Can we explain heterogeneity among randomized clinical trials of exercise for chronic back pain? A meta-regression analysis of randomized controlled trials

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CRD summary
This review found that exercise interventions resulted in small but significant reductions in pain and disability. These conclusions are supported by the results, but should be interpreted with some caution due to the possibility of missing studies, the unclear quality of the included studies and a lack of information with which to determine applicability.

Authors' objectives
To establish the effect of exercise on pain and disability in patients with chronic low back pain and to explain between-trial heterogeneity.

Searching
MEDLINE, CINAHL, PEDro, LILACS, Cochrane Central Register of Controlled Trials (CENTRAL) and EMBASE were searched to August 2008. Search strategies were reported in an appendix. Reference lists of systematic reviews were screened. No language restrictions were applied.

Study selection
Randomised controlled trials (RCTs) that evaluated the effects of exercise therapy in patients with nonspecific chronic low back pain were eligible for inclusion. Nonspecific chronic low back pain was defined as a nonspecific episode of low back pain (with or without leg pain) that lasted for 12 weeks or longer. Exercise therapy was defined as the performance of any physical activity in order to develop the body and improve health. Studies that included patients with mixed duration of back pain were eligible if it was possible to extract data separately for those with chronic low back pain. Studies that compared only two exercise groups, studies that evaluated post-surgical rehabilitation and trials of primary or secondary prevention were excluded. Outcomes of interest were pain and disability measured on a continuous scale.

Types of exercise evaluated in the included studies included various combinations of motor control, isotonic exercises, aerobic exercise, general exercise, hydrotherapy, postural, lumbar resistance training, massage, stretching, sit-ups, leg-press, McKenzie, back school, endurance, physical conditioning and flexion and extension. Some exercise programmes involved a cognitive-behavioural training (CBT) component, some were supervised exercise sessions and some were individualised exercises. The number of exercise sessions (where reported) ranged from one to 156. Comparison groups included no-treatment, usual care, psychotherapy, waiting list, surgery, traditional bone setting, whole-body vibration, steroid injection, laser and ultrasound therapy, usual physical therapy, osteopathy, TENS or sham TENS, education, spinal manipulative therapy, chiropractic care, advice, CBT, heat and massage and normal activity.

Two reviewers independently selected studies for inclusion; disagreements were resolved through consensus or referral to a third reviewer.

Assessment of study quality
Two reviewers independently assessed study quality using the 11-item PEDro scale to assign studies a score out of 10. Disagreements were resolved through consensus or referral to a third reviewer where necessary.

Data extraction
Two reviewers independently extracted data on post-treatment pain and disability scores. All outcome measures were rescaled to a scale of zero to 100. Mean differences (MDs) and 95% confidence intervals (CIs) between treatment and control groups were calculated. Where studies reported multiple exercise groups and a single control group, data for the exercise groups were combined. Where necessary, authors were contacted for further information. Where measures of variance were not reported or were unavailable from the authors, these were calculated from the average standard deviation from the remaining trials. Disagreements were resolved through consensus or referral to a third reviewer.
Methods of synthesis
Summary mean differences and 95% CIs were estimated using random-effects models. Fixed-effect models were used where heterogeneity was absent. Data were pooled separately for pain and disability and according to duration of follow-up (less than three months, three to six months and more than six or 12 months) and comparison group (minimal care, no treatment and conservative treatment). Heterogeneity was assessed using the $I^2$ statistic. Heterogeneity was investigated using meta-regression analysis based on the variables: baseline severity of symptoms, number of exercise hours and sessions, programme features (supervision, individually tailored programme, cognitive behavioural therapy component) and methodological features (analysis by intention-to-treat and concealment of treatment allocation). Univariate meta-regression was conducted with items that showed an association with the mean difference ($p<0.20$) entered into a multivariate model.

Results of the review
Forty-one studies (n=4,485 participants, range 20 to 240) were included in the review; one trial was unsuitable for pooling, so 40 trials contributed to the meta-analysis. Methodological quality ranged from 2 to 8 on the 10-point PEDro scale.

Pain intensity (30 RCTs, 33 comparisons): Exercise resulted in a significant improvement in pain compared to minimal care (MD -4.83, 95% CI -9.36 to -0.30; 11 studies) and no treatment (MD -9.27, 95% CI -17.0 to -1.55; three studies, five comparisons) at short-term follow-up (less than three months). The comparison with minimal care also suggested a significant beneficial effect at longer follow-up. There was no significant difference between exercise and other conservative treatments (14 studies) in the short term. There was a significant beneficial effect in favour of exercise compared to conservative treatment for studies that reported outcomes after three to six months follow-up (MD -5.56, 95% CI -10.06, -1.07; four studies, five comparisons) and after six to 12 months follow-up (MD -2.75, 95% CI -5.07 to -0.43; eight studies, nine comparisons). There was moderate to substantial heterogeneity for each comparison ($I^2$ ranged from 55% to 93%). Meta-regression found that the only covariate significantly associated with the effect of exercise on pain was number of exercise sessions (regression co-efficient 0.13, 95% CI 0.02 to 0.24; $p=0.028$). This variable explained 17% of between-study variance.

Disability (34 RCTs, 38 comparisons): Pooling of results from all trials found moderate heterogeneity ($I^2=44\%$) that was accounted for by two trials that had significant between-group differences at baseline; these two trials were excluded from further analyses. Exercise resulted in a significant improvement in disability compared to minimal care (MD -6.41, 95% CI -9.76 to -3.05; 14 studies) and no treatment (MD -3.31, 95% CI -4.83 to -1.79; six studies, nine comparisons) at short-term follow-up. There was no significant difference between exercise and other conservative treatments (12 studies, 13 comparisons). Results were similar for longer durations of follow-up. None of the variables investigated showed a significant association with the effects of exercise on disability.

Authors' conclusions
When all types of exercise are analysed, small but significant reductions in pain and disability were observed. The only variable significantly associated with exercise effect sizes on pain was the number of exercise sessions.

CRD commentary
The review addressed a clear question. Inclusion criteria were defined. The literature search included a broad range of databases. No language restrictions were applied. No specific attempts were made to locate unpublished studies and so there was a possibility of publication bias; this was not considered in the review. Appropriate steps were taken to minimise bias and errors at all stages of the review process. Study quality was assessed using appropriate criteria, but results were presented only as summary quality scores which were difficult to interpret and so the methodological quality of the included studies was unclear. The study details table included limited information, especially for participants and outcomes and this made it difficult to determine the generalisability of results. It appeared that appropriate methods were used to pool data. Heterogeneity was investigated.

The authors' conclusions are supported by the results, but should be interpreted with some caution due to the possibility of missing studies and the unclear quality of the included studies.
Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that systematic reviews should be conducted to examine the effects of specific exercise types on pain and disability in patients with chronic low back pain.

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