Critical Review

Comparative Effectiveness of Conservative Interventions for Nonspecific Chronic Spinal Pain: Physical, Behavioral/Psychologically Informed, or Combined? A Systematic Review and Meta-Analysis

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Abstract: Nonspecific chronic spinal pain (NSCSP) is highly disabling. Current conservative rehabilitation commonly includes physical and behavioral interventions, or a combination of these approaches. Physical interventions aim to enhance physical capacity by using methods such as exercise, manual therapy, and ergonomics. Behavioral/psychologically informed interventions aim to enhance behaviors, cognitions, or mood by using methods such as relaxation and cognitive behavioral therapy. Combined interventions aim to target physical and also behavioral/psychological factors contributing to patients’ pain by using methods such as multidisciplinary pain management programs. Because it remains unclear whether any of these approaches are superior, this review aimed to assess the comparative effectiveness of physical, behavioral/psychologically informed, and combined interventions on pain and disability in patients with NSCSP. Ten electronic databases were searched for randomized 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 (eg, if the study compared 2 physical interventions). Study quality was assessed using the Cochrane Back Review Group risk of bias criteria. The treatment effects of physical, behavioral/psychologically informed, and combined interventions were assessed using meta-analyses. Twenty-four studies were included. No clinically significant differences were found for pain and disability between physical, behavioral/psychologically informed, and combined interventions. The simple categorization of interventions into physical, behavioral/psychologically informed, and combined could be considered a limitation of this review, because 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, 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, behavioral/psychologically informed, and combined interventions.

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Key words: Nonspecific chronic spinal pain, physical, behavioral/psychological, combined, systematic review.
Nonspecific 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.\textsuperscript{25,66,124} Although 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.\textsuperscript{58,87,103,109} Although a plethora of interventions for NSCSP have been tested, heralding similar short-term outcomes,\textsuperscript{5,29,108} positive long-term outcomes are infrequent. One explanation for this relative ineffectiveness is the fact that many interventions used are unidimensional, either focusing on physical or behavioral/psychological factors, rather than combining/tailoring these approaches to the individual needs of the person with NSCSP.\textsuperscript{11,87} However, research on the tailoring of care to date has mixed results, with some studies showing encouraging findings,\textsuperscript{33,49} and others not showing an effect.\textsuperscript{46} Considering the increase in the number of randomized 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 that have been described among people with NSCSP include maladaptive postures,\textsuperscript{26,130} movement patterns associated with altered levels of muscle activity,\textsuperscript{31,50} altered body perception,\textsuperscript{14,98} pain behaviors (eg, propping, breath-holding, bracing),\textsuperscript{75} and muscular deconditioning.\textsuperscript{27,131} Behavioral/psychological factors that have been described among people with NSCSP include fear,\textsuperscript{83,84} maladaptive beliefs,\textsuperscript{6,89} catastrophic thoughts,\textsuperscript{13,126} hypervigilance,\textsuperscript{88,128} anxiety, depression, stress,\textsuperscript{17,119} poor pacing, maladaptive coping strategies,\textsuperscript{6,18} poor self-efficacy,\textsuperscript{109,129} physical inactivity,\textsuperscript{90} and sleep problems.\textsuperscript{50} Therefore, current rehabilitation for NSCSP comprises a range of interventions, primarily aimed at addressing physical, behavioral/psychological, or both of these factors.

Physical interventions aim to enhance physical capacity by using methods such as exercise, manual therapy, and ergonomics.\textsuperscript{115} Despite many treatment options, numerous trials have shown that most physical interventions have similar modest levels of effectiveness in the treatment of NSCSP.\textsuperscript{7,54,68,74,125} Furthermore, positive results for these physical interventions are most evident when compared with minimal interventions, placebo, or waiting list control groups.\textsuperscript{9,38,45,61,78}

Behavioral/psychologically informed interventions use educational, cognitive, or psychological strategies to enhance behaviors, cognitions, or moods. These include relaxation, biofeedback, cognitive-behavioral therapy, mindfulness-based stress reduction, as well as acceptance and commitment therapy.\textsuperscript{51} Similar to the evidence for physical interventions, no behavioral/psychologically informed intervention has been found to be superior to another.\textsuperscript{47,107,117,118} In addition, positive effects are once again most evident when compared with minimal interventions, placebo, or waiting list control groups.\textsuperscript{21,30,47,86,106,127}

Combined interventions aim to target physical and behavioral/psychological factors contributing to a Conservative Interventions for Nonspecific Chronic Spinal Pain patients’ pain. These include multidisciplinary team (MDT) pain management programs, functional restoration programs, yoga, graded activity, graded exposure, behaviorally-informed physiotherapy, or exercise combined with behavioral/psychologically informed interventions such as relaxation or cognitive-behavioral therapy.\textsuperscript{21,43,93,101,114} Combined interventions have been shown to be superior to minimal interventions, placebo, or waiting list control groups.\textsuperscript{56,79,90,112} One review\textsuperscript{26} conducted in chronic low back pain (CLBP) reported that MDT programs 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 review\textsuperscript{26} also suggests that combined interventions should be reserved for more complex patients.

Although it seems clear that physical, behavioral/psychologically informed, and combined interventions are superior to minimal or no treatment, it remains unclear whether either is superior to the other. Whereas 1 systematic review\textsuperscript{46} has compared the effectiveness of physical and multidisciplinary programs in people with CLBP, no systematic review has compared the effectiveness of the current interventions in an NSCSP population. Furthermore, no review has compared the effectiveness of behavioral and combined treatments in this population. Therefore, the primary objective of this systematic review was to assess the comparative effectiveness of physical, behavioral/psychologically informed, and combined interventions on pain and disability in patients with NSCSP.

Methods

\textbf{Literature Search Strategy}

The review was registered on the PROSPERO database (Registration number CRD42013005757) and has been reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.\textsuperscript{80} All relevant RCTs and cluster randomized trials meeting the inclusion criteria (see the section on Inclusion and Exclusion Criteria) were identified by the following:

- A computer-aided search of the Academic Search Complete, 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 (CBRG; Fig 1). The search was restricted to include trials that involved humans and were published in English.
- Scanning the reference lists of previous systematic reviews and included studies for further references.

Two independent reviewers (M.O.K. and K.O.S.) conducted the electronic searches. The strategy had 4 components, which were combined: 1) physical/behavioral/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) >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 (eg, pregnancy, fibromyalgia, rheumatoid arthritis, ankylosing spondylitis, stenosis, psoriatic arthritis, lupus erythematosus, Scheuermann disease, spondylolisthesis, or "red flag" disorders (eg, spinal cord compression/cauda equina, spinal cord injury, neoplasm, fracture) were excluded.

Interventions
Studies were required to involve a head-to-head comparison between 2 of our 3 chosen categories of interest.

Search Strategy
Academic Search Complete: (n = 3,270)
MEDLINE: (n = 2,196)
CINAHL: (n = 1,440)
SPORTDiscus: (n = 1,364)
Biomedical Reference Collection: (n = 925)
AMED: (n = 441)
PsycINFO: (n = 284)
PsycARTICLES: (n = 77)
EMBASE: (n = 471)
Web of Science: (n = 2,252)

Potentially relevant articles identified and screened for retrieval (n = 12,720)

Excluded after screening of title and abstract: (n = 7,727)
Excluded due to duplication: (n = 4,746)

Potentially appropriate articles for retrieval (n = 247)

Reasons for exclusion (n = 223)
1. Lack of “active” control group
2. Minimal intervention for control group
3. Lack of psychological component
4. Interventions from the same domain (physical, behavioral, combined)
5. Duration of symptoms <3 months
6. Follow-up <3 months

Finalized included articles (n = 24)

Figure 1. Literature search flowchart.
Clinical Outcomes

Studies had to report results from 1 or more outcome measures in the domains of pain intensity/level of functional disability. Because 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 3 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).

Selection of Studies

A standard protocol was followed for study selection and data abstraction.116 After the removal of duplicates, 2 reviewers (M.O.K. and J.H.) 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 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 2 reviewers. To minimize the risk of discarding studies incorrectly, articles that were initially chosen by only 1 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 e-mailed if clarification was needed on interventions provided.

Quality Assessment

Two reviewers (M.O.K. and M.C.) conducted the quality assessment independently, using the risk of bias criteria advised by the CBRG37 (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, cointerventions, 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 6 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 2 reviewers (M.O.K. and J.H.). 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 (H.P.). The treatment effects of physical interventions were compared with 1) behavioral/psychologically informed interventions, and 2) combined interventions using meta-analyses. Because only 1 study110 compared a behavioral/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. 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 standardized MD (SMD) to be computed because studies used a number of different measures to report disability including the Roland-Morris Disability Questionnaire, Oswestry Disability Index, Pain and Disability Index, Hannover Activities of Daily Living instrument, Neck Pain and Disability Index, Low Back Outcome Scale, and Neck Disability Index. Analyses were carried out at 3 assessment points, with data from studies included according to the time closest to the following 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 the CBRG and heterogeneity between treatment studies was reported using the I² statistic. Substantial heterogeneity was determined using the cutoff, I² ≥ 50%. In studies in which multiple contrasts were examined (eg, physical intervention vs behavioral/psychologically informed intervention 1 vs behavioral/psychologically informed intervention 2), the sample size in the shared comparison was halved 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 summarized using median and interquartile range values, the mean was approximated using the median and the width of the interquartile range was used as an approximation of 1.35 times the standard deviation. Pooled 95% confidence intervals (CIs) were computed for MD and SMD and CIs excluding 0 were considered statistically significant. Clinical relevance was determined using the following effect size classifications: 1) small: MD < 1 [ie, <10% of the 10-mm VAS]; SMD (Cohen d) of 0.2; 2) medium: MD < 2, SMD (Cohen d) of .5; and 3) large: MD ≥ 2, SMD (Cohen d) of .8.

The heterogeneity between studies was assessed visually from the Forest plots, using formal Q-tests (χ² test statistic and P value) and the I² 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 (RevMan) software (version 5.2; The Nordic Cochrane Centre, Copenhagen, Denmark).

Results

Literature Search

Study identification is summarized in Fig 1. The literature search of databases yielded 12,720 potentially relevant articles of which 4,746 duplicates were removed and 7,974 titles and abstracts were scanned. Two hundred forty-seven full-text articles were retrieved with 223 studies being excluded because 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 lack of an "active" control group.
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Sex</th>
<th>Mean Age, Years</th>
<th>Pain Condition</th>
<th>Interventions</th>
<th>Pain Intensity Measure</th>
<th>Disability Measure</th>
<th>Length of Follow-Up</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Results Summary</th>
</tr>
</thead>
</table>
| Christiansen et al    | 60          | 38 F/22 M | 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) | 3 Months      | LBP >6 months                                                                 | No significant difference in pain between groups  
Significant difference observed in disability between groups, favoring group 1 |
| Critchley et al       | 212         | 136 F/76 M | 44              | CLBP           | 1. Individual physiotherapy (exercise, joint mobilization, massage; physical)  
2. Spinal stabilization classes (physical)  
3. Pain management classes (education, exercise, CBT; combined) | NRS (0–100) | RMDQ (0–24)      | 6 Months; 12 months; 18 months | LBP >12 weeks       | No significant difference in pain and disability between groups |
| Dellve et al          | 73          | 73 F/0 M   | Chronic NP      | NP             | 1. Exercise (muscular strength training; physical)  
2. Myofeedback (behavioral/or psychologically informed) | NRS (0–10)  |                | 3 Months      | NP >12 months                                                                 | No significant difference in pain and disability between groups |
| Ferreira et al        | 240         | 165 F/74 M | 53.5            | CLBP           | 1. Spinal manipulation (physical)  
2. General exercise plus CBT (combined)  
3. Motor control exercises with CBT (combined) | VAS (0–10)  | RMDQ (0–24)      | 6 Months; 12 months      | LBP >3 months        | No significant differences in pain and disability between groups |
| Friedrich et al       | 93          | 47 F/46 M  | 44              | CLBP           | 1. Combined exercise and motivation program (combined)  
2. Exercise program (physical) | NRS (0–100) | Low back outcome scale (0–75) | 4 Months; 12 months | LBP >4 months        | Significant difference observed in pain and disability, favoring group 1 |

**Table 2. Overview of Characteristics of Included Studies**
<table>
<thead>
<tr>
<th>Study</th>
<th>Sample Size</th>
<th>Sex</th>
<th>Mean Age, Years</th>
<th>Pain Condition</th>
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<th>Length of Follow-Up</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Results Summary</th>
</tr>
</thead>
</table>
| Friedrich et al        | 93          | 47 F/46 M     | 44              | CLBP            | 1. Combined exercise and motivation program (combined)  
2. Exercise program (physical)                                           | NRS (0–100)             | Low back outcome scale (0–75)                     | 5 Years             | LBP >4 months       | Significant difference observed in pain and disability between groups, favoring group 1, massive dropout rate |
| Gustavsson and von Koch | 37          | 28 F/1 M      | 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)                     | 20 Weeks            | NP >3 months        | No significant difference in pain and disability between groups                 |
| Gustavsson et al       | 156         | 139 F/17 M    | 45.7            | Chronic NP     | 1. A multicomponent pain and stress self-management group intervention (combined)  
2. Individual physiotherapy (electrotherapy, exercise, massage, acupuncture, heat; physical) | NRS (0–10)             | NDI (0–100)                    | 20 Weeks            | NP >3 months        | No significant difference in pain and disability between groups                 |
| Gustavsson et al       | 156         | 139 F/17 M    | 45.7            | Chronic NP     | 1. A multicomponent pain and stress self-management group intervention (combined)  
2. Individual physiotherapy (electrotherapy, exercise, massage, acupuncture, heat; physical) | NRS (0–10)             | NDI (0–100)                    | 1 Year; 2 years     | NP >3 months        | No significant difference in pain and disability between groups                 |
<table>
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<tr>
<th>Study</th>
<th>Sample Size</th>
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<th>Pain Intensity Measure</th>
<th>Disability Measure</th>
<th>Length of Follow-Up</th>
<th>Inclusion and Exclusion Criteria</th>
<th>Results Summary</th>
<th>Included in Meta-Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kääpä et al.</td>
<td>120</td>
<td>120 F/0 M</td>
<td>46.3</td>
<td>CLBP</td>
<td>1. Multidisciplinary group rehabilitation (exercise, CBT, relaxation, back school education; combined) 2. Individual physiotherapy (exercise, massage, spinal traction, mobilization, ultrasound; physical)</td>
<td>NRS (0–10)</td>
<td>ODI (0–100)</td>
<td>6 Months; 12 months; 2 years</td>
<td>LBP &gt;3 months</td>
<td>No significant difference in pain and disability between groups</td>
<td></td>
</tr>
<tr>
<td>Kankaanpää et al.</td>
<td>59</td>
<td>22 F/37 M</td>
<td>39.6</td>
<td>CLBP</td>
<td>1. Exercise and behavioral support (combined) 2. Individual physiotherapy (physical)</td>
<td>VAS (0–100)</td>
<td>The Pain and Disability Index (0–70)</td>
<td>6 months; 12 months</td>
<td>LBP &gt;3 months</td>
<td>Significant difference observed both in pain and disability between groups</td>
<td></td>
</tr>
<tr>
<td>Macedo et al.</td>
<td>172</td>
<td>102 F/70 M</td>
<td>49</td>
<td>CLBP</td>
<td>1. Graded activity (combined) 2. Motor control exercises (physical)</td>
<td>NRS (0–10)</td>
<td>RMDQ (0–24)</td>
<td>6 Months; 12 months</td>
<td>LBP &gt;3 months</td>
<td>No significant difference in pain and disability between groups</td>
<td></td>
</tr>
<tr>
<td>Machado et al.</td>
<td>33</td>
<td>23 F/10 M</td>
<td>43.5</td>
<td>CLBP</td>
<td>1. Exercise (walking, stretching, strengthening; physical) 2. Client-centered therapy (behavioral/psychologically informed)</td>
<td>VAS (0–10)</td>
<td>RMDQ (0–24)</td>
<td>6 Months</td>
<td>LBP &gt;3 months</td>
<td>At short-term follow-up, significant difference observed in disability between groups, favoring group 1. At long-term, no significant difference in pain or disability between groups</td>
<td></td>
</tr>
<tr>
<td>Mehling et al.</td>
<td>36</td>
<td>26 F/10 M</td>
<td>49.2</td>
<td>CLBP</td>
<td>1. Breath therapy (behavioral/psychologically informed) 2. Individual physiotherapy (exercise, education, soft tissue and joint mobilization; physical)</td>
<td>VAS (0–10)</td>
<td>RMDQ (0–24)</td>
<td>6 Months</td>
<td>LBP &gt;3 months</td>
<td>No significant difference in pain and disability between groups</td>
<td></td>
</tr>
<tr>
<td>Monticone et al.</td>
<td>80</td>
<td>60 F/20 M</td>
<td>49.5</td>
<td>CLBP</td>
<td>1. Neck exercises with CBT (combined) 2. Neck exercises (physical)</td>
<td>NRS (0–10)</td>
<td>Neck Pain and Disability Scale (0–100)</td>
<td>12 Months</td>
<td>NP &gt;3 months</td>
<td>No significant difference in pain and disability between groups</td>
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<tr>
<td>Rendant et al</td>
<td>123</td>
<td>F/15 M</td>
<td>45.6</td>
<td>CLBP</td>
<td>1. Qigong (combined) 2. Exercise therapy (physical)</td>
<td>VAS (0–100)</td>
<td>Neck Pain and Disability Scale (0–100)</td>
<td>3 Months; 6 months</td>
<td>NP &gt;6 months</td>
<td>No significant difference in pain and disability between groups</td>
</tr>
<tr>
<td>Roche-Leboucher et al</td>
<td>132</td>
<td>F/86 M</td>
<td>39.8</td>
<td>CLBP</td>
<td>1. Functional restoration (exercise, occupational therapy, psychology; combined) 2. Individual physiotherapy (exercise, pain management; physical)</td>
<td>VAS (0–10)</td>
<td></td>
<td>12 months</td>
<td>LBP &gt;3 months</td>
<td>No significant difference in pain and disability between groups</td>
</tr>
<tr>
<td>Sahin et al</td>
<td>146</td>
<td>F/34 M</td>
<td>49.3</td>
<td>CLBP</td>
<td>1. Back school, with exercise and TENS, US, and heat (combined) 2. Exercise with TENS, US, and heat (physical)</td>
<td>VAS (0–10)</td>
<td>ODI (0–100)</td>
<td>3 Months</td>
<td>LBP &gt;12 weeks</td>
<td>Significant difference observed in pain and disability between groups favoring group 1</td>
</tr>
<tr>
<td>Sherman et al</td>
<td>228</td>
<td>F/82 M</td>
<td>48.4</td>
<td>CLBP</td>
<td>1. Yoga (combined) 2. Stretching (physical)</td>
<td>NRS (0–10)</td>
<td>RMDQ (0–23)</td>
<td>12 Weeks; 26 weeks</td>
<td>LBP &gt;3 months</td>
<td>No significant difference in pain and disability between groups</td>
</tr>
<tr>
<td>Smeets et al</td>
<td>223</td>
<td>F/118 M</td>
<td>41.6</td>
<td>CLBP</td>
<td>1. Exercise (physical) 2. Graded activity with problem solving (combined) 3. Exercise with graded activity and problem solving (combined)</td>
<td>VAS (0–100)</td>
<td>RMDQ (0–24)</td>
<td>6 Months; 12 months</td>
<td>LBP &gt;3 months</td>
<td>No significant difference in pain and disability between groups</td>
</tr>
<tr>
<td>Sorensen et al</td>
<td>207</td>
<td>F/99 M</td>
<td>39</td>
<td>CLBP</td>
<td>1. Exercise and educational program (combined) 2. Individual exercise therapy (physical)</td>
<td>NRS (0–10)</td>
<td>RMDQ (0–23)</td>
<td>6 Months; 12 months</td>
<td>LBP &gt;4 months</td>
<td>No significant difference in pain and disability between groups</td>
</tr>
<tr>
<td>Turner et al</td>
<td>96</td>
<td>F/50 M</td>
<td>44</td>
<td>CLBP</td>
<td>1. Group behavioral therapy with aerobic exercise (combined) 2. Behavioral therapy only (behavioral/psychologically informed) 3. Aerobic exercise only (physical)</td>
<td>McGill pain rating index (0–78)</td>
<td></td>
<td>6 Months; 12 months</td>
<td>LBP &gt;6 months</td>
<td>No significant difference in pain and disability between groups</td>
</tr>
</tbody>
</table>
Quality Assessment

The quality assessment scores are shown in Table 1. Forty-eight study authors were e-mailed about their studies (about treatment content and quality) and to clarify whether they were eligible to be included in this review. Twenty-six authors replied. Studies were excluded if no reply was received from the study author. Twenty-one studies included in this systematic review were deemed to have a low risk of bias, with 4 studies scoring the highest (9 of 12). Three studies were deemed to have a high risk of bias (<6 of 12). Common methodological limitations identified across studies included lack of information on cointerventions, 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. Eighteen studies investigated patients with CLBP, and 6 studies investigated participants with chronic NP.

Intervention Characteristics

The content and characteristics of the various physical, behavioral/psychologically informed, and combined interventions are shown in Table 2. Five studies compared physical and behavioral/psychologically informed interventions. Twenty studies compared physical and combined interventions. Only 1 study compared a behavioral/psychologically informed and combined intervention.

Clinical Outcome Measures

All studies reported results for pain intensity. Twenty-three of the 24 studies used the VAS or numeric rating scale to measure pain intensity, and 1 study used the McGill Pain Rating Index. Three studies did not report results for functional disability. The Oswestry Disability Index, Neck Disability Index, and Roland-Morris Disability Questionnaire were the commonly adopted functional disability assessment scales, being used in 18 studies. One study used the Pain and Disability Index. Another study used the Hannover Activities of Daily Living instrument. Furthermore, 2 studies chose the Low Back Outcome Scale and another 2 used the Neck Pain and Disability Scale.

Meta-Analysis

Twenty-two of the 24 studies were included in the meta-analysis of pain and disability. Therefore, 2 studies were excluded from the analysis. The first study was a 5-year follow-up and was excluded from the meta-analysis.
the meta-analysis because the remaining studies all had a long-term follow-up of a maximum of 24 months. The second study110 used an outcome measure (McGill Pain Rating Index) that was too heterogeneous to be pooled with the remaining studies in the physical versus behavioral/psychological and physical versus combined analyses. This was also the only study110 to compare a behavioral and combined intervention meaning that pooling of data was not possible and consequently there is no comparison between behavioral/psychologically informed versus combined interventions in the meta-analysis. These 2 studies35,110 also had a high risk of bias (<6 of 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 > .05).

A sensitivity analysis was conducted by limiting to studies with a low risk of bias. Twenty-one studies were included in the sensitivity analysis after those at high risk of bias35,94,110 were excluded. No significant differences between interventions in the effects on pain and disability were found (P > .05).

Effects of Physical Versus Behavioral/Psychologically Informed Interventions on Pain Intensity

No statistically significant difference was found for pain intensity between the physical and behavioral/psychologically informed groups at short-term (2 studies, n = 272; MD = .03; 95% CI, −.52 to .57; I² = 0%) and at medium-term (3 studies, n = 278; MD = −.50; 95% CI, −1.38 to 0.38; I² = 19%) follow-up (Fig 2).

Because only 1 study122 measured pain in the long-term in the physical versus behavioral/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 behavioral/psychologically informed groups.

Effects of Physical Versus Behavioral/Psychologically Informed Interventions on Disability

No statistically significant difference was found for disability between the physical and behavioral/psychologically informed groups at short-term (2 studies, n = 272; MD = .02; 95% CI, −.23 to 0.27; I² = 4%) and at medium-term (3 studies, n = 278; SMD = −.05; 95% CI, −.29 to .18; I² = 0%) follow-up (Fig 3).

Because only 1 study122 measured disability in the long-term in the physical versus behavioral/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 behavioral/psychologically informed groups.

Effect of Physical Versus Combined Interventions on Pain Intensity

A statistically significant difference was found for pain between groups (favoring the combined group) at short-term (5 studies, n = 529; MD = .52; 95% CI, .16–.88; I² = 4%) and at long-term (15 studies, n = 1,453; MD = .47; 95% CI, .13–.81; I² = 35%) follow-up (Fig 4).

No statistically significant difference was found for pain between physical and combined interventions at medium-term (15 studies, n = 1,535; MD = .14; 95% CI, −10 to .39; I² = 0%) follow-up (Fig 4).

Effect of Physical Versus Combined Interventions on Disability

A statistically significant difference was found for disability between groups (favoring the combined group) at short-term (5 studies, n = 529; MD = .52; 95% CI, .16–.88; I² = 4%) and at long-term (15 studies, n = 1,453; MD = .47; 95% CI, .13–.81; I² = 35%) follow-up (Fig 4).

No statistically significant difference was found for disability between physical and combined interventions at medium-term (15 studies, n = 1,535; MD = .14; 95% CI, −10 to .39; I² = 0%) follow-up (Fig 4).
group) at short-term (5 studies, n = 529; SMD = .27; 95% CI, .01–.54; I² = 56%) and at long-term (13 studies, n = 1,189; SMD = .25; 95% CI, .07–.43; I² = 54%) follow-up (Fig 5).

No statistically significant difference was found for disability between physical and combined interventions at medium-term follow-up (13 studies, n = 1,206; SMD = .12; 95% CI, −.06 to .30; I² = 55%; Fig 5).

**Effect of Behavioral/Psychologically Informed Versus Combined Interventions on Pain Intensity and Disability**

Because only 1 study compared a behavioral/psychologically informed and combined intervention, no meta-analysis for this category was completed. No statistically significant differences were found for pain and disability between the behavioral/psychologically informed intervention and combined groups.

**Discussion**

This systematic review and meta-analysis investigated the comparative effectiveness of physical, behavioral/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 behavioral/psychologically informed groups in the medium- and long-term. No statistically significant differences were found for pain and disability in the single study comparing behavioral/psychologically informed and combined interventions. Although a small statistically significant difference was found for pain and disability between the physical and combined group, favoring the combined group, this difference was small. This suggests that there are only small differences between physical, behavioral/psychologically informed, and combined interventions for reducing pain and disability in NSCSP patients.

Although it may appear surprising that these very different interventions show 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 acceptable to patients and also feasible for a health care service to provide, should be considered. Similarly, Kamper et al reported that combined multidisciplinary programs are significantly more effective than physical therapies for CLBP, but because of 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 physical and behavioral/psychologically informed interventions may in fact have similar mechanisms of effect. This is on the basis of trials showing that successful outcomes, even after a purely physical intervention, are often mediated by changes in cognitive and psychological factors (eg, fear, catastrophizing, self-efficacy, beliefs). Another possibility is that other important “nonspecific factors” such as clinician support, empathy, and 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 showing that a positive patient–therapist interaction is linked to reduced pain and disability.

It has been proposed that most RCTs have not adequately dealt with the multidimensional nature of NSCSP. This is significant considering the growing evidence that NSCSP is associated with a complex interplay of biopsychosocial factors. These may include pathoanatomical factors (eg, disc prolapse with radiculopathy, spondylosis/spondylolisthesis, lateral recess/central stenosis), physical factors (eg, maladaptive postures and movement patterns, altered body perception, pain behaviors and deconditioning), cognitive factors (eg, unhelpful beliefs, catastrophizing, hypervigilance, maladaptive coping strategies, poor self-efficacy), psychological factors (eg, fear, anxiety, depression), lifestyle factors (eg, physical inactivity, sleep problems, chronic life stress), neurophysiological factors (eg, peripheral and central nervous system sensitization), social factors (eg,
socioeconomic status, family, work, and culture), genetic factors. Even the "combined" treatment approaches did not target this wide range of factors, for example, commonly excluding factors such as sleep and life stress.

Another potential reason for the similar effectiveness of these conservative interventions is that the interventions are insufficiently tailored to the needs of patients. For example, 1 large RCT showed that people with LBP could be categorized into 3 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. 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 shown in this review. Attempts to

Figure 4. Effect of physical versus combined interventions on pain.
<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Physical</th>
<th>Combined</th>
<th>Std. Mean Difference</th>
<th>IV, Random, 95% CI</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean SD</td>
<td>Mean SD</td>
<td></td>
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<tr>
<td>4.1.1 Disability at short-term follow-up</td>
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</tr>
<tr>
<td>Christiansen 2010 (1)</td>
<td>31.9 23.7</td>
<td>20 25.3 16.8</td>
<td>30 15.6%</td>
<td>0.32 [-0.19, 0.83]</td>
<td></td>
</tr>
<tr>
<td>Friedrich 1998 (2)</td>
<td>24.15.7</td>
<td>47 17.8 15.7</td>
<td>43 18.6%</td>
<td>0.36 [-0.04, 0.02]</td>
<td></td>
</tr>
<tr>
<td>Rendant 2011 (3)</td>
<td>31.3 14.04</td>
<td>36 32.8 13.62</td>
<td>41 18.0%</td>
<td>-0.11 [-0.56, 0.34]</td>
<td></td>
</tr>
<tr>
<td>Sahin 2011 (4)</td>
<td>39.9 5.91</td>
<td>73 36.13 5.91</td>
<td>73 23.2%</td>
<td>0.64 [0.31, 0.97]</td>
<td></td>
</tr>
<tr>
<td>Sherman 2011 (5)</td>
<td>4.61 3.12</td>
<td>81 4.31 3.46</td>
<td>81 24.5%</td>
<td>0.09 [-0.22, 0.40]</td>
<td></td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>261</td>
<td></td>
<td></td>
<td>0.27 [0.01, 0.54]</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Tau^2 = 0.05; Chi^2 = 9.08; df = 4 (P = 0.08); I^2 = 56%</td>
<td></td>
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<tr>
<td>Test for overall effect: Z = 2.01 (P = 0.04)</td>
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<table>
<thead>
<tr>
<th>4.1.2 Disability at medium-term follow-up</th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Critchley 2007 (6)</td>
<td>7 5.41</td>
<td>56 6.2 5.45 25</td>
<td>7.2%</td>
<td>0.15 [-0.33, 0.62]</td>
<td></td>
</tr>
<tr>
<td>Critchley 2007 (7)</td>
<td>8 6.55</td>
<td>63 6.2 5.45 25</td>
<td>7.3%</td>
<td>0.28 [-0.18, 0.75]</td>
<td></td>
</tr>
<tr>
<td>Ferreira 2007 (8)</td>
<td>7.7 6.2 36 10.1 7 71 8.3%</td>
<td>-0.35 [-0.76, 0.05]</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Ferreira 2007 (9)</td>
<td>7.7 6.2 36 8.4 6.4 68 8.3%</td>
<td>-0.11 [-0.51, 0.29]</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Gustavsson 2006 (10)</td>
<td>14 12 16 14 9.26 13 4.2%</td>
<td>0.00 [-0.73, 0.73]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gustavsson 2010 (11)</td>
<td>33.7 16.5 62 23.9 13.3 63 9.1%</td>
<td>0.65 [0.29, 1.01]</td>
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<tr>
<td>Kankkapa 1999 (12)</td>
<td>12.6 10.2 22 5.7 6.6 28 5.7%</td>
<td>0.81 [0.23, 1.39]</td>
<td></td>
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<tr>
<td>Kapp 2006 (13)</td>
<td>18 11.5 57 20.4 11.6 58 9.0%</td>
<td>-0.21 [-0.57, 0.16]</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Macedo 2012 (14)</td>
<td>8 7.1 74 8.6 6.8 81 10.0%</td>
<td>-0.09 [-0.40, 0.23]</td>
<td></td>
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<tr>
<td>Rendant 2011 (15)</td>
<td>31.5 13.3 35 23 14 39 7.5%</td>
<td>0.11 [-0.35, 0.57]</td>
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<tr>
<td>Smeets 2008 (16)</td>
<td>11 3.7 25 10.09 3.65 58 7.2%</td>
<td>0.26 [-0.22, 0.72]</td>
<td></td>
<td></td>
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<tr>
<td>Smeets 2008 (18)</td>
<td>11 3.7 25 10.97 3.92 61 7.3%</td>
<td>0.01 [-0.46, 0.47]</td>
<td></td>
<td></td>
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<tr>
<td>Vonk 2009 (17)</td>
<td>26.5 13.9 59 22.5 14 50 8.8%</td>
<td>0.28 [-0.09, 0.06]</td>
<td></td>
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<tr>
<td>Subtotal (95% CI)</td>
<td>566</td>
<td></td>
<td></td>
<td>0.12 [-0.06, 0.30]</td>
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<tr>
<td>Heterogeneity: Tau^2 = 0.06; Chi^2 = 26.74; df = 12 (P = 0.008); I^2 = 55%</td>
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<tr>
<td>Test for overall effect: Z = 1.34 (P = 0.18)</td>
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<tr>
<th>4.1.3 Disability at long-term follow-up</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Critchley 2007</td>
<td>7.6 6   53 5.6 5.4 23 6.8%</td>
<td>0.31 [-0.19, 0.80]</td>
<td></td>
<td></td>
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<tr>
<td>Critchley 2007</td>
<td>8.1 7.8 55 5.9 5.4 23 6.9%</td>
<td>0.32 [-0.17, 0.81]</td>
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<tr>
<td>Ferreira 2007</td>
<td>9.2 6.6 36 9.6 6.9 73 8.4%</td>
<td>-0.06 [-0.46, 0.34]</td>
<td></td>
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<tr>
<td>Ferreira 2007</td>
<td>9.2 6.6 36 8.8 6.5 65 8.2%</td>
<td>0.06 [-0.35, 0.47]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friedrich 1998</td>
<td>24.1 18.7 35 16.1 12.6 34 7.0%</td>
<td>0.49 [0.02, 0.97]</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Gustavsson 2011</td>
<td>32.7 16 57 23.7 13.2 58 8.8%</td>
<td>0.61 [0.24, 0.98]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kankkapa 1999</td>
<td>11.4 11.4 22 5.7 8.1 27 5.7%</td>
<td>0.58 [0.00, 1.15]</td>
<td></td>
<td></td>
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<tr>
<td>Kappa 2006</td>
<td>18.5 12.4 54 18.9 12.8 53 8.7%</td>
<td>-0.03 [-0.41, 0.35]</td>
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<td></td>
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</tr>
<tr>
<td>Macedo 2012</td>
<td>7.4 6.7 75 8 6.9 80 9.9%</td>
<td>-0.09 [-0.40, 0.23]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Monticone 2012 (18)</td>
<td>47.01 16.79 35 30.88 17.02 40 7.0%</td>
<td>0.94 [0.48, 1.42]</td>
<td></td>
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</tr>
<tr>
<td>Smeets 2008</td>
<td>10.87 3.7 25 10 3.65 52 7.0%</td>
<td>0.23 [-0.24, 0.71]</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Smeets 2008</td>
<td>10.87 3.7 25 11.39 3.92 61 7.2%</td>
<td>-0.13 [-0.60, 0.33]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vonk 2009</td>
<td>26.6 14.2 47 21.9 16.5 45 8.1%</td>
<td>0.30 [-0.11, 0.71]</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>555</td>
<td>634 100.0%</td>
<td>0.25 [0.07, 0.43]</td>
<td></td>
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<tr>
<td>Heterogeneity: Tau^2 = 0.06; Chi^2 = 26.12; df = 12 (P = 0.01); I^2 = 54%</td>
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<tr>
<td>Test for overall effect: Z = 2.78 (P = 0.005)</td>
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Figure 5. Effect of physical versus combined interventions on disability.
individualize 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.\(^\text{140}\) However, because both of these RCTs offered combined rehabilitation in both intervention arms, they were ineligible for this review. It is important, however, to acknowledge that individualizing rehabilitation purely on the basis of biomedical and physical factors alone does not appear likely to enhance outcomes.\(^\text{3,15,33,46}\) Therefore, although biomedical and physical factors alone does not appear likely to enhance outcomes,\(^\text{3,15,33,46}\) it is crucial to consider the types of bias present in the included studies. For instance, the use of qualitative approaches where necessary.

**Future Research and Clinical Implications**

Because of the strong evidence that NSCSP is associated with a complex interplay of biopsychosocial factors, the challenge is to determine whether individualized care on the basis of targeting these factors offers greater benefits over other current approaches.\(^\text{49,53,76,87}\) Future RCTs 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,\(^\text{73,100}\) including consideration of the role of “nonspecific” factors such as therapeutic alliance, and the use of qualitative approaches where necessary.

**Strength and Limitations**

To our knowledge, this is the first comprehensive systematic review and meta-analysis to compare the effectiveness of physical, behavioral/psychologically informed, and combined interventions in NSCSP. Most studies that were included were of high methodological quality. Kamper et al\(^\text{56}\) 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 comparison by Kamper et al. The current review had also initially aimed to investigate behavioral/psychologically informed versus combined comparisons, but because only 1 study was found, a meta-analysis could not be completed on this comparison. Furthermore, our review expanded on the review by Kamper et al by including NSCSP, not just CLBP, and investigated physical versus behavioral/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 introduced 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 behavioral versus combined rehabilitation because there was only 1 studying comparing these interventions.\(^\text{110}\) This may indicate a preference for always including a physical component in interventions instead of a behavioral/psychological component, possibly showing the dominance of the biomedical model in practice and that most treatments assume peripheral nociception is the primary driver of NSCSP. Furthermore, review procedures have evolved since the authors of this report submitted the original review protocol. The authors of this report used a summary score out of 12 and specific cutoff values to distinguish high- from low-quality studies. Using this system means that a study that fulfills any 6 of the 12 criteria is deemed high-quality. This approach has limitations, however, because meta-epidemiological evidence suggests that failure on any 1 of the 12 criteria might alone explain a small positive effect on a subjective self-reported outcome. Some study authors did not reply to e-mails regarding their study interventions and methodology. This may have resulted in errors of eligibility and risk of bias rating. Furthermore, although this approach was previously recommended by Cochrane, it is no longer advocated for risk of bias assessment. Also, in this 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 these considerations for all studies. The authors of this report did not award a point for blinded assessment. This might be considered strict because 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 behavioral/psychologically informed versus combined. The authors chose these groupings on the basis of 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, because of the consistent evidence that physical, behavioral/psychologically informed, and combined interventions are superior to minimal interventions, placebo, or waiting list control groups.\(^\text{5,108}\) The meta-analysis pooled the results for NP and LBP together. It could be argued that the results may have been 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.85,87,103

Conclusions

No clinically significant differences were found for pain and disability between physical, behavioral/psychologically informed, and combined interventions for NSCSP. As a result, choosing the most cost-efficient, feasible rehabilitation option may be reasonable.

References

25. Dagfinrud H, Storheim K, Magnusen L, Ødegaard T, Hoffaniska J, Larsen R, Ringstad P, Hatlebrekke F, Grotle M: The predictive validity of the Orebro Musculoskeletal Pain Conservative Interventions for Nonspecific Chronic Spinal Pain 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.

Supplementary Data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jpain.2016.01.473.
O’Keeffe et al.

Questionnaire and the clinicians’ prognostic assessment following manual therapy treatment of patients with LBP and neck pain. Man Ther 18:124-129, 2013


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772 The Journal of Pain


Conservative Interventions for Nonspecific Chronic Spinal Pain


