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Physiotherapy rehabilitation for whiplash associated disorder II: a systematic review and meta-analysis of randomised controlled trials

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ABSTRACT

Objective: To evaluate effectiveness of physiotherapy management in patients experiencing whiplash associated disorder II, on clinically relevant outcomes in the short and longer term.

Design: Systematic review and meta-analysis. Two reviewers independently searched information sources, assessed studies for inclusion, evaluated risk of bias and extracted data. A third reviewer mediated disagreement. Assessment of risk of bias was tabulated across included trials. Quantitative synthesis was conducted on comparable outcomes across trials with similar interventions. Meta-analyses compared effect sizes, with random effects as primary analyses.

Data sources: Predefined terms were employed to search electronic databases. Additional studies were identified from key journals, reference lists, authors and experts.

Eligibility criteria for selecting studies: Randomised controlled trials (RCTs) published in English before 31 December 2010 evaluating physiotherapy management of patients (>16 years), experiencing whiplash associated disorder II. Any physiotherapy intervention was included, when compared with other types of management, placebo/sham, or no intervention. Measurements reported on ≥1 outcome from the domains within the international classification of function, disability and health, were included.

Results: 21 RCTs (2126 participants, 9 countries) were included. Interventions were categorised as active physiotherapy or a specific physiotherapy intervention. 20/21 trials were evaluated as high risk of bias and one as unclear. 1395 participants were incorporated in the meta-analyses on 12 trials. In evaluating short term outcome in the acute/sub-acute stage, there was some evidence that active physiotherapy intervention reduces pain and improves range of movement, and that a specific physiotherapy intervention may reduce pain. However, moderate/considerable heterogeneity suggested that treatments may differ in nature or effect in different trial patients. Differences between participants, interventions and trial designs limited potential meta-analyses.

ARTICLE SUMMARY

Article focus

- Physiotherapy intervention is recommended in whiplash associated disorder II, although the most beneficial intervention and the effectiveness of physiotherapy management are unclear.
- Systematic reviews have not focused on whiplash associated disorder II, which represents approximately 93% of patients presenting for management post-whiplash injury.
- The objective of this systematic review was to evaluate the effectiveness of physiotherapy management in patients experiencing whiplash associated disorder II, on clinically relevant outcomes in the short and longer term.

Key messages

- This systematic review demonstrates inconclusive very low/low quality evidence for the effectiveness of physiotherapy management for whiplash associated disorder II.
- There is potential benefit for improving pain and range of movement short term through active physiotherapy and for improving pain through specific physiotherapy interventions.
- This potential benefit merits further consideration in a properly powered clinical trial with attention to ensure low risk of bias.

Strengths and limitations of this study

- The strengths of this review are its focus to physiotherapy intervention and the most common whiplash associated disorder II classification requiring physiotherapy intervention.
- A limitation is that differences between participants, interventions and trial designs limited potential meta-analyses.
- Surprisingly, no chronic interventions were comparable for analysis, considering the high number of patients experiencing chronicity with whiplash associated disorder.

Conclusions: Inconclusive evidence exists for the effectiveness of physiotherapy management for whiplash associated disorder II. There is potential benefit for improving range of movement and pain short term through active physiotherapy, and for improving pain through a specific physiotherapy intervention.

INTRODUCTION

Road traffic accidents are the primary cause of whiplash, a soft tissue injury to the neck following an acceleration–deceleration mechanism of injury.[1] The cumulative incidence of patients seeking healthcare post-whiplash from a road traffic accident has increased during the last 30 years to recent estimates of >3/1000 inhabitants in North America and Western Europe[2] and 1.0–3.2/1000 inhabitants in Sweden.[3] In the UK, insurance statistics indicate that 300 000 patients present per annum with whiplash associated disorders.[4] Whiplash associated disorders are the resulting clinical presentations following the injury and can range in severity, clinical symptoms and physical findings.[1] Many patients with whiplash associated disorders experience persistent pain and disability, with reports suggesting that 40–60% of those injured have chronic symptoms.[5–8] The annual economic cost associated with management of whiplash associated disorders and associated time off work is estimated as $3.9 billion in the USA,[9] and €10 billion in Europe.[10]

Patients experiencing whiplash associated disorders may be regarded as a distinct group within the broader non-specific neck pain population,[1 2 7 11–13] although following review of trial data (n=4 trials), recent evidence questions this distinction for a primary care population and has identified a need for further research.[14] Whiplash associated disorders can be categorised as grades 0–IV,[1] where a higher grade indicates increased severity. The classification system is widely used in clinical practice[15] and guidelines.[16] Patients with whiplash associated disorder II who experience neck pain accompanied by stiffness or tenderness, and musculoskeletal signs, for example a reduced range of available movement, form the major group of patients (93.4%)[15] who might benefit from conservative management, commonly involving physiotherapy intervention. A recent best evidence synthesis[3] recommended a focus of research to the most common whiplash associated disorder I and II classifications, excluding classification III and above (ie, patients with neurological signs and fracture and/or dislocation) and classification 0 (no complaint at the neck, and no physical signs).[1] However, a classification of whiplash associated disorder I is less commonly seen by physiotherapists as there are no accompanying physical findings (neck pain, stiffness or tenderness but with no physical findings) and patients are known to recover within 6 months post-injury.[15]

Evidence of the effectiveness of physiotherapy intervention for the treatment of whiplash associated disorder II is scarce. Existing systematic reviews instead tend to focus on a range of whiplash associated disorder classifications and a broad range of conservative intervention strategies such as educational videos, include studies of non-traumatic neck pain, and lack rigorous assessment of the risk of bias of included studies. The most robust evidence, a Cochrane review,[17] on the management of whiplash associated disorder I/II patients does not specifically assess physiotherapy. No review has included trials published post-2006. The effectiveness of physiotherapy for the whiplash associated disorder II population is therefore unclear.

The objective of this systematic review was to investigate the short and longer term effectiveness of physiotherapy outpatient management of patients presenting with whiplash associated disorder II, in terms of function, disability and health,[18] in patients aged >16 years.

MATERIALS AND METHODS

A systematic review was conducted according to a predefined protocol based on the method guidelines of the Back Review Group of the Cochrane Collaboration[19] and the Cochrane handbook.[20] It is reported in line with the PRISMA statement.[21]

Eligibility criteria

Studies

Randomised controlled trials (RCTs) evaluating the effectiveness of physiotherapy outpatient management of patients experiencing whiplash associated disorder II were included. Studies not written in English were excluded rather than restricting the inclusion of studies, thereby providing information of potential bias.[22] No restrictions were placed on publication date.

Participants

Patients aged >16 years who had experienced a whiplash injury, classified as whiplash associated disorder II, were included. Acute and chronic presentations were included and analysed separately. Mixed populations of different classifications of whiplash associated disorder were included if patients presenting with whiplash associated disorder II formed part of the population.

Interventions

Any physiotherapy outpatient management intervention was included.

Outcome measures

Measures addressing domains within the international classification of function, disability and health,[18] in the short term (approximately 3 months post-injury/intervention) and/or longer term (approximately 12 months) were included.

Information sources

Each of the following databases was searched using sensitive topic based search strategies to the end of December 2010:

Box 1 Examples of search strategies

Medline (Ovid) 1948–31 December 2010

1. Acute whiplash or cervical spine disorder or cervical spine injury.mp
2. Manual therapy or manipulation or massage.mp
3. Clinical trial or randomised controlled trial or RCT.mp
4. 1 and 2
5. 3 and 4
6. WAD II or whiplash associated disorders or whiplash injury or whiplash patients or whiplash syndrome.mp
7. 2 and 6
8. 3 and 7
9. Conservative approach or conservative intervention or conservative management or conservative therapy.mp
10. Physical approach or physical intervention or physical management or physical therapy.mp
11. Exercise or active range of motion exercise$ or strengthening exercise$ or stretching exercise$ or therapeutic exercise$ or endurance training or home exercise$ or proprioception exercise$
12. Transcutaneous electrical nerve stimulation or TENS or thermotherapy or electrical stimulation or heat or electrotherapy.mp
13. Pain management program$.mp
14. Patient education or educational or self management program$.mp
15. Posture or (postural and balance) or traction.mp
16. 1 and 9
17. 3 and 16
18. 6 and 9
19. 3 and 18
20. 1 and 10
21. 3 and 20
22. 6 and 10
23. 3 and 22
24. 1 and 11
25. 3 and 24
26. 6 and 11
27. 3 and 26
28. 1 and 12
29. 3 and 28
30. 6 and 12
31. 3 and 30

Embase (Ovid) 1947–31 December 2010

1. Acute whiplash or cervical spine disorder or cervical spine injury.mp
2. Manual therapy or manipulation or massage.mp
3. Clinical trial or randomised controlled trial or RCT.mp
4. 1 and 2
5. 3 and 4
6. WAD II or whiplash associated disorders or whiplash injury or whiplash patients or whiplash syndrome.mp
7. 2 and 6
8. 3 and 7
9. Conservative approach or conservative intervention or conservative management or conservative therapy.mp
10. Physical approach or physical intervention or physical management or physical therapy.mp

Box 1 Continued

11. Exercise or active range of motion exercise$ or strengthening exercise$ or stretching exercise$ or therapeutic exercise$ or endurance training or home exercise$ or proprioception exercise$
12. Transcutaneous electrical nerve stimulation or TENS or thermotherapy or electrical stimulation or heat or electrotherapy.mp
13. Pain management program$.mp
14. Patient education or educational or self management program$.mp
15. Posture or (postural and balance) or traction.mp
16. 1 and 9
17. 3 and 16
18. 6 and 9
19. 3 and 18
20. 1 and 10
21. 3 and 20
22. 6 and 10
23. 3 and 22
24. 1 and 11
25. 3 and 24
26. 6 and 11
27. 3 and 26
28. 1 and 12
29. 3 and 28
30. 6 and 12
31. 3 and 30

- The Cochrane Library: Controlled Trials Register, Health Technology Assessment Database, NHS Economic Evaluation Database.
- CINAHL, EMBASE, MEDLINE, PEDro, ZETOC databases.
- Selected internet sites and indexes: Turning Research into Practice, Health Services/Technology Assessment, PUBMED.
- National Research Register, Current Controlled Trials website (York).
- Cochrane Back Review Group.
- Cochrane Cervical Overview Group.
- Hand searches in key journals, for example *Spine*, *Manual Therapy*, *Physiotherapy*, *Physical Therapy*, *Australian Journal of Physiotherapy*.
- Science Citation Index and Social Science Citation Index.
- Unpublished research[22]: British National Bibliography for Report literature, Dissertation Abstracts, Index to Scientific and Technical Proceedings, National Technical Information Service, System for Information on Grey Literature.
- Personal citations for key authors in the field.

The searches used predefined terms. Box 1 provides two examples of the searches utilised.

Study selection

Two subject experts independently searched information sources (GE/NH), and independently assessed identified studies for inclusion by grading each criterion

Table 1 Criteria for inclusion and exclusion of studies in the review

Criteria	
Inclusion criteria	
Study design	RCT
Population	
Age	16 years or older
Subjects	Human; outpatients
Condition	Post-whiplash injury Experiencing whiplash associated disorder II
Intervention	Conservative physiotherapy outpatient management
Comparison group(s)	At least one comparison group: placebo/other intervention/no intervention
Outcome	Measurement of at least one of the following outcomes: disability; functional status; physical impairment; impact on social and occupational levels of fitness; pain; quality of life; patient satisfaction Measurement of short term outcome (approx 3 months post-surgery) and/or long term outcomes (≥1 year post-surgery)
Time frame	All studies conducted from 1979 onwards
Exclusion criteria	
Study design	Initial search: studies stated as RCTs but do not have a comparison group or random allocation to groups
Participant characteristics	Multiple pathology Whiplash associated disorder not classified according to severity to provide clarity of whiplash associated disorder II population
Intervention	None
Outcome	None
Language	Full article not written in English

RCT, randomised controlled trial.

(table 1) as eligible/not eligible/might be eligible.[19] A study was potentially relevant and its full text was obtained, when it could not be unequivocally excluded on the basis of its title and abstract[22] following discussion between the two independent reviewers. In a situation of disagreement or when abstracts contained insufficient information, the full text was obtained. A study was included in the review when both reviewers independently assessed it as satisfying the inclusion criteria from the full text. If agreement was not obtained, a third reviewer (AR, subject and methodological expert) mediated following discussion.[19]

Risk of bias was independently assessed by the same reviewers for each included study. Risk of bias, and homogeneity of participants, interventions and outcomes were key considerations informing the potential for including trials in meta-analyses, in line with Cochrane.[20] The third reviewer again mediated.[20] Agreement between reviewers was evaluated using Cohen's κ.[23] All processes and tools were piloted.

Data collection process

Two reviewers (AR/CW) independently extracted the data[20 24] using a standardised form. A third independent reviewer (NH) checked for consistency and clarity.

Data items

Data extracted for each trial included: design, participants and indication, whiplash associated disorder categorisation, interventions, study setting, outcome measures, timing of assessments, power calculations, loss to follow-up, intention to treat analyses and main results. Key outcome measures were predefined as valid tools to measure pain, disability, function, physical impairment, social impact and patient satisfaction, reflecting domains from the International Classification of Functioning, Disability and Health.[18] Based on recommendations, a maximum of two primary outcomes were considered acceptable,[25] when more than one primary outcome was reported and alpha spend was not considered.

Risk of bias in individual studies

The Cochrane 'risk of bias' assessment tool was used to appraise the internal validity of each included trial.[21 26] In contrast to the majority of quality scales used in health research,[21 27 28] the Cochrane tool is informed by empirical research.[26] Each component of bias was reported independently and considered with regard to each key outcome measure.[26 29] The component including 'blinding' the treating therapist has been acknowledged as generally impossible[26] and this formed part of the appraisal by the reviewers as the Cochrane tool also permits evaluation of the likely influence of any lack of blinding. The rigour of the risk of bias assessment was ensured through strict application of the defined criteria to inform conclusions, making explicit the trials of high risk of bias or poor reporting.[30]

Summary measures

Quantitative synthesis was conducted in line with the protocol on comparable key outcomes across trials evaluating similar interventions (nature of intervention, and timing of assessments at approximately 3 months and/or 12 months post-injury or intervention). Results were reported in the context of overall risk of bias. Comparable outcomes were defined as tools developed to measure the same underlying domain. Two subject experts and two methodological experts identified the combinations of studies and outcomes on which to conduct meta-analyses.

Using RevMan,[31] meta-analyses compared standardised differences in means using DerSimonian–Laird random effects[32] for the principal analyses to allow for systematic differences in effects estimated across the included trials.[22 32] For summary statistics, 95% CIs were reported. Standardised mean differences were selected to make comparisons across studies that used different tools to measure the same outcome,[22] or reported a mixture of final value scores and change from baseline scores.[33] Hedges–Olkin fixed effects[34] were used as the supportive analyses.

Planned methods of analysis

Data were requested from all authors, except for those with no comparability of outcome measures to other trials.[35 36] Data defined by whiplash associated disorder classification was also requested from all authors of trials that reported combined whiplash associated disorder classifications. Analyses were conducted on final summary statistics when reported or the raw data where supplied. When necessary, standard deviations were estimated from reported CIs or percentiles.[33] In line with the use of random effects as primary analyses,[32] change scores were used for studies when no other data were forthcoming. Heterogeneity in treatment effects was evaluated through computation of I^2.

Risk of bias across studies

A summary assessment for risk of bias was tabulated across studies, and consensus agreed concerning the overall potential risk of bias. It was not helpful to attempt to assess potential publication bias visually using Funnel plots[22] as less than 10 trials were included in meta-analyses.[37]

Additional analyses

No post-hoc supportive analyses were conducted owing to the inconsistency of outcome measures across the trials.

RESULTS

Study selection

Included trials were grouped according to the whiplash associated disorder classification[1] into five categories:

- *Whiplash associated disorder II:* five articles and five trials,[36 38–41] from four countries were included.
- *Whiplash associated disorders I/II:* eight articles and eight trials,[42–49] from six countries were included.
- *Whiplash associated disorders II/III:* four articles and four trials,[35 50–52] from three countries were included.
- *Whiplash associated disorders 0/I/II:* three articles and two trials,[53–55] from two countries were included.
- *Whiplash associated disorders I/II/III:* three articles and two trials,[56–58] from one country were included.

Most retrieved trials were published in English with only two in other languages. One relevant unpublished study was found (Managing Injuries of the Neck Trial, accessible at http://www.hta.ac.uk/1399, due to be published 2011). Figure 1 presents the numbers of studies at each stage of selection. Complete inter-reviewer agreement was achieved on study inclusion across all categories following discussion.

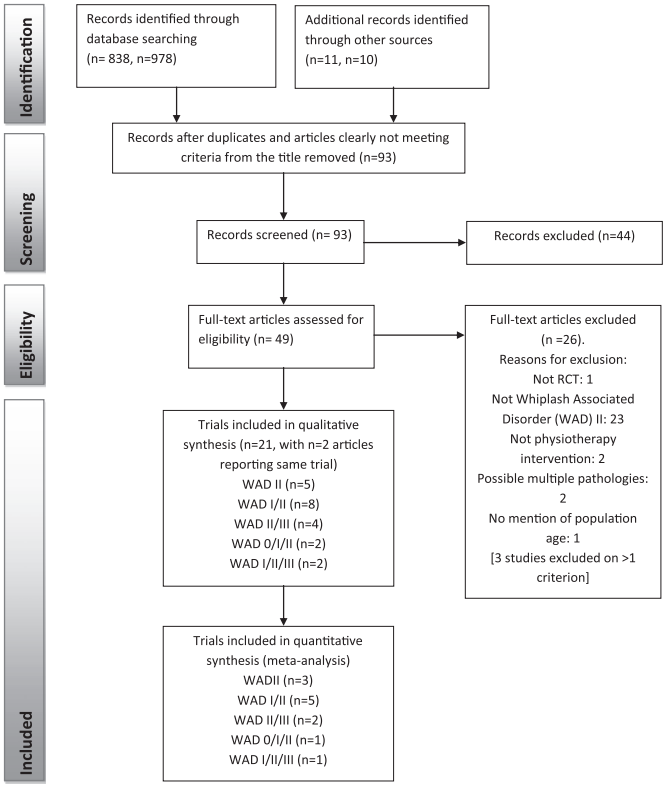


Figure 1 Study selection flow diagram (from Moher *et al*[21]). WAD, whiplash associated disorder.

Study characteristics

Descriptive data for the 21 included trials are summarised in online table 1.

Methods

Eighteen trials randomised participants across two groups, one trial across three groups, and two trials across four groups. Eight trials compared a specific physiotherapy intervention, for example manipulation, to no management, sham or placebo. Thirteen trials compared an active physiotherapy intervention to standard care; the active approaches were characterised by additional interventions, a multimodal intervention or a progressive intervention. Duration of interventions ranged from one treatment session to 12 months. The number of assessments varied from 1 to 4, occurring immediately post-treatment to 3 years.

Participants

The 21 trials randomised 2126 participants. Age varied from 16 to 70 years. A total of 271/2126 participants were randomised in trials focused to whiplash associated disorder II.[i] Of the authors who responded, no authors were able to provide data for their included whiplash

[i] In Aigner *et al*[38], three subject experts agreed that the Kramer grade II evaluated as equivalent to the WADII classification.

associated disorder classifications separately. In the eight whiplash associated disorder I/II category trials, 934 participants were randomised but no distinction of whiplash associated disorder II participants was possible. In the four whiplash associated disorder II/III category trials, 333/409 (81.5%, two trials) participants were classified as whiplash associated disorder II; in a further 111 participants (two trials), no distinction of whiplash associated disorder II participants was possible. In the two whiplash associated disorder O/I/II category trials, 302 participants were randomised with no distinction of whiplash associated disorder II participants possible. In the two whiplash associated disorder I/II/III category trials, 49/66 (74%, 1 trial) participants were classified as whiplash associated disorder II; in a further 33 participants (1 trial), no distinction of whiplash associated disorder II participants was possible. A total of 1395 participants were randomised in the 12 trials included in the meta-analyses.

Interventions

Eight trials were conducted at single centres that included physiotherapy clinics or outpatient departments. Both a clinic and home setting were used in one trial. The setting was unclear in 12 trials. One trial investigated a group intervention. Interventions could be grouped according to whether they were a specific physiotherapy intervention or an active intervention comprising different components. Timing of interventions included acute/sub-acute (13 trials) and chronic stages (8 trials), ranging from 2 days to 15 years post-injury.

Primary outcomes

Only six (28.5%) trials specified primary outcomes a priori that included: Neck Pain and Disability Index, Nociceptive Flexion Reflex, Neck Disability Index, Pain Visual Analogue Scale (VAS), Pain VAS and Work Activities VAS, and Pain VAS and Disability VAS. One trial[46] specified three primary outcome measures with no adjustment for alpha spend and was therefore evaluated as unacceptable in specifying primary outcomes.[25]

Secondary and additional outcomes

Most trials reported some assessment of pain (general or specific to the neck) (15 trials), and range of movement (ROM) (13 trials). Nine trials reported assessment of disability. A wide range of other outcomes included: work status, SF36, Tampa, patient satisfaction, muscle stability, posture and kinaesthetic sensibility. Two trials reported outcomes that were not consistent with any other trial, for example temperature pain threshold[36] and the tandem standing balance test.[35]

Risk of bias within studies

'Almost perfect'[59] 93% inter-reviewer agreement was achieved on risk of bias assessment prior to discussion (Cohen's κ=0.90, p<0.0005) and 100% agreement was reached following discussion. Only two trial protocols were available.[60 61] Of the 21 included trials, 20 were evaluated as high risk of bias and one as unclear risk of bias (table 2). The very high proportion of trials identified as high risk of bias should affect the interpretation of results.[26]

Risk of bias across studies

Only trials evaluated as high risk of bias were available for meta-analysis. Although reasons for the high risk components provided concern for potential bias, results from meta-analyses evaluated critically within this context enabled an overview of the evidence to be presented, strength of effect to be presented, and tentative conclusions to be proposed to advance research.

Results of individual studies and synthesis of results

Comparability of interventions, timing of assessments and outcome measures were considered to determine appropriate quantitative syntheses of trials.[22] In exploring the compatibility of outcomes for management in the acute/sub-acute and chronic stages, no possible quantitative syntheses within the five categories of whiplash associated disorders were possible. No further information regarding whiplash associated disorder classification was provided by authors to assist potential comparisons regarding whiplash associated disorder II. In comparing across categories, no comparison was possible for intervention in the chronic stage or long term. The following meta-analyses were conducted in the acute/sub-acute stage in the short term:

- Active intervention versus standard intervention for: pain, 4–12 weeks (n=6 trials); ROM flexion/extension (flex/ext), 12 weeks (n=3 trials); ROM rotation (Rot), 12 weeks (n=4); ROM side flexion (SF), 12 weeks (n=3); total ROM, 4–12 weeks (n=3)[ii]; disability, 6–12 weeks (n=5).
- Specific intervention versus control post-intervention for: pain (n=4 trials)[iii]; ROM flex/ext, ROM Rot, and ROM SF (n=3 trials).[iv]

Active versus standard intervention short term

Evidence from two trials[39 48] suggested that intervention might reduce pain, with active intervention being beneficial compared to standard intervention (figure 2). This was not supported by four trials.[42 45 55 56] The pooled random effects (−0.35, 95% CI −0.63 to −0.07) did support evidence of an effect short term. Evidence from one trial[43] suggested that intervention might improve ROM flex/ext and ROM SF, with active intervention being beneficial compared to standard intervention (figures 3 and 4). This was not supported by two trials.[42 45] The pooled random effects (ROM flex/ext: 0.39, 95% CI 0.04 to 0.74; ROM SF: 0.45, 95% CI 0.17 to 0.73) did support evidence of an effect short term. Evidence from three trials[43 45 56] suggested that

[ii]Excluded Rosenfeld *et al*[53 54] as short term assessment was 6 at months.
[iii]Included Thuile and Walzl[47] although timing of intervention and assessment was unclear from trial.
[iv]Aigner *et al*[38] n=5 loss to follow up but not clear from which group.

Table 2 Summary assessment of the overall risk of bias for each trial

Study (authors, year, country)	Components of risk of bias							Summary risk of bias	Comments, high risk components
	1	2	3	4	5a	5b	6		
WAD II									
Aigner *et al*[38] (2006)	U	U	U	U	U	U	H	**High (1)** Unclear (6)	One high risk component: 6 No primary outcome measure specified No primary endpoint specified No ITT reported
Dehner *et al*[39] (2009)	L	L	U	U	U	N/A	H	**High (1)** Unclear (3) Low (2) N/A (1)	One high risk component: 6 Design problematic with comparison to a previous non-randomised group. Assessment ROB excluded previous group No primary outcome measure specified No primary endpoint specified No ITT reported
Gonzalez-Inglesias *et al*[40] (2009)	L	L	L	L	U	N/A	H	**High (1)** Unclear (1) Low (4) N/A (1)	One high risk component: 6 No primary outcome measure specified No primary endpoint specified No ITT reported
Jull *et al*[41] (2007)	L	L	L	L	U	N/A	L	**Unclear (1)** Low (5) N/A (1)	No high risk components
Sterling *et al*[36] (2010)	L	U	L	L	U	N/A	H	**High (1)** Unclear (2) Low (3) N/A (1)	One high risk component: 6 No ITT reported
WAD I/II									
Ask *et al*[42] (2009)	U	L	L	L	U	U	H	**High (1)** Unclear (3) Low (3)	One high risk component: 6 No primary endpoint specified
Bonk *et al*[43] (2000)	U	U	H	L	U	N/A	H	**High (2)** Unclear (3) Low (1) N/A (1)	Two high risk components: 3, 6 3: Assessors not blinded beyond baseline 6: No primary outcome measure specified No primary endpoint specified No ITT reported
Pato *et al*[44] (2010)	U	U	L	L	U	N/A	H	**High (1)** Unclear (3) Low (2) N/A (1)	One high risk component: 6 No primary endpoint specified No ITT reported
Scholten-Peeters *et al*[45] (2006) [Scholten-Peeters *et al*[60] (2003) trial protocol]	L	L	L	L	L	L	H	**High (1)** Low (6)	One high risk component: 6 No primary endpoint specified

Continued

Table 2 Continued

Study (authors, year, country)	Components of risk of bias 1	2	3	4	5a	5b	6	Summary risk of bias	Comments, high risk components
Stewart *et al*[46] (2007), [Stewart *et al*[61] (2003) trial protocol]	L	L	L	L	L	N/A	H	**High (1)** Low (5) N/A (1)	One high risk component: 6 Co-interventions by 6 weeks: A: n=10 (15%) and B: n=15 (23%) reported seeking additional treatment Co-interventions by 12 months: A: n=18 (29%) and B: n=35 (56%) reported seeking additional treatment No primary outcome measure specified No primary endpoint specified
Thuile and Walzl[47] (2002)	U	U	U	U	U	N/A	H	**High (1)** Unclear (5) N/A (1)	One high risk component: 6 No primary outcome measure specified No primary endpoint specified No ITT reported Poor reporting, lacking detail across all components
Vassiliou *et al*[48] (2006)	L	L	L	H	U	N/A	H	**High (2)** Unclear (1) Low (3) N/A (1)	Two high risk component: 4, 6 4: Losses at 6 weeks (6 months): A: 15% (30%) B: 36% (46%) n=12 (6%) participants excluded due to incomplete outcome data. 6: No primary endpoint specified
Vikne *et al*[49] (2007)	U	L	L	H	U	U	H	**High (2)** Unclear (3) Low (2)	Two high risk components: 4, 6 4: Losses of 20% at 12 months (10% at 4 months) 6: No primary outcome measure specified No primary endpoint specified No ITT reported
WAD II/III									
Armstrong *et al*[50] (2005)	U	U	U	L	U	N/A	H	**High (1)** Unclear (4) Low (1) N/A (1)	One high risk component: 6 Problematic design and data analysis combining groups No primary outcome measure specified No ITT reported
Fernandez-de-las-Penas[51] (2004a)	L	U	U	U	U	N/A	H	**High (1)** Unclear (4) Low (1) N/A (1)	One high risk component: 6 No primary outcome measure specified No primary endpoint specified No ITT reported Selection bias as participants were volunteers

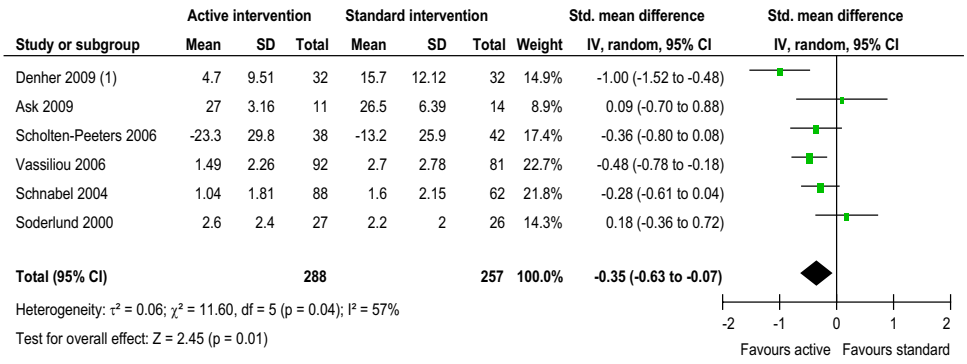
Continued

Table 2 Continued

Study (authors, year, country)	Components of risk of bias 1	2	3	4	5a	5b	6	Summary risk of bias	Comments, high risk components
Fernandez-de-las-Penas[52] (2004b)	L	U	U	U	U	N/A	H	**High (1)** Unclear (4) Low (1) N/A (1)	One high risk component: 6 No primary outcome measure specified No primary endpoint specified No ITT reported
Hansson *et al*[35] (2006)	L	L	L	H	U	N/A	H	**High (2)** Unclear (1) Low (3) N/A (1)	Two high risk components: 4, 6 4: Drop outs 38% 6: Differences at baseline on two outcomes No primary outcome measure specified No primary endpoint specified No ITT reported
WAD 0/I/II									
Rosenfeld *et al*[54] (2003), [Rosenfeld *et al* (2006) reporting same trial]	U	L	L	H	U	U	H	**High (2)** Unclear (3) Low (2)	Two high risk components: 4, 6 4: High loss to follow-up. Drop out at 6 months (and 3 years): 8% (13%). Exclusions at 6 months (and 3 years): 11% (8%). Includes eligibility errors with participants excluded post-randomisation for not meeting inclusion criteria 6: Co-interventions: 25% participants received treatment outside of study by 6 months; nearly 50% by 3 years No primary outcome measure specified No primary endpoint specified
Schnabel *et al*[55] (2004)	H	U	U	H	U	N/A	H	**High (3)** Unclear (3) N/A (1)	Three high risk components: 1, 4, 6 1: Inappropriate method of randomisation 4: Loss to follow-up from groups: A: 36% B: 15% 6: No primary outcome measure specified No ITT reported
WAD I/II/III									
Soderlund *et al*[56] (2000)	U	U	U	L	U	N/A	H	**High (1)** Unclear (4) Low (1) N/A (1)	One high risk component: 6 No primary outcome measure specified No primary endpoint specified No ITT reported
Soderlund and Lindberg[57] (2001), [Soderlund and Lindberg[58] (2007) reporting same trial]	U	U	L	L	U	N/A	H	**High (1)** Unclear (3) Low (2) N/A (1)	One high risk component: 6 No primary outcome measure specified No primary endpoint specified No ITT reported

Components of risk of bias: 1, sequence generation; 2, allocation concealment; 3, blinding of participants, personnel and outcome assessors; 4, incomplete outcome data; 5a, short term selective outcome reporting; 5b, long term selective outcome reporting; 6, other potential threats to validity.
Levels of risk of bias: H, high risk of bias; U, unclear risk of bias; L, low risk of bias. N/A, not applicable, no investigation of long term outcome.

Figure 2 Pain short-term.



(1) Scholten-Peeters reported change in pain

intervention might improve ROM Rot, with active intervention being beneficial compared to standard intervention (figure 5). This was not supported by one trial.[42] The pooled random effects (0.68, 95% CI 0.38 to 0.99) did support evidence of an effect short term.

Overall, there was no evidence of short term benefit of active over standard intervention on total ROM (pooled random effects 0.28, 95% CI −0.03 to 0.59) or disability (figure 6: −0.26, 95% CI −0.57 to 0.05).

Specific physiotherapy intervention versus control

Evidence from four trials[40 47 51 52] suggested that intervention might reduce pain short term, with specific physiotherapy intervention being beneficial compared to control. The pooled random effects (−2.11, 95% CI −3.85 to −0.36) did support evidence of an effect short term. Overall, there was no evidence of short term benefit of specific physiotherapy intervention over control on ROM flex/ext (pooled random effects 0.83, 95% CI −3.79 to 5.44), ROM Rot (pooled random effects −1.02, 95% CI −3.73 to 1.68) or ROM SF (pooled random effects −1.21, 95% CI −3.11 to 0.69).

DISCUSSION

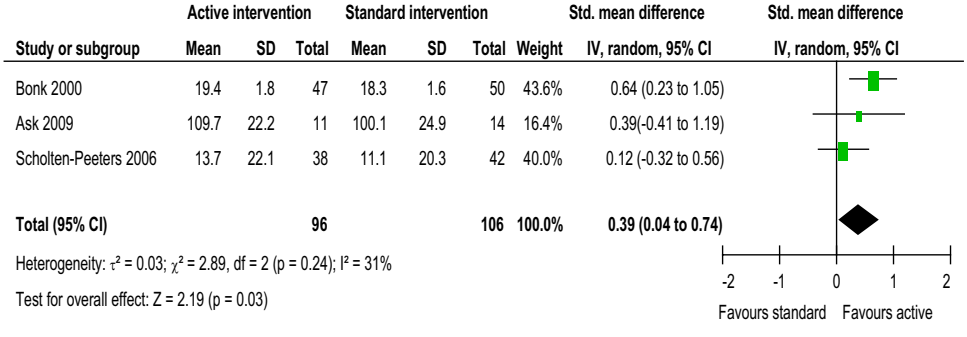
Summary of evidence

Evidence was assessed from 21 RCTs (2126 participants) conducted across nine countries. Only one trial investigated a group intervention. Interventions were grouped into active versus standard intervention, and specific physiotherapy intervention versus control. No meta-analyses were possible exclusively on a whiplash associated disorder II population, as most trials included combined classifications of whiplash associated disorders in their populations. Disappointingly, as many trials were recent, 20/21 trials were assessed as high risk of bias, and one as unclear risk. All 12 trials (1395 participants from six countries) included in the meta-analyses were assessed as high risk. Comparable outcomes across trials included pain, ROM flex/ext, ROM Rot, ROM SF, total ROM and disability in the short term. There was no evidence beyond individual results of benefit in the longer term as no meta-analyses were possible. The one trial that evaluated as unclear risk of bias was, therefore, not included in any meta-analyses.[41]

In evaluating short term outcome in the acute/subacute stage, there was some evidence that active physiotherapy intervention reduces pain. This was supported by statistically significant differences in two trials.[39 48] Although the finding is interesting, further trials are required since one trial possessed one high risk component of bias, and the other possessed two. Only one trial[43] suggested that active physiotherapy intervention changes ROM (flex/ext and SF); three trials[43 45 56] suggested a change in ROM Rot. There was evidence from the meta-analyses to support this. Again, risk of bias was high for all trials, with two high risk components for one trial[43] and one high risk component for the two other trials. There was no evidence that active physiotherapy intervention affects disability.

In evaluating short term outcome in the acute/subacute stage, there was some evidence that specific physiotherapy intervention reduces pain. This was supported by statistically significant differences found

Figure 3 ROM (range of movement) flexion/extension short-term.



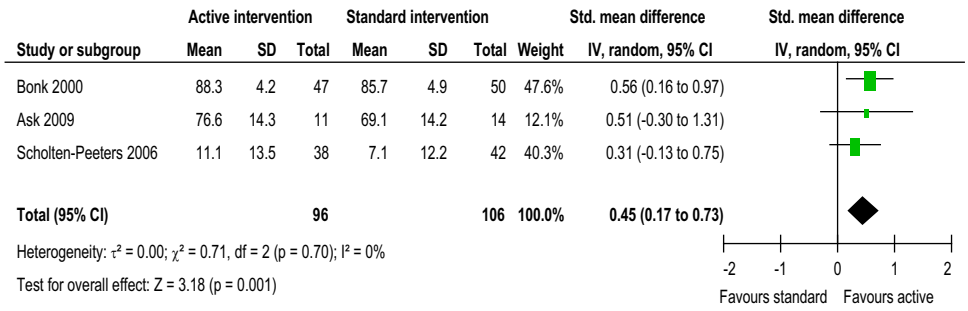


Figure 4 ROM (range of movement) right side flexion/left side flexion short-term.

in four trials[40 47 51 52] using interventions of Kinesio taping, magnetic therapy and manipulation. Although the finding is interesting, further trials are required because all trials possessed one high risk component of bias and two trials had an additional four unclear risks. Only one individual trial[47] suggested that specific physiotherapy intervention (magnetic therapy) changes ROM (flex/ext or Rot or SF) in the short term. There was no evidence from the meta-analyses to support this.

Limitations

The strengths of this review are its focus to physiotherapy intervention and the most common whiplash associated disorder II classification requiring physiotherapy intervention. Heterogeneity in treatment effects can be explained by variation in the quality of administration of interventions. Differences were evident in the outcome measures, assessment points, and classification of whiplash associated disorder participants, where many trials combined whiplash associated disorder classifications even though interventions in practice would vary between classifications.[15 16] Differences in components of the physiotherapy interventions were also evident, with some variation explained by diversity in practice across countries. The differences limited the possible comparisons in the meta-analyses. Surprisingly, no chronic interventions were comparable for analysis, considering the high number of patients experiencing chronicity with whiplash associated disorder.[7 8] Also surprisingly, work status was not possible for analysis considering the economic implications of whiplash associated disorder.[9 10]

Moderate heterogeneity (I^2=57%) was present in the evidence for active intervention for pain,[33] identifying significant difference in treatment effects between trials. However, heterogeneity might not be important for ROM flex/ext, Rot and SF (I^2=31%, 25% and 0%, respectively). Substantial heterogeneity (I^2=64%) was

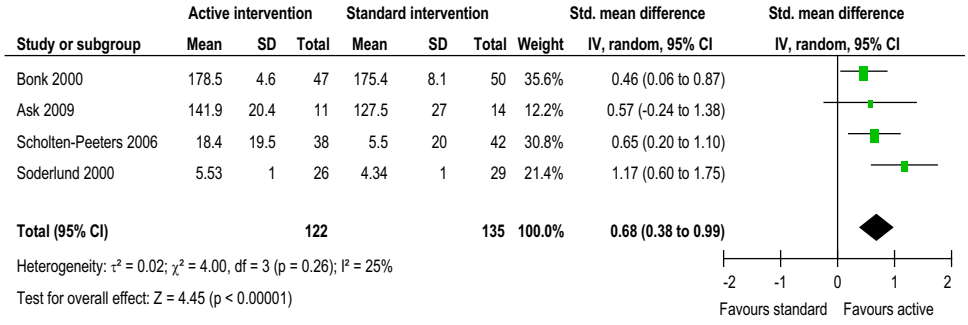


Figure 5 ROM (range of movement) rotation right/left short-term.

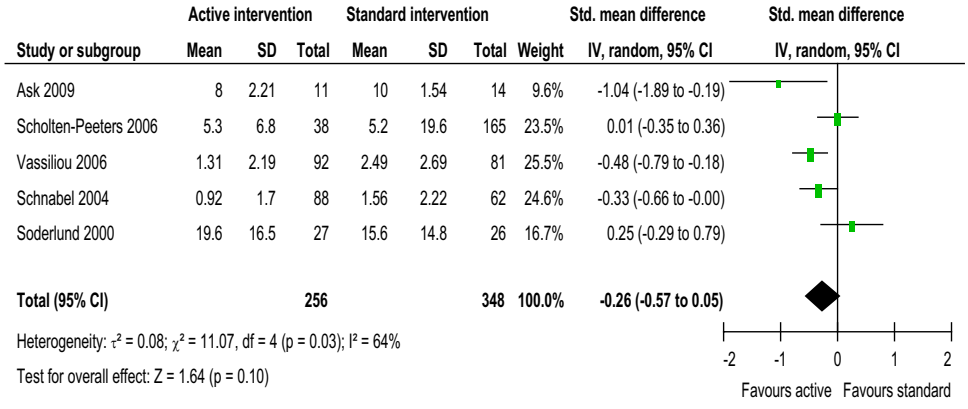


Figure 6 Disability short-term.

present in the evidence for active intervention for disability, perhaps explaining the lack of evidence of an effect. Considerable heterogeneity[33] was present in the evidence for specific physiotherapy intervention for pain, ROM flex/ext, Rot, and SF (I^2=98.1%, 99.0%, 98.1% and 96.6%, respectively), perhaps explaining the lack of evidence of an effect for all ROM evaluations. This anticipated heterogeneity was accounted for by using the random effects model.

Using GRADE[62] (the Grading of Recommendations Assessment, Development and Evaluation system), the quality of the body of evidence for physiotherapy rehabilitation in the management of whiplash associated disorder II, based on the 12 trials included in the meta-analyses, is 'very low' for pain, ROM flex/ext and SF (active vs standard intervention), and 'low' for ROM Rot (active vs standard intervention) and pain (specific intervention vs control) in the short term. These estimates are interpreted as 'little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect' (very low) and 'confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect' (low).[62] Downgrading of quality was due to high risk of bias, and issues of imprecision and inconsistency.[62]

The limitations in the context of the high risk of bias and number of trials available necessitate urgent attention to focus a future high quality and properly powered trial to evaluate a whiplash associated disorder II population. The very low/low quality of trials is consistent with earlier findings for physiotherapy management post-lumbar discectomy.[30 63] There is limited scope at present for good quality meta-analyses in physiotherapy with rigorous and well reported trial inclusion. Physiotherapy trials need to avoid risk of bias. Planning for quality is important, particularly for issues that present known problems for physiotherapy trials, for example loss to follow-up. Consensus for minimum core sets of outcome measures for specific populations is also required.

Conclusions

This systematic review has identified inconclusive very low/low quality evidence for the effectiveness of physiotherapy management for whiplash associated disorder II. Inclusion of large numbers of participants in the poorly designed trials published to date is unethical. Best practice for physiotherapy management, therefore, remains unclear. This lack of clarity might explain the variability of interventions across the trials that made comparability of interventions difficult. There is potential benefit for improving pain and ROM flex/ext, Rot and SF short term through active physiotherapy, and for improving pain through specific physiotherapy interventions. This potential benefit merits further consideration in a properly powered clinical trial with attention to ensure low risk of bias.

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Contributors AR and GE are senior lecturers in Physiotherapy and NH is a lecturer. MC and CW are both senior lecturers. NF is Professor of Clinical Epidemiology and Biostatistics. AR, MC, CW and NF have longstanding professional interests in the quality and reporting of randomised controlled trials in medicine and physiotherapy. AR, NH and GE have a professional focus to musculoskeletal physiotherapy. AR and CW were responsible for the conception of the study. All authors have contributed to the systematic review and have been involved in developing the content of the article. AR wrote the first draft of the paper and developed it initially with CW. AR has worked with all authors reworking content into subsequent drafts. All authors gave final approval of the version to be published. AR is the guarantor.

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