

## Effects of Cognitive Behavior Therapy on Patients with Chronic Whiplash-Associated Disorders: A Systematic Review and Meta-analysis

Yu Kondo<sup>1</sup> • Takahiro Miki<sup>1,2,3</sup> • Hiroshi Kurakata<sup>4</sup> • Tsuneo Takebayashi<sup>5</sup> • Hiroshi Takasaki<sup>6</sup>

Accepted: 27 November 2022 / Published online: 8 December 2022 © The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

## Abstract

To determine the effectiveness of cognitive behavioral therapy (CBT) alone and in combination with physical interventions on pain, disability, quality of life, and psychological parameters in patients with chronic whiplash-associated disorders (WADs). 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 evidence quality using the Grading of Recommendations, Assessment, Development, and Evaluation approach. Of the 2287 studies identified, 8 were included in the review, of which, 7 were suitable for meta-analysis. We found moderate-quality evidence that CBT does not provide different degrees of short-term (6 RCTs; SMD, -0.20; 95% CI, -0.50 to 0.10) or long-term improvement in disability (3 RCTs; SMD, -0.18; 95% CI, -0.46 to 0.10) than is indicated by other types of intervention comparison. Subgroup analyses indicated low-quality evidence that CBT alone has a medium to large effect on shortterm improvement in disability (2 RCTs; SMD, -0.61; 95% CI, -1.21 to -0.01) compared with wait-and-see control. Additionally, we found moderate-quality evidence that CBT, combined with physical interventions, has a small effect on longterm improvement in disability (2 RCTs; SMD, -0.29; 95% CI, -0.53 to -0.06) compared with advice alone. No differences were found for pain or long-term quality of life. The study found moderately favorable evidence of the combined effect of physical interventions and CBT against advice alone in long-term disability.

**Keywords** Whiplash-associated disorders · Cognitive behavior therapy · Systematic review · Bio-psycho-social model

⊠ Takahiro Miki tkhr.mk@gmail.com

Extended author information available on the last page of the article

#### Introduction

Chronic whiplash-associated disorders (WADs) often include not only physical but also diverse psychological and cognitive impairments (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 et al., 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 metaanalysis 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., 2007a, 2007b), 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 on pain, disability, quality of life (QoL), and psychological parameters in patients with chronic WADs. Second is to investigate the effects of 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 et al., 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  $\geq 3$  months, which was revised from symptoms lasting for  $\geq 6$  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 Online 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 ( $\geq$  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 musculo-skeletal 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 et al., 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 et al., 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  $\geq 6$  (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 () 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  $\geq 3$  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  $\geq 12$  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<sup>2</sup> 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 et al., 2019). Effect sizes proposed were used with 0.2 representing a small effect, 0.5 a moderate effect, and 0.8 a large effect (Cohen, 1988).

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<sup>2</sup> 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.

#### Subgroup Analysis

Subgroup analyses were conducted to compare the effectiveness of CBT alone and in combination with physical interventions with that of specific interventions.

## Results

#### **Study Selection**

Figure 1 presents the flow of the study selection. Two studies by Söderlund and Lindberg (2001, 2007) and two studies by Wicksell et al., (2008, 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 et al., 2012; Ehrenborg & Archenholtz, 2010; Michaleff et al., 2014; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b; Wicksell et al., 2008; Wicksell et al., 2010). Table 1 demonstrates the results of the risk of bias assessment. Six studies (Andersen et al., 2020; Dunne et al., 2012; Michaleff et al., 2014; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2012; Michaleff et al., 2014; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2012; Michaleff et al., 2014; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b; Wicksell et al., 2008; Wicksell et al., 2010; Dunne et al., 2007a, 2007b; Wicksell et al., 2008; Wicksell et al., 2010; Dunne et al., 2010; Michaleff et al., 2014; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b; 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.

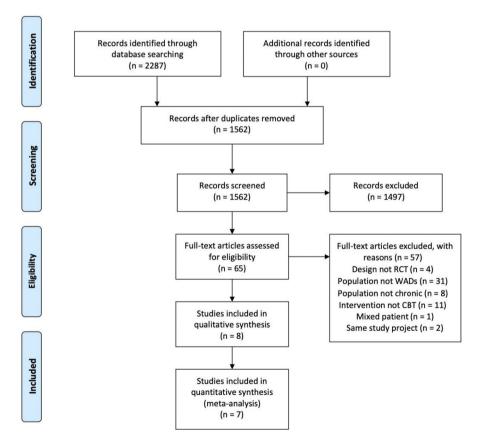


Fig. 1 PRISMA flow chart demonstrating the study search results

Study	Random alloca- tion	Concealed allocation	Groups similar at baseline	Par- ticipant blinding	Therapist blinding	Therapist Assessor blinding blinding	<15% drop- outs	Intention-to- treat analysis	Between-group difference reported	Point estimate and variability reported	Total
Andersen (2020)	Y	Y	Y	Z	Y	Y	Y	Y	Y	Y	6
Dunne (2012)	Y	Z	Υ	Z	z	z	Y	Y	Y	Υ	9
Ehrenborg (2010)	Z	Z	Υ	Z	z	Z	Y	Υ	Y	Υ	5
Michaleff (2014)	Υ	Υ	Υ	Z	z	Y	Y	Y	Y	Υ	8
Pato (2010)	Υ	N	Υ	Z	z	Z	z	Z	Y	Υ	4
Soderlund (2001, 2007)	Υ	Z	Υ	Z	z	Υ	Y	Z	Y	Υ	9
Stewart (2007)	Y	Υ	Υ	z	z	Y	Υ	Y	Y	Y	8
Wicksell (2008, 2010)	Υ	Y	Y	Z	N	Z	Y	Y	Y	Y	7

c re	İ
ystemati	
in this s	
n tl	
ded	
Ē.	
inclu	
·=	İ
studies included i	
the	
s of	
scores o	
PEDro	
-	

#### **Study Characteristics**

The summary of the eight studies is presented in Table 2. Detailed characteristics of the eight studies are presented in Online Appendix 2. Andersen et al. (2020) have compared trauma-focused CBT in addition to exercise with Supportive therapy and exercise. Söderlund and Lindberg (2001, 2007) have compared CBT in addition to physical therapy with physical therapy alone. Pato et al. (2010) have compared CBT in addition to other treatments (physical therapy, infiltration, or medication) with other treatments alone. Ehrenborg and Archenholtz (2010) have compared CBT in addition to surface electromyography biofeedback training with CBT alone. Dunne et al. (2012) and Wicksell et al., (2008, 2010) have compared CBT with the wait-and-see control group. Michaleff et al. (2014) and Stewart et al., (2007a, 2007b) have compared CBT combined with a comprehensive exercise program with advice alone.

One study (Ehrenborg & Archenholtz, 2010) was deemed ineligible for the metaanalysis because it compared CBT combined with surface electromyography biofeedback training with CBT alone. Therefore, seven studies (Andersen et al., 2020; Dunne et al., 2012; Michaleff et al., 2014; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis comparing CBT effect sizes with those in all types of comparisons. Furthermore, two studies that have compared CBT with the wait-and-see control group (Dunne et al., 2012; Wicksell et al., 2008, 2010), were considered eligible for inclusion in the subgroup analysis to investigate the effects of CBT alone. Two studies comparing CBT combined with a comprehensive exercise program with advice alone (Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b), were considered eligible for inclusion in the subgroup analysis to investigate the combined effects of CBT and physical interventions.

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, 2010) and by physical therapists in four studies (Ehrenborg & Archenholtz, 2010; Michaleff et al., 2014; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b). 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., 2007a, 2007b) 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.

Study, data collection country Sample size (Experimental/ control) Andersen et al., (2020); Australia 53/50 and Denmark	Interventions (Duration, Sessions)	Commentions (Duration (contract)	Outcome maneurae Follow un	;
	Laur	Comparisons (Duration/contact)	Ouroine incasures	Follow up
	Trauma-focused CBT 10 weekly 60–90-min sessions Additional exercise 10 sessions for over 6 weeks	Supportive therapy 10 weekly 60-min sessions Exercise 10 sessions for over 6 weeks	NRS NDI PSFS SF-12 DASS TSK PCS PSEQ Adverse events	10 weeks 16 weeks 6 months 12 months
Dunne et al., (2012); Australia 13/13	Trauma-focused CBT 10 weekly 60-min sessions	Wait-and-see control	NRS NDI SF-36 DASS PDS TSK IES-R	Post-treatment 6 months
Ehrenborg and Lindberg., (2010); 36/29 Sweden	Interdisciplinary rehabilitation based on CBT 5 h/day, 5 days/week for 4–6 weeks Additional biofeedback training 55-min sessions/week for 4 weeks	Interdisciplinary rehabilitation based on CBT 5 h/day, 5 days/week for 4–6 weeks	Multidimensional Pain Inventory	4–6 weeks 6 months
Michaleff et al., (2014); Australia 86/86	Exercise based on CBT 20 sessions lasting 1 h for 12 weeks	Advice 30-min	NRS NDI SF-36 PSFS Adverse events	14 weeks 6 months 12 months

Table 2 (continued)					
Study, data collection country	Sample size (Experimental/ control)	Interventions (Duration, Sessions)	Comparisons (Duration/contact)	Outcome measures Follow up	Follow up
Pato et al., (2010); Switzerland	43/33	CBT 2 weekly sessions for 8 weeks Additional infiltration or physical therapy or medication	Infiltration or physical therapy or medication	VAS HAQ	8 weeks 3 months 6 months
Soderlund et al., (2007); Sweden	16/17	Physical therapy based on CBT 12 sessions	Physical therapy 12 sessions	NRS PDI	Post-treatment 3 months 6 months
Stewart et al., (2007a, 2007b); Australia	68/68	Exercise based on CBT 6-weeks	Advice One consultation and two follow- ups	NRS NDI SF-36 PSFS Adverse events	6 weeks 12 months
Wicksell et al., (2008); (2010); Sweden	01/11	CBT 10 sessions (60 min each) for 8 weeks	Wait-and-see control	VAS PDI HADS TSK IES-R	Post-treatment 4 months 7 months
<i>CBT</i> cognitive behavioral therapy; <i>N</i> <i>SF-12</i> 12-item short form health sur matic stress diagnostic scale; <i>PCS</i> p	VRS numerical ratin vey, DASS depression ain catastrophizing	<i>CBT</i> cognitive behavioral therapy; <i>NRS</i> numerical rating scale; <i>NDI</i> neck disability index; <i>PSFS</i> patient-specific functional scale; <i>SF</i> -36 36-item short form health survey; <i>SF-12</i> 12-item short form health survey, <i>DASS</i> depression anxiety and stress scale; <i>IES-R</i> impact of events scale-revised; <i>TSK</i> tampa scale of kinesiophobia; <i>PDS</i> posttraumatic stress diagnostic scale; <i>PCS</i> pain catastrophizing scale; <i>VAS</i> visual analog scale; <i>HAQ</i> health assessment questionnaire; <i>HADS</i> hospital anxiety and depression scale;	<sup>55</sup> patient-specific functional scale; <i>Si</i> tet of events scale-revised; <i>TSK</i> tampa talth assessment questionnaire; <i>HADS</i>	7-36 36-item short for scale of kinesiophobi hospital anxiety and	m health survey; a; <i>PDS</i> posttrau- depression scale;

PDI pain disability index; PSEQ pain self-efficacy questionnaire

#### **CBT versus All Types of Comparisons**

For pain in the short-term, 372 patients with chronic WADs from six studies (Andersen et al., 2020; Dunne et al., 2012; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose forest plot is presented in Fig. 2. No statistically significant overall effect was observed (p=0.17; SMD, -0.21; 95% CI, -0.50 to 0.09), indicating that CBT was not more effective than all types of comparisons in reducing pain at the short-term follow-up. The I<sup>2</sup> value was 43%, indicating moderate heterogeneity. Due to a serious impression with one levels downgraded from the GRADE score, the quality evidence was deemed moderate (Online Appendix 3).

For pain in the intermediate-term, 348 patients with chronic WADs from five studies (Andersen et al., 2020; Michaleff et al., 2014; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; Wicksell et al., 2008, 2010) were included in the metaanalysis, whose forest plot is presented in Fig. 2. No statistically significant overall effect was observed (p=0.73; SMD, -0.04; 95% CI, -0.25 to 0.17), indicating that CBT was not more effective than all types of comparisons in reducing pain at the intermediate-term follow-up. The I<sup>2</sup> value was 0%, indicating insignificant heterogeneity. Due to a serious impression with one levels downgraded from the GRADE score, the quality evidence was deemed moderate (Online Appendix 3).

For pain in the long-term, 361 patients with chronic WADs from studies (Andersen et al., 2020; Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b) were included in the meta-analysis, whose forest plot is presented in Fig. 2. No statistically significant overall effect was observed (p=0.58; SMD, -0.08; 95% CI, -0.36

		СВТ		C	ontrol		:	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Pain in the sho	ort term								
Andersen 2020	6.6	1.72	43	6.28	1.97	46	22.5%	0.17 [-0.25, 0.59]	- <b>+</b>
Dunne 2012	3.23	1.24	13	3.92	1.44	13	10.4%	-0.50 [-1.28, 0.29]	
Pato 2010	32	24	40	41	26	33	20.2%	-0.36 [-0.82, 0.11]	
Soderlund 2007	3.5	1.8	16	2.9	1.8	16	12.3%	0.32 [-0.37, 1.02]	
Stewart 2007	3.2	2.2	66	4.3	2.5	66	26.2%	-0.46 [-0.81, -0.12]	
Wicksell 2008	4.8	2.1	11	5.7	1.6	9	8.5%	-0.46 [-1.35, 0.44]	
Subtotal (95% CI)			189			183	100.0%	-0.21 [-0.50, 0.09]	•
Heterogeneity: Tau <sup>2</sup>	= 0.05; 0	Chi <sup>2</sup> =	8.73, 0	lf = 5 (I	P = 0.1	12); I <sup>2</sup> =	= 43%		
Test for overall effect	t: Z = 1.	38 (P =	= 0.17)						
1.1.2 Pain in the inte	ermedia	te teri	m						
Andersen 2020	5.39	2.39	38	4.9	2.06	40	22.4%	0.22 [-0.23, 0.66]	<b></b>
Michaleff 2014	4.4	2.7	74	4.7	2.3	71	41.8%	-0.12 [-0.44, 0.21]	
Pato 2010	39	27	40	40	24	33	20.9%	-0.04 [-0.50, 0.42]	
Soderlund 2007	3.3	1.8	16	3.5	2.3	16	9.2%	-0.09 [-0.79, 0.60]	
Wicksell 2008	5.2	1.9	10	5.8	1.4	10	5.7%	-0.34 [-1.23, 0.54]	
Subtotal (95% CI)			178			170	100.0%	-0.04 [-0.25, 0.17]	<b></b>
Heterogeneity: Tau <sup>2</sup>	= 0.00; 0	Chi <sup>2</sup> =	1.99, c	f = 4 (1)	P = 0.7	74); I <sup>2</sup> =	= 0%		
Test for overall effect	t: Z = 0.1	35 (P =	= 0.73)						
1.1.3 Pain in the lon	g term								
Andersen 2020	5.43	2.21	36	4.86	2.21	43	26.2%	0.26 [-0.19, 0.70]	
Michaleff 2014	3.7	2.6	76	4.4	2.5	74	38.0%	-0.27 [-0.59, 0.05]	
Stewart 2007	3.5	2.3	66	3.8	2.7	66	35.8%	-0.12 [-0.46, 0.22]	
Subtotal (95% CI)			178			183	100.0%	-0.08 [-0.36, 0.20]	<b>+</b>
Heterogeneity: Tau <sup>2</sup>	= 0.03; 0	Chi <sup>2</sup> =	3.58, c	lf = 2 (I	P = 0.1	17); I <sup>2</sup> =	= 44%		
Test for overall effect	t: Z = 0.	55 (P =	= 0.58)						
								-	
									Favours [CBT] Favours [control]
									ravours [CB1] Favours [Control]

Fig.2 Forest plot of CBT versus all types of comparisons on pain in the short, intermediate and long term

to 0.20), indicating that CBT was not more effective than all types of comparisons in reducing pain at the long-term follow-up. The  $I^2$  value was 44%, indicating moderate heterogeneity. Due to a serious impression with one levels downgraded from the GRADE score, the quality evidence was deemed moderate (Online Appendix 3).

For disability in the short-term, 372 patients with chronic WADs from six studies (Andersen et al., 2020; Dunne et al., 2012; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b; Wicksell et al., 2008; Wicksell et al., 2010) were included in the meta-analysis, whose forest plot is presented in Fig. 3. No statistically significant overall effect was observed (p=0.18; SMD, -0.20; 95% CI, -0.50 to 0.10), indicating that CBT was not more effective than all types of comparisons in reducing disability at the short-term follow-up. The I<sup>2</sup> value was 45%, indicating moderate heterogeneity. Due to a serious impression with one levels downgraded from the GRADE score, the quality evidence was deemed moderate (Online Appendix 3).

For disability in the intermediate-term, 348 patients with chronic WADs from five studies (Andersen et al., 2020; Michaleff et al., 2014; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; Wicksell et al., 2008, 2010) were included in the meta-analysis, whose forest plot is presented in Fig. 3. No statistically significant overall effect was observed (p=0.68; SMD, -0.05; 95% CI, -0.31 to 0.20), indicating that CBT was not more effective than all types of comparisons in reducing disability at the intermediate-term follow-up. The I<sup>2</sup> value was 23%, indicating insignificant heterogeneity. Due to a serious impression with one levels downgraded from the GRADE score, the quality evidence was deemed moderate (Online Appendix 3).

For disability in the long-term, 361 patients with chronic WADs from studies (Andersen et al., 2020; Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b)

		CBT		c	ontrol		:	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.4.1 Disability in th	e short	term							
Andersen 2020	47.29	14.76	43	46.66	15.94	46	22.4%	0.04 [-0.38, 0.46]	_ <b>_</b> _
Dunne 2012	38.69	12.58	13	43.85	12.88	13	10.8%	-0.39 [-1.17, 0.38]	
Pato 2010	5.1	6	40	5.1	4	33	20.4%	0.00 [-0.46, 0.46]	
Soderlund 2007	25.3	18.6	16	20.4	16.7	16	12.6%	0.27 [-0.43, 0.97]	
Stewart 2007	12	6.8	66	15.7	7.9	66	25.8%	-0.50 [-0.85, -0.15]	
Wicksell 2008	24.3	14	11	38.3	15.2	9	8.1%	-0.92 [-1.86, 0.02]	
Subtotal (95% CI)			189			183	100.0%	-0.20 [-0.50, 0.10]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.06; C	Chi <sup>2</sup> = 9	.12, df	= 5 (P =	= 0.10);	$l^2 = 45$	%		-
Test for overall effect	: Z = 1.3	83 (P =	0.18)						
1.4.2 Disability in th	e intern	nediate	term						
Andersen 2020	42.04	19.65	38	39.07	17.9	40	23.6%	0.16 [-0.29, 0.60]	<b>_</b>
Michaleff 2014	26.8	18	74	31.7	18.5	71	35.3%	-0.27 [-0.59, 0.06]	
Pato 2010	6.4	7.6	40	5.7	4.4	33	22.4%	0.11 [-0.35, 0.57]	<b>_</b>
Soderlund 2007	23.4	17.2	16	19.6	16	16	11.5%	0.22 [-0.47, 0.92]	
Wicksell 2008	31.6	14.3	10	40.9	13.2	10	7.2%	-0.65 [-1.55, 0.26]	
Subtotal (95% CI)			178			170	100.0%	-0.05 [-0.31, 0.20]	+
Heterogeneity: Tau <sup>2</sup> =	= 0.02; 0	$Chi^2 = 5$	.22, df	= 4 (P =	= 0.27);	$I^2 = 23$	8%		
Test for overall effect	: Z = 0.4	12 (P =	0.68)						
1.4.3 Disability in th	e long t	erm							
Andersen 2020	41.68	21.52	36	38.78	17.98	43	26.1%	0.15 [-0.30, 0.59]	_ <b>_</b>
Michaleff 2014	25.9	19.6	76	30	18.9	74	38.3%	-0.21 [-0.53, 0.11]	
Stewart 2007	12.1	7.5	66	15.5	9.9	66	35.6%	-0.38 [-0.73, -0.04]	
Subtotal (95% CI)			178				100.0%	-0.18 [-0.46, 0.10]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.03; C	Chi <sup>2</sup> = 3	.45, df	= 2 (P =	= 0.18);	$I^2 = 42$	2%		
Test for overall effect	: Z = 1.2	27 (P =	0.20)						
									Favours [CBT] Favours [control]

Fig.3 Forest plot of CBT versus all types of comparisons on disability in the short, intermediate and long term

were included in the meta-analysis, whose forest plot is presented in Fig. 3. No statistically significant overall effect was observed (p=0.20; SMD, -0.18; 95% CI, -0.46 to 0.10), indicating that CBT was not more effective than all types of comparisons in reducing disability at the long-term follow-up. The I<sup>2</sup> value was 42%, indicating moderate heterogeneity. Due to a serious impression with one levels downgraded from the GRADE score, the quality evidence was deemed moderate (Online Appendix 3).

For QoL in the short-term, 247 patients with chronic WADs from three studies (Andersen et al., 2020; Dunne et al., 2012; M. J. Stewart et al., 2007a, 2007b) 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 Fig. 4, and that of the mental component summary score is presented in Fig. 5. No statistically significant overall effect was observed (p=0.08; SMD, -0.26; 95% CI, -0.55 to 0.03), indicating that CBT was not more effective than all types of comparisons in improving QoL (physical component summary) at the short-term follow-up. CBT had a statistically significant overall small effect (p=0.007; SMD, -0.35; 95% CI, -0.60 to -0.10), indicating that CBT was more effective than all types of comparisons in improving QoL (mental component summary) at the short-term follow-up. The I<sup>2</sup> value was 18% for the physical component summary score, and 0% for the mental component summary score, indicating insignificant heterogeneity. Due to a serious impression with one level downgraded from the GRADE score, the quality evidence was considered moderate (Online Appendix 3).

For QoL in the intermediate-term, 223 patients with chronic WADs from two studies (Andersen et al., 2020; Michaleff et al., 2014) were included in the metaanalysis with the SF-36 scores. The forest plot of the physical component summary score in the SF-36 is presented in Fig. 4, and that of the mental component summary score is presented in Fig. 5. CBT had no statistically significant overall effect (p=0.90; SMD, -0.02; 95% CI, -0.33 to 0.29 for the physical component summary

		CBT		Co	ontrol		5	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.8.1 Quality of life	in the sho	ort term	(phys	ical com	poner	nt sumi	mary)		
Andersen 2020	-37.26	8.96	43	-37.12	9.42	46	37.6%	-0.02 [-0.43, 0.40]	
Dunne 2012	-42.31	20.54	13	-31.31	12.3	13	12.3%	-0.63 [-1.42, 0.16]	
Stewart 2007	-42.1	8.9	66	-38.9	9.3	66	50.0%	-0.35 [-0.69, -0.01]	
Subtotal (95% CI)			122			125	100.0%	-0.26 [-0.55, 0.03]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.01; Ch	$1i^2 = 2.4$	3. df =	2 (P = 0)	0.30); 1	$^{2} = 189$	%		
Test for overall effect	: Z = 1.76	5 (P = 0.	08)						
1.8.2 Quality of life	in the int	ermedia	te teri	n (physi	cal co	mpone	nt summa	ary)	
Andersen 2020	-38.82	10.13	38	-40.45	7.97	40	38.5%	0.18 [-0.27, 0.62]	
Michaleff 2014	-44.5	9.7	74	-43.1	9.5	71	61.5%	-0.15 [-0.47, 0.18]	
Subtotal (95% CI)			112				100.0%	-0.02 [-0.33, 0.29]	
Heterogeneity: Tau <sup>2</sup> =	= 0.01: Cł	$ni^2 = 1.3$	1. df =	1 (P = 0)	).25): I	$^{2} = 249$	%		
Test for overall effect									
1.8.3 Quality of life	in the lon	ıq term	(physi	cal com	onen	t sumn	nary)		
Andersen 2020	-39.59		36	-40.9		43		0.12 [-0.32, 0.56]	
Michaleff 2014	-45.1	9.2	76	-42.7	9.9	74	41.5%	-0.25 [-0.57, 0.07]	
Stewart 2007	-42.3	9.8	66	-40.7		66	36.7%	-0.15 [-0.49, 0.19]	
Subtotal (95% CI)			178			183	100.0%	-0.13 [-0.34, 0.07]	•
Heterogeneity: Tau <sup>2</sup> =	= 0.00: Ch	$ni^2 = 1.7$	7. df =	2 (P = 0)	).41):	$^{2} = 0\%$			
Test for overall effect									
			/						
								-	<u> </u>
									-2 -1 0 1 2
									Favours [CBT] Favours [control]

Fig. 4 Forest plot of CBT versus all types of comparisons on quality of life in the short, intermediate and long term (physical component summary)

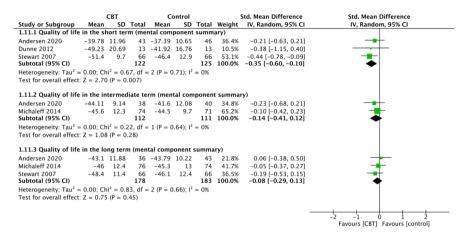


Fig. 5 Forest plot of CBT versus all types of comparisons on quality of life in the short, intermediate and long term (mental component summary)

score; p = 0.28; SMD, -0.14; 95% CI, -0.41 to 0.12 for the mental component summary score), indicating that CBT was not more effective than all types of comparisons in improving the QoL at the intermediate-term follow-up. The I<sup>2</sup> value was 24% for the physical component summary score, and 0% for the mental component summary score, indicating insignificant heterogeneity. Due to a serious impression with one level downgraded from the GRADE score, the quality evidence was considered moderate (Online Appendix 3).

For QoL in the long-term, 361 patients with chronic WADs from three studies (Andersen et al., 2020; Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b) 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 Fig. 4, and that of the mental component summary score is presented in Fig. 5. CBT had no statistically significant overall effect (p=0.21; SMD, -0.13; 95% CI, -0.34 to 0.07 for the physical component summary score; p=0.45; SMD, -0.08; 95% CI, -0.29 to 0.13 for the mental component summary score), indicating that CBT was not more effective than all types of comparisons in improving the QoL at the long-term follow-up. The I<sup>2</sup> 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 (Online Appendix 3).

For secondary outcomes (fear of physical activity, anxiety, depression, posttraumatic stress) in the short-term, 135 patients with chronic WADs from three studies (Andersen et al., 2020; Dunne et al., 2012; Wicksell et al., 2008, 2010) were included in the meta-analysis, whose forest plot is presented in Online Appendix 4. More details of the results of secondary outcomes is available in Online Appendix 4. CBT was more effective than all types of comparisons in reducing the fear of physical activity (p=0.03; SMD, -0.70; 95% CI, -1.34 to -0.07), anxiety (p=0.02; SMD, -0.62; 95% CI, -1.16 to -0.08), and depression (p=0.005; SMD, -0.68; 95% CI, -1.15 to -0.20) at the short-term follow-up. CBT was not more

		CBT		Wa	it-lis	t	5	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	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: Tau <sup>2</sup> = Test for overall effect					P = 0.9	94); I <sup>2</sup> =	= 0%		-4 -2 0 2 4 Favours [CBT] Favours [Wait-list]

Fig. 6 Forest plot of CBT alone versus wait-and-see control on pain in the short term

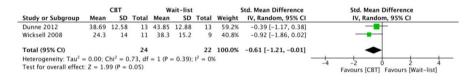


Fig. 7 Forest plot of CBT alone versus wait-and-see control on disability in the short term

effective than all types of comparisons in reducing posttraumatic stress (p=0.34; SMD, -0.28; 95% CI, -0.87 to 0.30) at the short-term follow-up. Due to a very serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low for all secondary outcomes (Online Appendix 3).

For secondary outcomes (fear of physical activity, anxiety, depression) in the intermediate-term, 98 patients with chronic WADs from two studies (Andersen et al., 2020; Wicksell et al., 2008, 2010) were included in the meta-analysis, whose forest plot is presented in Online Appendix 4. More details of the results of secondary outcomes is available in Online Appendix 4. CBT was more effective than all types of comparisons in reducing anxiety (p=0.03; SMD, -0.44; 95% CI, -0.84 to -0.04) at the intermediate-term follow-up. CBT was not more effective than all types of comparisons in reducing fear of physical activity (p=0.48; SMD, -0.24; 95% CI, -0.92 to 0.43), and depression (p=0.10; SMD, -0.70; 95% CI, -1.53 to 0.14) at the intermediate-term follow-up. Due to a very serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low for all secondary outcomes (Online Appendix 3).

#### Subgroup Analysis: CBT Alone Versus Wait-and-See Control

For pain in the short-term, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008, 2010) were included in the meta-analysis, whose forest plot is presented in Fig. 6. No statistically significant overall effect was observed (p=0.11; SMD, -0.48; 95% CI, -1.07 to 0.11), indicating that CBT alone was not more effective than the wait-and-see control in reducing pain at the short-term follow-up. The I<sup>2</sup> value was 0%, indicating insignificant heterogeneity. The number of participants within the pooled analysis was a very small sample. Due to a very serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low (Online Appendix 3).

For disability in the short-term, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008, 2010) were included in the meta-analysis, whose plot is presented in Fig. 7. CBT alone had a statistically significant overall

medium effect (p=0.05; SMD, -0.61; 95% CI, -1.21 to -0.01), indicating that CBT alone was more effective than the wait-and-see control in terms of disability reduction at the short-term follow-up. The I<sup>2</sup> value was 0%, indicating insignificant heterogeneity. The number of participants within the pooled analysis was a very small sample. Due to a very serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low (Online Appendix 3).

For secondary outcomes (fear of physical activity, anxiety, depression, posttraumatic stress) in the short-term, 46 patients with chronic WADs from two studies (Dunne et al., 2012; Wicksell et al., 2008, 2010) were included in the meta-analysis, whose forest plot is presented in Online Appendix 4. More details of the results of secondary outcomes is available in Online Appendix 4. CBT alone had a statistically significant overall large effect, indicating that CBT alone was more effective than the wait-and-see control in reducing the fear of physical activity (p=0.001; SMD, -1.04; 95% CI, -1.67 to -0.41), anxiety (p=0.002; SMD, -0.97; 95% CI, -1.59 to -0.35), and depression (p=0.001; SMD, -1.04; 95% CI, -1.66to -0.41) at the short-term follow-up. CBT alone was not more effective than the wait-and-see control in reducing posttraumatic stress (p=0.34; SMD, -0.28; 95% CI, -0.87 to 0.30) at the short-term follow-up. Due to a very serious impression with two levels downgraded from the GRADE score, the quality evidence was considered low for all secondary outcomes (Online Appendix 3).

#### Subgroup Analysis: CBT in Addition to Physical Interventions versus Advice Only

For pain in the long-term, 282 patients with chronic WADs from two studies (Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b) were included in the meta-analysis, whose forest plot is presented in Fig. 8. CBT in addition to physical interventions had no statistically significant overall effect (p=0.09; SMD, -0.20; 95% CI, -0.43 to 0.03), 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<sup>2</sup> 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 (Online Appendix 3).

For disability in the long-term, 282 patients with chronic WADs from two studies (Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b) were included in the meta-analysis, whose forest plot is presented in Fig. 9. CBT in addition to physical interventions had a statistically significant overall small effect (p = 0.01; SMD, -0.29; 95% CI, -0.53 to -0.06), indicating that CBT in addition to

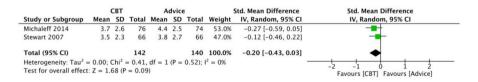


Fig.8 Forest plot of CBT in addition to physical interventions versus advice only on pain in the long term

		CBT		A	dvice			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Michaleff 2014	25.9	19.6	76	30	18.9	74	53.5%	-0.21 [-0.53, 0.11]	
Stewart 2007	12.1	7.5	66	15.5	9.9	66	46.5%	-0.38 [-0.73, -0.04]	
Total (95% CI)			142			140	100.0%	-0.29 [-0.53, -0.06]	•
Heterogeneity: Tau <sup>2</sup> = Test for overall effect					P = 0.4	17); l <sup>2</sup> =	= 0%	-	-2 -1 0 1 2 Favours [CBT] Favours [Advice]

Fig.9 Forest plot of CBT in addition to physical interventions versus advice only on disability in the long term

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 (Online Appendix 3).

For QoL in the long-term, 282 patients with chronic WADs from two studies (Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b) 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 Fig. 10, and that of the mental component summary score is presented in Fig. 11. CBT in addition to physical interventions had no statistically significant overall effect (p=0.09; SMD, -0.20; 95% CI, -0.44 to 0.03 for the physical component summary score; p=0.32; SMD, -0.12; 95% CI, -0.35 to 0.11 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<sup>2</sup> 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 (Online Appendix 3).

		СВТ		A	dvice		1	Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Michaleff 2014	-45.1	9.2	76	-42.7	9.9	74	53.1%	-0.25 [-0.57, 0.07]	
Stewart 2007	-42.3	9.8	66	-40.7	11.3	66	46.9%	-0.15 [-0.49, 0.19]	
Total (95% CI)			142			140	100.0%	-0.20 [-0.44, 0.03]	•
Heterogeneity: Tau <sup>2</sup> Test for overall effect					(P = 0	.68); I <sup>2</sup>	= 0%	_	-2 -1 0 1 2 Favours [CBT] Favours [Advice]

**Fig. 10** Forest plot of CBT in addition to physical interventions versus advice only on quality of life in the long term (physical component summary)

		CBT		A	dvice			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Michaleff 2014	-46	12.4	76	-45.3	13	74	53.3%	-0.05 [-0.37, 0.27]	-
Stewart 2007	-48.4	11.4	66	-46.1	12.4	66	46.7%	-0.19 [-0.53, 0.15]	
Total (95% CI)			142			140	100.0%	-0.12 [-0.35, 0.11]	•
Heterogeneity: Tau <sup>2</sup> = Test for overall effect				f = 1 (F)	9 = 0.5	(7); I <sup>2</sup> =	0%	-	-2 -1 0 1 2 Favours [CBT] Favours [Advice]

Fig. 11 Forest plot of CBT in addition to physical interventions versus advice only on quality of life in the long term (mental component summary)

### 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. Eight studies were considered in detail. Most RCTs were of high quality. This analysis indicated with moderate-quality evidence that CBT was no more effective for most primary outcomes than any other intervention included in a comparison. In subgroup analyses, when considering 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, 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., 2007a, 2007b), resulting in the moderate quality of evidence of all findings.

## The Meta-Analysis for the Effects of CBT Compared with those of All Types of Comparisons

No statistically significant overall effect was observed for most primary outcomes, except QoL (mental component summary) at short-term follow-up, thereby indicating that CBT was no more effective than any other intervention included in a comparison. However, this result may be affected by heterogeneity in the interventions and comparisons of the studies included in the meta-analysis. Several studies (Andersen et al., 2020; Michaleff et al., 2014; Pato et al., 2010; Söderlund & Lindberg, 2001, 2007; M. J. Stewart et al., 2007a, 2007b) demonstrated the effectiveness of CBT as a supplement to other treatments and as part of a comprehensive exercise program. Additionally, the comparison group varied between trials, with two trials (Dunne et al., 2012; Wicksell et al., 2008, 2010) using a waiting list control and other studies comparing the CBT group to other treatments (e.g., medication, acupuncture, physical therapy, naprapathy, and osteopathy) or advice alone. Therefore, these results should be interpreted with caution due to the difficulty in separating the effects of CBT from those of other treatments or exercises.

None of the comparisons provided high-quality evidence either for or against the effectiveness of CBT. The main reason for downgrading the evidence quality was high imprecision. There are methodological reasons for this. Small sample sizes are considered acceptable in behavioral science research (Shearer et al., 2016), and the sample size was less than 400 for all outcomes in the studies considered. Therefore, further RCTs are required to improve the evidence quality for CBT effectiveness.

## 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 et al., 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., 2007a, 2007b).

## 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. (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 et al., 2020; Suzuki & Takasaki, 2020; Takasaki et al., 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 et al., 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 et al., 2006; M. Stewart et al., 2007a, 2007b) 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 et al., 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 et al., 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.

Both in the two RCTs (Michaleff et al., 2014; M. J. Stewart et al., 2007a, 2007b) included in the meta-analysis to investigate the combined effects of CBT and physical interventions, CBT was provided by physical therapists. Therefore, 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. However, we believe that it is important to involve psychologists when planning future studies in order to enhance the quality of the intervention. Previous studies have shown the benefits of a multidisciplinary approach for chronic pain conditions (Casey et al., 2020; Kamper et al., 2014), and further research is needed.

#### Limitations

Our meta-analysis had some limitations. The first and greatest limitation is the limited number of studies included in the meta-analysis. We were unable to compare the advantages of a combination of physical interventions and CBT with other treatments other than advice because of heterogeneity regarding interventions, comparison, and outcomes. In the future, when more RCTs reporting the effects of CBT are available, the results of this study can be strengthened. Secondly, the analysis was performed with a limited number of participants. Therefore, studies with a larger sample size should be performed in the future. 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 moderate-quality evidence that CBT was no more effective for most primary outcomes than any other intervention included in a comparison. We also performed subgroup analysis and found a low level of evidence on the favorable effects of CBT alone compared with those of the wait-and-see control on disability and psychological status 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.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10942-022-00490-y.

Acknowledgements None.

Author contributions Conceptualization: YK, TM, HT. Data curation: YK, TM, HK. Formal analysis: YK, TM, HK. Investigation: YK, TM, HK. Methodology: YK, TM, HK, HT. Project administration: MT, TT, HT. Supervision: TT, HT. Visualization: TT. Writing – original draft: YK, TM, HT. Writing – review & editing: TT, HK.

Funding No funding.

#### Declarations

Conflict of interest The authors declare that they have no conflict of interest.

**Data availability** All data generated or analysed during this study are included in this published article (and its supplementary information files).

## References

- Alperstein, D., & Sharpe, L. (2016). The efficacy of motivational interviewing in adults with chronic pain: A meta-analysis and systematic review. *The Journal of Pain*, 17, 393–403.
- Andersen, T. E., Ravn, S. L., Armfield, N., Maujean, A., Requena, S. S., & Sterling, M. (2020). Traumafocused cognitive behavioural therapy and exercise for chronic whiplash with comorbid posttraumatic stress disorder: A randomised controlled trial. *Pain*, 162, 1221–1232.
- Anstey, R., Kongsted, A., Kamper, S., & Hancock, M. J. (2016). Are people with whiplash-associated neck pain different from people with nonspecific neck pain? *Journal of Orthopaedic and Sports Physical Therapy*, 46, 894–901.
- 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. *Physical Therapy*, 89, 456–469.
- Butler, A. C., Chapman, J. E., Forman, E. M., & Beck, A. T. (2006). The empirical status of cognitivebehavioral therapy: A review of meta-analyses. *Clinical Psychology Review*, 26, 17–31.
- Casey, M. B., Smart, K. M., Segurado, R., & Doody, C. (2020). Multidisciplinary-based rehabilitation (MBR) compared with active physical interventions for pain and disability in adults with chronic pain: A systematic review and meta-analysis. *Clinical Journal of Pain*, 36(11), 874–886.
- 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.

Cohen, J. (1988). Statistical power analysis for the behavioral sciences (2nd ed.). Routledge.

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. *Physical Therapy*, 97, 338–353.

- Deeks, J.J., Higgins, J.P., Altman, D., (2019). Analysing data and undertaking meta-analyses. Cochrane Hand- book for Systematic Reviews of Interventions, 10. https://training.cochrane.org/handbook/curre nt/chapter-10.
- 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. *Clinical Journal of Pain, 28*, 755–765.
- 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. *Clinical Rehabilitation*, 24, 715–726.
- 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 of Systematic Reviews*, 9(9), 3968.
- Flor, H., & Turk, D. C. (1984). Etiological theories and treatments for chronic back pain. I. Somatic models and interventions. *Pain*, 19, 105–121.
- Furlan, A. D., Malmivaara, A., Chou, R., Maher, C. G., Deyo, R. A., & Schoene, M. (2015). 2015 updated method guideline for systematic reviews in the Cochrane back and neck group. *Spine (Phila Pa 1976)*, 40, 1660–1673.
- 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. *Psychological Bulletin*, 133, 581–624.
- Gross, A., Kay, T. M., Paquin, J. P., Blanchette, S., Lalonde, P., & Christie, T. (2015). Exercises for mechanical neck disorders. *Cochrane Database of Systematic Reviews*, 1, 4250.
- Kamper, S. J., Apeldoorn, A. T., Chiarotto, A., Smeets, R. J., Ostelo, R. W., Guzman, J., & van Tulder, M. W. (2014). Multidisciplinary biopsychosocial rehabilitation for chronic low back pain. *Cochrane Database* of Systematic Reviews, 9, 963.
- 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.
- 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. *Physical Therapy*, 83, 713–721.
- 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.
- 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.
- 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. *Musculoskeletal Science and Practice*, 51, 102300.
- Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Annals of Internal Medicine*, 151, 264–269.
- 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 of Systematic Reviews*. https://doi.org/10.1002/14651858.CD010664.pub2
- Morley, S. (2011). Efficacy and effectiveness of cognitive behaviour therapy for chronic pain: Progress and some challenges. *Pain*, 152, 99–106.
- 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.
- 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. *Physical Therapy*, 98, 408–423.
- 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.
- 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. *Journal of Clinical Epidemiology*, 70, 106–110.

- 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.
- 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. *Scandinavian Journal of Pain*, 14, 1–8.
- 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.
- 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. *The Spine Journal*, 16, 1566–1581.
- 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.
- Söderlund, A., & Lindberg, P. (2007). Cognitive behavioural components in physiotherapy management of chronic whiplash associated disorders (WAD)–a randomised group study. *Giornale Italiano Di Medicina Del Lavoro Ed Ergonomia*, 29, 5–11.
- 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.
- Sterling, M. (2014). Physiotherapy management of whiplash-associated disorders (WAD). Journal of Physiotherapy, 60, 5–12.
- Stewart, M., Maher, C. G., Refshauge, K. M., Bogduk, N., & Nicholas, M. (2007). Responsiveness of pain and disability measures for chronic whiplash. *Spine (Phila Pa 1976)*, 32, 580–585.
- 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.
- 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.
- 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.
- Turk, D. C., & Flor, H. (1984). Etiological theories and treatments for chronic back pain. II. Psychological models and interventions. *Pain*, 19, 209–233.
- 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. *Current Pain and Headache Reports*, 23, 57.
- Walton, D. M., Macdermid, J. C., & Nielson, W. (2010). Recovery from acute injury: Clinical, methodological and philosophical considerations. *Disability and Rehabilitation*, 32, 864–874.
- 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 Orthopaedics Journal*, 8, 316–325.
- 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. *Cognitive Behaviour Therapy*, 37, 169–182.
- 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. *European Journal of Pain*, 14, 1059.e1051-1059.e1011.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.

## **Authors and Affiliations**

# Yu Kondo<sup>1</sup> • Takahiro Miki<sup>1,2,3</sup> • Hiroshi Kurakata<sup>4</sup> • Tsuneo Takebayashi<sup>5</sup> • Hiroshi Takasaki<sup>6</sup>

Yu Kondo y.kondo.reha@gmail.com

Hiroshi Kurakata pt.makuhari.tsukuba@gmail.com

Tsuneo Takebayashi takebaya@dream.com

Hiroshi Takasaki physical.therapy.takasaki@gmail.com

- <sup>1</sup> Department of Rehabilitation, Sapporo Maruyama Orthopedic Hospital, Sapporo, Japan
- <sup>2</sup> Graduate School, Hokkaido University, Sapporo, Japan
- <sup>3</sup> Graduate School, Saitama Prefectural University, Koshigaya, Japan
- <sup>4</sup> Department of Rehabilitation, Yumenomachi Home Nursing Care and Rehabilitation Service, Chiba, Japan
- <sup>5</sup> Department of Orthopedic, Sapporo Maruyama Orthopedic Hospital, Sapporo, Japan
- <sup>6</sup> Division of Physical Therapy, Saitama Prefectural University, Koshigaya, Japan