375*, 916-923.
17. Maher, C. G., Sherrington, C., Herbert, R. D., Moseley, A. M., & Elkins, M. (2003). Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther, 83*, 713-721.
18. Michaleff, Z. A., Maher, C. G., Lin, C.-W. C., Rebbeck, T., Jull, G., Latimer, J., . . . Sterling, M. (2014). Comprehensive physiotherapy exercise programme or advice for chronic whiplash (PROMISE): a pragmatic randomised controlled trial. *The Lancet, 384*, 133-141.
19. Miki, T., Kondo, Y., Takebayashi, T., & Takasaki, H. (2020). Difference between physical therapist estimation and psychological patient-reported outcome measures in patients with low back pain. *PLoS One, 15*, e0227999.
20. Modarresi, S., & Walton, D. M. (2020). Reliability, discriminative accuracy, and an exploration of response shift as measured using the satisfaction and Recovery Index over 12 months from musculoskeletal trauma. *Musculoskelet Sci Pract, 51*, 102300.
21. Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & Group, P. (2009). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med, 6*, e1000097.
22. Monticone, M., Cedraschi, C., Ambrosini, E., Rocca, B., Fiorentini, R., Restelli, M., . . . Moja, L. (2015). Cognitive-behavioural treatment for subacute and chronic neck pain. *Cochrane Database Syst Rev*, CD010664.
23. Morley, S. (2011). Efficacy and effectiveness of cognitive behaviour therapy for chronic pain: Progress and some challenges. *Pain, 152*, 99-106.
24. Murray, A., Hall, A., Williams, G. C., McDonough, S. M., Ntoumanis, N., Taylor, I., . . . Matthews, J. (2019). Assessing physiotherapists' communication skills for promoting patient autonomy for self-management: reliability and validity of the communication evaluation in rehabilitation tool. *Disability and Rehabilitation, 41*, 1699-1705.

25. O'Sullivan, P. B., Caneiro, J. P., O'Keeffe, M., Smith, A., Dankaerts, W., Fersum, K., & O'Sullivan, K. (2018). Cognitive Functional Therapy: An Integrated Behavioral Approach for the Targeted Management of Disabling Low Back Pain. *Phys Ther, 98*, 408-423.
26. Pato, U., Di Stefano, G., Fravi, N., Arnold, M., Curatolo, M., Radanov, B. P., . . . Sturzenegger, M. (2010). Comparison of randomized treatments for late whiplash. *Neurology, 74*, 1223-1230.
27. Pollock, A., Farmer, S. E., Brady, M. C., Langhorne, P., Mead, G. E., Mehrholz, J., . . . Wiffen, P. J. (2016). An algorithm was developed to assign GRADE levels of evidence to comparisons within systematic reviews. *J Clin Epidemiol, 70*, 106-110.
28. Richmond, H., Hall, A. M., Copsey, B., Hansen, Z., Williamson, E., Hoxey-Thomas, N., . . . Lamb, S. E. (2015). The Effectiveness of Cognitive Behavioural Treatment for Non-Specific Low Back Pain: A Systematic Review and Meta-Analysis. *PLoS One, 10*, e0134192.
29. Ris, I., Juul-Kristensen, B., Boyle, E., Kongsted, A., Manniche, C., & Søgaard, K. (2017). Chronic neck pain patients with traumatic or non-traumatic onset: Differences in characteristics. A cross-sectional study. *Scand J Pain, 14*, 1-8.
30. Ritchie, C., Hendrikz, J., Kenardy, J., & Sterling, M. (2013). Derivation of a clinical prediction rule to identify both chronic moderate/severe disability and full recovery following whiplash injury. *Pain, 154*, 2198-2206.
31. Scholten-Peeters, G. G., Bekkering, G. E., Verhagen, A. P., van Der Windt, D. A., Lanser, K., Hendriks, E. J., & Oostendorp, R. A. (2002). Clinical practice guideline for the physiotherapy of patients with whiplash-associated disorders. *Spine (Phila Pa 1976), 27*, 412-422.
32. Shearer, H. M., Carroll, L. J., Wong, J. J., Cote, P., Varatharajan, S., Southerst, D., . . . Taylor-Vaisey, A. L. (2016). Are psychological interventions effective for the management of neck pain and whiplash-associated disorders? A systematic review by the Ontario Protocol for Traffic Injury Management (OPTIMa) Collaboration. *Spine J, 16*, 1566-1581.
33. Söderlund, A., & Lindberg, P. (2001). Cognitive behavioural components in physiotherapy management of chronic whiplash associated disorders (WAD)–a randomised group study. *Physiotherapy Theory and Practice, 17*, 229-238.
34. Söderlund, A., & Lindberg, P. (2007). Cognitive behavioural components in physiotherapy management of chronic whiplash associated disorders (WAD)–a randomised group study. *G Ital Med Lav Ergon, 29*, 5-11.
35. Spitzer, W. O., Skovron, M. L., Salmi, L. R., Cassidy, J. D., Duranceau, J., Suissa, S., & Zeiss, E. (1995). Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders: redefining "whiplash" and its management. *Spine (Phila Pa 1976), 20*, 1-73.
36. Sterling, M. (2014a). Physiotherapy management of whiplash-associated disorders (WAD). *Journal of physiotherapy, 60*, 5-12.
37. Sterling, M. (2014b). Physiotherapy management of whiplash-associated disorders (WAD). *J Physiother, 60*, 5-12.
38. Stewart, M., Maher, C. G., Refshauge, K. M., Bogduk, N., & Nicholas, M. (2007a). Responsiveness of pain and disability measures for chronic whiplash. *Spine (Phila Pa 1976), 32*, 580-585.
39. Stewart, M. J., Maher, C. G., Refshauge, K. M., Herbert, R. D., Bogduk, N., & Nicholas, M. (2007b). Randomized controlled trial of exercise for chronic whiplash-associated disorders. *Pain, 128*, 59-68.
40. Suzuki, K., & Takasaki, H. (2020). Ability of Therapists Trained in Mechanical Diagnosis and Therapy to Guess Pain Catastrophizing and Kinesiophobia Scores for Patients with Low Back Pain. *Open Journal of Therapy and Rehabilitation, 8*, 119-130.
41. Takasaki, H., Saiki, T., & Iwasada, Y. (2014). McKenzie Therapists Adhere More to Evidence-Based Guidelines and Have a More Biopsychosocial Perspective on the Management of Patients with Low Back Pain than General Physical Therapists in Japan. *Open Journal of Therapy and Rehabilitation, 02*, 173-181.
42. Turk, D. C., & Flor, H. (1984). Etiological theories and treatments for chronic back pain. II. Psychological models and interventions. *Pain, 19*, 209-233.
43. Urits, I., Hubble, A., Peterson, E., Orhurhu, V., Ernst, C. A., Kaye, A. D., & Viswanath, O. (2019). An Update on Cognitive Therapy for the Management of Chronic Pain: a Comprehensive Review. *Curr Pain Headache Rep, 23*, 57.
44. Walton, D. M., Macdermid, J. C., & Nielson, W. (2010). Recovery from acute injury: clinical, methodological and philosophical considerations. *Disabil Rehabil, 32*, 864-874.
45. Walton, D. M., MacDermid, J. C., Pulickal, M., Rollack, A., & Veitch, J. (2014). Development and Initial Validation of the Satisfaction and Recovery Index (SRI) for Measurement of Recovery from Musculoskeletal Trauma. *Open Orthop J, 8*, 316-325.
46. Wicksell, R. K., Ahlqvist, J., Bring, A., Melin, L., & Olsson, G. L. (2008). Can exposure and acceptance strategies improve functioning and life satisfaction in people with chronic pain and whiplash-associated disorders (WAD)? A randomized controlled trial. *Cogn Behav Ther, 37*, 169-182.
47. Wicksell, R. K., Olsson, G. L., & Hayes, S. C. (2010). Psychological flexibility as a mediator of improvement in Acceptance and Commitment Therapy for patients with chronic pain following whiplash. *Eur J Pain, 14*, 1059.e1051-1059.e1011.

Tables

Table 1.

PEDro scores of the studies included in this systematic review

Study	Random allocation	Concealed allocation	Groups similar at baseline	Participant blinding	Therapist blinding	Assessor blinding	< 15% dropouts	Intention-to-treat analysis	Between-group difference reported	Point estimate and variability reported	Total
Andersen 2020	Y	Y	Y	N	N	Y	N	Y	Y	Y	7
Dunne 2012	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Ehrenborg 2010	N	N	Y	N	N	N	Y	Y	Y	Y	5
Michaleff 2014	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Pato 2010	Y	N	Y	N	N	N	N	N	Y	Y	4
Soderlund 2001, 2007	Y	N	Y	N	N	Y	Y	N	Y	Y	6
Stewart 2007	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Wicksell 2008, 2010	Y	Y	Y	N	N	N	Y	Y	Y	Y	7

Table 2.

Summary of the eight studies included in this systematic review

Study, data collection country, the source of funding, and study design	Participants	Interventions	Comparisons	Outcome
Andersen et al., 2020; Australia and Denmark, NHMRC Project Grant and Danish Victims Fund Project, RCTs	Total n (completing) = 103 (79) (from recruited advertisements and clinical practices in Southeast Queensland in Australia and the region of Zealand in Denmark between). Participants were aged between 18 and 70 years and diagnosed with chronic WADs grade II and PTSD. CBT group: Age: 39.7 ± 13.3 years. Gender: 14 males, 39 females. Mean duration of symptoms: 2.49 ± 1.9 years. Control group: Age: 44.5 ± 11.6 years. Gender 14 males, 36 females. Mean duration of symptoms: 3.33 ± 4.2 years.	10 weekly 60–90-minute sessions of individually delivered trauma-focused CBT (PTSD-related psychoeducation, teaching anxiety management strategies, such as progressive muscle relaxation, initiating cognitive restructuring of unhelpful thoughts and assumptions, and applying prolonged imaginal and *in vivo* exposure relapse prevention) by psychologists who were trained in appropriate protocols and had training in the trial interventions. After receiving the aforementioned psychological interventions, the exercise program was delivered by physical therapists who were trained in appropriate protocols and had training in the trial interventions and comprised 10 sessions for over 6 weeks (specific exercises to improve mobility, strength, and endurance of the neck and shoulder girdle muscles and exercises to improve eye/head coordination).	Supportive therapy was given in 10 weekly 60-minute individual sessions including psychoeducation about PTSD symptomatology and the rationale for ST and discussion of current issues and general problem-solving skills. Supportive intervention would specifically avoid exposure, cognitive restructuring, and anxiety management techniques. After receiving the aforementioned psychological interventions, the exercise program was delivered by physical therapists who were trained in appropriate protocols and had training in the trial interventions and comprised 10 sessions for over 6 weeks (specific exercises to improve mobility, strength, and endurance of the neck and shoulder girdle muscles and exercises to improve eye/head coordination).	Other obje were not i this meta- Pain: Wee Disability: Functiona Quality of Depressio DASS Fear phys Pain cata Self-effica PTSD: CA checklist Global pe point scal Adverse e Follow-up weeks, 6 r
Dunne et al., 2012; Australia, no funding, RCTs	Total n (completing) = 26 (22) (recruited through newspaper, poster, and email advertisements in Southeast Queensland, Australia). Participants were aged between 20 and 49 years and diagnosed with chronic WADs grade II or III and motor vehicle crash-related PTSD. Gender: 13 males, 13 females. Duration of symptoms ranged from 3 months to 5years with a mean of 28.5 months.	10 weekly 1-hour sessions of individually delivered CBT based on the Australian guidelines for the treatment of adults with acute stress disorder and PTSD (cognitive strategies, coping self-talk, and cognitive restructuring) administered by a graduate psychologist with post- graduate clinical training and 12 months of prior experience delivering CBT interventions.	Wait-and-see control.	Pain: curr Disability NDI Depressio DASS Posttraum Fear phys Other obje were exclu analysis. Quality of Psycholo Pressure p Digital pre Follow-up 6 months
Ehrenborg and Lindberg., 2010; Sweden, no funding, RCTs	Total n (completing) = 65 (59) (from the pain unit of the Department of Rehabilitation Medicine, Boras Hospital). Participants were aged 39.4 ± 11.1 years and diagnosed with chronic WADs. Gender: 31 males, 34 females. Duration of symptoms ranged from 4 to 177 mouths with a mean of 25.0 ± 30.2 months.	Interdisciplinary rehabilitation based on cognitive behavioral perspectives of pain provided 5 hours/day, 5 days/week for 4–6 weeks by occupational therapists, physical therapists, physicians, nurses, nurse assistants, psychologists, and social workers. In addition, eight sessions of biofeedback training (55-minute sessions/week for 4 weeks) conducted during engagement in	Interdisciplinary rehabilitation based on cognitive behavioral perspectives of pain provided 5 hours/day, 5 days/week for 4–6 week by occupational therapists, physical therapists, physicians, nurses, nurse assistants, psychologists, and social workers. The control group was active in handicraft on the same terms as the treatment group but without surface electromyography biofeedback.	Other obje were exclu analysis. Occupatio and satisf performar Occupatio Measure Psychoso functionir Pain Inver Follow-up months

		occupational therapy handicraft with surface electromyography.		
Michaleff et al., 2014; Australia, no funding, RCTs	Total n (completing) = 172 (150) (from sites in Sydney and Brisbane, Australia). Participants were aged between 18 and 65 years and diagnosed with chronic WADs grade I or II. CBT group: Age: 42.6 ± 12.3 years. Gender: 38 males, 48 females. Mean duration of symptoms: 20.9 ± 15.1 months. Control group: Age: 43.1 ± 12.7 years. Gender: 26 males, 60 females. Mean duration of symptoms: 22.0 ± 18.2 months.	Individually tailored and supervised comprehensive exercise program provided by physical therapists who were trained at a 1-day workshop. Twenty sessions lasting 1 h for 12 weeks (two sessions per week for 8 weeks; one session per week for 4 weeks). CBT strategies were used for a comprehensive exercise program (encouraging skill acquisition by modeling, setting progressive goals, and self-monitoring, and positively reinforcing progress). The comprehensive exercise program included specific cervical spine exercises, neck extensor endurance exercises, specific neck motor relearning exercises, aerobic exercises, and manual therapy techniques provided with the patient educational booklet.	The participants received a 30-min consultation with a physical therapist during which they read the educational booklet, practiced the exercises with minimum guidance (verbal or physical) from the physical therapist. The participants were then required to implement the advice provided and practice the exercises independently at their own discretion. No additional supervision was provided. The participants had the opportunity to contact the physical therapist by telephone on two occasions if they needed further verbal clarification of the information covered in the consultation.	Pain: Wee Disability/ NDI Quality of Other obje were exclu analysis. Global pe Global pe Disability/ status: W Questionn Functiona PSFS Cer motion: In Adverse e Follow-up 6 months,
Pato et al., 2010; Switzerland, no funding, RCTs	Total n (completing) = 87 (73) (from Swiss Accident Insurance Fund (SUVA) and the Swiss Insurance Association registers). Participants were aged 41.61 ± 12.0 years and diagnosed with chronic WADs grade I or II. CBT group: Age: 42.6 ± 12.3 years. Gender: 38 males, 48 females. Mean duration of symptoms: 20.9 ± 15.1 months. Control group: Age: 43.1 ± 12.7 years. Gender: 26 males, 60 females. Mean duration of symptoms: 22.0 ± 18.2 months.	All patients received two weekly sessions for 8 weeks (16 sessions) of CBT by the same (male) psychologist and were randomly assigned to one of following additional treatments: infiltration, physical therapy, medication for 8 weeks prescribed by the physician or physical therapist, or CBT focused on pain aspects, teaching control of pain, stress reduction, and chronic pain management techniques. Specific skills taught during the sessions were imagery, cognitive therapy for stressful situations, progressive muscle relaxation training, and application of guided mastery for stress/pain management.	The infiltration group had 16 sessions, the physical therapy group had 16 sessions, and the medication group were medicated once a day for 8 weeks by the physician or physical therapist.	Other obje were exclu analysis. Pain: VAS questionn Disability/ HAQ Well-being Cognitive Failures Q Follow-up and 6 mo
Soderlund and Lindberg, 2001; 2007; Sweden, Swedish Foundation, RCTs	Total n (completing) = 33 (32) (from an orthopedic clinic). Participants were aged between 18 and 60 years and diagnosed with chronic WADs grade I, II, or III. Duration of symptoms: 3 months or more. CBT group: Age: 37.7 years. Gender: seven males, nine females. Control group: Age: 43.5 years. Gender: seven males, 10 females.	Patients underwent 12 individual sessions, which included learning of basic physical and psychological skills, application and generalization of these basic skills in everyday activities, and a phase for maintenance of these skills by a physical therapist. The basic skill phase included coping strategies, relaxation training, re-education of a balanced cervicothoracic posture, and exercises aimed to increase neck range of motion, coordination, and endurance.	Patients underwent 12 individual sessions of exercises designed to enhance muscular stabilization of the neck, mobility of the neck and shoulders with stretching, and coordination of head movements and exercises to maintain the body posture and arm muscle strength provided by physical therapist. The treatment could also include pain-relieving methods including relaxation, transcutaneous electric nerve stimulation, acupuncture, and heat.	Other obje were exclu analysis. Pain: Wee Disability/ PDI Cervicoth universal Cervical ra Rehab Ca goniomet Follow-up interventi months
Stewart et al., 2007; Australia,	Total n (completing) = 132 (125) (from two physical therapy clinics in Sydney).	The 6-week exercise program (three sessions in the first and second weeks; two sessions in the third and fourth	Patients received standardized education, reassurance, and encouragement to resume light activity alone assisted by a physical therapist. The advice was given in one consultation and two follow-up phone contacts. Two and 4 weeks later,	Pain: Aver hours, NR Disability/ status: ND

NSW Motor Accidents Authority, RCTs	Participants were aged 20 years or more and diagnosed with chronic WADs grade I, II, or III. CBT group: Age: 42.7 ± 14.4 years. Gender: 27 males, 41 females. Mean duration of symptoms: 8.6 ± 2.5 months. Control group: Age: 43.9 ± 15.1 years. Gender: 18 males, 48 females. Mean duration of symptoms: 9.5 ± 2.1 months.	weeks each; and one session in the fifth and sixth weeks each) after advice was an individualized, progressive program designed by a physical therapist. A treatment manual was developed, and each physical therapist was trained in the study protocol and interventions and were educated by an experienced clinical psychologist about the principles of CBT. The therapist used principles of CBT including setting goals of progressively increasing difficulty, shaping, encouraging self-monitoring of progress, and self-reinforcing. Each participant performed aerobic exercises; stretches; functional activities; activities to enhance speed, endurance, and coordination; and trunk- and limb-strengthening exercises.	patients were contacted via telephone, and the standardized advice was reinforced.	Quality of Other obje were exclu analysis. Functiona Global pe Global pe Adverse e Follow-up months
Wicksell et al., 2008; 2010; Sweden, Swedish Research Council, RCTs	Total n (completing) = 22 (19) (from Swedish Association of Survivors of Traffic Accidents and Polio). Participants were diagnosed with chronic WADs grade I, II, or III. CBT group: Age 48.2 ± 7.8 years. Gender: two males, nine females. Mean duration of symptoms: 79.7 ± 42.2 months. Control group: Age: 55.1 ± 11.2 years. Gender: three males, seven females. Mean duration of symptoms: 76.0 ± 40.9 months.	The 10 individual sessions (60 minutes each) for 8 weeks. Eight sessions were conducted by psychologists and two sessions by a physician specializing in pain. Both the psychologists and physician had experience and formal training in CBT. The basic skill phase included pain education, values assessment, shifting perspective, exposure, acceptance, and diffusion.	Wait-and-see control.	Pain: Wee Disability/ PDI Depressio HADS. Posttraum Fear phys Other obje were exclu analysis. Global life Psycholog PIPS Follow-up 4 months

RCTs, randomized controlled trials; WADs, whiplash-associated disorders; PTSD, posttraumatic stress disorder; CBT, cognitive behavioral therapy; NRS, numer Functional Scale; SF-36, 36-Item Short Form Health Survey; SF-12, 12-Item Short Form Health Survey, DASS, Depression Anxiety and Stress Scale; CAPS-5, Cli Revised; TSK, Tampa Scale of Kinesiophobia; PDS, Posttraumatic Stress Diagnostic Scale; PCS, *Pain Catastrophizing* Scale; VAS, visual analog scale; HAQ, H Depression Scale; PDI, Pain Disability Index; PSEQ, Pain Self-Efficacy Questionnaire; SWLS, Satisfaction with Life Scale; PIPS, Psychological Inflexibility in Pa

Table 3

A summary of the quality of the evidence using the GRADE approach

Quality assessment						Summary of findings		
No of studies	Risk of bias	Imprecision	Inconsistency	Indirectness	Publication bias	No of participants	Pooled standardized mean difference (95% confidence intervals)	Quality of evidence
CBT versus wait-and-see control on pain in the short term								
2	Not serious	Very serious[1]	Not serious	Not serious	Undetected	46	−0.48 (−1.07 to 0.11)	⊕⊕●● LOW
CBT versus wait-and-see control on disability in the short term								
2	Not serious	Very serious[1]	Not serious	Not serious	Undetected	46	−0.61 (−1.21 to −0.01)	⊕⊕●● LOW
CBT versus wait-and-see control on fear of physical activity in the short term								
2	Not serious	Very serious[1]	Not serious	Not serious	Undetected	46	−1.04 (−1.67 to −0.41)	⊕⊕●● LOW
CBT versus wait-and-see control on anxiety in the short term								
2	Not serious	Very serious[1]	Not serious	Not serious	Undetected	46	−0.97 (−1.59 to −0.35)	⊕⊕●● LOW
CBT versus wait-and-see control on depression in the short term								
2	Not serious	Very serious[1]	Not serious	Not serious	Undetected	46	−1.04 (−1.66 to −0.41)	⊕⊕●● LOW
CBT versus wait-and-see control on posttraumatic stress in the short term								
2	Not serious	Very serious[1]	Not serious	Not serious	Undetected	46	−0.28 (−0.87 to 0.30)	⊕⊕●● LOW
CBT in addition to physical interventions versus advice only on pain in the long term								
2	Not serious	Serious[2]	Not serious	Not serious	Undetected	282	−0.20 (−0.43 to 0.03)	⊕⊕⊕● MODERATE
CBT in addition to physical interventions versus advice only on disability in the long term								
2	Not serious	Serious[2]	Not serious	Not serious	Undetected	282	−0.29 (−0.53 to −0.06)	⊕⊕⊕● MODERATE
CBT in addition to physical interventions versus advice only on quality of life in the long term (physical component summary)								
2	Not serious	Serious[2]	Not serious	Not serious	Undetected	282	−0.20 (−0.44 to 0.03)	⊕⊕⊕● MODERATE
CBT in addition to physical interventions versus advice only on quality of life in the long term (mental component summary)								
2	Not serious	Serious[2]	Not serious	Not serious	Undetected	282	−0.12 (−0.35 to 0.11)	⊕⊕⊕● MODERATE

CBT, cognitive behavioral therapy.

[1]Due to the limited sample sizes (fewer than 100 participants), significance was rated down two levels.

[2]Due to the limited sample sizes (fewer than 200 participants), significance was rated down one level.

Figures

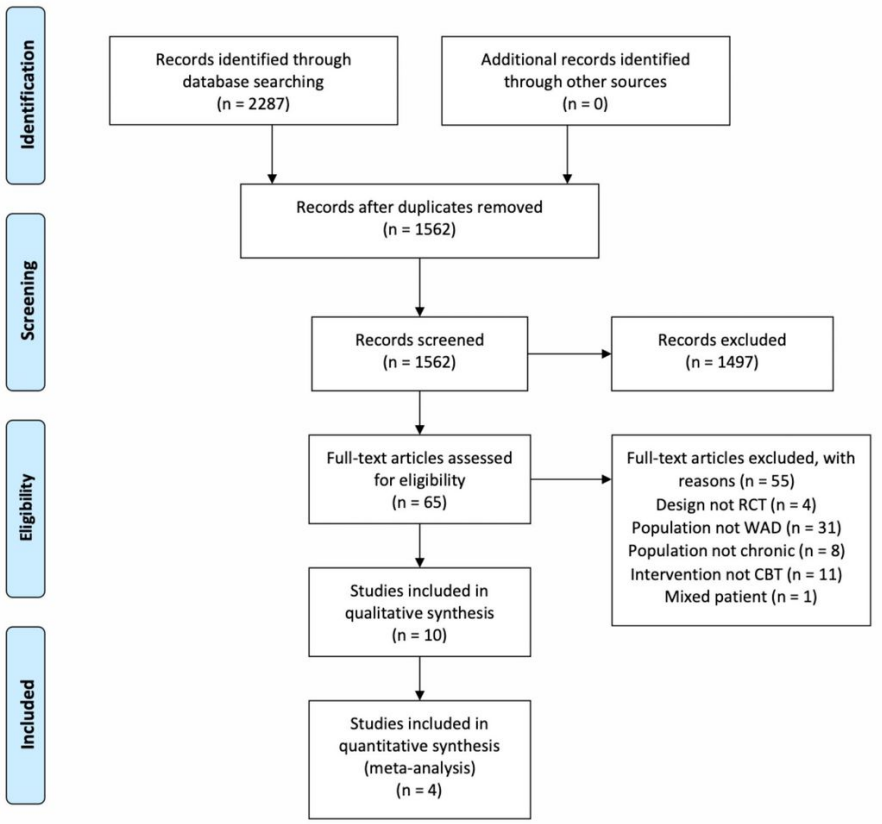
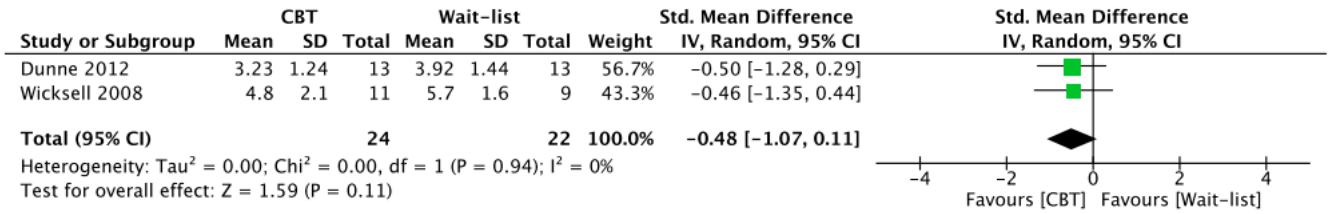


Figure 1.

Figure 1

PRISMA flow chart demonstrating the study search results.



Study or Subgroup	CBT Mean	CBT SD	CBT Total	Wait-list Mean	Wait-list SD	Wait-list Total	Weight	Std. Mean Difference IV, Random, 95% CI
Dunne 2012	3.23	1.24	13	3.92	1.44	13	56.7%	-0.50 [-1.28, 0.29]
Wicksell 2008	4.8	2.1	11	5.7	1.6	9	43.3%	-0.46 [-1.35, 0.44]
Total (95% CI)			**24**			**22**	**100.0%**	**-0.48 [-1.07, 0.11]**

Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.94); I² = 0%
Test for overall effect: Z = 1.59 (P = 0.11)

Figure 2.

Figure 2

Forest plot of CBT versus wait-and-see control on pain in the short term.

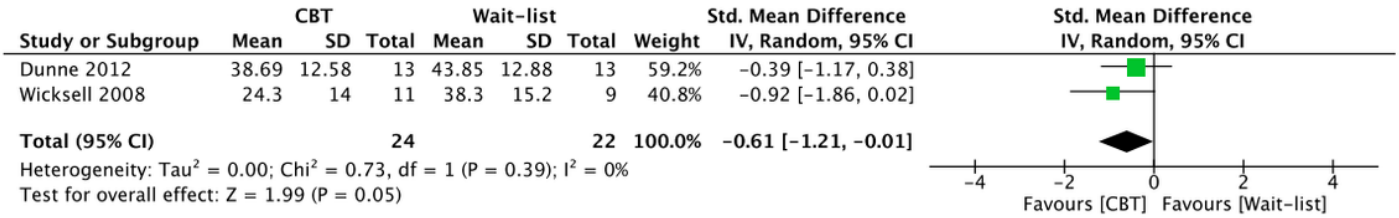


Figure 3.

Figure 3

Forest plot of CBT versus wait-and-see control on fear of physical activity in the short term.

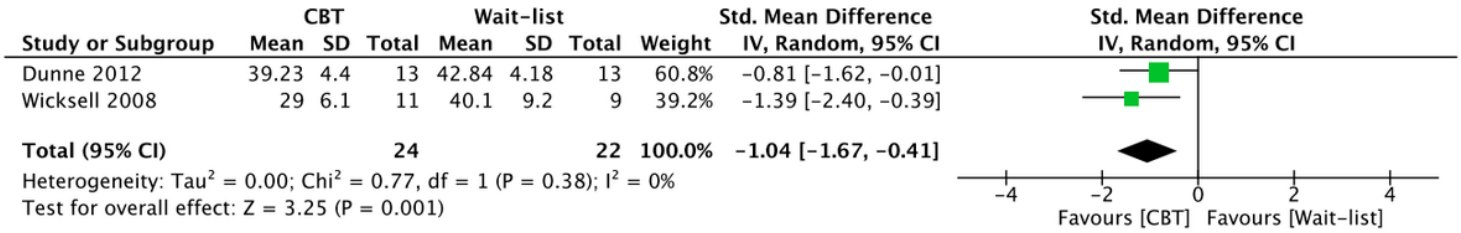


Figure 4.

Figure 4

Forest plot of CBT versus wait-and-see control on fear of physical activity in the short term.

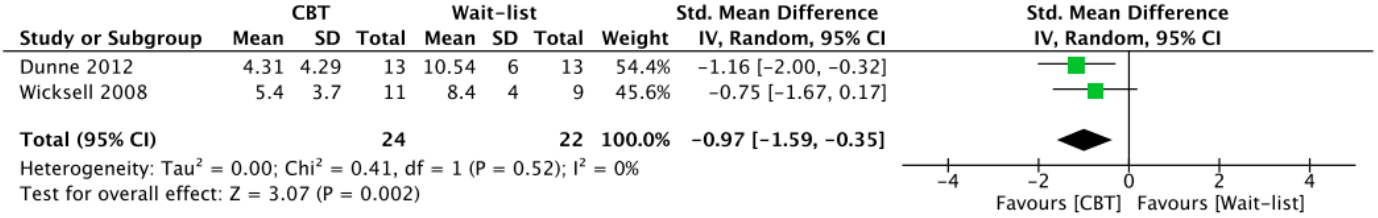


Figure 5.

Figure 5

Forest plot of CBT versus wait-and-see control on anxiety in the short term.

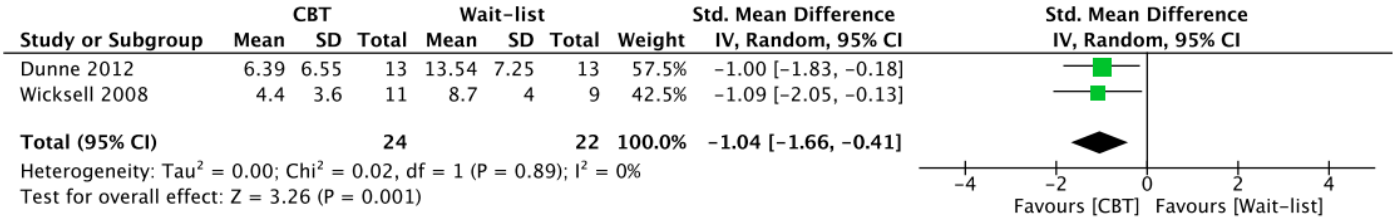


Figure 6.

Figure 6

Forest plot of CBT versus wait-and-see control on depression in the short term.

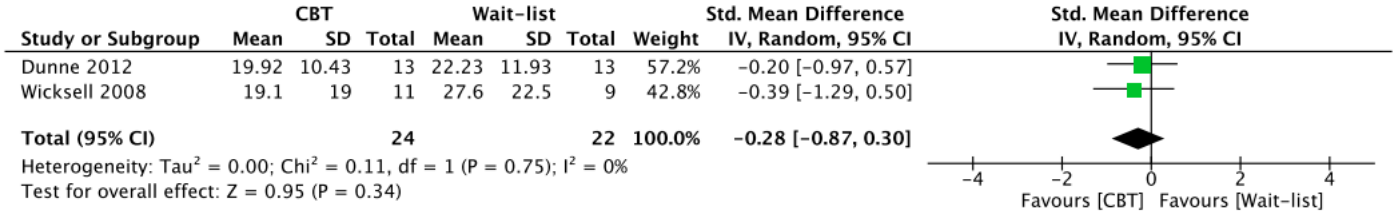


Figure 7.

Figure 7

Forest plot of CBT versus wait-and-see control on posttraumatic stress in the short term.

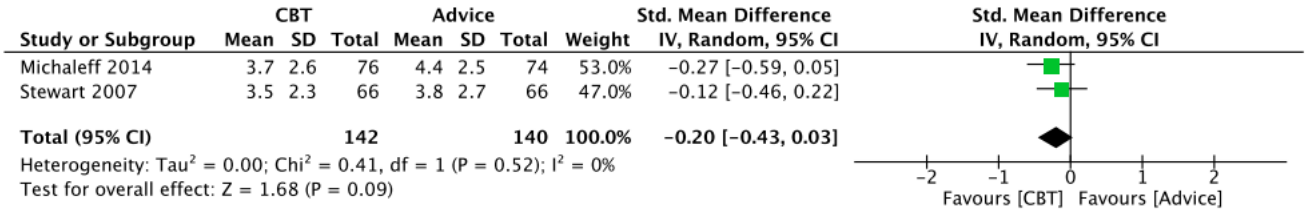


Figure 8.

Figure 8

Forest plot of CBT in addition to physical interventions versus advice only on pain in the long term.

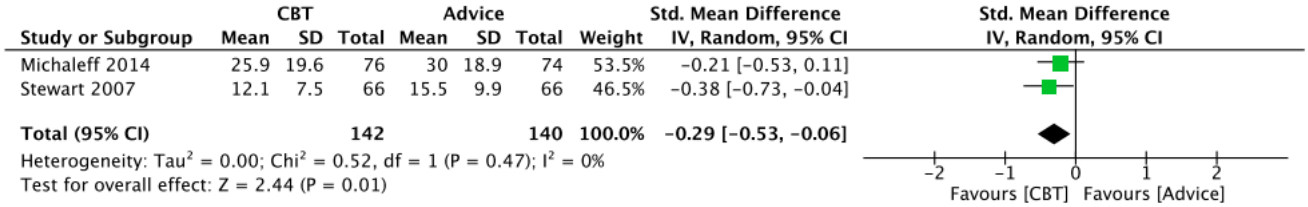


Figure 9.

Figure 9

Forest plot of CBT in addition to physical interventions versus advice only on disability in the long term.

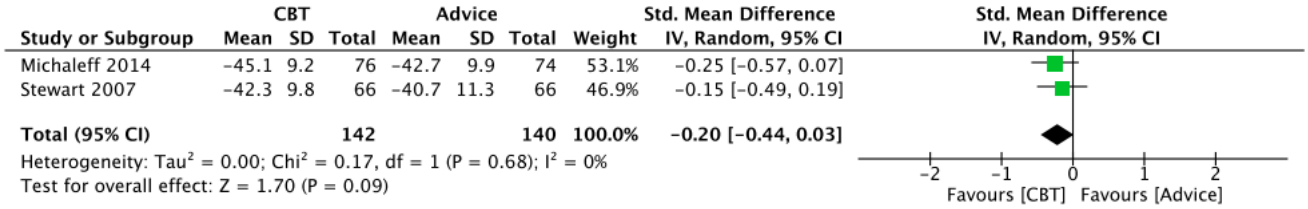


Figure 10.

Figure 10

Forest plot of CBT in addition to physical interventions versus advice only on quality of life in the long term (physical component summary).

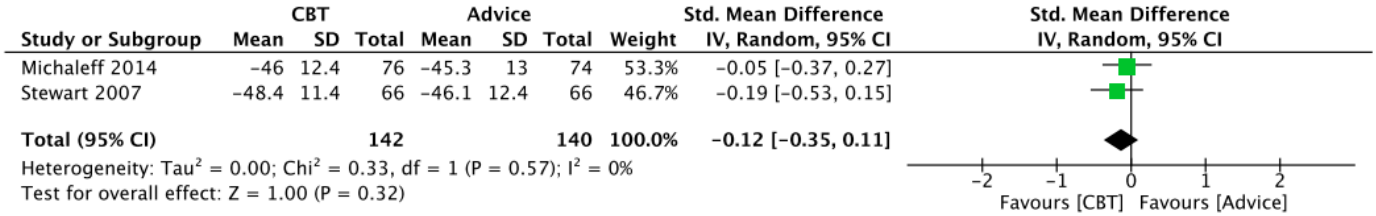


Figure 11.

Figure 11

Forest plot of CBT in addition to physical interventions versus advice only on quality of life in the long term (mental component summary).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Appendix1.Searchstrategy.docx