Physiotherapy Pain Association

Effectiveness of additional cognitive behavioural interventions on pain, catastrophising, kinesiophobia and anxiety in people with whiplash-associated disorders compared to physiotherapy alone: A systematic review

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Abstract

Background

Among patients with whiplash-associated disorders (WAD), psychological distress can appear in forms of anxiety, depression or behavioural irregularities. Cognitive behavioural interventions (CBI) aim to influence such issues and thereby the pain experience.

Objectives

The purpose of this review is to synthesise the current state of evidence regarding the effectiveness of additional CBIs on pain, kinesiophobia, catastrophising and anxiety in people with WAD compared to physiotherapy alone.

Data sources

AMED, CINAHL, MEDLINE, PsycARTICLES, SPORTDiscus, PubMed and PEDro were searched from inception to 9 February 2019, complemented with a search update up to September 2021.

Study selection

Randomised controlled trials were included.

Study appraisal and synthesis methods

Quality appraisal and reporting incorporated the Cochrane Risk of Bias 2 tool and GRADE approach.

Results

Six studies were included. The evidence for all outcomes was uncertain. The findings as to whether CBIs in addition to physiotherapy are more effective in reducing pain intensity, kinesiophobia and anxiety than physiotherapy alone are conflicting. Regarding catastrophising, there are consistent findings that additional CBIs are not more effective.

Limitations

The review was not registered beforehand. Only one reviewer performed study selection, appraisal and data synthesis.

Conclusion and implications of key findings

Due to high risk of bias and very low methodological quality, the evidence is very uncertain about the effectiveness of additional CBIs. Their general addition to physiotherapy should be recommended cautiously.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Systematic review registration number

Not applicable.

Contributions of the paper

- Currently, there is scarce scientific evidence on which decisions regarding the appropriate treatment of WAD as a distinct entity could be based.
- This review shows that additional CBIs could not be recommended to reduce pain, catastrophising, kinesiophobia and anxiety in patients with WAD.
- Future research should focus on administering standardised CBI protocols as well as transparent reporting of training and skills of therapists providing the intervention.

Keywords

Whiplash Injuries; Cognitive Behavioural Therapy; Pain; Catastrophising; Anxiety

Introduction

Whiplash is defined as 'an acceleration–deceleration mechanism of energy transfer to the neck. It may result from rear-end or side-impact motor vehicle collisions but can also occur during diving or other mishaps. The impact may result in bony or soft-tissue injuries (whiplash injury [WI]), which

in turn may lead to a variety of clinical manifestations called whiplash associated disorders (WAD) (1). The worldwide annual prevalence of symptomatic injuries ranges between 16 and 200 per 100 000 people (2). Most patients recover from whiplash injuries within 8 weeks (1); however, 18 to 40% report persisting symptoms for more than six months.

The most common symptoms found in people after WI are neck pain, stiffness in the neck and headache, but paraesthesia, arm pain, dysphagia, visual and auditory symptoms and dizziness can also occur (3, 4). The Quebec Severity Classification of Whiplash-Associated Disorder differentiates these disorders into five grades of severity, ranging from Grade 0 (no symptoms or physical signs) to Grade 4 (neck symptoms and fracture or dislocation) (1).

The diagnosis and management of cervical musculoskeletal disorders are increasingly considering pathophysiological approaches or processes concerning recognition (5). Compared to healthy controls, people with low back pain (LBP) show functional and anatomical brain abnormalities (6). Alterations in the nervous system encoding or processing of sensory information can be more relevant for perceived pain than ongoing injury or the dysfunction of local structures, allowing hypotheses regarding cognitive abnormalities in people with chronic pain (6). Persistent neck pain independent of insidious or traumatic onset is accompanied by psychological distress. In WAD, this includes affective disturbances, anxiety, depression and behavioural irregularities or moderate levels of posttraumatic stress reaction. Sterling et al. (7) found that pronounced initial disability, decreased pain thresholds and a higher level of acute emotional distress were associated with higher disability at six months post injury. Es pecially in this WAD subgroup, they recommended multiprofessional approaches combining psychological interventions, physical therapy and adequate pain medication (7).

A current guideline for people after WI recommends reassuring and staying active, a return to usual activities and specific exercises such as low load isometric, postural endurance, motion-promoting and strengthening exercises for the first 12 weeks after injury (8). For patients with negative expectations regarding recovery, monitoring and an eventual referral to a clinician specialised in WAD is suggested (8).

Physiotherapists started recognising the broader psychosocial impact of pain (9) and adopting cognitive behavioural approaches. Cognitive behavioural therapy bases on the assumption that maladaptive cognitions contribute to the maintenance of emotional distress and behavioural problems (10) and aims to influence such maladaptive thoughts, feelings and behaviours and thereby the experience of pain (11). Cognitive behavioural interventions (CBI) might include different techniques such as using a guided-discovery delivery style, appraising thoughts and challenging unhelpful thoughts, goal setting, activity pacing, graded activity, problem solving and homework (12). Research findings show that in the presence of chronic spinal pain, combined physiotherapy and psychology interventions are more effective for the enhancement of physical functioning than physiotherapy alone (13). With additional training and resources, physiotherapists are capable of successfully translating and implementing effective CBI (12). Combining psychosocial interventions with physiotherapy might serve as a feasible and cost-effective approach to target persistent pain (14, 15).

Currently, there is no clear evidence to support the application of CBIs to the physiotherapeutic treatment of people with WAD. In an extensive review, Shearer et al. (16) evaluated the effectiveness of psychological interventions compared with other interventions, placebo or sham interventions or no intervention in improving the self-rated recovery, functional recovery or clinical outcomes of patients with neck pain or WAD. Regarding the effectiveness of additional CBI compared to physiotherapy alone for people with WAD, the evidence was found to be conflicting. In contrast to chronic idiopathic neck pain, WAD is characterised by a clear onset of complaints. Stenneberg et al. (17) found higher pain intensities, a wider distribution of the neck pain, more restricted cervical range of motion, less muscle endurance and more disability in people with WAD compared to those with non-traumatic neck pain and concluded that WAD was a more severe condition. They recommend considering WAD as a separate subgroup that requires a different approach in clinical practice and research. Coppieters et al. (18) found that women with traumatic neck pain such as WAD suffered from distant hyperalgesia and decreased conditioned pain modulation, whereas participants with chronic idiopathic neck pain showed significantly lower disability and fewer cognitive deficits (18). Considering these findings, the current review focused solely on people with WAD as an independent entity. In contrast to the work of Shearer et al. (16), it aimed to synthesise the current state of evidence regarding the effectiveness of additional CBIs on pain intensity, kinesiophobia, catastrophising and anxiety compared to physiotherapy alone in people with WAD and provide updated and specifically tailored information for this population only.

Materials and Methods

This systematic review of randomised controlled trials (RCTs) followed the Preferred Reporting Items of Systematic Review and Meta-analyses: The PRISMA statement (19) (see Appendix A). AMED, CINAHL, MEDLINE, PsycARTICLES, SPORTDiscus, PubMed and PEDro were searched from inception to 9 February 2019. The search terms were defined beforehand and applied in all databases (see Appendix B). The search in PubMed was complemented by MeSH terms. After removing duplicates, titles and abstracts were screened to identify potentially eligible studies. Full text versions were obtained where appropriate and screened for eligibility. The reasons for exclusion were documented during the whole process.

RCTs written in English or German including participants at least 18 years of age with diagnosed acute or chronic WAD were eligible. Studies that involved participants with major structural pathology (i.e., fractures, dislocations, spinal cord injury) or other chronic musculoskeletal conditions were excluded. The studies needed to apply an additional approach of CBI compared to any form of physiotherapy or usual care alone and report data for at least one of the outcomes pain intensity, catastrophising, kinesiophobia or anxiety at baseline and follow-up evaluations. To ensure an adequate comparison, short educational aspects via advice booklets, short reconnaissance, or advice to stay physically active were considered not to be sufficient for inclusion as well as the comparison of CBIs to 'no treatment' or 'waiting list control'. According to the limited literature available and to avoid overly narrowing the initial earch, these requirements were only applied during the screening process.

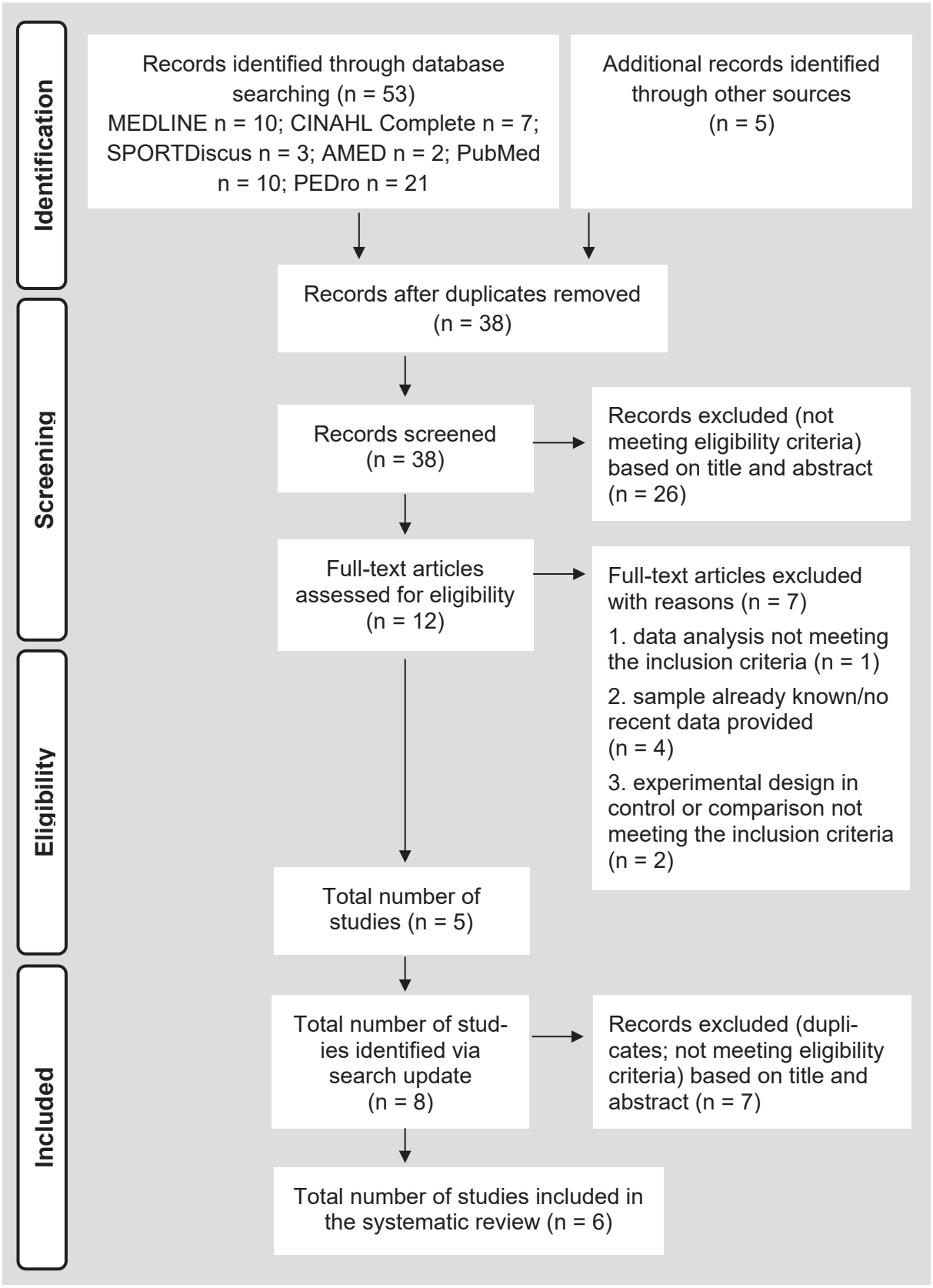
The methodological quality of the included trials was appraised using the Cochrane risk of bias (RoB) tool for randomised trials (RoB 2) (20).

Data regarding study characteristics, participant characteristics and outcome measures were extracted to an Excel template by one researcher. The follow-up periods were categorised as short-term (> 24 hours ≤ 3 months), intermediate (> 3 months < 12 months) and long-term (≥ 12 months) (21). Descriptive statistics were used to report the characteristics of the studies included. Where possible, quantitative pooling of multiple studies via meta-analysis was planned to be conducted. When this was not appropriate due to insufficient comparability of study designs, intervention protocols and outcome measures, the 'difference in means' with calculated confidence intervals was given (22). 'Effect sizes' of therapy were indicated as Hedges' g, which is the difference in mean outcome between groups divided by the weighted pooled standard deviation (23), also referred to as standardised mean difference (SMD). The subtraction of the mean values was done so that positive SMDs indicate improvement for the intervention group (24). The effect sizes were categorised into small (0.2), medium (0.5) and large (0.8) effects (23).The certainty of the body of evidence was summarised by means of the Grade of Recommendation, Assessment, Development and Evaluation (GRADE) (25, 26). This involves the appraisal of RoB, inconsistency/heterogeneity, indirectness of evidence, imprecision of the effect estimates and risk of publication bias as well as domains that may act to increase or decrease confidence in the effect estimate. The level of certainty rating can be 'High', 'Moderate', 'Low' or 'Very low' (27).

Results

Initially, 53 studies were identified. Five further studies were found by hand searching. After emoving duplicates, the titles and abstracts of 38 articles were screened, with 26 classified as ineligible. Twelve full texts were reviewed, with seven not matching the inclusion criteria and excluded. The search update, extending from the initial 9 February 2019 date to 24 September 2021, yielded eight additional studies; however, only one further study was included in the final list of six studies (see Figure 1)

Figure 1. PRISMA flow diagram



A total of 309 people after WI (103 male; 33%) were included. The mean age of the participants ranged from 38 (no SD given) to 55 ± 11.2 years. Most of the participants had been involved in car crashes (n = 278; 90%). The studies included participants with complaints ranging from 16 days up to 36 months after injury (see Table 1). Three studies recited different outcome data from different measurement points from the same sample.

Tables

Table 1 Participant characteristics

Reference	Age (y) Mean ± SD	n (Male/Female)	Type of Whiplash n (%)	WAD grade* n 2/3	Time since Whiplash (mo) Mean ± SD	Pain Duration (mo) Mean ± SD
Wicksell (2008)	IG: 48.2 ± 7.8	IG: 11 (2/9)	IG: Rear end: 8 (73) Other: 3 (27)	NR	NR	IG: 84.1 ± 41.8
	CG: 55.1 ± 11.2	CG: 10 (3/7)	CG: Rear end: 8 (80) Other: 2 (20)			CG: 81.8 ± 41.5
Ludvigsson (2016)	IG: 40 ± 11.6 CG: 38 ± 11.3	IG: 76 (19/57) CG: 71 (24/47)	NR Same sample as Overmeer (2016) & Ludvigsson (2015)	IG: 33/38 CG: 49/27	IG: 20 ± 8.9 CG: 19 ± 8.7	NR
Ludvigsson (2015)	IG: 40 ± 11.6 CG: 38 ± 11.3	IG: 71 (24/47) CG: 76 (19/57)	IG: Motor accident: 54 (76) CG: Motor accident: 65 (86)	IG: 33/38 CG: 49/27	IG: 20 ± 8.9 CG: 19 ± 8.7	NR
Overmeer (2016)	IG: 39.0 ± 11.0	IG: 68 (24/44)	IG: Motor accident: 53 (78) Other: 15 (22)	IG: 31/37	NR	NR
	CG: 40.0 ± 11.7	CG: 67 (16/51)	CG: Motor accident: 56 (84) Other: 11 (16)	CG: 44/31		
Söderlund (2001)	IG: 37.7 CG: 43.5	IG: 16 (7/9) CG: 17 (7/10)	IG + CG: Car crashes 30 (91)	NR (Inclusion: 1-3)	NR	NR
Sterling (2019)	IG: 43.4 ± 14.3	IG: 53 (17/36)	IG: Rear end: 19 (36) Front end: 17 (32) Rear and front end: 7 (13) Side impact: 10 (18.9)	IG: 53/-	IG + CG: 16.4 ± 7.7 days	NR
	CG: 39.3 ± 13.9	CG: 55 (24/31)	CG: Rear end: 22 (40.0) Front end: 15 (27.3) Rear and front end: 8 (14.5) Side impact: 9 (16.4)	CG: 55/-		

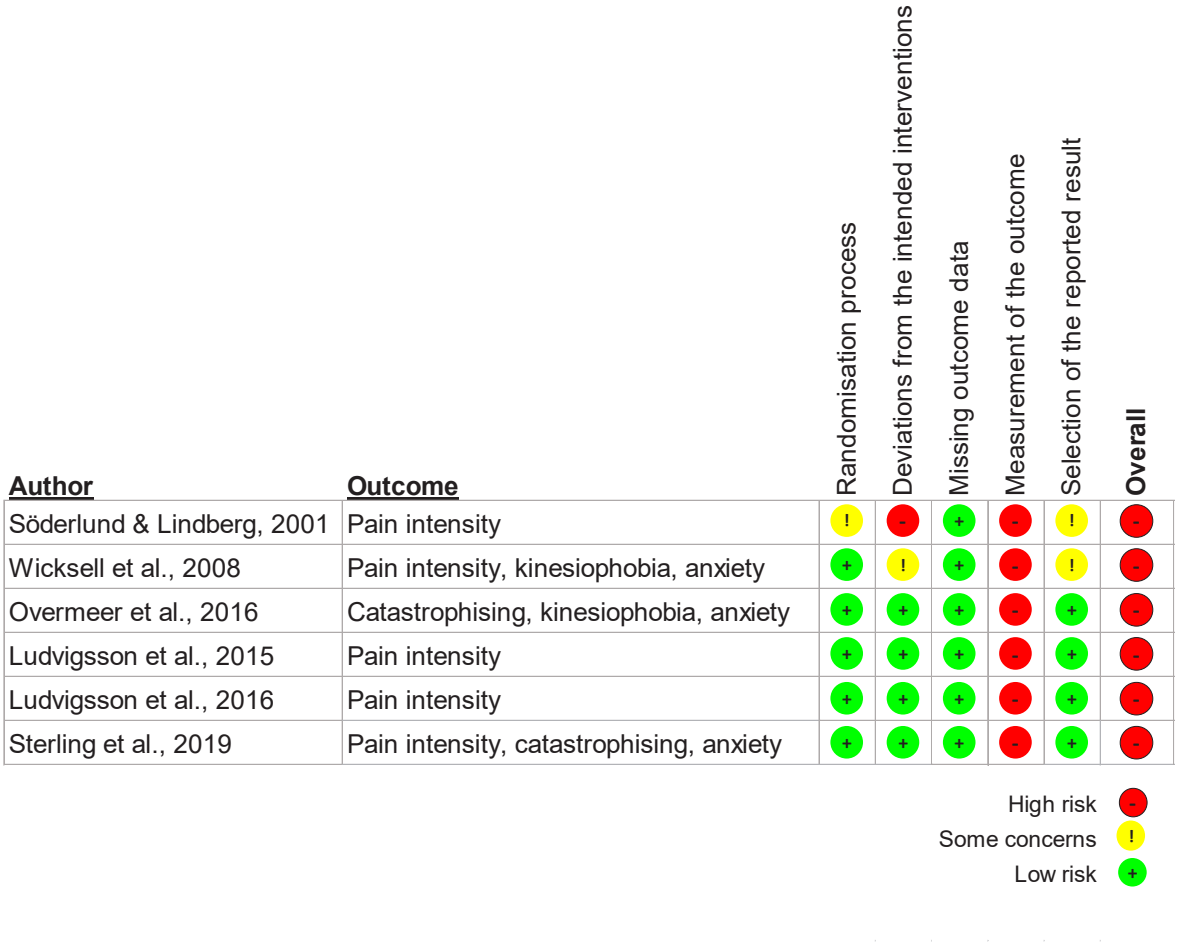
IG = Intervention Group; **CG** = Comparison Group; **NR** = Not Reported; **SD** = Standard Deviation; **mo** = months; **y** = year.
***** WAD severity according to the Quebec Task Force Classification (52).

The CBI protocols of the studies implied pain education/management, values assessment, shifting perspective, exposure, acceptance/defusion, problem solving and coping strategies. They were delivered by psychologists, physicians specialised in pain management or physiotherapists. Physiotherapy included neck-specific exercises for the muscular stabilisation of the neck, neck and shoulder mobility or pain-relieving methods such as relaxation or transcutaneous electric nerve stimulation (TENS). The interventions were summarised according to the TIDieR checklist (28) (see Appendix C).

Pain intensity was assessed in five studies (29-33) using the Visual Analogue Scale (VAS) (0-100) (30, 31), the 10-cm VAS (0-100) (32), respectively, or the unidimensional numeric rating scale (NRS) (29, 33). Catastrophising was assessed in two studies (33, 34). Both used the Pain Catastrophising Scale (PCS), consisting of 13 items scored on a five-point Likert 187 scale from zero (not at all) to four (always) (34). Kinesiophobia was assessed in two studies (32, 34), both using the Tampa Scale of Kinesiophobia (TSK). Overmeer et al. (34) used a short version with 11 items and a score ranging from 11 to 44 points. Wicksell et al. (32) used a scale with 17 items and a score ranging from 17 to 68. Items are rated on a four-point scale with higher scores indicating stronger fear of (re)injury. Anxiety was assessed in three studies. Two used the Hospital Anxiety and Depression Scale (HADS) (32, 34), which combines two subscales (depression and anxiety), each consisting of seven items. The other study used the Depression, Anxiety and Stress Scale (DASS), consisting of 42 items (33). In both questionnaires, the items are rated on a four-point scale from zero (not at all) to three (very often/most of the time). In the context of the present review, only the anxiety subscales were considered.

All individual studies included were rated to be associated with high RoB (see Figure 2). The RoB in the domain 'Measurement of the outcome' was rated as high for all studies. High RoB was also detected for the 'Deviations from the intended interventions' domain in one individual study (29). Some concerns were detected for the 'Randomisation process', 'Selection of the reported results' and 'Deviations from the intended interventions' domains. A judgement of 'High' RoB for any individual domain led to the overall result for a study being at 'High' RoB. A judgement of 'Some concerns' for any individual domain led to the overall result being at 'Some concerns' or 'High' risk (35). The quality of the body of evidence per outcome was downgraded across all domains except for indirectness and was based on high RoB, inconsistency due to the large clinical heterogeneity of the interventions and imprecision due to small sample sizes (see Appendix D). Based on the recommendations by Ryan and Hill (36), no quantitative pooling was conducted as the studies were too heterogeneous on factors such as participants, comparisons and outcomes.

Figure 2. Risk of bias assessment by means of the Cochrane RoB 2



Effects of the interventions

The main findings of this review are shown in the summary of findings table (see Table 2). Regarding pain intensity, only one of four studies found significant differences in favour of the intervention group at all follow-ups (33). In the other studies, no significant improvements from baseline at three-, six- or 12- months' follow-up (30, 31) or significant positive effects at short-term follow-up were found in both groups (29). Thus, there is uncertain evidence from the conflicting findings in four studies of low methodological quality as to whether CBIs in addition to physiotherapy are more effective in reducing pain intensity in people with WAD than physiotherapy alone at short-, intermediate- and long-term follow-up.

Overmeer et al. (34) were not able to detect any significant effects of additional CBIs in terms of catastrophising between two groups performing neck-specific exercises. The unadjusted results by Sterling et al. (33) initially indicated effects in favour of the intervention group. When adjusted for baseline characteristics, these effects were not significant. Hence, there is uncertain evidence from the consistent findings in two studies of low methodological quality that CBIs in addition to physiotherapy are not more effective in reducing catastrophising in people with WAD compared to physiotherapy alone at short-, intermediate- and long-term follow-up.

Regarding kinesiophobia, Wicksell et al. (32) found significant group differences in favour of the intervention group in the short- and intermediate-term follow-ups. Overmeer et al. (34) did not find significant group differences in the intermediate- or long-term follow-ups. Thus, there is uncertain evidence from the conflicting findings in two studies of low methodological quality as to whether CBIs in addition to physiotherapy are more effective in reducing kinesiophobia in people with WAD than physiotherapy alone at short-, intermediate- and long-term follow up.

Wicksell et al. (32) did not report any significant effects of an additional CBI on anxiety though the mean differences calculated in the context of this review showed significant confidence intervals in the short- and intermediate-term follow-ups. Overmeer et al. (34) found no significant group differences for the intermediate- or long-term follow-ups. Sterling et al. (33) reported significant group differences in favour of the intervention group for the intermediate term follow-up for the adjusted data. The mean differences

calculated in this review suggested no significant group differences in the short- and intermediate-term follow-ups but significant group differences in favour of the control group in the long-term follow-up. However, these values have not been adjusted. Thus, there is uncertain evidence from the conflicting findings in three studies of low methodological quality as to whether CBIs in addition to physiotherapy are more effective in reducing anxiety in people with WAD than physiotherapy alone at short-, intermediate- and long-term follow-up.

Table 2 Summary of findings for the studies included

Cognitive behavioural interventions (CBI) for people with whiplash-associated disorders

Patient or population: people with WAD
Settings: primary care physiotherapy practice, orthopaedic clinic, home-based
Intervention: physiotherapy and additional CBI
Comparison: physiotherapy alone

	Illustrative comparative risk				
	Physiotherapy alone *M* ± SD	**Additional CBI** *M* ± SD MD (95% CI) [a]	Standardised mean differences (SMD) Hedges' *g*	Number of participants (studies)	Quality of the evidence (GRADE)
Outcomes					
Pain intensity					Very Low ⊕○○○
Short-term follow-up					
Wicksell (8 wks) VAS 0-10	5.7 ± 1.6	4.8 ± 2.1 MD: 0.9 (-0.38 to 2.17)	*g* = 0.48	20	
Ludvigsson 2015 (3 mo) [b, c] VAS 0-100	change score from baseline: -10 ± 28	-9 ± 24	NA	131	
Söderlund (post-treatment, n. d.) NRS 0-10	2.9 ± 1.8	3.5 ± 1.8 MD: -0.6 (-0.37 to 1.57)	*g* = 0.33	32	
Sterling (6 wks) NRS 0-10	3.7 ± 2.4	2.5 ± 2.2 **MD: 1.2 (0.60 to 1.80)**	*g* = 0.52	102	
Overall MD (VAS 0-10, NRS 0-10)	The mean pain intensity ranged across control groups from 3 to 6.	The mean pain intensity in the intervention groups was on average 0.5 lower.		154 (3)	
Intermediate-term follow-up					
Wicksell (4 mo)	5.8 ± 1.4	5.2 ± 1.9 MD: 0.6 (-0.60 to 1.80)	*g* = 0.36	20	
Ludvigsson 2015 (6 mo) [b, c]	change score from baseline: -10 ± 24	-16 ± 24	NA	114	
Sterling (6 mo)	3.4 ± 2.5	2.6 ± 2.4 **MD: 0.8 (0.17 to 1.43)**	*g* = 0.33	98	

Cognitive behavioural interventions (CBI) for people with whiplash-associated disorders

Patient or population: people with WAD
Settings: primary care physiotherapy practice, orthopaedic clinic, home-based
Intervention: physiotherapy and additional CBI
Comparison: physiotherapy alone

	Illustrative comparative risk				
	Physiotherapy alone *M* ± SD	**Additional CBI** *M* ± SD MD (95% CI) [a]	Standardised mean differences (SMD) Hedges' *g*	Number of participants (studies)	Quality of the evidence (GRADE)
Outcomes					
Overall MD (VAS 0-10, NRS 0-10)	The mean pain intensity ranged across control groups from 3 to 6.	The mean pain intensity in the intervention groups was on average 0.7 lower.		118 (2)	
Long-term follow-up					
Ludvigsson 2016 (12 mo) [b, c]	change score from baseline: -13 ± 23	-12 ± 25	NA	134	
Ludvigsson 2016 (24 mo) [b, c]	change score from baseline: -14 ± 22	-14 ± 22	NA		
Sterling (12 mo)	3.7 ± 2.7	2.9 ± 2.3 **MD: 0.8 (0.16 to 1.44)**	*g* = 0.32	98	
Overall MD (12 mo)	NA as data from only one study per time point/outcome measure were available.			98 (1)	
Catastrophising PCS (0-52)					Very Low ⊕○○○
Short-term follow-up					
Overmeer (3 mo) [b, c]	15.59 ± 13.84	14.74 ± 11.29 MD: 0.85 (-0.39 to 2.09)	*g* = 0.09	129	
Sterling (6 wks)	11.3 ± 11.3	8.8 ± 9.7 **MD: 2.5 (1.23 to 3.77)**	*g* = 0.24	102	
Overall MD	The mean catastrophising ranged across control groups from 11 to 16.	The mean catastrophising in the intervention groups was on average 1.7 lower.		231 (2)	
Intermediate-term follow-up					

Cognitive behavioural interventions (CBI) for people with whiplash-associated disorders

Patient or population: people with WAD
Settings: primary care physiotherapy practice, orthopaedic clinic, home-based
Intervention: physiotherapy and additional CBI
Comparison: physiotherapy alone

Outcomes	Illustrative comparative risk: Physiotherapy alone *M* ± SD	Illustrative comparative risk: Additional CBI *M* ± SD MD (95% CI) [a]	Standardised mean differences (SMD) Hedges' *g*	Number of participants (studies)	Quality of the evidence (GRADE)
Overmeer (6 mo) [b, c]	13.77 ± 11.17	16.32 ± 11.75 **MD: -2.55 (-3.81 to -1.29)**	*g* = 0.22	113	
Sterling (6 mo) PCS	10.7 ± 10.5	9.9 ± 13.1 MD: 0.8 (-0.58 to 2.18)	*g* = 0.07	98	
Overall MD	The mean catastrophising ranged across control groups from 11 to 14.	The mean catastrophising in the intervention groups was on average 0.9 higher.		211 (2)	
Long-term follow-up					
Overmeer (12 mo) [b, c]	12,26 ± 10.89	16.80 ± 12.55 **MD: -4.54 (-5.79 to -3.29)**	*g* = -0.39	118	
Overmeer (24 mo) [b, c]	14. 93 ± 12.39	14.03 ± 10.18 MD: 0.9 (-0.54 to 2.34)	*g* = 0.08	86	
Sterling (12 mo)	10.6 ± 12.4	10.0 ± 12.1 MD: 0.6 (-0.80 to 2.00)	*g* = 0.05	98	
Overall MD (12mo)	The mean catastrophising ranged across control groups from 11 to 12.	The mean catastrophising in the intervention group was on average 2 higher.		216 (2)	
Kinesiophobia TSK (17-68)					Very Low ⊕○○○
Short-term follow-up					
Wicksell (8 wks)	40.1 ± 9.2	29.0 ± 6.1 **MD: 11.1 (8.50 to 13.70)**	*g* = 1.45	20	
Overall MD	NA as Data from only one study per time point was available.			20 (1)	
Intermediate-term					

Cognitive behavioural interventions (CBI) for people with whiplash-associated disorders

Patient or population: people with WAD
Settings: primary care physiotherapy practice, orthopaedic clinic, home-based
Intervention: physiotherapy and additional CBI
Comparison: physiotherapy alone

Outcomes	Illustrative comparative risk: Physiotherapy alone *M* ± SD	Illustrative comparative risk: Additional CBI *M* ± SD MD (95% CI) [a]	Standardised mean differences (SMD) Hedges' *g*	Number of participants (studies)	Quality of the evidence (GRADE)
follow-up					
Wicksell (4 mo)	35.2 ± 10.4	28.7 ± 6.4 **MD: 5.5 (2,78 to 8.22)**	*g* = 0.75	20	
Overmeer (6 mo) [b, c]	20.87 ± 6.95	20.90 ± 6.73 MD: -0.03 (-1.01 to 0.95)	*g* = -0.004	113	
Overall MD	NA as data from only one study per outcome measure were available (short version of the TSK in one study).			133 (2)	
Long-term follow-up					
Overmeer (12 mo) [b, c]	19.12 ± 6.24	18.87 ± 7.05 MD: 0.25 (-1.66 to 2.16)	*g* = 0.04	118	
Overmeer (24 mo) [b, c]	20.79 ± 5.98	19.55 ± 6.30 **MD: 1.24 (0.18 to 2.30)**	*g* = 0.20	86	
Overall MD (12mo)	NA as data from only one study per time point were available.			118 (1)	
Anxiety					Very Low ⊕○○○
Short-term follow-up					
Wicksell (8 wks) HADS Anxiety (0-21)	8.4 ± 5.6	5.4 ± 3.7 **MD: 3 (0.97 to 5.03)**	*g* = 0.64	20	
Sterling (6 wks) DASS Anxiety (0-42)	7.0 ± 7.9	7.0 ± 8.4 MD: 0 (-1.12 to 1.12)	*g* = 0	102	
Overall MD	NA as data from only one study per outcome measure were available.			122 (2)	
Intermediate-term					

Cognitive behavioural interventions (CBI) for people with whiplash-associated disorders

Patient or population: people with WAD
Settings: primary care physiotherapy practice, orthopaedic clinic, home-based
Intervention: physiotherapy and additional CBI
Comparison: physiotherapy alone

	Illustrative comparative risk				
Outcomes	**Physiotherapy alone** *M* ± SD	**Additional CBI** *M* ± SD MD (95% CI) [a]	Standardised mean differences (SMD) Hedges' *g*	Number of participants (studies)	Quality of the evidence (GRADE)
follow-up					
Wicksell (4 mo)	8.9 ± 6.2	5.0 ± 2.5 **MD: 3.9 (1.9 to 5.86)**	*g* = 0.83	20	
Sterling (6 mo)	7.5 ± 7.7	7.5 ± 7.8 MD: 0 (-1.12 to 1.12)	*g* = 0	98	
Overmeer (6 mo) HADS Anxiety (0-21) [b, c]	5.46 ± 4.91	5.87 ± 5.01 MD: -0.41 (-1.24 to 0.42)	*g* = -0.08	113	
Overall MD (HADS Anxiety)	The mean anxiety ranged across control groups from 6 to 9	The mean anxiety in the intervention group was on average 2 lower.		133 (2)	
Long-term follow-up					
Sterling (12 mo)	7.0 ± 6.9	9.3 ± 9.8 **MD: -2.3 (-3.46 to -1,14)**	*g* = -0.27	98	
Overmeer (12 mo) [b, c]	5.32 ± 4.03	5.58 ± 5.11 MD: -0.26 (-1.04 to 0.52)	*g* = -0.06	118	
Overmeer (24 mo) [b, c]	5.25 ± 3.70	5.66 ± 4.43 MD: 0.41 (-1.28 to 0.46)	*g* = -0.1	86	
Overall MD (12 mo) (HADS Anxiety)	NA as data from only one study per outcome measure were available.			216 (2)	

[a] Bold values indicating significant differences.
[b] In the research article, only baseline values and change scores to 3, 6, 12 and 24 months were provided. Data were requested.
[c] Based on the inclusion criteria, participants from only two of three arms of the study were included (third arm: prescription of physical activity).

VAS = Visual Analogue Scale; **NRS** = Numeric Rating Scale; **PCS** = Pain Catastrophising Scale; **TSK** = Tampa Scale of Kinesiophobia; **HADS** = Hospital Anxiety and Depression Scale; **DASS** = Depression, Anxiety and Stress Scale, **wks** = weeks; **mo** = month; **NA** = not applicable; **MD** = mean difference.

Discussion

The findings of this review show that there is uncertain evidence from the conflicting findings of multiple studies as to whether CBIs in addition to physiotherapy compared to physiotherapy alone are more effective in reducing pain, kinesiophobia and anxiety in people with WAD (29-34). There is uncertain evidence from the consistent findings of two studies that CBIs in addition to physiotherapy are not more effective in reducing catastrophising in people with WAD compared to physiotherapy alone (33, 34).

The ambivalent results for pain might be due to sample differences as Sterling et al. (33) included people with acute WAD, whereas participants in the other studies were diagnosed with chronic WAD, probably associated with a higher risk for central sensitisation and abnormal nociceptive processing (37). Moreover, in patients with neck pain, a minimal clinically important change of two points was determined (38). Hence, the clinical importance of the improvement of one out of 10 points on the NRS experienced by people with WAD should be critically evaluated.
The ambivalent results for kinesiophobia may be due to the insufficient comparability of the two samples (32, 34) due to higher average baseline values (more than 10 points difference) and ambiguity in terms of treatment in the control group in one study (32). Regarding anxiety, significant effects of additional CBIs were found in one out of three studies only for the short- and intermediate-term follow-ups (32). Nevertheless, the results of small sample sizes should be interpreted cautiously.

Further, the possibility of the interventions to demonstrate effectiveness for the outcomes catastrophising, kinesiophobia and anxiety might have been hampered due to ceiling effects. The mean baseline values for catastrophising ranged between 17 and 19 out of 52 possible points (33, 34), which was scarcely below the cut-off threshold for being distressed of 20 points (39). The baseline values for kinesiophobia in two studies (32, 34) were below the cut-off threshold for being 'distressed' of 41 points (39). Finally, the mean baseline values for anxiety of seven to 10 points (32, 34) were below the cut-off values for the HADS anxiety scale of 11 points (40).

The results of the review suggest that when compared to no treatment, the effects of both CBI and physiotherapy, respectively, converge and that treatment effects might be characterised by comparable mechanisms of action. These assumptions are in line with the findings of Overmeer et al. (34), who found positive effects on general disability and psychological factors such as anxiety, kinesiophobia and catastrophising for neck-specific exercises both with and without additional CBI when compared to a control group receiving the advice to stay active only. Ludvigsson et al. (30) reported comparable findings for the effects on pain reduction but which dissolved after two years, generally questioning the long-term benefits of conervative treatments.

A secondary analysis of an RCT revealed that improvements in stress and pain-related coping were causal mechanisms for the effectiveness of an integrated psychological and exercise intervention for patients at risk of poor recovery after acute WI. The authors concluded that reducing stress was crucial in this population (41). Willaert et al. (42) attribute the low effectiveness of bio-psychologically oriented multimodal interventions to the fact that these mostly focus on the rehabilitation of physical symptoms rather than on concomitant cognitive and psychological symptoms, such as posttraumatic stress and associated dysregulated stress system responses. Therefore, it is conceivable that physiotherapy and CBI might achieve comparable effects when stress is addressed appropriately and that sophisticated interventions might not even be necessary. Regarding their costs, educational approaches are even preferable to multimodal treatment approaches (43).

Further, the high RoB detected for all individual studies should also be considered. High RoB in the domain 'Measurement of the outcome' mainly arose from a lack of blinding of outcome assessors. For participant-reported outcomes such as pain or anxiety, participants are considered as outcome assessors. It is likely that the assessment of the outcome was influenced by knowledge of the intervention received as patients who believe that they will improve with therapy tend to report better outcome ratings (44). High RoB for the 'Deviations from the intended interventions' domain could have been avoided by ensuring and reporting arrangements to keep the allocation secret. The results in both domains emphasise the importance of placebo controlled trials and the usage of appropriate analyses to estimate the effect of assignment to intervention (e.g. intention to treat analyses). Further, researchers should aim to analyse all participants in the assigned group as excluding participants from the analysis might have a significant impact on the result (20). Judgements of 'Some concerns' in the 'Selection of the reported results' domain are avoidable by providing sufficient information, which allows reviewers to estimate whether the data underlying the results are in accordance with a pre-specified analysis plan (20). This is also crucial for the 'Randomisation process' domain. A lack of reporting can consequently lead to an unjustified high RoB judgement.

Strengths of the review

This review adds to the findings of the review by Shearer et al. (16), who also investigated the effectiveness of psychological interventions for patients with neck pain or WAD. They did not find clear evidence to support or refute the application of CBIs in patients with recent onset WAD (16). The current review provides specifically tailored updated evidence regarding the effectiveness of additional CBIs compared to physiotherapy alone in people with WAD and reaches similar conclusions.

Limitations

There were some limitations to this review. Due to personal and time constraints of this review, the setting did not allow for several reviewers to realise the processes of study selection, assessment of methodological quality or data extraction. This might have led to the inappropriate exclusion of eligible studies or a misjudgement of the methodological quality, potentially influencing the quality of the body of evidence. To reduce potential bias in the review design, the research questions were refined during the initial phase with the help of an experienced statistician, who also assisted with the definition of structured and objective PICOs that were refined in collaboration with a subject librarian and incorporated during study selection.

Additionally, the review was not registered beforehand, and retrospective registration was no longer designated by PROSPERO, possibly leading to undesirable duplication.

All studies included applied the principles of CBIs without being based on a standardised protocol for implementation, hampering comparability across studies. The level of training, qualification and experience of therapists as well as different interpretations or weightings of single aspects of CBIs can differ. Within the included studies, only one investigated CBIs provided by psychologists or physicians specialised in pain education (32). Shearer et al. (16) stated a possible slight benefit in favour of CBIs provided by pain specialists. Hall et al. (45) found high-quality evidence showing that CBIs provided by trained physiotherapists within the physiotherapy setting were effective for the treatment of LBP. Currently, there is no evidence concerning the advantages and disadvantages of physiotherapist-guided CBIs for people with WAD.

Recommendations for future studies

There is a lack of knowledge as to whether specific subgroups demonstrating impairments or deficits regarding psychological factors, coping strategies and self-efficacy could benefit more from additional CBIs. A potential approach to overcoming this issue might be the application of precise classification tools to detect those patients (46, 47) . In most of the studies, included physiotherapy involved forms of neck-specific exercises, which is in line with guide line recommendations for WAD. However, the effects of exercise compared to control interventions vary between modest,

low or non-existent, questioning the appropriateness of exercise in this clinical population (48). Regarding factors that might affect the responsiveness to exercise in acute and chronic WAD, Griffin et al. (49) highlighted the therapeutic relationship. They emphasised the importance of providing specific education around the significance of therapist-patient rapport and effective communication skills that give a rationale behind prescribed exercises as well as the ability to give hope and optimism for healthcare practitioners in this field. Further determinants affecting responsiveness are immediate effectiveness and symptom responsiveness as well as psychological factors such as fear avoidance behaviours, pain catastrophising and sense of justice (49). The authors suggest including an initial assessment of the presence of discrete physical impairments that respond immediately to exercise and psychological attributes and investigate their role in mediating outcomes in WAD (49).

Varying outcome measures hamper data and quantitative pooling via meta-analyses. Using a pre-defined core outcome set could help to overcome this issue (50). Chen et al. (50) recom mend addressing the core domains of physical functioning, perceived recovery, work and social functioning, psychological functioning, quality of life and pain for clinical trials in WAD.

Besides the abovementioned aspects, future research should consider longer follow-up periods as patients with WAD can suffer from frequent residual symptoms more than 10 years after the accident (51). Placebo-controlled or 'do nothing/ waiting list control' study designs can contribute to further knowledge regarding the natural healing process and possible common mechanisms of either physiotherapy, psychological or combined interventions in addition to insights regarding time points where possible effects may align with placebo interventions.

Conclusion

The body of evidence found in the current review is so small that deriving recommendations for clinical practice requires caution. There is scarce scientific evidence on which decisions regarding the appropriate treatment of WAD could be based. Considering these findings and that additional CBIs require greater financial and personnel resources, their clinical application cannot hitherto be recommended to reduce pain intensity, kinesiophobia, catastrophising or anxiety in people with WAD. Future research should focus on administering standardised CBI protocols and core outcome sets. Further, researchers should transparently report study designs as well as the training and skills of the therapists providing the intervention to facilitate comparison and analysis across studies.

- Ethical approval by an ethics committee was not necessary. Thus, there is no ethics protocol reference number available.
- This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.
- Declarations of interest: none

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Appendices

Appendix A: PRISMA 2009 Checklist (19)

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2, 3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4, 5, 6
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes and study design (PICOS).	5, 6
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g. web address) and, if available, provide registration information including registration number.	No registration
Eligibility criteria	6	Specify study characteristics (e.g. PICOS, length of follow-up) and report characteristics (e.g. years considered, language, publication status) used as criteria for eligibility, giving rationale.	7, 8
Information sources	7	Describe all information sources (e.g. databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7
Study selection	9	State the process for selecting studies (i.e. screening, eligibility, included in systematic review and, if applicable, included in the meta-analysis).	7, 8
Data collection process	10	Describe method of data extraction from reports (e.g. piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7, 8

Data items	11	List and define all variables for which data were sought (e.g. PICOS, funding sources) and any assumptions and simplifications made.	7, 8
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level) and how this information is to be used in any data synthesis.	7, 8
Summary measures	13	State the principal summary measures (e.g. risk ratio, difference in means).	8
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g. I^2) for each meta-analysis.	8
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g. publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g. sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	No additional analyses
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility and included in the review with reasons for exclusions at each stage, ideally with a flow diagram.	9
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g. study size, PICOS, follow-up period) and provide the citations.	9, 10, 11, 12
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	10, 11
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11, 12
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	No meta-analysis
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see item 15).	11, 12
Additional analysis	23	Give results of additional analyses, if done (e.g. sensitivity or subgroup analyses, meta-regression [see item 16]).	No additional analyses
DISCUSSION			
Summary of evidence	24	Summarise the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g. healthcare providers, users and policy makers).	13, 14, 15, 16

Limitations	25	Discuss limitations at study and outcome level (e.g. risk of bias), and at review-level (e.g. incomplete retrieval of identified research, reporting bias).	16, 17
Conclusions	26	Provide a general interpretation of the results in the context of other evidence and implications for future research.	17, 18
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g. supply of data); role of funders for the systematic review.	No funding

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix B: Search strategy

The list of search terms included the following groups of keywords:

- ‘whiplash associated disorder*’ OR ‘whiplash injur*’
- ‘cognitive behavioural therapy’ OR ‘cognitive functional therapy’ OR ‘graded activity’
- ‘standard treatment’ OR ‘usual care’ OR ‘physiotherapy’ OR ‘physical therapy’ OR ‘exercise*’
- ‘pain*’ OR ‘kinesiophobia’ OR ‘catastrophising’ OR ‘anxiety’
- MeSH terms for ‘whiplash injury’, ‘cognitive behavioural therapy’, ‘exercise therapy’, ‘pain’, ‘anxiety’ (Pubmed)

These components were combined using the Boolean operators ‘AND’ and ‘OR’

Search strategy PubMed database

Search	Query	Results
#1	Whiplash associated disorder*	785
#2	Whiplash injur*	1510
#3	Whiplash injuries MeSH	3158
#4	graded activity	191
#5	cognitive behavioral therapy	3449
#6	cognitive behavioral therapy MeSH	24923
#7	cognitive functional therapy	15
#8	standard treatment	22110
#9	usual care	14048
#10	physiotherapy	17432
#11	physical therapy	18767
#12	exercise*	271076
#13	Exercise therapy MeSH	45136
#14	pain*	632999
#15	MeSH pain	639719
#16	kinesiophobia	652
#17	catastrophizing	2629
#18	anxiety	169967
#19	Anxiety MeSH	76841
#20	#1 OR #2 OR #3	3528
#21	#4 OR #5 OR #6 OR #7	26462
#22	# 8 OR #9 OR #10 OR #11 OR #12 OR #13	349406
#23	#14 OR #15 OR #16 OR #17 OR #18 OR #19	945277
#24	#20 AND #21	28
#25	#24 AND #22	21
#26	#25 AND #23	19
#27	Filter: Clinical Trial	10
#28	Filter: Language (English, German)	10

((((((((whiplash associated disorder*[Title/Abstract]) OR whiplash injur*[Title/Abstract]) OR 'Whiplash Injuries'[Mesh])) AND ((((‘cognitive functional therapy’[Title/Abstract]) OR ‘cognitive behavioural therapy’[Title/Abstract]) OR ‘Cognitive Behavioral Therapy’[Mesh]) OR ‘graded activity’[Title/Abstract]))) AND ((((((exercise*[Title/Abstract]) OR physical therapy[Title/Abstract]) OR physiotherapy[Title/Abstract]) OR usual care[Title/Abstract]) OR standard treatment[Title/Abstract]) OR ‘Exercise Therapy’[Mesh]))) AND ((((((pain*[Title/Abstract]) OR ‘Pain’[Mesh]) OR kinesiophobia[Title/Abstract]) OR catastrophizing[Title/Abstract]) OR anxiety[Title/Abstract]) OR ‘Anxiety’[Mesh])

Search strategy EBSCOhost

The databases AMED, CINAHL, MEDLINE, PsycARTICLES and SPORTDiscus were simultaneously searched via the EBSCOhost Research Platform. During the second search update, the platform no longer allowed the incorporation of CINAHL and AMED in the search.

Search	Query	Results
#1	Whiplash associated disorder*	1849
#2	Whiplash injur*	2721
#3	graded activity	1478
#4	cognitive behavioral therapy	16670
#5	cognitive functional therapy	384
#6	standard treatment	68532
#7	usual care	29747
#8	physiotherapy	37817
#9	physical therapy	50019
#10	exercise*	513041
#11	pain*	919799
#12	kinesiophobia	1417
#13	catastrophizing	4836
#14	anxiety	252772
#15	#1 OR #2	4092
#16	#3 OR #4 OR #5	18409
#17	#6 OR #7 OR #8 OR #9 OR #10	676721
#18	#11 OR #12 OR #13 OR #14	1143728
#19	#15 AND #16	31
#20	#19 AND #17	23
#21	#20 AND #18	22

https://search.ebscohost.com/login.aspx?direct=true&db=pdx&db=cmedm&db=s3h&bquery=((AB+pain*)+OR+(AB+kinesiophobia)+OR+(AB+catastrophizing)+OR+(anxiety))+AND+((((AB+whiplash+associated+disorder*)+OR+(AB+whiplash+injur*))+AND+((AB+cognitive+behavioral+therapy)+OR+(AB+cognitive+functional+therapy)+OR+(AB+graded+activity)))+AND+(((AB+standard+treatment)+OR+(AB+usual+care)+OR+(AB+physiotherapy)+OR+(physical+therapy)+OR+(exercise*))+AND+(((AB+whiplash+associated+disorder*)+OR+(AB+whiplash+injur*))+AND+((AB+cognitive+behavioral+therapy)+OR+(AB+cognitive+functional+therapy)+OR+(AB+graded+activity)))))&lang=de&type=1&searchMode=Standard&site=ehost-live

Search strategy Physiotherapy Evidence Database PEDro

Abstract & Title:	
Therapy:	behaviour modification
Problem:	pain
Body Part:	head or neck
Subdiscipline:	
Topic:	whiplash
Method:	clinical trial
Author/Association:	
Title Only:	
Source:	
Published Since:	[YYYY]
New records added since:	[DD/MM/YYYY]
Score of at least:	[/10]
Return:	20 records at a time
When Searching:	Match all search terms (AND)
	Match any search term (OR)

Start Search

Appendix C: Characteristics of the protocols for the intervention and control group (TIDieR checklist)

Author	Overmeer, 2016	Ludvigsson, 2015	Ludvigsson, 2016	Wicksell, 2008	Söderlund, 2001	Sterling, 2019
1. NAME	Neck-specific exercise with a behavioural approach (NSEB)	Neck-specific exercise with a behavioural approach (NSEB)	Neck-specific exercise with a behavioural approach (NSEB)	Exposure and acceptance delivered in addition to treatment as usual (TAU)	Physiotherapy management complemented with cognitive-behavioural components	Physiotherapist-delivered stress inoculation training (SIT) integrated with exercise
2. WHY	- to investigate the effect of NSE with or without a behavioural approach and prescribed physical activity (PPA) on general pain disability and psychological factors in chronic WADs, grades 2 and 3, with a 2-year follow-up.	- to compare the effect of 3 interventions in chronic WAD management on self-rated pain, disability and self-efficacy: 1. Neck-specific exercise (NSE) 2. (NSEB).	- to explore whether, after 1 and 2 years, neck-specific exercise with or without a behavioural approach has long-term benefits over PPA regarding pain, self-rated functioning/disability and self-efficacy in the management of grade 2 or grade 3 chronic WAD.	- to investigate whether exposure and acceptance delivered in addition to treatment as usual (TAU) could increase functions and life satisfaction in people with WAD compared to a control group receiving TAU only. - to investigate the relationship of improvements to changes in psychological flexibility.	- to study the effects of physiotherapy management complemented with cognitive-behavioural components in a group study. - to study if patients with high self-efficacy differed from those with low self-efficacy in reported use of coping strategies, disability and pain intensity.	- to establish the effectiveness of SIT and a physiotherapy exercise programme in decreasing pain-related disability in individuals with acute whiplash injury (< 4 weeks duration). - to investigate the effect on posttraumatic stress symptoms, depression, anxiety, catastrophising, self-efficacy and coping.
3. WHAT						
Materials:	**Physiotherapy + CBI**					
	See Ludvigsson, 2015	- resistive exercise bands. - written individualised exercise programme including prescription of physical activity.	See Ludvigsson, 2015	NI	- oral or written information (or both). - written exercise programme.	- patient educational booklet with information and advice about WAD and self-management. - written and illus-

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						trated exercise instructions. - logbook to record compliance with exercises.
Materials: Physiotherapy Alone						
	See Ludvigsson,	- basic information regarding motor function of the neck, and therapeutic exercise. - resistive exercise bands. - written individualised exercise programme including prescription of physical activity.	See Ludvigsson, 2015	NI	- oral or written information (or both). - written exercise programme.	- patient educational booklet. - written and illustrated exercise instructions. - logbook. - specific smartphone application to assist with required daily practise. - iPod for those without smartphone.
Procedures: CBI Design (Physiotherapy + CBI)						
	See Ludvigsson, 2015	<u>Oral education:</u> <u>Week 1:</u> - pain management education, relaxation exercises, activity goal setting. <u>Week 3:</u> - awareness of the influence of thoughts on behaviour. <u>Week 4:</u> - activity-based goal-specific exercise. <u>Week 5:</u> - breathing exercises.	See Ludvigsson, 2015	<u>Pain education:</u> - mechanisms involved in longstanding pain syndromes. - difference to acute nociceptive pain. - emphasis on the dysfunctional character of non-nociceptive pain and lack of effective treatments. Values assessment: - individual values in life domains.	<u>Basic skills phase:</u> - discussion with the patients about the aims of the treatment and ways of coping with increased pain and self-efficacy. - relaxation training. - re-education of a balanced cervicothoracic posture based on cervi-	<u>1. Phase:</u> - identifying and understanding stress/stressors and how these impact on pain, behaviour, emotions, physical performance and thoughts. <u>2. Phase:</u> - developing skills for managing stress

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		- discussion of personal activity level/pacing. <u>Week 7:</u> - reinforcement of pain management education. <u>Week 8:</u> - follow-up of activity goal setting. <u>Week 10:</u> - reinforcement of strategies to handle relapse. <u>Week 11-12:</u> - follow-up of activity goal setting.		- behaviourally oriented goal setting. Shifting perspective: - evaluation of previous strategies to reduce pain and distress, effects and impact on functionality and valued life. - acceptance of a certain amount of pain to enable engagement in behaviours towards an increase in valued life. Exposure: - gradual values-based exposure to increase frequency of values-directed behaviours in situations that previously resulted in pain-related avoidance. Acceptance and defusion: - addressing negative private experiences that functionally led to avoidance of actions. - acknowledging and accepting these events without acting on their content.	cothoracic muscular stabilisation techniques. - re-education of normal humeroscapular rhythm. Next two phases: - application and generalisation of basic skills on the everyday activities derived from the functional behavioural analysis. Last phase: - maintenance of skills trained earlier. - repetition of key components.	through relaxation, problem solving and helpful coping self-statements. - practise of these skills on a weekly basis at home. <u>3. Phase:</u> - applying skills in various stressful situations to develop tolerance and confidence. - strategies such as progressive muscle relaxation, breathing control exercises, simple cognitive behavioural skills and problem-solving skills.

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				- distinguishing between experiencing a thought and following its content.		
Procedures: Exercise Design (Physiotherapy + CBI)						
	See Ludvigsson, 2015	Week 1: - individual examination. - daily unresisted neck-specific exercise to facilitate deep cervical muscle activity. Week 2-3: - isometric neck-specific exercise. - postural control. Week 3-12: - neck-specific gym exercising. - introduction of home exercises with resistive exercise bands. Week 12: - instruction regarding continuation of neck-specific exercise after the intervention period. - prescription of physical activity. - same exercise protocol as in control group, initially progressed slower to accommodate the ad-	See Ludvigsson, 2015	- treatment protocol did not include physiotherapy. - all participants received TAU during the study period, which could include: - medication - acupuncture - physiotherapy - naprapathy - osteopathy	- exercises aiming at enhancing muscular stabilisation of the neck, and neck and shoulder mobility. - stretching and coordination of head movements. - exercises to maintain body posture and arm muscle strength. - pain-relieving methods such as relaxation, transcutaneous electric nerve stimulation (TENS), acupuncture and heat.	- examination - activating/improving coordination and endurance capacity of the neck flexor, extensor and scapular muscles in specific exercises and functional tasks. - graded programme directed to postural control system, including balance exercises, head relocation exercises and exercises for eye movement control. - physiotherapeutic advice and guidance for return to normal activities, including work, and on undertaking general aerobic exercise. - participants were encouraged to perform exercises at home once per day.

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		ditional behavioural component. - individually complemented by exercises for lower back, abdomen and scapulae as well as stretching exercises.				- at the physiotherapist's discretion, manual therapy (but not grade V manipulation) was allowed if not a major component of the intervention.
Procedures: Exercise Design (Physiotherapy/alone) see Physiotherapy + CBI						
4. WHO PROVIDED						
	See Ludvigsson, 2015	- physiotherapists experienced in managing neck pain disorders. - provided with standardised oral and written information about their interventions. - one day of standardised theoretical and practical training from project leaders for PTs delivering exercise. - physiotherapists were encouraged to become familiar with any of the specific neck exercises before receiving study patients. - behavioural approach was designed to be basic and manageable by experienced physiotherapists in primary care with	See Ludvigsson, 2015	- 8 sessions by psychologists. - 2 sessions by physician specialising in pain and trained in cognitive behaviour therapy. - both with experience and formal training in acceptance and commitment therapy.	- one physiotherapist. - no formal psychotherapeutic training.	- community-based primary care physiotherapists experienced in the management of whiplash-injured people. - completion of a face-to-face training workshop. - different physiotherapists for delivery of SIT + exercise and exercise. - those delivering exercise only have never been trained in the SIT intervention. - SIT therapists were assessed for accreditation via audiotape of each session. - session-by-session checklist of protocol

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		some previous knowledge of behavioural approaches.				adherence. - physiotherapy exercise audited twice to check for adherence to the exercise protocol.
5. HOW						
	See Ludvigsson, 2015	- supervised exercise. - all physiotherapist visits were made within the ordinary publicity funded reimbursement system.	See Ludvigsson, 2015	- conducted individually. - behavioural activation was carried out by the patients between sessions.	- face-to-face. - individually tailored. - skills training done at home.	- supervised by physiotherapist. - face-to-face. - individually tailored.
6. WHERE						
	See Ludvigsson, 2015	<u>Setting:</u> - primary-care setting. - in the gym. - practise of relevant pain management skills at home between sessions.	See Ludvigsson, 2015	<u>Setting:</u> - not further defined.	<u>Setting:</u> - orthopaedic clinic. - exercise practise at home or at the physiotherapy departments' gym (or at both places). - pain-relieving methods were given in the physiotherapy department.	<u>Setting:</u> - assessment: university research laboratory if online assessment was not possible. - interventions: primary care physiotherapy practices. - participants will also perform the exercises at home once per day.
7. WHEN and HOW MUCH						
	See Ludvigsson, 2015	<u>Intervention period:</u> 12 weeks. <u>Week 1:</u> - 2-3 times daily.	See Ludvigsson, 2015	<u>Intervention period:</u> 8 weeks. - 10 sessions (60 min each).	<u>Intervention period:</u> not further defined. - max. 12 sessions.	<u>Intervention period:</u> 6 weeks. - 10 sessions exercise.

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		Weeks 2 and 3: - introduction to gym exercises. - 2 sessions/week. - exercise pain provocation was avoided. Progression: - higher repetitions (up to 3 sets of 30 repetitions) within the symptom tolerance. - tailored individually.		Progression: not applicable as no standardised protocol for the control group exists.		- 6 sessions of SIT strategies (1/week). Weeks 1-4: - 2 sessions/week. Weeks 5-6: - 1 session/week. Progression: - low load nature. - progressed by the physiotherapist (increasing difficulty and load). - pain free.

CBI = Cognitive behavioural intervention; PT = Physiotherapist; NSEB = Neck-specific exercise with a behavioural approach; NSE = Neck-specific exercise; NI = No information available.

Appendix D: Quality of the body of evidence

Outcome	Risk of Bias	Inconsistency/ Heterogeneity	Indirectness	Imprecision	Publication Bias	Other Factors	Rating
Pain	- all information is from results at high risk of bias. - therefore, the level of evidence was downgraded by 2 levels.	- large clinical heterogeneity of the interventions. So, the results of a meta-analysis can be misleading (53). - the point estimate I^2 has lower reliability in meta-analyses with few studies (54). - therefore, the level of evidence was downgraded by 1 level.	- comparison for all outcomes: Ludvigsson et al. (2015, 2016) and Overmeer et al. (34) compared, respectively, neck-specific exercise and neck-specific exercises with additional CBI to the prescription of physical activity alone. No comparison of the two neck specific exercise groups. - population: one study included participants with acute WAD (33). - providing of the intervention: by both physiotherapists and psychologists. - no indirectness for the chosen outcomes. - indirectness among the studies is not considered, leading to differences in the anticipated effects. - therefore, the level of evidence was not downgraded.	- sample sizes of less than 400 participants can lead to imprecision, and it is recommended to consider rating down (26). - therefore, the level of evidence was downgraded by 1 level.	- assessment via graphical or statistical methods and by qualitative signals (55). - funnel plots should only be used when at least 10 studies are included in the meta-analysis; otherwise the power is low. -therefore, the rating was carried out qualitatively. - various databases were searched, and registration was not required for inclusion. -there is no concern that relevant studies have not yet reached phase III testing and could therefore have been missed during the search. So, the risk of publication bias is considered negligible (55). - therefore, the level of evidence was not downgraded.	- as no domains that may lead to increasing the certainty level of the body of evidence such as large effects, dose response or plausible confounding were detected, there is no upgrading.	Very Low ⊕◯◯◯
Catastrophising	downgraded by 2 levels.	downgraded by 1 level.	no downgrading.	downgraded by 1 level.	no downgrading.	no upgrading.	Very Low ⊕◯◯◯

Kinesio-phobia	downgraded by 2 levels.	downgraded by 1 level.	no downgrading.	downgraded by 1 level.	no downgrading.	no upgrading.	Very Low ⊕◯◯◯
Anxiety	downgraded by 2 levels.	downgraded by 1 level.	no downgrading.	downgraded by 1 level.	no downgrading.	no upgrading.	Very Low ⊕◯◯◯

CBI = Cognitive behavioural intervention