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Comparative effectiveness of conservative interventions for non-specific chronic spinal pain: Physical, behavioural/psychologically informed or combined? A systematic review and meta-analysis

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Abstract

Non-specific chronic spinal pain (NSCSP) is highly disabling. Current conservative rehabilitation commonly includes physical and behavioural interventions, or a combination of these approaches. Physical interventions aim to enhance physical capacity by using methods such as exercise, manual therapy and ergonomics. Behavioural and/or psychologically informed interventions aim to enhance behaviours, cognitions or mood by using methods such as relaxation and cognitive behavioural therapy (CBT). Combined interventions aim to target both physical and behavioural and/or psychological factors contributing to patients' pain by using methods such as multidisciplinary pain management programmes. Since it remains unclear whether any of these approaches are superior, this review aimed to assess the comparative effectiveness of physical, behavioural and/or psychologically informed, and combined interventions on pain and disability in patients with NSCSP. Nine electronic databases were searched for randomised controlled trials (RCTs) including participants reporting NSCSP. Studies were required to have an "active" conservative treatment control group for comparison. Studies were not eligible if the interventions were from the same domain (e.g. if the study compared two physical interventions). Study quality was assessed used the Cochrane Back Review Group risk of bias criteria. The treatment effects of physical, behavioural and/or psychologically informed, and combined interventions were assessed using meta-analyses. 24 studies were included. No clinically significant differences were found for pain and disability between physical, behavioural and/or psychologically informed and combined interventions. The simple categorisation of interventions into physical, behavioural and/or psychologically informed and combined could be considered a limitation of this review, as these interventions may not be easily differentiated to allow accurate comparisons to be made. Further work should consider investigating whether tailoring

rehabilitation to individual patients and their perceived risk of chronicity, as seen in recent RCTs for low back pain (LBP), can enhance outcomes in NSCSP.

Perspective: In this systematic review of RCTs in NSCSP, only small differences in pain or disability were observed between physical, behavioural and/or psychologically informed and combined interventions.

Keywords: non-specific chronic spinal pain; physical; behavioural/psychological; combined; systematic review

Introduction

Non-specific chronic spinal pain (NSCSP), particularly low back pain (LBP) and neck pain (NP), remains a common musculoskeletal disorder, resulting in a significant personal, social and economic burden. ^{50, 64, 121} While LBP and NP occupy different body regions, strong evidence exists that both are best considered multidimensional disorders, associated with a complex interaction of contributory factors. ^{56, 83, 99, 101} While a plethora of interventions for NSCSP have been tested, heralding similar short-term outcomes, ^{5, 105} positive long-term outcomes are infrequent. One explanation for this relative ineffectiveness is the fact that many interventions used are uni-dimensional, either focusing on physical or behavioural and/or psychological factors, rather than combining these approaches and/or tailoring them to the individual needs of the person with NSCSP. ^{68, 83} However, research on the tailoring of care to date has mixed results, with some studies showing encouraging findings ^{33, 47}, and others not showing an effect. ⁴⁴ Considering the increase in the number of randomised controlled trials (RCTs) conducted on NSCSP there is a need for a systematic review to determine which of these interventions has the greatest level of evidence.

Physical factors which have been described among people with NSCSP include maladaptive postures, ^{27, 127} movement patterns associated with altered levels of muscle activity ^{32, 48}, altered body perception, ^{14, 94} pain behaviours (e.g propping, breath-holding, bracing), ⁷² and muscular deconditioning. ^{28, 128} Behavioural and/or psychological factors which have been described among people with NSCSP include fear, ^{80, 81} maladaptive beliefs, ^{16, 86} catastrophic thoughts, ^{13, 123} hypervigilance, ^{85, 125} anxiety, depression, stress, ^{17, 116} poor pacing, maladaptive coping strategies, ^{1, 18} poor self-efficacy, ^{106, 126} physical inactivity ³⁹ and sleep problems. ⁵⁸

Therefore, current rehabilitation for NSCSP comprises a range of interventions, primarily aimed at addressing physical, behavioural and/or psychological or both of these factors.

Physical interventions aim to enhance physical capacity by using methods such as exercise, manual therapy and ergonomics. ¹¹² Despite many treatment options, numerous trials have shown that most physical interventions have similar modest levels of effectiveness in the treatment of NSCSP. ^{7, 52, 65, 71, 122} Furthermore, positive results for these physical interventions are most evident when compared to minimal interventions, placebo or waiting list control groups. ^{9, 38, 43, 59, 75}

Behavioural and/or psychologically informed interventions use educational, cognitive or psychological strategies to enhance behaviours, cognitions or moods. These include relaxation, biofeedback, cognitive-behavioural therapy (CBT), mindfulness-based stress reduction (MBSR) as well as acceptance and commitment therapy (ACT). Similar to the evidence for physical interventions, no behavioural and/or psychologically informed intervention has been found to be superior to another. In addition, positive effects are once again most evident when compared to minimal interventions, placebo or waiting list control groups. 22, 31, 45, 84, 102, 124

Combined interventions aim to target both physical and behavioural and/or psychological factors contributing to a patients' pain. These include multidisciplinary pain management programmes, functional restoration programmes (FRP), yoga, graded activity, graded exposure, behaviourally-informed physiotherapy or exercise combined with behavioural

and/or psychologically informed interventions such as relaxation or CBT.^{23, 41, 89, 97, 111}
Combined interventions have been shown to be superior to minimal interventions, placebo or waiting list control groups.^{54, 76, 87, 109}. One review⁵⁴ conducted in CLBP found that MDT programmes were more effective than physical treatments and concluded that cost and resources should be considered when deciding whether such interventions are worthwhile, considering the small size of the effect. This review⁵⁴ also suggests that combined interventions should be reserved for more complex patients.

While it seems clear that physical, behavioural/psychologically informed and combined interventions are superior to minimal or no treatment, ^{6,57,84} it remains unclear whether either is superior to the other. While one systematic review ⁵⁴ has compared the effectiveness of physical and multidisciplinary programmes in people with CLBP, no systematic review has compared the effectiveness of the current interventions in a NSCSP population. Furthermore, no review has compared the effectiveness of behavioural and combined treatments in this population. Therefore, the primary objective of this systematic review was to assess the comparative effectiveness of physical, behavioural/psychologically informed, and combined interventions on pain and disability in patients with NSCSP.

Methods

Literature Search Strategy

The review was registered on the PROSPERO database (Registration number CRD42013005757) and has been reported in accordance with the PRISMA statement.⁷⁷ All relevant RCTs and cluster randomised trials meeting the inclusion criteria (see below) were identified by;

- A computer aided search of the Medline, Cinahl, SPORTDiscus, Biomedical Reference Collection, AMED, PsycINFO, PsycARTICLES, Embase and Web of Science databases from the period of inception to January 2013 using the search strategy recommended by the Cochrane Back Review Group (Figure 1). The search was restricted to include trials that involved humans and which were published in English.
- Scanning the reference lists of previous systematic reviews and included studies for further references.

Two independent reviewers conducted the electronic searches. The strategy had four components which were combined: (1) physical/behavioural/psychological/combined intervention, (2) spinal pain, (3) chronic and (4) RCT (see Supplementary appendix A for details).

Inclusion and exclusion criteria

Study design

Only published reports of completed RCTs published in peer-reviewed journals were included. Studies were required to have a minimum follow-up period of 12 weeks after completion of treatment.

Population

Studies including participants with NSCSP (neck, thoracic, low back, or pelvic) greater than 12 weeks duration and between 18 and 65 years of age, were eligible. Participants with previous spinal surgery (>6 months previously) were eligible. Studies that involved participants with specific pathologies/conditions (e.g. pregnancy, fibromyalgia, rheumatoid arthritis, anklylosing spondylitis, stenosis, psoriatic arthritis, lupus erythematosus, scheurmann's disease, spondylolisthesis or "red flag" disorders (e.g spinal cord compression/cauda equina, spinal cord injury, neoplasm, fracture) were excluded.

Interventions

Studies were required to involve a head-to-head comparison between two of our three chosen categories of interest (i.e. active physical or behavioural/psychologically informed or combined interventions). Therefore, studies that had "no treatment", "waiting list" "treatment as usual" or usual medications as a control group were excluded. If however, "usual treatment" involved some form of therapy other than GP/medications (e.g. usual outpatient physiotherapy/pain clinic rehabilitation), a study was eligible for inclusion. Comparisons to

surgery, percutaneous procedures or pharmacology were excluded, as these were not deemed to be active physical or behavioural and/or psychologically informed interventions. Studies deemed to have a minimalist control group only (e.g. short duration education sessions/seminars or merely provision of education or advice booklets) were excluded, based on data highlighting that physical, behavioural and/or psychologically informed and combined interventions have established superiority over minimalist intervention efforts. Studies were not eligible if the interventions were from the same domain (e.g. if the study compared physical to physical). Education was defined as physical if it was pertaining to physical aspects such as posture, anatomy, exercise or biomechanics. Education was defined as behavioural and or psychologically informed if it was pertaining to cognitive and psychological aspects such as beliefs, fear, stress, relaxation. An intervention was only deemed to have an education component if it was a major aspect of the intervention provided. For example, if an intervention had a large physical component and had an educational leaflet that was behaviour focussed, such an educational leaflet was not adequate to be defined as behavioural. Therefore this intervention would still be defined as physical, not combined.

Clinical Outcomes

Studies had to report results from one or more outcome measures in the domains of pain intensity and/or level of functional disability. Since research highlights that interventions for NSCSP have similar outcomes immediately after treatment,⁶ eligible studies were required to have data at least 12 weeks after the completion of treatment. Outcome data were then only abstracted for three time periods: short-term follow-up (12 weeks to <6 months), medium-term follow-up (6 months to <12 months) and long-term follow-up (12 months or more).

Selection of studies

A standard protocol was followed for study selection and data abstraction.¹¹³ After the removal of duplicates, two reviewers independently screened the titles and abstracts from the articles found and discarded the irrelevant citations according to the selection criteria. If no abstract was available, or when it was not clear if the study should be included, full-text articles were retrieved in order to determine inclusion or exclusion. Both reviewers kept a record of their reasons for the inclusion or the exclusion of articles. The screened lists were compared between the two reviewers. To minimize the risk of discarding studies incorrectly, articles that were initially chosen by only one reviewer were included for the next stage of the review. The full-text version of an article was obtained if the title and abstract seemed to fulfil the inclusion criteria or if the eligibility of the study was unclear. Any disagreements on study eligibility were resolved by discussion and a consensus meeting. Original study authors were emailed if clarification was needed on interventions provided.

Quality assessment

Two reviewers conducted the quality assessment independently, using the risk of bias criteria advised by the Cochrane Back Review Group (CBRG)³⁷ (see Supplementary appendix B for details) which consists of 12 items: random sequence generation; allocation concealment; blinding of participants; blinding of personnel/care providers; blinding of outcome assessor; incomplete outcome data; selective reporting; group similarity at baseline; co-interventions; intention-to-treat analysis; timing of outcome assessment; and any other bias not covered elsewhere. Each item was scored as "Yes" if it fulfilled the criteria, as "No" when there was a risk of bias and as "Unclear" if there was insufficient information. When it was unclear whether a study did or did not meet an item, or if no clear information regarding the item was stated, the author of the original study was contacted for clarification. A total score was

calculated by using the number of items scored as "Yes". Differences in the reviewers' assessment of risk of bias were discussed during a consensus meeting. A total score was computed, and high quality was defined as fulfilling six or more (>50%) of the internal validity criteria (range 0–12). The quality assessment scores for all studies are shown in Table 1.

Data extraction

Data regarding each study were extracted and cross-checked by two reviewers. The following data were extracted from the studies: (1) characteristics of the studies: number of participants, sex, age, area of pain and inclusion/exclusion criteria (2) characteristics of the interventions: the type and content of interventions; (3) characteristics of the outcomes: pain and disability outcome measures, length of follow-up and (4) results summary of each study. Similarities in the outcome measures used, the subjects included and the interventions examined allowed for pooled analysis of most of the data.

The data extracted from all studies are shown in Table 2.

Data analysis

Data analysis was performed by a statistician (HP). The treatment effects of physical interventions were compared to (1) behavioural and/or psychologically informed interventions and (2) combined interventions using meta-analyses. Since only one study compared a behavioural and/or psychologically informed and combined intervention, no meta-analysis for this category was completed. The primary outcomes of interest were pain intensity and functional disability. Pain intensity was measured using a visual analogue scale

(VAS) or a numeric rating scale (NRS). The reported pain intensity scores were converted to a 10 point scale, where necessary, and a mean difference (MD) was computed. The analysis of functional disability required a standardised mean difference (SMD) to be computed as studies used a number of different measures to report disability including; Roland-Morris Disability Questionnaire (RMDQ), Oswestry Disability Index (ODI), Pain and Disability Index (PDI), Hannover Activities of Daily Living (ADL) instrument, Neck Pain and Disability Index, Low Back Outcome Scale and Neck Disability Index (NDI). Analyses were carried out at three assessment points, with data from studies included according to the time closest to these intervals: (1) Short-term follow-up (minimum of 12 weeks and <6 months), (2) Medium-term follow-up (minimum of 6 months and <12 months and (3) Long-term follow-up (minimum of 12 months).

A random-effects model was selected for all analyses a priori, as recommended by CBRG⁴⁶ and heterogeneity between treatment studies was reported using the I^2 statistic. Substantial heterogeneity was determined using the cut-off; $I^2 \ge 50\%$. In studies where multiple contrasts were examined (e.g. physical intervention vs. behavioural and/or psychologically informed intervention 1 vs. behavioural and/or psychologically informed intervention 2), the sample size in the shared comparison was halved in order to avoid double-counting of participants in the analyses.

In cases where standard deviations were not reported at follow-up times, the baseline standard deviation was used in the analysis. In studies where data were summarised using median and interquartile range (IQR) values, the mean was approximated using the median and the width of the IQR was used as an approximation of 1.35 times the standard deviation. Pooled 95% confidence intervals were computed for MD and SMD and confidence intervals excluding zero were considered statistically significant. Clinical relevance was determined using the following effect size classifications: (1) Small: MD < 1

(i.e. less than 10% of the 10-mm VAS); SMD (Cohen's d) of 0.2; (2) Medium: MD < 2, SMD (Cohen's d) of 0.5; (3) Large: MD \geq 2, SMD (Cohen's d) of 0.8.).²¹

The heterogeneity between studies was assessed visually from the forest plots, using formal Q-tests (chi-square test statistic and p-value) and the I^2 statistic. Subgroup analyses were conducted by testing pooled differences in pain and disability between NP and LBP at each follow-up time. A sensitivity analysis was conducted to assess if limiting the analysis to low risk of bias studies changed the results. In this review, a negative effect size indicates that physical interventions are more beneficial than the comparison. All analyses were conducted in Review Manager 5.2. 104

Results

Literature search

Study identification is summarised in Figure 1. The literature search of databases yielded 12,720 potentially relevant articles. 4,746 duplicates were removed and 7,974 titles and abstracts were scanned. 247 full-text studies were retrieved with 223 studies being excluded as they did not meet the eligibility criteria. Searching the reference lists of these articles did not yield any further articles. The major reasons for exclusion were of lack of an "active" control group and comparison of interventions from the same domain (physical, behavioural and/or psychologically informed or combined). 24 articles met the selection criteria. ^{19, 24, 29, 35, 36, 40, 53, 55, 65, 67, 74, 78, 88, 90, 91, 93, 95, 98, 107, 119, 120}

Quality assessment

The quality assessment scores are shown in Table 1. 48 study authors were emailed about their studies (about treatment content and quality) and to clarify whether they were eligible to be included in this review. 26 authors replied. Studies were excluded if no reply was received from the study author. 21 studies included in this systematic review were deemed to have a low risk of bias (>6/12) when scored using the CBRG bias assessment tool, with four studies ^{19, 74, 78, 95} scoring the highest (9/12). Three studies ^{35, 90, 107} were deemed to have a high risk of bias (<6/12). Common methodological limitations identified across studies included lack of information on co-interventions, blinding and compliance to treatment.

Population

The sample sizes of the included studies ranged from 30 to 393 participants. The average age of the participants in these studies ranged from 39 to 53.5 years. 18 studies investigated patients with CLBP, while six studies investigated participants with chronic neck pain (CNP).

Intervention characteristics

The content and characteristics of the various physical, behavioural/psychologically informed and combined interventions can be seen in Table 2. Five studies compared physical and behavioural/psychologically informed interventions. 20 studies compared physical and combined interventions. Only one study compared a behavioural/psychologically informed and combined intervention. ¹⁰⁷

Clinical outcome measures

All studies reported results for pain intensity. 23 of the 24 studies employed the VAS or NRS to measure pain intensity, while one study¹⁰⁷ utilised the McGill Pain Rating Index. Three studies did not report results for functional disability.^{29, 90, 107} The ODI, NDI and RMDQ were the commonly adopted functional disability assessment scales, being used in 18 studies. One study employed the PDI.⁵⁵ Another study employed the Hannover ADL instrument.²⁰ Furthermore, two studies chose the Low Back Outcome Scale^{35, 36} and another two utilised the Neck Pain and Disability Scale.^{78, 88}

Meta-analysis

22 of the 24 studies were included in the meta-analysis of pain and disability. Therefore, two studies^{35, 107} were excluded from the analysis. The first study ³⁵ was a five year follow-up and was excluded from the meta-analysis since the remaining studies all had a long-term follow-up of a maximum of 24 months. The second study¹⁰⁷ used an outcome measure (McGill Pain Rating Index) that was too heterogeneous to be pooled with the remaining studies in the physical versus behavioural/psychological and physical vs combined analyses. This was also the only study¹⁰⁷ to compare a behavioural and combined intervention meaning that pooling of data was not possible and consequently there is no comparison between behavioural and/or psychologically informed versus combined interventions in the meta-analysis. These two studies^{35, 107} also had a high risk of bias (<6/12).

Subgroup and sensitivity analyses

Subgroup analyses were conducted by testing pooled differences in pain and disability between NP and LBP studies at each follow-up time. No significant differences were found between subgroups in the effects on pain or disability (p>0.05).

A sensitivity analysis was conducted by limiting to studies with a low risk of bias. 21 studies were included in the sensitivity analysis after those at high risk of bias^{35, 90, 107} were excluded. No significant differences between interventions in the effects on pain and disability were found (p>0.05).

Effects of Physical versus Behavioural/psychologically informed interventions on pain intensity

No statistically significant difference was found for pain intensity between the physical and behavioural and/or psychologically informed groups at short term (two studies, n=272, MD= 0.03, 95% CI -0.52 to 0.57, I^2 =0%) and at medium term (three studies, n=278, MD= -0.50, 95% CI -1.38 to 0.38, I^2 =19%) follow-up (Figure 2).

Since only one study¹¹⁹ measured pain in the long-term in the physical versus behavioural and or psychologically informed groups, there is no long-term plot in this section of meta-analysis. This study found no statistically significant difference for pain intensity between the physical and behavioural and/or psychologically informed groups.

Effects of Physical versus Behavioural/psychologically informed interventions on disability

No statistically significant difference was found for disability between the physical and behavioural and/or psychologically informed groups at short term (two studies, n=272, MD= 0.02, 95% CI -0.23 to 0.27, $I^2 = 4\%$) and at medium term (three studies, n=278, SMD= -0.05, 95% CI -0.29 to 0.18, $I^2 = 0\%$) follow-up (Figure 3).

Since only one study¹¹⁹ measured disability in the long-term in the physical versus behavioural and/or psychologically informed groups, there is no long-term plot in this section of meta-analysis. This study found no statistically significant difference for disability between the physical and behavioural and/or psychologically informed groups.

Effect of Physical versus Combined interventions on pain intensity

A statistically significant difference was found for pain between groups (favouring the combined group) at short term (five studies, n=529, MD= 0.52, 95% CI 0.16 to 0.88, I^2 = 4%) and at long term (11 studies, n=1341, MD= 0.46, 95% CI 0.09 to 0.83, I^2 =40%) follow-up (Figure 4).

No statistically significant difference was found for pain between physical and combined at medium term follow-up (12 studies, n=1535, MD= 0.14~95% CI -0.10 to 0.39, I^2 =0%) (Figure 4).

Effect of Physical versus Combined interventions on disability

A statistically significant difference was found for disability between groups (favouring the combined group) at short term (five studies, n=529, SMD= 0.27 95% CI 0.01 to 0.54, I^2 = 56%) and at long term (10 studies, n=1189, SMD= 0.25 95% CI 0.07 to 0.43, I^2 = 54%) follow-up (Figure 5).

No statistically significant difference was found for disability between physical and combined at medium term follow-up (10 studies, n=1206, SMD= 0.12 95% CI -0.06 to 0.30, $I^2=55\%$) (Figure 5).

Effect of Behavioural/psychologically informed versus Combined interventions on pain intensity and disability

Since only one study¹⁰⁷ compared a behavioural and/or psychologically informed and combined intervention, no meta-analysis for this category was completed. No statistically significant differences were found for pain and disability between behavioural and/or psychologically informed and combined groups.

Discussion

This systematic review and meta-analysis investigated the comparative effectiveness of physical, behavioural and/or psychologically informed and combined interventions for pain and disability in NSCSP populations. No statistically significant differences were found for pain and disability between physical and behavioural and/or psychologically informed groups

in the medium and long-term. No statistically significant differences were found for pain and disability in the single study¹⁰⁷ comparing behavioural and/or psychologically informed and combined interventions. While a small statistically significant difference was found for both pain and disability between the physical and combined group, favouring the combined group, this difference was small. This suggests that there are only small differences between physical, behavioural and/or psychologically informed and combined interventions for reducing pain and disability in NSCSP patients.

While it may appear surprising that these very different interventions demonstrate such similar effects for NSCSP, it is clear that simply combining them offers only a small additional benefit. Consequently, choosing the most cost-efficient, rehabilitation choice which is both acceptable to patients and feasible for a healthcare service to provide should be considered. Similarly, Kamper et al⁵⁴ found that combined multidisciplinary programmes are significantly more effective than physical therapies for CLBP, but given the small effect, the decision to choose a combined intervention should be balanced against the time and resources available.

One possible reason for the lack of differences is that both physical and behavioural and/or psychologically informed interventions may in fact have similar mechanisms of effect. This is based on trials showing that successful outcomes, even after a purely physical intervention, are often mediated by changes in cognitive and psychological factors (e.g fear, catastrophising, self-efficacy, beliefs). Another possibility is that other important "non-specific factors" such as clinician support, empathy, ability to motivate and encourage and accommodate patients' treatment preferences and expectations may be common to these seemingly different interventions. This is supported by data demonstrating that a positive patient-therapist interaction is linked to reduced pain and disability.

It has been proposed that most RCT's have not adequately dealt with the multidimensional nature of NSCSP. 34, 76, 83, 100 This is significant considering the growing evidence that NSCSP is associated with a complex interplay of biopsychosocial factors. These may include patho-anatomical factors (e.g. disc prolapse with radiculopathy, spondylolysis/spondylolisthesis, lateral recess/central stenosis), 92 physical factors (e.g. maladaptive postures and movement patterns, altered body perception, pain behaviours and deconditioning), 60 cognitive factors (e.g. unhelpful beliefs, catastrophising, hypervigilance, maladaptive coping strategies, poor self-efficacy), ⁶² psychological factors (e.g. fear, anxiety, depression), 8, 11 lifestyle factors (e.g. physical inactivity, sleep problems, chronic life stress), 10, 58, 118 neuro-physiological factors (e.g. peripheral and central nervous system sensitisation), 25, 82 social factors (e.g. socio-economic status, family, work and culture), 4, 61 and genetic factors.⁶⁶ Even the "combined" treatment approaches did not target this wide range of factors, for example commonly excluding factors such as sleep^{58, 108} and life stress.⁶²

Another potential reason for the similar effectiveness of these conservative interventions is that the interventions are insufficiently tailored to the needs of patients. ^{51, 68, 68}. For example, one large RCT⁴⁷ demonstrated that people with LBP could be categorised into three different "risk" profiles, each with different natural histories for their LBP. Consequently, some groups may benefit from combined physical and psychological support more than others, and identification of these patients could be facilitated by using suitable screening measures. ^{26, 47, 54, 63} However, when the type (physical or combined) and amount of rehabilitation was matched to the perceived needs of each group, outcomes were improved. The effect sizes for this trial were small however, and in line with the effect sizes displayed in this review. Attempts to individualise rehabilitation in a biopsychosocial manner according to the needs of LBP patients, as opposed to targeting broad "risk" groups, resulted in significantly less pain and disability in another recent RCT. ¹¹⁷ However, since both of these

RCTs offered combined rehabilitation in both interventions arms, they were ineligible for this review. It is important however to acknowledge that individualising rehabilitation based on purely biomedical and physical factors alone does not appear likely to enhance outcomes.^{3, 15, 33, 44} Therefore, while the findings of this review demonstrate that simply combining physical and behavioural and/or psychologically informed interventions does not increase effectiveness very much, there is a need for further studies investigating whether tailoring these rehabilitation options to the needs of patients can enhance effectiveness. The possibility that NSCSP will remain highly resistant to treatment in some patients, even when an individualised biopsychosocial approach is used, cannot be discounted. Additionally, the similar effects seen across interventions may also reflect the use of outcome measures which are influenced by the types of bias present in the included studies.

Future Research and Clinical implications

Given the strong evidence that NSCSP is associated with a complex interplay of biopsychosocial factors, the challenge is to determine whether individualised care based on targeting these factors offers greater benefits over other current approaches. ^{47, 51, 73, 83} Future RCT's should also incorporate mediation analysis to investigate and better understand particular patient profiles who respond best to specific treatment approaches, and the mechanisms underlying different interventions, ^{70, 96} including consideration of the role of "non-specific" factors such as therapeutic alliance, and the use of qualitative approaches where necessary.

Strength and limitations

This is the first comprehensive systematic review and meta-analysis to compare the effectiveness of physical, behavioural and/or psychologically informed and combined interventions in NSCSP. Most studies that were included were of high methodological quality. Kamper et al⁵⁴ published a systematic review during the completion of the current review, investigating physical versus combined interventions in CLBP. From this perspective, our physical versus combined comparison is a repeat (and therefore confirmation) of the Kamper comparison. The current review had also initially aimed to investigate behavioural and/or psychologically informed versus combined comparisons, but since only one study was found, a meta-analysis could not be completed on this comparison. Furthermore, our review expanded on the Kamper review by including NSCSP, not just CLBP and investigated physical versus behavioural and/or psychologically informed interventions, as well as physical versus combined interventions. However, there are significant issues in our review methodology which need to be acknowledged. Only RCTs published in English were included, therefore potentially relevant studies in other languages may have been excluded. In addition, searches were limited to published studies only, which introduce a risk of publication bias. Not all studies could be included in the meta-analysis. For example, there was no plot showing the effect of behavioural versus combined rehabilitation since there was only one studying comparing these interventions. 107 This may indicate a preference for always including a physical component in interventions instead of a behavioural/psychological component, possibly displaying the dominance of the biomedical model in practice and that most treatments assume peripheral nocioception is the primary driver of NSCSP. Furthermore, review procedures have evolved since the current authors submitted the original review protocol. The current authors used a summary score out of 12 and specific cut-off values to distinguish high from low quality studies. Using this system

means that a study that fulfils any six of the 12 criteria is deemed high quality. This approach has limitations however as meta-epidemiological evidence suggests that failure on any one of the 12 criteria might alone explain a small positive effect on a subjective self-reported outcome. Some study authors did not reply to emails regarding their study interventions and methodology. This may have resulted in errors of eligibility and risk of bias rating. Furthermore, while this approach was previously recommended by Cochrane, it is no longer advocated for risk of bias assessment. Also, in the current review all the primary outcome measures were subjective self-report scales (pain or disability) and the primary outcome data assessors were the patients themselves- hence high risk of bias for both of the above considerations for all studies. The current authors did not award a point for blinded assessment. This might be considered strict as the scoring is an arbitrary process, and it is simply not possible to get this point in studies of pain.

A further significant limitation of this review is the method used to group interventions; physical versus behavioural and/or psychologically informed versus combined. The authors chose these groupings based on their interpretation of the biopsychosocial model and their experience of different interventions. Therefore, the groupings are purely subjective, creating major difficulties for interpretation of the data. In reality, interventions cannot be easily differentiated and separated which introduces a lot of heterogeneity, making meaningful comparisons very difficult.

Only studies featuring an active control group were included which may have contributed to the small effect sizes. This was deemed appropriate however given the consistent evidence that physical, behavioural and/or psychologically informed and combined interventions are superior to minimal interventions, placebo or waiting list control groups.^{5, 105} The meta-analysis pooled the results for NP and LBP together. It could be argued that the results may

have being different if plots were formed separately. However, the subgroup and sensitivity analyses performed showed no difference, further supporting the contention that LBP and NP both involve an interaction of multiple factors across the biopsychosocial spectrum. ^{82, 83, 99}

Conclusion

No clinically significant differences were found for pain and disability between physical, behavioural and/or psychologically informed and combined interventions for NSCSP. As a result, choosing the most cost-efficient, feasible rehabilitation option may be reasonable. Further work may be needed to investigate whether tailoring rehabilitation to the needs of individual patients, which has been seen in recent RCTs for LBP, can enhance outcomes in NSCSP.

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Figure Legends

Figure 1 Literature search flowchart

Supplementary Appendix A Literature search strategy

Supplementary Appendix B CBRG risk of bias assessment tool

Table 1 CBRG risk of bias scores for included studies

Table 2 Overview of characteristics of included studies

Figure 2 Effect of Physical vs Behavioural and/or psychologically informed interventions on pain

Figure 3 Effect of Physical vs Behavioural and/or psychologically informed interventions on disability

Figure 4 Effect of Physical vs Combined interventions on pain

Figure 5 Effect of Physical vs Combined interventions on disability

Table 1 CBRG risk of bias scores for included studies

Author	1	2	3	4	5	6	7	8	9	10	11	12	Total
Christensen	+	+	-	-	-	+	+	+	+	+	+	+	9
et al. 2010													
Critchley et	+	+	-	-	-	-	+	+	+	-	+	+	7
al. 2007													
Dellve et al.	+	+	-	-	-	+	+	+	?	+	+	+	8
2011													
Ferreira et	+	+	-	-	-	+	+	+	?	+	+	4	8
al. 2007													
Friedrich et	+	?	-	-	-	-	+	+	?	-	+	+	5
al. 2005													
Friedrich et	+	?		-	-	-	+	+	?	+	+	+	6
al.1998													
Gustavsson	+	+	-	-		?	+	+	?	?	+	+	6
et al. 2006													
Gustavsson	+	+	•	-	-	-	+	+ 🗸	?	?	+	+	6
et al. 2010													
Gustavsson	+	+	•	-	-	-	+	+	?	?	+	+	6
et al. 2011							· ·						
Kankaanpaa	+	?	•	-	-	+	+ ~	+	?	+	+	+	7
et al. 1999								Y					
Kaapa et al	+	+	-	-	-	+	+	+	?	?	+	+	7
2006													
Macedo et	+	+	-	-	-	4	+	+	?	+	+	+	8
al. 2012													
Machado et	+	+	-	-	-	+	+	+	?	+	+	+	8
al. 2007													
Mehling et	+	+	-	-		+	+	+	+	+	+	+	9
al. 2005						·							
Monticone	+	+		- /	-	+	+	+	+	+	+	+	9
et al. 2012													
Rendant et	+	+	-	9	-	+	+	+	?	+	+	+	8
al. 2011													
Roche-	+	+	〈 〉	\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	-	-	+	+	?	?	?	+	5
Leboucher													
et al. 2011													
Sahin et al.	+	+	(-		+	+	+	+	+	?	+	8
2011													
Sherman et	+	+		-		+	+	+	+	?	+	+	8
al. 2011													
Smeets et al.	+	_+_	-	-	-	+	+	+	+	+	+	+	9
2008		7											
Sorenson et	+	+		-		+	+	+	•	-	+	+	7
al 2010													
Turner et al.	+	?	-	-	?	-	+	+	?	+	?	+	5
1990													
Viljanen et	+	+		-	-	+	+	+	+	?	+	+	8
al. 2003													
Vonk et al.	+	+	-	-	-	-	+	+	+	+	+	+	8
2009													

Table 2 Overview of characteristics of included studies

Study	Sample size	Gender	Mean age	Pain condition	Interventions	Pain intensity measure	Disability Measure	Length of follow-up	Inclusion and exclusion criteria	Results summary	Included in meta- analysis
Christiansen et al., 2010	60	38F/22M	47.7	CLBP	1.Exercise therapy and education plus goal setting, CBT and a goal pursuit strategy (Combined) 2. Exercise therapy and education (Physical)	NRS (0- 10)	Hannover ADL instrument (0-100)	3mths	LBP >6mths	No significant difference in pain between groups Significant difference observed in disability between groups, favouring group 1	✓
Critchley et al., 2007	212	136F/76M	44	CLBP	1.Individual physiotherapy (exercise, joint mobilization, massage) (Physical) 2.Spinal stabilisation classes (Physical) 3. Pain management	NRS (0- 100)	RMDQ (0-24)	6mths 12mths 18mths	LBP>12wks	No significant difference in pain and disability between groups	✓

Dellve et al., 2011	73	73F/0M		Chronic NP	classes (education, exercise, CBT) (Combined) 1.Exercise (Muscular strength training) (Physical) 2. Myofeedback (Behavioural/or psychologically informed)	NRS (0- 10)		3mths	NP>12mths	No significant difference in pain and disability between groups	✓
Ferreira et al 2007	240	165F/74M	53.5	CLBP	1.Spinal manipulation (Physical) 2.General exercise plus CBT (Combined) 3.Motor control exercises plus CBT (Combined)	VAS (0- 10)	RMDQ (0-24)	6mths 12mths	LBP>3mths	No significant differences in pain and disability between groups	
Friedrich et al 1998	93	47F/46M	44	CLBP	1.Combined exercise and motivation program (Combined) 2.Exercise program (Physical)	NRS (0- 100)	Low back outcome scale (0- 75)	4mths 12mths	LBP>4mths	Significant difference observed in both pain and disability, favouring group 1	√
Friedrich et al 2005	93	47F/46M	44	CLBP	1.Combined exercise and motivation program (Combined)	NRS (0- 100)	Low back outcome scale (0- 75)	5years	LBP>4mths	Significant difference observed both in	X

	-										
					2.Exercise program (Physical)			2	8	pain and disability between groups, favouring group 1, massive dropout	
Gustavsson and von Koch 2006	37	28F/1M	39.5	Chronic NP	1.Pain and stress management group intervention with applied relaxation (Combined) 2.Individual physiotherapy (electrotherapy, exercise, massage, acupuncture, heat) (Physical)	NRS (0- 10)	NDI (0- 50)	20wks	NP>3mths	No significant difference in pain and disability between groups	√
Gustavsson et al., 2010	156	139F/17M	45.7	Chronic NP	1.A multi- component pain and stress self- management group intervention (Combined) 2.Individual physiotherapy (electrotherapy, exercise, massage, acupuncture, heat) (Physical)	NRS (0- 10)	NDI (0- 100)	20wks	NP>3mths	No significant difference in pain and disability between groups	√
Gustavsson	156	139F/17M	45.7	Chronic	1.A multi-	NRS (0-	NDI (0-	1 year	NP>3mths	No	✓

						4.63	100				1
et al., 2011				NP	component pain and stress self- management group intervention (Combined) 2.Individual physiotherapy (electrotherapy, exercise, massage, acupuncture, heat) (Physical)	10)	100)	2years	S -	significant difference in pain and disability between groups	
Kaapa et al., 2006	120	120F/0M	46.3	CLBP	1.Multidisciplinary group rehabilitation (exercise, CBT, relaxation, back school education) (Combined) 2.Individual physiotherapy (exercise, massage, spinal traction, mobilisation, ultrasound) (Physical)	NRS (0- 10)	ODI (0- 100)	6mths 12mths 2years	LBP>3mths	No significant difference in pain and disability between groups	✓
Kankaanpaa et al., 1999	59	22F/37M	39.6	CLBP	1.Exercise and behavioural support (Combined) 2.Individual physiotherapy (Physical)	VAS (0- 100)	The Pain and Disability Index (0- 70)	6mths 12mths	LBP>3mths	Significant difference observed both in pain and disability between groups, favouring	√

										group 1	
Macedo et al., 2012	172	102F/70M	49	CLBP	1.Graded activity (Combined) 2.Motor control exercises (Physical)	NRS (0- 10)	RMDQ (0-24)	6mths 12mths	LBP>3mths	No significant difference in pain and disability between	✓
Machado et al. 2007	33	23F/ 10M	43.5	CLBP	1.Exercise (walking, stretching, strengthening) (Physical) 2.Client-centered therapy (Behavioural and/or psychologically informed)	VAS (0- 10)	RMDQ (0-24)	6mths	LBP>3mths	groups At short- term follow-up, significant difference observed in disability between groups, favouring group 1. At long- term, no significant difference in pain or disability between groups	•
Mehling et al., 2005	36	26F/10M	49.2	CLBP	1.Breath therapy (Behavioural and/or psychologically informed)	VAS (0- 10)	RMDQ (0-24)	6mths	LBP>3mths	No significant difference in pain and disability	✓

_											
					2.Individual physiotherapy (exercise, education, soft tissue and joint mobilisation) (Physical)			Q	B.	between groups	
Monticone et al., 2012	80	60F/20M	49.5	CLBP	1.Neck exercises plus CBT (Combined) 2.Neck exercises (Physical)	NRS (0- 10)	Neck pain and disability scale (0- 100)	12mths	NP>3mths	No significant difference in pain and disability between groups	√
Rendant et al., 2011	123	107F/15M	45.6	CLBP	1.Qigong (Combined) 2.Exercise therapy (Physical)	VAS (0- 100)	Neck pain and disability scale (0- 100)	3mths 6mths	NP>6mths	No significant difference in pain and disability between groups	√
Roche Leboucher et al., 2011	132	46F/86M	39.8	CLBP	1. Functional restoration (exercise, occupational therapy, psychology) (Combined) 2. Individual physiotherapy (exercise, pain management) (Physical)	VAS (0- 10)		12mths	LBP>3mths	No significant difference in pain and disability between groups	√

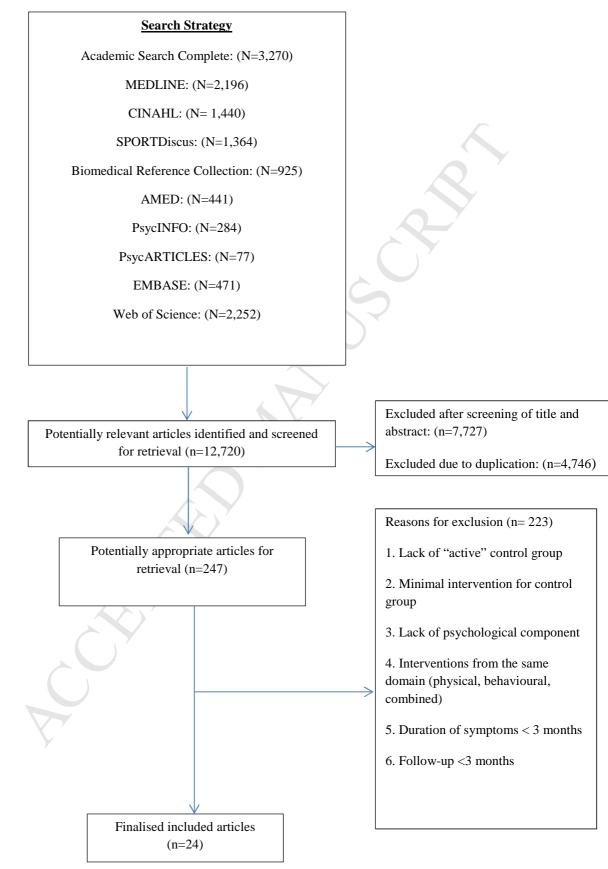
Sahin et al., 2011	146	112F/34M	49.3	CLBP	1.Back school, plus exercise plus TENS, US and heat (Combined) 2.Exercise plus TENS, US and heat (Physical)	VAS (0- 10)	ODI (0- 100)	3mths	LBP>12weeks	Significant difference observed in pain and disability between groups, favouring group 1	√
Sherman et al., 2011	228	146F/82M	48.4	CLBP	1.Yoga (Combined) 2.Stretching (Physical)	NRS (0- 10)	RMDQ (0-23)	12wks 26wks	LBP>3mths	No significant difference in pain and disability between groups	√
Smeets et al., 2008	223	105F/118M	41.6	CLBP	1.Exercise (Physical) 2.Graded activity plus problem solving (Combined) 3.Exercise plus graded activity and problem solving (Combined)	VAS (0- 100)	RMDQ (0-24)	6mths 12mths	LBP>3mths	No significant difference in pain and disability between groups	√
Sorensen et al., 2010	207	108F/ 99M	39	CLBP	1.Exercise and Educational programme (Combined)	NRS (0- 10)	RMDQ (0-23)	6mths 12mths	LBP>4mths	No significant difference in pain and disability	√

					2.Individual exercise therapy (Physical)					between groups	
Turner et al., 1990	96	46F/50M	44	CLBP	1.Group behavioural therapy plus aerobic exercise (Combined) 2.Behavioural therapy only (Behavioural and/or psychologically informed) 3.Aerobic exercise only (Physical)	McGill pain rating index (0-78)		6mths 12mths	LBP>6mths	No significant difference in pain and disability between groups	X
Viljanen et al., 2003	393	393F/0M	45	Chronic NP	1.Dynamic muscle training (Physical) 2.Relaxation (Behavioural and/or psychologically informed) 3.Ordinary activity (Physical)	NRS (0- 10)	NDI (0- 80)	3mths 6mths	NP>12wks	No significant difference in pain and disability between groups	√
Vonk et al., 2009	30	9F/21M	45.7	Chronic NP	1.Behaviour graded activity (Combined)	NRS (0- 10)	NDI (0- 100)	26wks 12mths	NP>3mths	No significant difference	✓

		2. Individual physiotherapy (exercise, massage, mobilizations) (Physical)			in pain and disability between groups	
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mths: months; CBT: cognitive behavioural therapy; LBP: low back pain; APT: active physical training; NP: neck pain; MET: motivational enhancement treatment

Figure 1 Literature Search Flowchart



	Ph	iysical		Behav a	nd/or Ps	sych		Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
1.1.1 Pain at short-te	erm follo	w-up							
Delive 2011 (1)	6	1.4	20	5.9	1.9	20	27.9%	0.10 [-0.93, 1.13]	-
Viljanen 2003 (2)	2.9	2.6	116	2.9	2.4	116	72.1%	0.00 [-0.64, 0.64]	-
Subtotal (95% CI)			136			136	100.0%	0.03 [-0.52, 0.57]	•
Heterogeneity: Tau ² =	0.00; CI	hi² = 0	.03, df=	1 (P = 0.	87); l² = I	0%			
Test for overall effect:	Z = 0.10	(P = 0	0.92)						
1.1.2 Pain at mediun	n-term fo	ollow-u	ıp						
Machado 2007 (3)	4.57	3.76	14	5.77	2.98	13	10.9%	-1.20 [-3.75, 1.35]	
Mehling 2005 (4)	1.92	2.55	11	3.44	2.04	15	19.7%	-1.52 [-3.35, 0.31]	
Viljanen 2003 (5)	2.9	2.8	112	3	2.7	113	69.3%	-0.10 [-0.82, 0.62]	
Subtotal (95% CI)			137			141	100.0%	-0.50 [-1.38, 0.38]	◆
Heterogeneity: Tau² =	0.16; CI	hi = 2	47, df=	2 (P = 0.	29); l² = 1	19%			
Test for overall effect:	Z = 1.11	(P = 0)	0.27)						
									, , , , ,
									Favours Physical Favours Rehavle

- (1) Exercise vs. Myofeedback; change scores presented in text; SD used from baseline; neck
- (2) Exercise vs. relaxation; neck
- (3) Exercise vs. client-centred therapy; data from author; low back
- (4) Individual physiotheraphy vs. breath therapy; change scores presented in text; SD from baseline; low back
- (5) Exercise vs. relaxation; neck

	D.			Б.				0.1. II. D.F.	0.1.1
		iysica		Benav a	and/or Ps			Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
2.1.1 Disability at she	ort-term	follow	/-up						
Delive 2011 (1)	33.1	6.9	20	35.2	7.9	20	16.0%	-0.28 [-0.90, 0.35]	
Viljanen 2003 (2)	15	14.6	116	14	12.5	116	84.0%	0.07 [-0.18, 0.33]	-
Subtotal (95% CI)			136			136	100.0%	0.02 [-0.23, 0.27]	*
Heterogeneity: Tau* =	= 0.00; CI	hi² = 1	.04, df=	1 (P = 0.	31); I² = 4	4%			
Test for overall effect	Z = 0.14	(P = 0	0.89)						
2.1.2 Disability at me	edium-te	rm fol	low-up						
Machado 2007 (3)	9.64	7.25	14	11.54	5.9	13	9.6%	-0.28 [-1.04, 0.48]	
Mehling 2005 (4)	4.72	6	11	6.28	5	15	9.1%	-0.28 [-1.06, 0.50]	
Vilianen 2003 (5)	15	15.4	112	15	14.5	113	81.3%	0.00 [-0.26, 0.26]	-
Subtotal (95% CI)			137			141	100.0%	-0.05 [-0.29, 0.18]	•
Heterogeneity: Tau ² =	= 0.00: CI	hi² = 0	.81. df=	2 (P = 0.	67): $I^2 = I$	3%			
Test for overall effect:				- (,,				
			,						
									
									-2 -1 0 1 2
									Favours Physical Favours Behav/Psy

- (1) Exercise vs. Myofeedback; SD used from baseline; Work Ability Index (scores reversed); neck
- (2) Exercise vs. relaxation; NDI; neck
- (3) Exercise vs. client-centred therapy; data from author; RMDQ; low back
- (4) Individual physiotherapy vs. breath therapy; change scores presented in text; SD from baseline; RMDQ; low back
- (5) Exercise vs. relaxation; NDI; neck

	DE	nysical		Cou	mbine	d		Mean Difference	Mean Difference		
Study or Subgroup	Mean	•					Woight		IV, Random, 95% CI		
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI IV, Random, 95% CI 3.1.1 Pain at short-term follow-up											
		•	20	2.5	2.7	20	0.40	0.001.045.2051	<u> </u>		
Christiansen 2010 (1)	4.3	2.2	30	3.5	2.7	30	8.1%	0.80 [-0.45, 2.05]	<u> </u>		
Friedrich 1998 (2)		2.66	41	3.27	2.43	43	10.5%	0.71 [-0.38, 1.80]			
Rendant 2011 (3)		1.92	36		2.17	41	14.7%	-0.13 [-1.04, 0.78]			
Sahin 2011 (4)		1.33	73		1.33	73	58.5%	0.71 [0.28, 1.14]			
Sherman 2011 (5)	4.43	3.75	81 261	4.59	4.23	81	8.3%	-0.16 [-1.39, 1.07]			
Subtotal (95% CI)	4.053				N . 17		100.0%	0.52 [0.16, 0.88]	▼		
Heterogeneity: Tau ² = 0.0				P = 0.38	3); 1*=	4%					
Test for overall effect: $Z = 2.86$ (P = 0.004)											
3.1.2 Pain at medium-term follow-up											
		-	60		0.04	25	0.70	0.0014.07.4.071			
Critchley 2007 (6)		2.58	63		2.81	25	3.7%	0.00 [-1.27, 1.27]			
Critchley 2007 (7)		2.62	56	4.2	2.81	25	3.6%	-0.30 [-1.60, 1.00]			
Ferreira 2007 (8)	4.3	2.6	36	4.3	2.6	68	5.5%	0.00 [-1.05, 1.05]	T T		
Ferreira 2007 (9)	4.3	2.6	36	4.8	2.6	71	5.6%	-0.50 [-1.54, 0.54]	 T		
Gustavsson 2006 (10)	. 7	2.81	16	5	4.07	13	0.9%	2.00 [-0.61, 4.61]	 		
Gustavsson 2010 (11)	4.9	2.2	62	4.2	2.5	63	8.9%	0.70 [-0.13, 1.53]	T-		
Kankannpaa 1999 (12)	4.34	1.98	22	2.66	2.84	28	3.4%	1.68 [0.34, 3.02]	 -		
Kappa 2006 (13)	3.4	2.5	57	3.3	2.5	58	7.3%	0.10 [-0.81, 1.01]	-		
Macedo 2012 (14)	4.1	2.5	74	4.1	2.7	81	9.1%	0.00 [-0.82, 0.82]	+		
Rendant 2011		1.64	36	2.67	1.9	39	9.4%	0.07 [-0.73, 0.87]			
Sherman 2011		2.13	80	3.59	2.15	83	14.0%	-0.25 [-0.91, 0.41]			
Smeets 2008 (15)	4.84	2.66	25	4.81	2.4	53	4.0%	0.03 [-1.20, 1.26]			
Smeets 2008 (16)	4.84	2.66	25	4.48	2.35	55	4.1%	0.36 [-0.85, 1.57]			
Sorensen 2010 (17)	4.8	2.1	89	4.5	2.3	87	14.3%	0.30 [-0.35, 0.95]	 -		
Vonk 2009 (18)	4.3	2.9	59	4.2	2.4	50	6.1%	0.10 [-0.90, 1.10]			
Subtotal (95% CI)			736			799	100.0%	0.14 [-0.10, 0.39]	•		
Heterogeneity: Tau² = 0.0	0; Chi² =	= 12.71	, df = 1	4 (P = 0)	.55); P	°= 0%					
Test for overall effect: Z=	1.13 (P	= 0.26)									
3.1.3 Pain at long-term f	ollow-up)									
Critchley 2007		2.54	53	3.8	3.16	23	4.8%	0.40 [-1.06, 1.86]			
Critchley 2007	4.2	2.59	55	3.8	3.16	23	4.8%	0.40 [-1.06, 1.86]			
Ferreira 2007	4.9	2.7	36	5.2	2.8	73	7.1%	-0.30 [-1.39, 0.79]			
Ferreira 2007	4.9	2.7	36	4.9	2.9	65	6.8%	0.00 [-1.13, 1.13]			
Friedrich 1998	4.19	2.96	35	2.64	2.22	34	6.1%	1.55 [0.32, 2.78]			
Gustavsson 2011	5.1	2.2	57	4.2	2.6	54	8.9%	0.90 [0.00, 1.80]	 -		
Kankannpaa 1999	4.51	2.22	22	2.39	1.78	27	6.7%	2.12 [0.97, 3.27]			
Kappa 2006	3.4	2.5	54	3.6	2.7	53	8.0%	-0.20 [-1.19, 0.79]	-		
Macedo 2012	3.7	2.7	75	3.7	2.6	80	9.5%	0.00 [-0.84, 0.84]	+		
Monticone 2012 (19)	4.04	2.11	35	2.83	2.14	40	8.2%	1.21 [0.25, 2.17]			
Smeets 2008	4.89	2.66	25	4.57	2.35	52	6.1%	0.32 [-0.90, 1.54]			
Smeets 2008	4.89	2.66	25	5.17	2.4	53	6.1%	-0.28 [-1.51, 0.95]			
Sorensen 2010	4.8	2.2	78	4.5	2.4	86	11.1%	0.30 [-0.40, 1.00]	 -		
Vonk 2009	4.3	3	47	4.1	3.2	45	5.8%	0.20 [-1.07, 1.47]			
Subtotal (95% CI)			633			708	100.0%	0.46 [0.09, 0.83]	◆		
Heterogeneity: Tau² = 0.19; Chi² = 21.53, df = 13 (P = 0.06); l² = 40%											
Test for overall effect: Z = 2.46 (P = 0.01)											
									-4 -2 0 2 4		
									Favours Physical Favours Combined		
									r avours r nysicar i avours combined		

- (1) Exercise vs. exercise + goal setting; low back
- (2) Exercise vs. exercise + motivation; low back
- (3) Exercise vs. qigong; neck
- (4) Individual physiotherapy vs. individual physiotherapy + back school; low back
- (5) Exercise vs. yoga; adjusted scores from regression; low back
- (6) Individual physiotherapy vs. physiotherapy pain management; number of pain management subjects was halved; low back
- (7) Spinal stabilisation vs. physiotherapy pain management, number of pain management subjects was halved; low back
- (8) SMT vs. motor control exercises + CBT; number of subjects in SMT was halved; neck
- (9) SMT vs. general exercises + CBT; number of subjects in SMT was halved; neck
- (10) Individual physiotherapy vs. pain management + stress management; mean and SD estimated from median and IQR; neck
- (11) Individual physiotherapy vs. pain management + stress management; neck
- (12) Individual physiotherapy vs. exercise + behavioural support, low back
- (13) Individual physiotherapy vs. exercise + relaxation + CBT + education; low back
- (14) Motor control exercises vs. graded activity; low back
- (15) Exercise vs. exercise + graded activity + problem solving; number of subjects in exercise was halved; SD from baseline; low back
- (16) Exercise vs. graded activity + problem solving; number of subjects in exercise was halved; SD from baseline; low back
- (17) Exercise vs. education; low back
- (18) Exercise vs. graded activity; neck
- (19) Neck exercises vs. neck exercises + CBT; neck

								C44 M D:#	044 M D:#		
Study Sub		hysical	T-4-1		mbined			Std. Mean Difference	Std. Mean Difference		
Study or Subgroup	Mean		Total	wean	20	rotai	Weight	IV, Random, 95% CI	IV, Random, 95% CI		
4.1.1 Disability at short-t							45.00		_		
Christiansen 2010 (1)	31.9	23.7	30	25.3	16.8	30	15.6%	0.32 [-0.19, 0.83]	T-		
Friedrich 1998 (2)	24	15.7	41	17.8	15.7	43	18.6%	0.39 [-0.04, 0.82]			
Rendant 2011 (3)		14.04	36	32.8	13.62	41	18.0%	-0.11 [-0.56, 0.34]	 -		
Sahin 2011 (4)	39.93	5.91	73	36.13	5.91	73	23.2%	0.64 [0.31, 0.97]			
Sherman 2011 (5)	4.61	3.12	81	4.31	3.46	81	24.5%	0.09 [-0.22, 0.40]	_		
Subtotal (95% CI)			261			268	100.0%	0.27 [0.01, 0.54]	-		
Heterogeneity: Tau² = 0.05; Chi² = 9.08, df = 4 (P = 0.06); I² = 56%											
Test for overall effect: Z = 2.01 (P = 0.04)											
4.1.2 Disability at medium-term follow-up											
Critchley 2007 (6)	7	5.41	5 6	6.2	5.45	25	7.2%	0.45 (0.22 0.62)			
	8							0.15 [-0.33, 0.62]	<u> </u>		
Critchley 2007 (7)		6.55	63	6.2	5.45	25	7.3%	0.28 [-0.18, 0.75]			
Ferreira 2007 (8)	7.7	6.2	36	10.1	7	71	8.3%	-0.35 [-0.76, 0.05]			
Ferreira 2007 (9)	7.7	6.2	36	8.4	6.4	68	8.3%	-0.11 [-0.51, 0.29]			
Gustavsson 2006 (10)	14	12	16	14	9.26	13	4.2%	0.00 [-0.73, 0.73]			
Gustavsson 2010 (11)	33.7	16.5	62	23.9	13.3	63	9.1%	0.65 [0.29, 1.01]			
Kankannpaa 1999 (12)	12.6	10.2	22	5.7	6.6	28	5.7%	0.81 [0.23, 1.39]	_		
Kappa 2006 (13)	18	11.5	57	20.4	11.6	58	9.0%	-0.21 [-0.57, 0.16]	-		
Macedo 2012 (14)	8	7.1	74	8.6	6.8	81	10.0%	-0.09 [-0.40, 0.23]	-		
Rendant 2011	31.5	13.3	35	30	14	39	7.5%	0.11 [-0.35, 0.57]			
Smeets 2008 (15)	11	3.7	25	10.09	3.65	58	7.2%	0.25 [-0.22, 0.72]	 		
Smeets 2008 (16)	11	3.7	25	10.97	3.92	61	7.3%	0.01 [-0.46, 0.47]			
Vonk 2009 (17)	26.5	13.9	59 566	22.5	14	50	8.8%	0.28 [-0.09, 0.66]			
Subtotal (95% CI)	0.01:3	00.74		/D 0/		640	100.0%	0.12 [-0.06, 0.30]	_		
Heterogeneity: Tau ² = 0.0			at = 12	(P = 0.0	JU8); I*=	: 55%					
Test for overall effect: Z=	1.34 (P	= 0.18)									
4.1.3 Disability at long-te	rm follo	w-up									
Critchley 2007	7.6	6	53	5.8	5.4	23	6.8%	0.31 [-0.19, 0.80]			
Critchley 2007	8.1	7.8	55	5.8	5.4	23	6.9%	0.32 [-0.17, 0.81]			
Ferreira 2007	9.2	6.6	36	9.6	6.9	73	8.4%	-0.06 [-0.46, 0.34]			
Ferreira 2007	9.2	6.6	36	8.8	6.5	65	8.2%	0.06 [-0.35, 0.47]			
Friedrich 1998	24.1	18.7	35	16.1	12.6	34	7.0%	0.49 [0.02, 0.97]			
Gustavsson 2011	32.7	16.7	57	23.7	13.2	58	8.8%	0.61 [0.24, 0.98]			
Kankannpaa 1999	11.4	11.4	22	5.7	8.1	27	5.7%	0.58 [0.00, 1.15]			
Kappa 2006	18.5	12.4	54	18.9	12.8	53	8.7%	-0.03 [-0.41, 0.35]			
Macedo 2012	7.4	6.7	75	8	6.9	80	9.9%	-0.09 [-0.40, 0.23]			
Monticone 2012 (18)		16.79	35	30.88	17.02	40	7.0%	0.94 [0.46, 1.42]			
Smeets 2008	10.87	3.7	25	10	3.65	52	7.0%	0.23 [-0.24, 0.71]			
Smeets 2008	10.87	3.7	25	11.39	3.92	61	7.2%	-0.13 [-0.60, 0.33]			
Vonk 2009	26.6	14.2	47	21.9	16.5	45	8.1%	0.30 [-0.11, 0.71]	 -		
Subtotal (95% CI)	20.0	14.2	555	21.3	10.3	634		0.25 [0.07, 0.43]	•		
Heterogeneity: Tau* = 0.06; Chi* = 26.12, df = 12 (P = 0.01); I* = 54%											
Test for overall effect: Z = 2.78 (P = 0.005)											
		0.000	,								
											
									-2 -1 0 1 2		
									Favours Physical Favours Combined		

- (1) Exercise vs. exercise + goal setting; Hannover ADL Instrument (scores reversed); low back
- (2) Exercise vs. exercise + motivation; low back outcome scale (scores reversed); low back
- (3) Exercise vs. qigong; pain and neck disability scale; neck
- (4) Individual physiotherapy vs. individual physiotherapy + back school; ODI; low back
- (5) Exercise vs. yoga; adjusted scores from regression; RMDQ; low back
- (6) Spinal stabilisation vs. physiotherapy pain management; number of pain management subjects was halved; RMDQ; low back
- (7) Individual physiotherapy vs. physiotherapy pain management; number of pain management subjects was halved; RMDQ; low back (8) SMT vs. general exercises + CBT; number of subjects in SMT was halved; RMDQ; neck (9) SMT vs. motor control exercises + CBT; number of subjects in SMT was halved; RMDQ; neck

- (10) Individual physiotherapy vs. pain management + stress management; mean and SD estimated from median and IQR; NDI; neck (11) Individual physiotherapy vs. pain management + stress management; NDI; neck
- (12) Individual physiotherapy vs. exercise + behavioural support; PDI; low back
- (13) Individual physiotherapy vs. exercise + relaxation + CBT + education; ODI; low back
- (14) Motor control exercises vs. graded activity; RMDQ; low back
- (15) Exercise vs. graded activity + problem solving; number of subjects in exercise was halved; SD from baseline; RMDQ; low back
- (16) Exercise vs. exercise + graded activity + problem solving; number of subjects in exercise was halved; SD from baseline; RMDQ; low back
- (17) Exercise vs. graded activity; NDI; neck
- (18) Neck exercises vs. neck exercises + CBT; neck pain and disability scale; neck

Highlights

- Conservative rehabilitation for NSCSP includes physical, behavioural and/or psychologically informed or combined interventions.
- We performed a systematic review and meta-analysis to compare the effectiveness of physical, behavioural and/or psychologically informed, and combined interventions on pain and disability in patients with NSCSP.
- No clinically significant differences were found for pain and disability between physical, behavioural and/or psychologically informed and combined interventions.