

Spinal Manipulative Therapy for Low Back Pain

A Meta-Analysis of Effectiveness Relative to Other Therapies

Willem J.J. Assendelft, MD, PhD; Sally C. Morton, PhD; Emily I. Yu, MPH; Marika J. Suttorp, MS; and Paul G. Shekelle, MD, PhD

Background: Low back pain is a costly illness for which spinal manipulative therapy is commonly recommended. Previous systematic reviews and practice guidelines have reached discordant results on the effectiveness of this therapy for low back pain.

Purpose: To resolve the discrepancies related to use of spinal manipulative therapy and to update previous estimates of effectiveness by comparing spinal manipulative therapy with other therapies and then incorporating data from recent high-quality randomized, controlled trials (RCTs) into the analysis.

Data Sources: MEDLINE, EMBASE, CINAHL, the Cochrane Controlled Trials Register, and previous systematic reviews.

Study Selection: Randomized, controlled trials of patients with low back pain that evaluated spinal manipulative therapy with at least 1 day of follow-up and at least one clinically relevant outcome measure.

Data Extraction: Two authors, who served as the reviewers for all stages of the meta-analysis, independently extracted data from unmasked articles. Comparison treatments were classified into the following seven categories: sham, conventional general practitioner care, analgesics, physical therapy, exercises, back school, or a collection of therapies judged to be ineffective or even harmful

(traction, corset, bed rest, home care, topical gel, no treatment, diathermy, and minimal massage).

Data Synthesis: Thirty-nine RCTs were identified. Meta-regression models were developed for acute or chronic pain and short-term and long-term pain and function. For patients with acute low back pain, spinal manipulative therapy was superior only to sham therapy (10-mm difference [95% CI, 2 to 17 mm] on a 100-mm visual analogue scale) or therapies judged to be ineffective or even harmful. Spinal manipulative therapy had no statistically or clinically significant advantage over general practitioner care, analgesics, physical therapy, exercises, or back school. Results for patients with chronic low back pain were similar. Radiation of pain, study quality, profession of manipulator, and use of manipulation alone or in combination with other therapies did not affect these results.

Conclusions: There is no evidence that spinal manipulative therapy is superior to other standard treatments for patients with acute or chronic low back pain.

Ann Intern Med. 2003;138:871-881.

www.annals.org

For author affiliations, see end of text.

See related article on pp 898-906.

Low back pain is a disabling disorder that greatly affects Western society; it is a burden for the individual patient and an additional cost for society because of loss of work and medical expenses (1, 2). Therefore, adequate treatment of low back pain is an important issue for patients, treating clinicians, and health care policymakers. Spinal manipulative therapy is widely used for low back pain. It has been studied in many randomized, controlled trials (RCTs), which are heterogeneous in size, design, and quality of performance. These trials have been summarized in numerous systematic reviews (3).

The conclusions of systematic reviews (4–6), which provided input for national guidelines, are partially discordant. None of these reviews has included the larger high-quality trials that have been published over the past few years (7–16). Furthermore, all of these reviews and meta-analyses have considered the treatments to which spinal manipulative therapy is being compared as equivalent, meaning, for example, that no distinction was made among studies comparing spinal manipulative therapy with bed rest and studies comparing spinal manipulative therapy with physical therapy. Only two recent reviews (17, 18) compared spinal manipulative therapy with a homogeneous control group (sham treatment in both reviews).

Spinal manipulation has a prominent role in all national guidelines on the management of back pain (19). However, the recommendations in these guidelines vary.

In most countries, spinal manipulative therapy is recommended for acute low back pain. However, in the Netherlands, Australia, and Israel, the evidence is interpreted differently (19). Recommendations also vary for chronic low back pain; spinal manipulative therapy is recommended in the Danish and Dutch guidelines but is not recommended or is absent in the other national guidelines.

Our goal in this review is to update, improve, and resolve inconsistencies in previous systematic reviews through collaboration with the Cochrane Back Review Group (20). We incorporate relevant clinical variables and combine them with meta-analytic techniques to estimate the effectiveness of spinal manipulative therapy relative to other commonly used therapies (21). By presenting the most current information on this complicated issue, we provide support for individual and collective treatment decisions.

METHODS

Literature Search

One reviewer searched the following computerized bibliographic databases without language restrictions (22, 23): MEDLINE from January 1966 to January 2000, EMBASE from January 1988 to January 2000, and CINAHL from January 1982 to January 2000. The highly sensitive Cochrane Collaboration search strategy, which aims to

Context

The role of spinal manipulation in the treatment of low back pain remains controversial, possibly because previous summaries of the evidence have compared spinal manipulation with a combination of traditional therapies rather than with individual therapies.

Contribution

This meta-analysis of randomized clinical trials found that spinal manipulation was more effective than sham therapy but was no more or less effective than general practitioner care, analgesics, physical therapy, exercise, or back school.

Implications

While some patients with low back pain may prefer spinal manipulation to traditional therapies, there is no evidence that it achieves better outcomes than standard treatments.

—The Editors

identify all randomized, controlled trials, was used (20, 24). The same reviewer also searched for systematic reviews on low back pain and spinal manipulation (25).

Additional specific subject headings and free text words were used to identify papers on low back pain and spinal manipulation (20). The Cochrane Controlled Trial Register was searched (24). Finally, references from retrieved articles were screened. To determine whether a study should be included, the abstracts of all identified papers were assessed by the same reviewer who performed the computerized bibliographic search. If there was any doubt, the full article was retrieved and read independently by both reviewers. Disagreements were resolved by consensus.

Literature Selection

We included studies that met the following conditions: 1) adult patients with low back pain, regardless of radiation pattern; 2) comparison of manipulation or mobilization for low back pain with another treatment or control (manipulation differs from mobilization in that it focuses on a different range of motion of the involved joint; unless otherwise indicated, spinal manipulative therapy refers to both hands-on treatments in this review; co-interventions were allowed); 3) at least one clinically relevant outcome measure (pain, global improvement, back pain-specific functional status, or generic functional status) (26); 4) follow-up of at least 1 day; 5) publication as a full report before January 2001.

Quality Assessment

Quality can be assessed by using different checklists or scales. We used the quality list from the Cochrane Back Review Group (20) to assess methodologic quality. This list contains items relevant to the description, internal validity, and statistical issues of the study (Table 1). Each criterion was rated as positive, negative, or inconclusive

(insufficient information presented). Equal weights were applied, resulting in a total score for internal validity of each study, by adding the number of positive criteria (range, 0 to 10); higher scores indicated a lower likelihood of bias. In addition, we scored the list of Jadad and colleagues (27, 28). We used multiple criteria and scales because of the absence of a consensus on a “gold standard” for quality, especially for interventions such as spinal manipulative therapy, for which true double-blinding is not feasible.

The articles were not blinded for authors, journal, or year of publication (27) because the two reviewers were familiar with most of the articles from their previous reviews. Included articles were independently assessed for methodologic quality by the two authors. Disagreements were discussed and resolved in a consensus meeting.

Data Extraction

Data were independently extracted by the two reviewers and checked for accuracy by two other authors.

Statistical Analysis

We briefly describe the analysis here. The Appendix (available at www.annals.org) describes the analysis in detail. We classified studies by the duration of back pain (acute, chronic, mixed, and unsure), presence of leg pain, profession of manipulator, comparison therapy, outcome measured, and follow-up time. “Short-term” follow-up was less than 6 weeks; for the meta-analysis, we chose the outcome measurement closest to 3 weeks. “Long-term” follow-up was more than 6 weeks; for the meta-analysis, we chose the outcome measurement closest to 6 months. For each study that had data available for each of the four outcomes (short-term pain, long-term pain, short-term function, and long-term function), we calculated the effect sizes of the changes in outcome between the reference spinal manipulative therapy group and all comparison therapy

Table 1. Criteria for the Methodologic Assessment of Randomized Clinical Trials (Cochrane Back Review Group and Editorial Board Quality List)*

Cochrane Back Pain Group Score	Criteria
V1	Adequate randomization: adequate procedure for generation of a random-number sequence
V2	Concealed randomization
V3	Care provider blinded
V4	Control for co-interventions
V5	Co-interventions reported for each group separately
V6	Patient blinded
V7	Outcome assessor blinded
V8	Withdrawals and dropouts: $\leq 20\%$ for short-term follow-up; $\leq 30\%$ for intermediate-term and long-term follow-up and no substantial bias (numeric inequality between groups or differences in reasons for withdrawal or dropout)
V9	Identical timing of outcome assessment
V10	Intention-to-treat analysis

* From van Tulder et al. (20).

groups in the study. An effect size is the ratio of the difference in mean outcomes between the spinal manipulative therapy and comparison therapy groups divided by its standard deviation; it is a unitless measure of comparison for results reported by using different measurement scales (for example, pain measured by using a 100-mm visual analogue scale [VAS] or a 7-point pain rating scale). A positive effect size indicates that spinal manipulative therapy was beneficial, that is, function increased or pain decreased, as compared with the alternative therapy. For each outcome, we assessed the degree of heterogeneity in all effect sizes within each back pain stratum by use of a forest plot and chi-square test (29).

Ideally, we would have liked to compare spinal manipulative therapy with each different therapy for each outcome within each back pain stratum, but this was not possible because the data were sparse. Therefore, we used available research evidence and the clinical judgment of similar effectiveness of the Editorial Board of the Cochrane Back Review Group to group the comparison therapies into the following clusters of presumed effectiveness:

1. Sham: Used to assess efficacy rather than effectiveness.

2. Conventional general practitioner care and analgesics: Although general practitioners may suggest other therapy for back pain in addition to prescribing medication, empirical evidence shows that 80% of initial visits to primary care providers for back pain result in an analgesic prescription (38); consequently, we considered these two categories sufficiently similar to pool.

3. Physical therapy and exercise: Both are considered to be activating therapies; in general, exercises are often a key component of physical therapy, making up 30%, 33%, and 100% of the treatment delivered in three studies of “physical therapy” for patients with low back pain (7–10, 39).

4. Traction, corset, bed rest, home care, topical gel, no treatment, diathermy, and minimal massage: Treatments that were considered to lack evidence of benefit or have evidence of harm (40).

5. Back school: Treatments that did not conceptually fit with any other group.

For each outcome, we fit a random-effects meta-regression (33) model, in which effect size is the unit of observation, to compare the effect of spinal manipulative therapy with that of alternative therapies while controlling for other variables. The model contained indicator variables for the five alternative therapy clusters and main effects for duration of back pain (chronic, acute, mixed, or unsure). Although we also developed estimates for patients with mixed pain patterns and “unsure,” we do not present them because the number of studies was too small. We also fit a series of models with increasingly complex parameterizations of the treatment effect to investigate the robustness of our results (see Appendix, available at www.annals.org).

We tested for interactions between duration of back

pain and therapy cluster; we also investigated the effect of adjustments for the presence of leg pain and the profession of the manipulator. Because some studies provided spinal manipulative therapy in combination with other therapies, we also repeated our analysis on the subset of studies that assessed “manipulation” (as defined by the use of this word in the description of the intervention) as the sole or predominant treatment. Because a study can have more than one comparison group, it can contribute more than one effect size to the analysis. Multiple effect sizes from a single study may be correlated because they are based on comparison to the same spinal manipulative therapy group. We assessed the possible effect of this correlation on our results by conducting a sensitivity analysis. We also conducted sensitivity analyses to determine how excluding outlying effect sizes or including only studies with continuous or dichotomous outcomes affected our results. Finally, we checked for publication bias for each outcome by using both graphic and statistical testing techniques (36, 37).

For interpretability, the observed effect sizes shown in the forest plots and the estimated effect sizes from the models were backtranslated into clinically relevant values by using the 100-mm VAS scale for pain and the Roland Disability Questionnaire (RDQ) for function (assuming a standard deviation of 25 for the VAS and 6 for the RDQ). As an example, if the effect size for pain was 0.2, we present the result as 5 mm on the VAS, which indicates that spinal manipulative therapy is associated with a 5-mm reduction in pain as compared with the relevant comparison group. We used a standard *P* value of 0.05 to assess statistical significance. On the basis of discussion with the Cochrane Back Editorial Board, we considered a 10-mm difference on the VAS and a 2-point or greater difference on the RDQ as clinically relevant.

RESULTS

Our search strategy identified 1153 potentially relevant abstracts. After review of the full text of articles, 53 articles were included (7–16, 39, 41–82), representing 39 studies meeting our inclusion criteria. The **Appendix Figure** (available at www.annals.org) is a flow chart of the selection. We excluded one study because it did not report sample sizes by group (82). **Table 2** is a condensed version of an evidence table describing the key clinical and methodologic characteristics of each included study. **Appendix Table 1** (available at www.annals.org) is a complete version of this table. **Appendix Table 2** (available at www.annals.org) describes the excluded studies. There were 29 comparisons of spinal manipulative therapy for patients with acute or subacute pain, 29 comparisons of spinal manipulative therapy for patients with subacute or chronic pain, and 14 comparisons of spinal manipulative therapy for patients with mixed or unsure durations of pain. Most studies excluded patients with sciatica; 12 comparisons were restricted to patients with sciatica. The studies included a

Table 2. Evidence Table

Study (Reference), Year*	Duration	Presence of Sciatica	Sample Size†	Comparison Group	Quality Score‡	Outcomes Reported
Glover et al. (41), 1974	Acute/semi-acute	Unsure	84	Diathermy	6; 3; 3	Short-term pain
Doran and Newell (42), 1975	Mixed	Excludes sciatica	395	Analgesic, corset, or physical therapy	4; 2; 2	Short-term pain Short-term function Long-term pain
Bergquist-Ullman and Larsson (43), 1977	Acute/semi-acute	Excludes sciatica	150	Back school or diathermy	3; 2; 2	Short-term pain
Evans et al. (44), 1978	Semi-acute/chronic	Includes sciatica	32	Analgesic	5; 2; 2	Short-term pain Short-term function
Sims-Williams et al. (45), 1978	Mixed	Includes sciatica	87	Diathermy	5; 1; 1	Short-term pain Long-term pain
Rasmussen (46), 1979	Acute	Excludes sciatica	24	Diathermy	4; 2; 2	Short-term pain
Sims-Williams et al. (47), 1979	Mixed	Includes sciatica	90	Diathermy	5; 1; 1	Short-term pain Long-term pain
Coxhead et al. (48), 1981	Mixed	Restricted to sciatica	572	Traction, exercise, or corset	5; 3; 3	Short-term pain Short-term function Long-term function
Hoehler et al. (49–51), 1981	Mixed	Excludes sciatica	58	Sham	3; 1; 3	Short-term pain Short-term function
Zylbergold and Piper (52), 1981	Unsure	Excludes sciatica§	28	Exercise or home care	3; 1; 1	Short-term pain Short-term function
Farrell and Twomey (53), 1982	Acute	Excludes sciatica§	24	Physical therapy	5; 2; 2	Short-term pain
Godfrey et al. (54), 1984	Acute	Unsure	72	Physical therapy	5; 2; 2	Short-term pain Short-term function
Gibson et al. (55), 1985	Semi-acute/chronic	Excludes sciatica§	71	Diathermy	6; 2; 2	Short-term pain Long-term pain
Waterworth and Hunter (56), 1985	Acute	Excludes sciatica§	108	Analgesics or physical therapy	4; 2; 2	Short-term pain
Waagen et al. (57), 1986	Semi-acute/chronic	Excludes sciatica§	19	Sham	5; 2; 4	Short-term pain
Hadler et al. (58, 59), 1987	Acute	Unsure	28	Sham	6; 2; 3	Short-term function
Mathews et al. (60), 1987	Acute/semi-acute	Excludes sciatica	53	Diathermy	6; 2; 2	Short-term pain Short-term function Short-term function
	Acute/semi-acute	Restricted to sciatica	207	Diathermy		Short-term pain Short-term function
Ongley et al. (61), 1987	Chronic	Excludes sciatica	81	Sham	7; 3; 4	Short-term pain Short-term function Long-term pain Long-term function
Postacchini et al. (62), 1988	Acute	Excludes sciatica	82	Analgesics, back school, physical therapy, or topical gel	3; 2; 2	Long-term pain
	Semi-acute/chronic	Excludes sciatica	66	Analgesics, back school, physical therapy, or topical gel		Long-term pain
	Acute	Restricted to sciatica	66	Analgesics, bed rest, physical therapy, or topical gel		Long-term pain
	Semi-acute/chronic	Restricted to sciatica	80	Analgesics, back school, physical therapy, or topical gel		Long-term pain
	Acute	Excludes sciatica	82	Analgesics, back school, physical therapy, or topical gel		Short-term pain
	Acute	Excludes sciatica	76	Analgesics, bed rest, physical therapy, or topical gel		Short-term pain
	Semi-acute/chronic	Excludes sciatica	77	Analgesics, back school, physical therapy, or topical gel		Short-term pain
	Acute	Restricted to sciatica	83	Analgesics, bed rest, physical therapy, or topical gel		Short-term pain
	Semi-acute/chronic	Restricted to sciatica	80	Analgesics, back school, physical therapy, or topical gel		Short-term pain
Kinalski et al. (63), 1989	Unsure	Unsure	111	Physical therapy	1; 1; 1	Short-term pain
Bronfort (64), 1989	Mixed	Includes sciatica	19	Usual care	4; 2; 2	Short-term pain Short-term function Long-term pain Long-term function
MacDonald and Bell (65), 1990	Acute/semi-acute	Includes sciatica	66	Usual care	5; 1; 1	Short-term function Long-term function
Herzog et al. (66), 1991	Semi-acute/chronic	Unsure	29	Back school	3; 2; 2	Short-term pain
Koes et al. (67–70), 1992	Semi-acute/chronic	Excludes sciatica	214	Usual care, physical therapy, or diathermy	8; 3; 3	Short-term pain Short-term function Long-term pain Long-term function

Continued on following page

Table 2—Continued

Study (Reference), Year*	Duration	Presence of Sciatica	Sample Size†	Comparison Group	Quality Score‡	Outcomes Reported
Pope et al. (71, 72), 1992	Semi-acute/chronic	Excludes sciatica	144	Corset, diathermy, or minimal massage	6; 3; 3	Short-term pain Short-term function
Wreje et al. (73), 1992	Acute/semi-acute	Excludes sciatica	39	Sham	3; 2; 2	Short-term pain
Cramer et al. (74), 1993	Acute	Excludes sciatica	35	Diathermy	4; 1; 1	Short-term pain Short-term function
Delitto et al. (75), 1993	Acute/semi-acute	Includes sciatica	24	Exercise	3; 2; 2	Short-term function
Blomberg et al. (11–15), 1994	Acute/semi-acute	Includes sciatica	101	Usual care	7; 2; 2	Short-term pain Short-term function Long-term pain Long-term function
Erhard et al. (76), 1994	Acute/semi-acute	Includes sciatica	12	Exercise	3; 3; 3	Short-term function
Timm (77), 1994	Chronic	Excludes sciatica	200	Exercise, diathermy, or no treatment	3; 2; 2	Long-term function
Meade et al. (39, 78), 1995	Mixed	Excludes sciatica	666	Physical therapy	5; 1; 1	Short-term pain Long-term pain
Triano et al. (79), 1995	Semi-acute/chronic	Excludes sciatica	129	Back school or sham	5; 3; 4	Short-term pain Short-term function
Bronfort et al. (80), 1996	Semi-acute/chronic	Includes sciatica	105	Analgesics	7; 2; 2	Short-term pain Short-term function Long-term pain
Hemmilä et al. (81), 1997	Semi-acute/chronic	Unsure	113	Exercise or physical therapy	6; 3; 3	Long-term pain
Skargren et al. (8–10), 1997	Acute	Excludes sciatica	105	Physical therapy	3; 2; 2	Long-term function
	Semi-acute/chronic	Excludes sciatica	146	Physical therapy		Long-term function
	Acute (<1 wk)	Excludes sciatica	59	Physical therapy		Long-term pain
	Acute (1–4 wk)	Excludes sciatica	105	Physical therapy		Long-term pain
	Semi-acute/chronic	Excludes sciatica	146	Physical therapy		Long-term pain
	Acute	Excludes sciatica	164	Physical therapy		Short-term function
	Semi-acute/chronic	Excludes sciatica	147	Physical therapy		Short-term function
	Acute (<1 wk)	Excludes sciatica	69	Physical therapy		Short-term pain
	Acute (1–4 wk)	Excludes sciatica	105	Physical therapy		Short-term pain
	Semi-acute/chronic	Excludes sciatica	147	Physical therapy		Short-term pain
Cherkin et al. (7), 1998	Acute/semi-acute	Excludes sciatica	307	Physical therapy or home care	5; 1; 1	Short-term pain Short-term function Long-term pain Long-term function
Andersson et al. (16), 1999	Semi-acute/chronic	Excludes sciatica	155	Usual care	7; 3; 3	Long-term pain Long-term function

* Given in chronological order.

† Represents number or analysis pairs that include spinal manipulative therapy—not the actual sample size of the study.

‡ Quality scores are given in this order: Cochrane Back Review Group (ratings, 0–10); Jadad (ratings, 0–5); “modified” Jadad (ratings, 0–5). For explanation, see Methods section.

§ Presence of sciatica not reported in this study; determination is based on judgment of reviewers.

total of 5486 patients; study sample sizes ranged from 19 to 666 (median, 92). Quality varied but tended to be higher in the more recent studies.

Except for long-term function for patients with acute low back pain, the null hypothesis of no heterogeneity was rejected for all outcomes for patients with acute and chronic low back pain. Figures 1 and 2 show the forest plots for short-term pain for patients with acute and chronic low back pain.

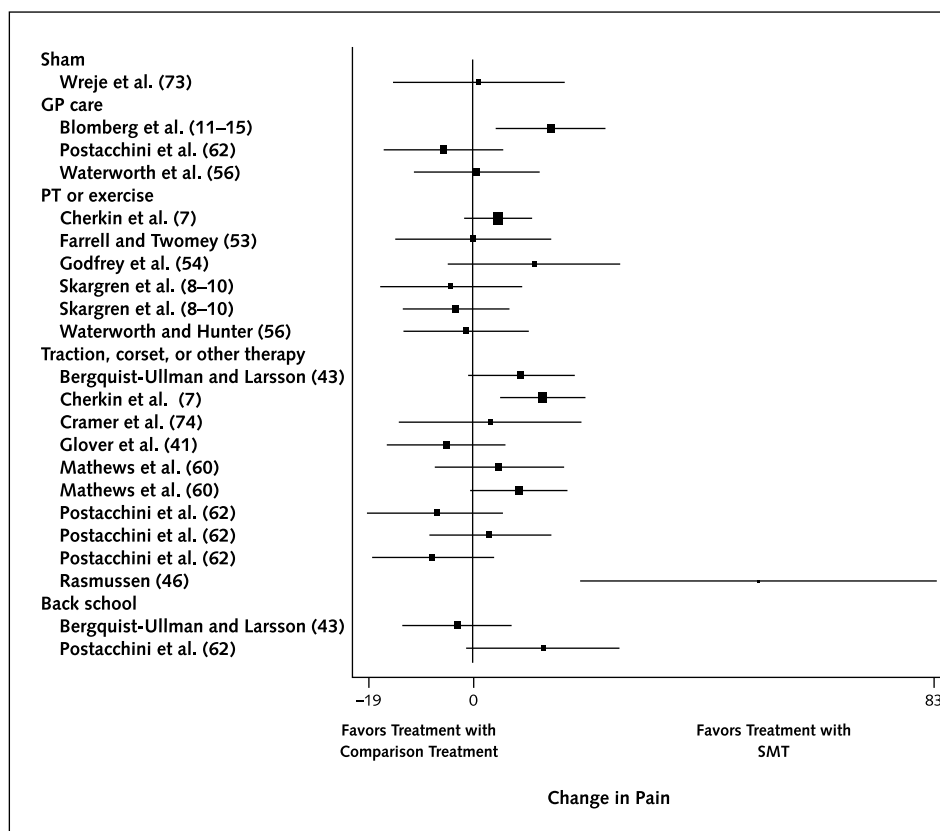
Effectiveness of Spinal Manipulative Therapy Compared with Other Specific Therapies

Figure 3 presents studies of patients with acute low back pain. Compared with sham therapy, patients receiving treatment that included spinal manipulative therapy had clinically important short-term improvements in pain and on the RDQ (10-mm difference in pain [95% CI, 2 to 17 mm]; 2.8-mm difference on the RDQ [CI, –0.1 to 5.6]). However, the improvement in function did not reach a conventional level of statistical significance. Com-

pared with other therapies, the only finding of statistical significance favoring spinal manipulative therapy was an improvement in short-term pain, which was seen when spinal manipulative therapy was compared with the group of therapies judged to be ineffective or possibly even harmful. However, the clinical significance of this finding is questionable (4-mm difference in pain). The point estimate of improvement in short-term function for treatment with spinal manipulative therapy compared with the ineffective therapies was clinically significant but did not reach a conventional level of statistical significance (2.1-point difference on the RDQ [CI, –0.2 to 4.4]). The differences between patients treated with spinal manipulative therapy and those treated with any of the conventionally advocated therapies were not statistically or clinically important.

Figure 3 also reports the results for patients with chronic low back pain. Results are similar to those seen for patients with acute low back pain. The only findings of statistical or clinical significance are the comparisons of

Figure 1. Effect of spinal manipulative therapy (SMT) on short-term pain for acute low back pain.



GP = general practitioner; PT = physical therapy.

spinal manipulative therapy with either a sham manipulation (improvement in short-term pain, 10 mm [CI, 3 to 17 mm]; improvement in long-term pain, 19 mm [CI, 3 to 35 mm]; improvement in short-term function, 3.3 points on the RDQ [CI, 0.6 to 6.0]) or the group of therapies judged to be ineffective or perhaps harmful (improvement in short-term pain, 4 mm [CI, 0 to 8]; improvement in short-term function, 2.6 points on the RDQ [CI, 0.5 to 4.8]).

Other Clinical Variables and Sensitivity Analyses

We assessed the effect of leg pain as an effect modifier and found it made little difference. Data were insufficient to allow us to assess the effect of spinal manipulative therapy as a treatment for patients with clearly defined sciatica. A sensitivity analysis using the 25 studies that used manipulation (instead of mobilization) alone or predominantly instead of combining it with other therapies showed essentially the same results as stated earlier. In addition, our results did not differ when we assessed only those studies that scored 3 or more on the Jadad scale (which has previously been shown to be a threshold associated with bias [28]) or only those studies that scored 3 or more on a “modified” Jadad scale (because true double-blinding cannot be achieved in studies of spinal manipulative therapy, we gave 1 point if the control patients were treated with a sham and another point if a post-treatment assessment

showed that patients could not guess whether they received “real” or “sham” spinal manipulative therapy). We also found no difference in effectiveness depending on the profession of the manipulator (chiropractor or other).

Our visual assessment and formal statistical tests did not detect any publication bias.

DISCUSSION

Spinal manipulative therapy had clinically and statistically significant benefits only when it was compared with either sham manipulation or the group of therapies judged to be ineffective or even harmful. Compared with other advocated therapies for low back pain, including analgesics, physical therapy, exercises, or back school, therapy that included spinal manipulative therapy had neither statistically nor clinically significant benefits. Our comparison of spinal manipulative therapy with a sham therapy suggests that spinal manipulative therapy is probably more effective than a placebo, but its effectiveness compared with other advocated therapies is substantially less than previous reviews and meta-analyses have suggested. Our sensitivity analyses supported the robustness of our results with respect to the type of manipulative therapy, profession of manipulator, and the quality of the studies included.

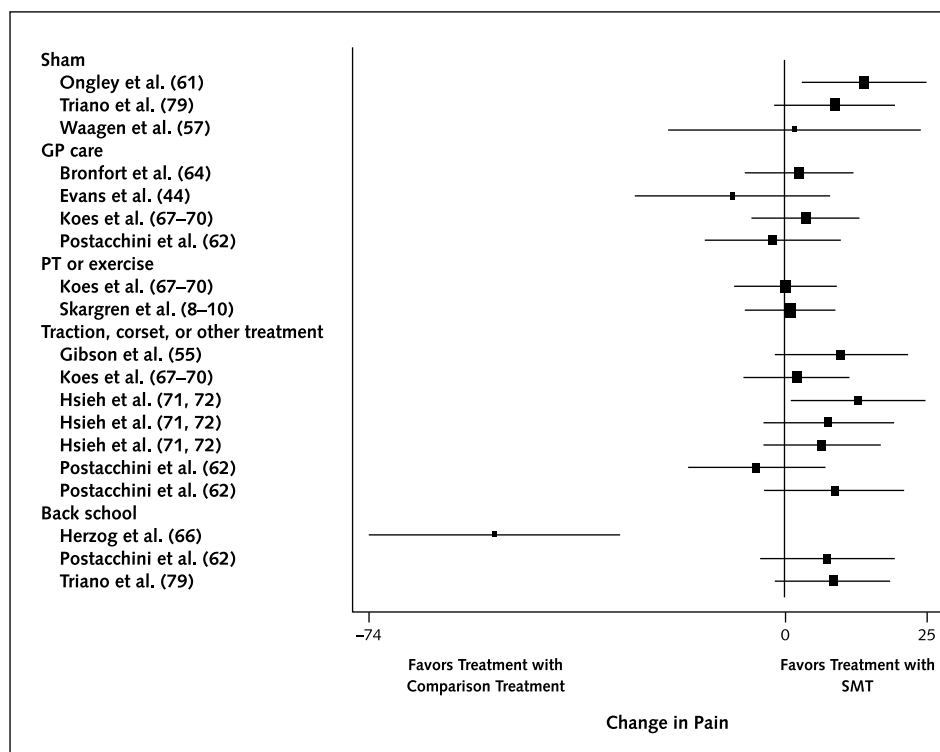
The effectiveness of spinal manipulative therapy has been the subject of persistent debate. We concluded that there is no evidence for increased effectiveness of spinal manipulative therapy compared with other advocated therapies for acute and chronic low back pain. We identified 13 systematic reviews (5, 6, 104–114). Of these, 8 reported favorable outcomes for patients with acute low back pain or chronic low back pain (5, 6, 104–106, 108–110). These reviews predate the more recent trials, and none could assess the relative effectiveness of spinal manipulative therapy compared with different kinds of control groups. Our meta-analysis includes the newer RCTs comparing spinal manipulative therapy with other active therapies. Furthermore, advances in meta-analysis methods allowed us to more precisely compare spinal manipulative therapy with other specific therapies. These two factors are the main reasons why results from our meta-analysis differ from those of previous reviews.

A methodologic implication of our study is that accounting for potential differences in the comparison groups is important in assessing the effect of spinal manipulative therapy. In the past, overall pooled results were statistically and clinically significant in favor of manipulative therapy; however, when spinal manipulative therapy was compared with specific alternative therapies, this benefit was consistent for only two comparison groups. This may be true for other meta-analyses that have heterogeneous comparison groups.

Our results also have implications for future clinical research on spinal manipulative therapy. While not all of the 95% CIs in our analysis exclude improvements of moderate clinical importance, most do. We interpret this to mean that spinal manipulative therapy is very unlikely to be a particularly effective therapy for any group of patients with back pain. While it is conceivable that spinal manipulative therapy is very effective for a subgroup of patients with back pain, this subgroup is probably small. Therefore, future clinical trials of spinal manipulative therapy, if undertaken at all, should concentrate not on effectiveness but rather on cost-effectiveness, which is primarily a function of the number of treatments needed to achieve the most benefit.

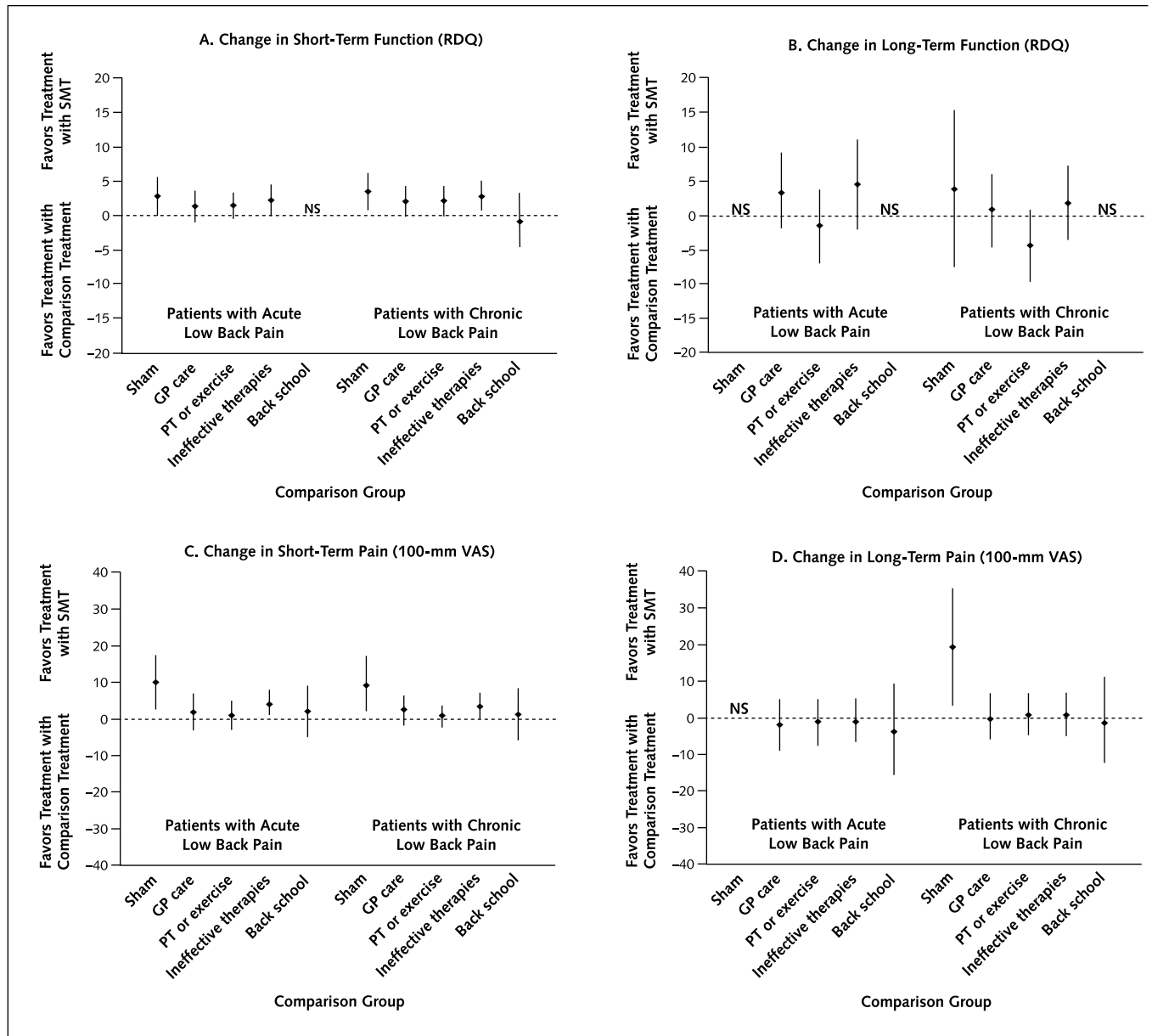
The primary limitation of this review, common to many such systematic reviews, is the uneven quantity and quality of the original studies. Although our meta-regression models adjust for study-level differences, we cannot correct for any biases inherent in individual studies. There is little consensus on how study quality should be assessed and on the optimal method of incorporating study quality in statistical pooling (115). We used different techniques for assessing quality because there is no gold standard. Our sensitivity analysis using the only scale with empirical evidence supporting it (the Jadad scale) upheld our primary analysis. A third limitation is the possibility of publication bias, which we attempted to minimize through an extensive database search without language restrictions. We did

Figure 2. Effect of spinal manipulative therapy (SMT) on short-term pain for chronic low back pain.



GP = general practitioner; PT = physical therapy.

Figure 3. Spinal manipulative therapy (SMT) for acute and chronic low back pain.



The bars represent CIs, and the values are scores for either the Roland Disability Questionnaire (RDQ) or visual analogue scale (VAS). Ineffective therapies are traction, corset, bed rest, home care, topical gel, no treatment, diathermy, or minimal massage. GP = general practitioner; NS = no studies; PT = physical therapy.

not actively seek unpublished studies but no such data have been brought to our attention, despite the widespread knowledge in the low back pain community that we were conducting this review. We assessed publication bias both visually and statistically. The power of these methods, however, is limited (116). An earlier report concluded that not including “grey literature” leads to an overestimation of the effect of therapy (117). Because our results do not indicate that the effect of spinal manipulative therapy is greater than that achieved with other advocated therapies, we doubt that grey literature would have had a substantial effect on our conclusions. Finally, there are several statisti-

cal issues. First, only a subgroup of studies assessed spinal manipulative therapy given alone, some studies presented continuous outcome measures, and some presented dichotomous measures. Second, our meta-regression model contained only main effects because the data were sparse and did not control for the correlation between multiple effect sizes in the same study. We conducted sensitivity analyses to assess the possible effect of the measurement differences, test for possible interactions, and assess the effect of possible correlation. All sensitivity analyses upheld the conclusions of our main analysis.

For patients, clinicians, and policymakers, our findings

that spinal manipulative therapy is substantially less effective than previously estimated should temper enthusiasm for this treatment as “the” recommended therapy for patients with low back pain. We found no evidence that spinal manipulative therapy is superior to other advocated therapies, including analgesics, exercises, physical therapy, and back schools. Neither did we find evidence that these therapies are superior to spinal manipulative therapy. Therefore, we conclude that spinal manipulative therapy is one of several options of only modest effectiveness for patients with low back pain. Truly effective therapy for such patients remains elusive.

From The Cochrane Back Review Group, Toronto, Ontario, Canada, and Amsterdam, the Netherlands; Dutch College of General Practitioners, Utrecht, the Netherlands; RAND, Santa Monica, California; and Greater Los Angeles Veterans Affairs Healthcare System, Los Angeles, California.

Grant Support: No external funding was obtained for this study.

Acknowledgments: The authors thank the members of the Editorial Board of the Cochrane Back Review Group for constructive comments on the protocol and draft version of this article. They also thank Bart W. Koes, PhD, and Maurits W. van Tulder, PhD, for helping develop some of the methods of searching and quality assessment used in this review.

Potential Financial Conflicts of Interest: None disclosed.

Requests for Single Reprints: Paul G. Shekelle, MD, PhD, RAND, 1700 Main Street, PO Box 2138, Santa Monica, CA 90407; e-mail, shekelle@rand.org.

Current author addresses and author contributions are available at www.annals.org.

References

1. Waddell G. Low back pain: a twentieth century health care enigma. *Spine*. 1996;21:2820-5. [PMID: 9112705]
2. van Tulder MW, Koes BW, Bouter LM. A cost-of-illness study of back pain in The Netherlands. *Pain*. 1995;62:233-40. [PMID: 8545149]
3. Assendelft WJ, Koes BW, Knipschild PG, Bouter LM. The relationship between methodological quality and conclusions in reviews of spinal manipulation. *JAMA*. 1995;274:1942-8. [PMID: 8568990]
4. Bronfort G. Spinal manipulation: current state of research and its indications. *Neurol Clin*. 1999;17:91-111. [PMID: 9855673]
5. Shekelle PG, Adams AH, Chassin MR, Hurwitz EL, Brook RH. Spinal manipulation for low-back pain. *Ann Intern Med*. 1992;117:590-8. [PMID: 1388006]
6. Koes BW, Assendelft WJ, van der Heijden GJ, Bouter LM. Spinal manipulation for low back pain. An updated systematic review of randomized clinical trials. *Spine*. 1996;21:2860-71; discussion 2872-3. [PMID: 9112710]
7. Cherkin DC, Deyo RA, Battié M, Street J, Barlow W. A comparison of physical therapy, chiropractic manipulation, and provision of an educational booklet for the treatment of patients with low back pain. *N Engl J Med*. 1998;339:1021-9. [PMID: 9761803]
8. Skargren EI, Oberg BE, Carlsson PG, Gade M. Cost and effectiveness analysis of chiropractic and physiotherapy treatment for low back and neck pain. Six-month follow-up. *Spine*. 1997;22:2167-77. [PMID: 9322328]
9. Skargren EI, Carlsson PG, Oberg BE. One-year follow-up comparison of the cost and effectiveness of chiropractic and physiotherapy as primary management for back pain. Subgroup analysis, recurrence, and additional health care utilization. *Spine*. 1998;23:1875-83; discussion 1884. [PMID: 9762745]
10. Skargren EI, Oberg BE. Predictive factors for 1-year outcome of low-back and neck pain in patients treated in primary care: comparison between the treatment strategies chiropractic and physiotherapy. *Pain*. 1998;77:201-7. [PMID: 9766838]
11. Blomberg S, Hallin G, Grann K, Berg E, Sennerby U. Manual therapy with steroid injections—a new approach to treatment of low back pain. A controlled multicenter trial with an evaluation by orthopedic surgeons. *Spine*. 1994;19:569-77. [PMID: 8184352]
12. Blomberg S, Svärdsudd K, Tibblin G. A randomized study of manual therapy with steroid injections in low-back pain. Telephone interview follow-up of pain, disability, recovery and drug consumption. *Eur Spine J*. 1994;3:246-54. [PMID: 7866845]
13. Blomberg S, Svärdsudd K, Mildnerberger F. A controlled, multicentre trial of manual therapy in low-back pain. Initial status, sick-leave and pain score during follow-up. *Scand J Prim Health Care*. 1992;10:170-8. [PMID: 1410946]
14. Blomberg S, Svärdsudd K, Tibblin G. Manual therapy with steroid injections in low-back pain. Improvement of quality of life in a controlled trial with four months' follow-up. *Scand J Prim Health Care*. 1993;11:83-90. [PMID: 8356370]
15. Blomberg S, Tibblin G. A controlled, multicentre trial of manual therapy with steroid injections in low-back pain: functional variables, side effects and complications during four months follow-up. *Clin Rehab*. 1993;7:49-62.
16. Andersson GB, Lucente T, Davis AM, Kappler RE, Lipton JA, Leurgans S. A comparison of osteopathic spinal manipulation with standard care for patients with low back pain. *N Engl J Med*. 1999;341:1426-31. [PMID: 10547405]
17. Ernst E. Does spinal manipulation have specific treatment effects? *Fam Pract*. 2000;17:554-6. [PMID: 11120730]
18. Ernst E, Harkness E. Spinal manipulation: a systematic review of sham-controlled, double-blind, randomized clinical trials. *J Pain Symptom Manage*. 2001;22:879-89. [PMID: 11576805]
19. Koes BW, van Tulder MW, Ostelo R, Kim Burton A, Waddell G. Clinical guidelines for the management of low back pain in primary care: an international comparison. *Spine*. 2001;26:2504-13; discussion 2513-4. [PMID: 11707719]
20. van Tulder MW, Assendelft WJ, Koes BW, Bouter LM. Method guidelines for systematic reviews in the Cochrane Collaboration Back Review Group for Spinal Disorders [Editorial]. *Spine*. 1997;22:2323-30. [PMID: 9355211]
21. Lau J, Ioannidis JP, Schmid CH. Quantitative synthesis in systematic reviews. *Ann Intern Med*. 1997;127:820-6. [PMID: 9382404]
22. Gregoire G, Derderian F, Le Lorier J. Selecting the language of the publications included in a meta-analysis: is there a Tower of Babel bias? *J Clin Epidemiol*. 1995;48:159-63. [PMID: 7853041]
23. Moher D, Fortin P, Jadad AR, Juni P, Klassen T, Le Lorier J, et al. Completeness of reporting of trials published in languages other than English: implications for conduct and reporting of systematic reviews. *Lancet*. 1996;347:363-6. [PMID: 8598702]
24. Dickersin K, Larson K. Optimal search strategy for RCTs. From establishing and maintaining an international register of RCTs. In: *The Cochrane Library*. Oxford: Update Software; 1996.
25. Hunt DL, McKibbin KA. Locating and appraising systematic reviews. *Ann Intern Med*. 1997;126:532-8. [PMID: 9092319]
26. Deyo RA, Andersson G, Bombardier C, Cherkin DC, Keller RB, Lee CK, et al. Outcome measures for studying patients with low back pain. *Spine*. 1994;19:2032S-2036S. [PMID: 7801179]
27. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials*. 1996;17:1-12. [PMID: 8721797]
28. Moher D, Pham B, Jones A, Cook DJ, Jadad AR, Moher M, et al. Does quality of reports of randomised trials affect estimates of intervention efficacy reported in meta-analyses? *Lancet*. 1998;352:609-13. [PMID: 9746022]
29. Hedges LV, Olkin I. *Statistical Methods for Meta-Analysis*. San Diego, CA: Academic Pr; 1985.
30. Rosenthal R. *Meta-Analytic Procedures for Social Research*. Newbury Park: Sage Publications; 1991.
31. Hedges LV, Olkin I. Nonparametric estimators of effect size in meta-analysis. *Psychol Bull*. 1984;96:573-80.

32. Mood AM, Graybill FA, Boes DC. Introduction to the Theory of Statistics. London: McGraw-Hill; 1974.
33. Berkey CS, Hoaglin DC, Mosteller F, Colditz GA. A random-effects regression model for meta-analysis. *Stat Med*. 1995;14:395-411. [PMID: 7746979]
34. Stata Statistical Software Manual. College Station, TX: Stata Corp.; 1999.
35. SAS/STAT Software Manual. Cary, NC: SAS Institute, Inc.; 1999.
36. Begg CB, Mazumdar M. Operating characteristics of a rank correlation test for publication bias. *Biometrics*. 1994;50:1088-101. [PMID: 7786990]
37. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315:629-34. [PMID: 9310563]
38. Cherkin DC, Wheeler KJ, Barlow W, Deyo RA. Medication use for low back pain in primary care. *Spine*. 1998;23:607-14. [PMID: 9530793]
39. Meade TW, Dyer S, Browne W, Townsend J, Frank AO. Low back pain of mechanical origin: randomised comparison of chiropractic and hospital outpatient treatment. *BMJ*. 1990;300:1431-7. [PMID: 2143092]
40. van Tulder M, Koes B. Low back pain and sciatica. In: Barton SW, ed. *Clinical Evidence*. London: BMJ Publishing Group; 2002.
41. Glover JR, Morris JG, Khosla T. Back pain: a randomized clinical trial of rotational manipulation of the trunk. *Br J Ind Med*. 1974;31:59-64. [PMID: 4274488]
42. Doran DM, Newell DJ. Manipulation in treatment of low back pain: a multicentre study. *Br Med J*. 1975;2:161-4. [PMID: 123815]
43. Bergquist-Ullman M, Larsson U. Acute low back pain in industry. A controlled prospective study with special reference to therapy and confounding factors. *Acta Orthop Scand*. 1977;1:117. [PMID: 146394]
44. Evans DP, Burke MS, Lloyd KN, Roberts EE, Roberts GM. Lumbar spinal manipulation on trial. Part I—clinical assessment. *Rheumatol Rehabil*. 1978;17:46-53. [PMID: 153574]
45. Sims-Williams H, Jayson MI, Young SM, Baddeley H, Collins E. Controlled trial of mobilisation and manipulation for patients with low back pain in general practice. *Br Med J*. 1978;2:1338-40. [PMID: 152663]
46. Rasmussen GG. Manipulation in treatment of low back pain: a randomized clinical trial. *Manuelle Medizin*. 1979;1:8-10.
47. Sims-Williams H, Jayson MI, Young SM, Baddeley H, Collins E. Controlled trial of mobilisation and manipulation for low back pain: hospital patients. *Br Med J*. 1979;2:1318-20. [PMID: 160266]
48. Coxhead CE, Inskip H, Meade TW, North WR, Troup JD. Multicentre trial of physiotherapy in the management of sciatic symptoms. *Lancet*. 1981;1:1065-8. [PMID: 6112444]
49. Hoehler FK, Tobis JS, Buerger AA. Spinal manipulation for low back pain. *JAMA*. 1981;245:1835-8. [PMID: 6453240]
50. Buerger AA. A controlled trial of rotational manipulation in low back pain. *Manuelle Medizin*. 1980;2:17-26.
51. Tobis JS, Hoehler FK. Musculoskeletal manipulation in the treatment of low back pain. *Bull N Y Acad Med*. 1983;59:660-8. [PMID: 6226331]
52. Zylbergold RS, Piper MC. Lumbar disc disease: comparative analysis of physical therapy treatments. *Arch Phys Med Rehabil*. 1981;62:176-9. [PMID: 6453571]
53. Farrell JP, Twomey LT. Acute low back pain. Comparison of two conservative treatment approaches. *Med J Aust*. 1982;1:160-4. [PMID: 6210835]
54. Godfrey CM, Morgan PP, Schatzker J. A randomized trial of manipulation for low-back pain in a medical setting. *Spine*. 1984;9:301-4. [PMID: 6233718]
55. Gibson T, Grahame R, Harkness J, Woo P, Blagrove P, Hills R. Controlled comparison of short-wave diathermy treatment with osteopathic treatment in non-specific low back pain. *Lancet*. 1985;1:1258-61. [PMID: 2860453]
56. Waterworth RF, Hunter IA. An open study of diflunisal, conservative and manipulative therapy in the management of acute mechanical low back pain. *N Z Med J*. 1985;98:372-5. [PMID: 3157894]
57. Waagen GN, Haldeman S, Cook G, Lopez D, DeBoer KF. Short term trial of chiropractic adjustments for the relief of chronic low back pain. *Manual Medicine*. 1986;2:63-7.
58. Hadler NM, Curtis P, Gillings DB, Stinnett S. A benefit of spinal manipulation as adjunctive therapy for acute low-back pain: a stratified controlled trial. *Spine*. 1987;12:702-6. [PMID: 2961085]
59. Hadler NM, Curtis P, Gillings DB, Stinnett S. Der Nutzen von Manipulationen als zusätzliche Therapie bei akuten Lumbalgie: eine gruppenkontrollierte Studie. *Manuelle Medizin*. 1990;28:2-6.
60. Mathews JA, Mills SB, Jenkins VM, Grimes SM, Morkel MJ, Mathews W, et al. Back pain and sciatica: controlled trials of manipulation, traction, sclerosant and epidural injections. *Br J Rheumatol*. 1987;26:416-23. [PMID: 2961394]
61. Ongley MJ, Klein RG, Dorman TA, Eek BC, Hubert LJ. A new approach to the treatment of chronic low back pain. *Lancet*. 1987;2:143-6. [PMID: 2439856]
62. Postacchini F, Facchini M, Palieri P. Efficacy of various forms of conservative treatment in low back pain: a comparative study. *Neuro-Orthopedics*. 1988;6:28-35.
63. Kinalski R, Kuwik W, Pietrzak D. The comparison of the results of manual therapy versus physiotherapy methods used in treatment of patients with low back pain syndromes. *Journal of Manual Medicine*. 1989;4:44-6.
64. Bronfort G. Chiropractic versus general medical treatment of low back pain: a small scale controlled clinical trial. *Am J Chiropractic Med*. 1989;2:145-50.
65. MacDonald RS, Bell CM. An open controlled assessment of osteopathic manipulation in nonspecific low-back pain. *Spine*. 1990;15:364-70. [PMID: 2141951]
66. Herzog W, Conway PJ, Willcox BJ. Effects of different treatment modalities on gait symmetry and clinical measures for sacroiliac joint patients. *J Manipulative Physiol Ther*. 1991;14:104-9. [PMID: 1826920]
67. Koes BW, Bouter LM, van Mameren H, Essers AH, Verstegen GM, Hofhuizen DM, et al. Randomised clinical trial of manipulative therapy and physiotherapy for persistent back and neck complaints: results of one year follow up. *BMJ*. 1992;304:601-5. [PMID: 1532760]
68. Koes BW, Bouter LM, van Mameren H, Essers AH, Verstegen GM, Hofhuizen DM, et al. A blinded randomized clinical trial of manual therapy and physiotherapy for chronic back and neck complaints: physical outcome measures. *J Manipulative Physiol Ther*. 1992;15:16-23. [PMID: 1531487]
69. Koes BW, Bouter LM, van Mameren H, Essers AH, Verstegen GM, Hofhuizen DM, et al. The effectiveness of manual therapy, physiotherapy, and treatment by the general practitioner for nonspecific back and neck complaints. A randomized clinical trial. *Spine*. 1992;17:28-35. [PMID: 1531552]
70. Koes BW, Bouter LM, van Mameren H, Essers AH, Verstegen GJ, Hofhuizen DM, et al. A randomized clinical trial of manual therapy and physiotherapy for persistent back and neck complaints: subgroup analysis and relationship between outcome measures. *J Manipulative Physiol Ther*. 1993;16:211-9. [PMID: 8340715]
71. Hsieh CY, Phillips RB, Adams AH, Pope MH. Functional outcomes of low back pain: comparison of four treatment groups in a randomized controlled trial. *J Manipulative Physiol Ther*. 1992;15:4-9. [PMID: 1531488]
72. Pope MH, Phillips RB, Haugh LD, Hsieh CY, MacDonald L, Haldeman S. A prospective randomized three-week trial of spinal manipulation, transcutaneous muscle stimulation, massage and corset in the treatment of subacute low back pain. *Spine*. 1994;19:2571-7. [PMID: 7855683]
73. Wreje U, Nordgren B, Aberg H. Treatment of pelvic joint dysfunction in primary care—a controlled study. *Scand J Prim Health Care*. 1992;10:310-5. [PMID: 1480873]
74. Cramer GD, Humphreys CR, Hondras MA, McGregor M, Triano JJ. The Hmax/Mmax ratio as an outcome measure for acute low back pain. *J Manipulative Physiol Ther*. 1993;16:7-13. [PMID: 8423429]
75. Delitto A, Cibulka MT, Erhard RE, Bowling RW, Tenhula JA. Evidence for use of an extension-mobilization category in acute low back syndrome: a prescriptive validation pilot study. *Phys Ther*. 1993;73:216-22; discussion 223-8. [PMID: 8456141]
76. Erhard RE, Delitto A, Cibulka MT. Relative effectiveness of an extension program and a combined program of manipulation and flexion and extension exercises in patients with acute low back syndrome. *Phys Ther*. 1994;74:1093-100. [PMID: 7991650]
77. Timm KE. A randomized-control study of active and passive treatments for chronic low back pain following L5 laminectomy. *J Orthop Sports Phys Ther*. 1994;20:276-86. [PMID: 7849747]
78. Meade TW, Dyer S, Browne W, Frank AO. Randomised comparison of chiropractic and hospital outpatient management for low back pain: results from extended follow up. *BMJ*. 1995;311:349-51. [PMID: 7640538]
79. Triano JJ, McGregor M, Hondras MA, Brennan PC. Manipulative therapy versus education programs in chronic low back pain. *Spine*. 1995;20:948-55.

[PMID: 7644961]

80. Bronfort G, Goldsmith CH, Nelson CF, Boline PD, Anderson AV. Trunk exercise combined with spinal manipulative or NSAID therapy for chronic low back pain: a randomized, observer-blinded clinical trial. *J Manipulative Physiol Ther.* 1996;19:570-82. [PMID: 8976475]
81. Hemmilä HM, Keinänen-Kiukaanniemi SM, Levoska S, Puska P. Does folk medicine work? A randomized clinical trial on patients with prolonged back pain. *Arch Phys Med Rehabil.* 1997;78:571-7. [PMID: 9196462]
82. Rupert RL, Ezzeldin MT. Chiropractic adjustments: results of a controlled clinical trial in Egypt. *ICA International Review of Chiropractic.* 1985;winter:58-60.
83. Moher D, Cook DJ, Eastwood S, Olkin I, Rennie D, Stroup DF. Improving the quality of reports of meta-analyses of randomised controlled trials: the QUOROM statement. Quality of Reporting of Meta-analyses. *Lancet.* 1999;354:1896-900. [PMID: 10584742]
84. Arkuszewski Z. The efficacy of manual treatment in low back pain: a clinical trial. *Manual Medicine.* 1986;2:68-71.
85. Brennan PC, Graham MA, Triano JJ, Hondras MA, Anderson RJ. Lymphocyte profiles in patients with chronic low back pain enrolled in a clinical trial. *J Manipulative Physiol Ther.* 1994;17:219-27. [PMID: 8046277]
86. Cibulka MT, Delitto A, Koldehoff RM. Changes in innominate tilt after manipulation of the sacroiliac joint in patients with low back pain. An experimental study. *Phys Ther.* 1988;68:1359-63. [PMID: 2971233]
87. Côté P, Mior SA, Vernon H. The short-term effect of a spinal manipulation on pain/pressure threshold in patients with chronic mechanical low back pain. *J Manipulative Physiol Ther.* 1994;17:364-8. [PMID: 7964196]
88. Coyer AB, Curwin I. Low back pain treated by manipulation. *BMJ.* 1955;1:705-7.
89. Ellestad SM, Nagle RV, Boesler DR, Kilmore MA. Elektromyographische und Hautwiderstandsreaktionen auf die osteopathische manipulative Behandlung des Kreuzschmerzes. *Manuelle Medizin.* 1990;28:7-12.
90. Ellestad SM, Nagle RV, Boesler DR, Kilmore MA. Electromyographic and skin resistance responses to osteopathic manipulative treatment for low-back pain. *J Am Osteopath Assoc.* 1988;88:991-7. [PMID: 2975645]
91. Gemmill HA, Jacobson BH. The immediate effect of activator vs. meric adjustment on acute low back pain: a randomized controlled trial. *J Manipulative Physiol Ther.* 1995;18:453-6. [PMID: 8568427]
92. Gibson H, Ross J, Allen J, Latimer J, Maher C. The effect of mobilization on forward bending range. *J Manual Manipulative Therapy.* 1993;1:142-7.
93. Gilbert JR, Taylor DW, Hildebrand A, Evans C. Clinical trial of common treatments for low back pain in family practice. *Br Med J (Clin Res Ed).* 1985;291:791-4. [PMID: 2931153]
94. Haas M, Panzer D, Peterson D, Raphael R. Short-term responsiveness of manual thoracic end-play assessment to spinal manipulation: a randomized controlled trial of construct validity. *J Manipulative Physiol Ther.* 1995;18:582-9. [PMID: 8775019]
95. Helliwell PS, Cunliffe G. Manipulation in low back pain. *The Physician.* 1987;187-8.
96. Indahl A, Velund L, Reikeraas O. Good prognosis for low back pain when left untampered. A randomized clinical trial. *Spine.* 1995;20:473-7. [PMID: 7747232]
97. Khalil TM, Asfour SS, Martinez LM, Waly SM, Rosomoff RS, Rosomoff HL. Stretching in the rehabilitation of low-back pain patients. *Spine.* 1992;17:311-7. [PMID: 1533060]
98. Kokjohn K, Schmid DM, Triano JJ, Brennan PC. The effect of spinal manipulation on pain and prostaglandin levels in women with primary dysmenorrhea. *J Manipulative Physiol Ther.* 1992;15:279-85. [PMID: 1535359]
99. Nwuga VC. Relative therapeutic efficacy of vertebral manipulation and conventional treatment in back pain management. *Am J Phys Med.* 1982;61:273-8. [PMID: 6216814]
100. Petty NJ. The effect of posteroanterior mobilisation on sagittal mobility of the lumbar spine. *Man Ther.* 2000;1:25-9. [PMID: 11327791]
101. Sanders GE, Reinert O, Tepe R, Maloney P. Chiropractic adjustive manipulation on subjects with acute low back pain: visual analog pain scores and plasma beta-endorphin levels. *J Manipulative Physiol Ther.* 1990;13:391-5. [PMID: 2145384]
102. Siehl D, Olson DR, Ross HE, Rockwood EE. Manipulation of the lumbar spine with the patient under general anesthesia: evaluation by electromyography and clinical-neurologic examination of its use for lumbar nerve root compression syndrome. *J Am Osteopath Assoc.* 1971;70:433-40. [PMID: 5203536]
103. Terrett AC, Vernon H. Manipulation and pain tolerance. A controlled study of the effect of spinal manipulation on paraspinal cutaneous pain tolerance levels. *Am J Phys Med.* 1984;63:217-25. [PMID: 6486245]
104. Ottenbacher K, DiFabio RP. Efficacy of spinal manipulation/mobilization therapy. A meta-analysis. *Spine.* 1985;10:833-7. [PMID: 2935951]
105. DiFabio RP. Efficacy of manual therapy. *Physical Therapy.* 1992;72:853-64.
106. Anderson R, Meeker WC, Wirrick BE, Mootz RD, Kirk DH, Adams A. A meta-analysis of clinical trials of spinal manipulation. *J Manipulative Physiol Ther.* 1992;15:181-94. [PMID: 1533416]
107. Assendelft WJ, Koes BW, van der Heijden GJ, Bouter LM. The effectiveness of chiropractic for treatment of low back pain: an update and attempt at statistical pooling. *J Manipulative Physiol Ther.* 1996;19:499-507. [PMID: 8902660]
108. van Tulder MW, Koes BW, Bouter LM. Conservative treatment of acute and chronic nonspecific low back pain. A systematic review of randomized controlled trials of the most common interventions. *Spine.* 1997;22:2128-56. [PMID: 9322325]
109. Bronfort G. Efficacy of manual therapies of the spine [thesis]. Amsterdam: Instituut voor Extramuraal Geneeskundig Onderzoek;1997.
110. van der Weide WE, Verbeek JH, van Tulder MW. Vocational outcome of intervention for low-back pain. *Scand J Work Environ Health.* 1997;23:165-78. [PMID: 9243726]
111. Scheer SJ, Watanabe TK, Radack KL. Randomized controlled trials in industrial low back pain. Part 3. Subacute/chronic pain interventions. *Arch Phys Med Rehabil.* 1997;78:414-23. [PMID: 9111463]
112. Scheer SJ, Radack KL, O'Brien DR Jr. Randomized controlled trials in industrial low back pain relating to return to work. Part 1. Acute interventions. *Arch Phys Med Rehabil.* 1995;76:966-73. [PMID: 7487440]
113. Ferreira ML, Ferreira PH, Latimer J, Herbert R, Maher CG. Does spinal manipulative therapy help people with chronic low back pain? *Aust J Physiother.* 2002;48:277-84. [PMID: 12443522]
114. Pengel HM, Maher CG, Refshauge KM. Systematic review of conservative interventions for subacute low back pain. *Clin Rehabil.* 2002;16:811-20. [PMID: 12501942]
115. Juni P, Altman DG, Egger M. Systematic reviews in health care: Assessing the quality of controlled clinical trials. *BMJ.* 2001;323:42-6. [PMID: 11440947]
116. Sterne JA, Gavaghan D, Egger M. Publication and related bias in meta-analysis: power of statistical tests and prevalence in the literature. *J Clin Epidemiol.* 2000;53:1119-29. [PMID: 11106885]
117. McAuley L, Pham B, Tugwell P, Moher D. Does the inclusion of grey literature influence estimates of intervention effectiveness reported in meta-analyses? *Lancet.* 2000;356:1228-31. [PMID: 11072941]

APPENDIX: DETAILED METHODS OF ANALYSIS

Effect Size Calculations

Within each study, effect sizes were calculated for each alternative therapy group relative to the spinal manipulative therapy group in the study. The calculations were done separately for the four outcomes: short-term pain, short-term function, long-term pain, and long-term function. Both continuous and dichotomous outcomes were transformed into comparable effect sizes, as described in the following sections.

Effect Size Calculations for Continuous Outcomes

For each study, the means and standard deviations of each outcome for each alternative therapy group and spinal manipulative therapy group were extracted, if available. In the 4 studies that reported the median instead of the mean, we assumed that the median equaled the mean. For the 12 studies that reported a range of observed values or did not report a measure of variation, a standard deviation of 0.25 of the theoretical range for the specific measure was assumed; for example, the theoretical range was 0 to 100 for the visual analogue scale (VAS) and 0 to 24 for the Roland Disability Questionnaire (RDQ).

For each treatment and spinal manipulative therapy comparison, an unbiased estimate (29) of Hedges' g effect size (30) and a 95% CI were calculated. A positive effect size indicated that spinal manipulative therapy was beneficial, that is, it increased function or decreased pain as compared with the alternative therapy.

Effect Size Calculations for Dichotomous Outcomes

Effect sizes were calculated by using the Kraemer and Andrews estimator (31), which uses the inverse normal cumulative distribution function to transform from a dichotomous to continuous scale. Associated 95% CIs were constructed by using the Delta method (32). A positive effect size may be interpreted as discussed earlier.

Statistical Analysis

If both a continuous and dichotomous outcome were available for an outcome, only the continuous outcome was included in the primary analysis. For each outcome, we assessed the degree of heterogeneity in all effect sizes within each back pain stratum via a forest plot and chi-square test (29). We fit models to predict effect size by using random-effects meta-regression (33) in Stata statistical software, version 6.0 (Stata Corp., College Station, Texas) (34), via the procedure called *metareg*; restricted maximum likelihood was used to estimate the between-study variation.

For each outcome separately, four models were fit. Each model contained main effects for duration of back pain (chronic, acute, mixed, or unsure) as well as a particular parameterization of the treatment effect. The treatment variables in the four models were: overall alternative therapy effect only; sham versus other alternative therapies; alternative therapy clusters (sham; conventional general practitioner care or analgesic; physical therapy or exercise; traction, corset, bed rest, home care, topical gel, no treatment, diathermy, or minimal massage; and back school); and all alternative therapies as separate individual variables.

We examine the alternative therapy clusters model for short-

term pain as an example. To compare the effect of spinal manipulative therapy with sham therapy in patients with acute back pain, for example, the model combines the main effect for sham therapy with the main effect for patients with acute back pain. The modeling approach allows us to borrow strength across all effect sizes that involve sham therapy or patients with acute back pain to estimate the treatment effect. We chose the alternative therapy cluster parameterization as our primary model because it allowed the most detailed examination of the alternative therapies, given sample size constraints. For this model, we tested specific interactions, such as the interaction between duration of back pain and alternative therapy; none were found to be significant. Therefore, we believe a main-effects model is warranted. We also tested whether adjustments for the presence of leg pain (sciatica) or profession of manipulator influenced the effect; neither did. We did fit a reduced model that examined effect of provider by combining across outcome domains and developing models for patients with acute and chronic low back pain separately.

We conducted three sensitivity analyses that consisted of determining whether our results were consistent for three subgroups of studies. The three subgroups were as follows: studies that used manipulation alone instead of combining it with other therapies, studies that had continuous outcomes, and studies that had dichotomous outcomes only. All sensitivity analysis results were comparable to the primary analysis results.

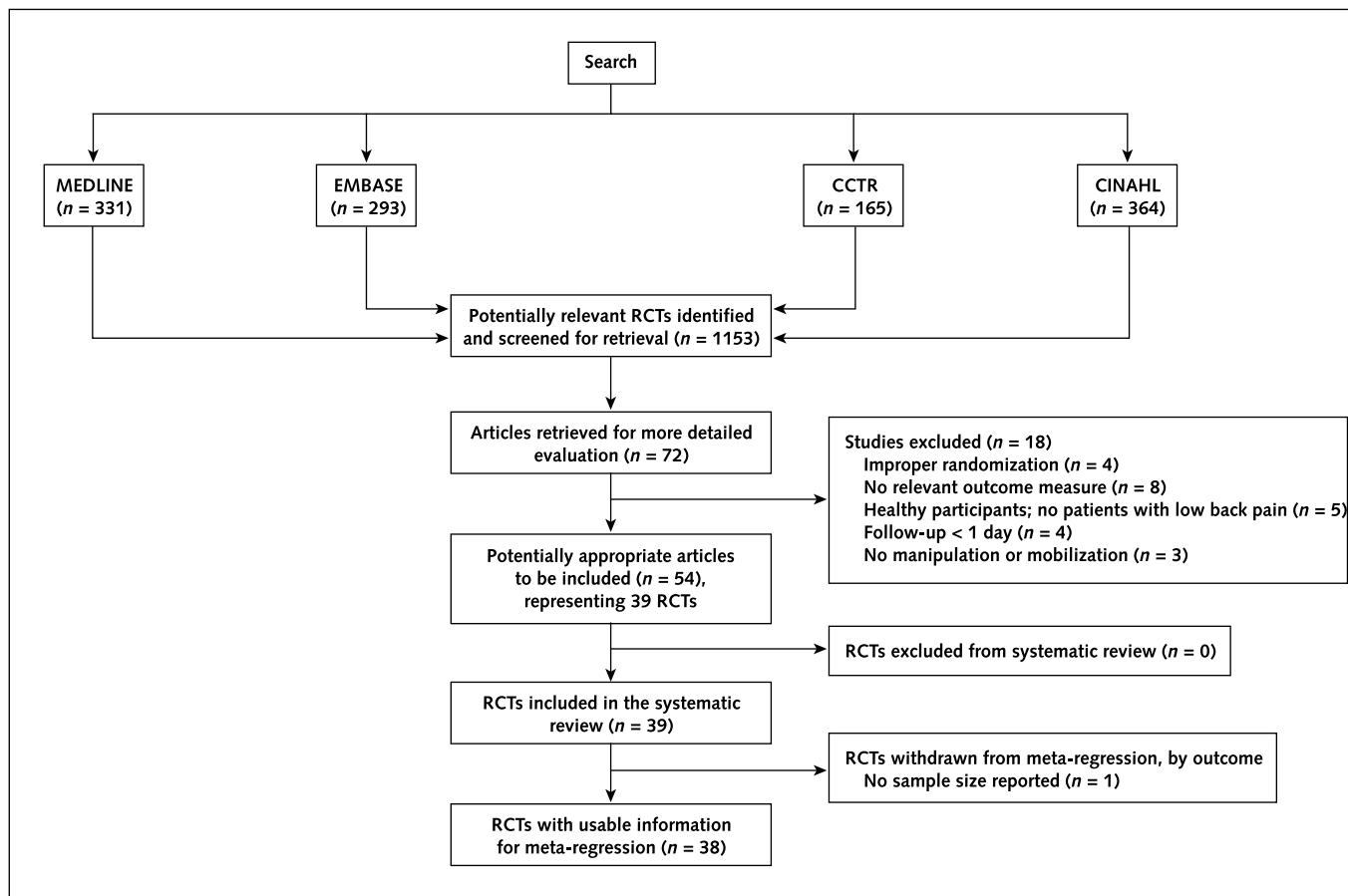
If a study has more than one comparison group, it can contribute more than one effect size to the analysis. Effect sizes from the same study may be correlated because they are based on comparison to the same group of patients receiving spinal manipulative therapy. We conducted a sensitivity analysis to assess the possible effect of this correlation between effect sizes from the same study. In this sensitivity analysis, we added another level of random effects at the comparison level to our model in addition to the random effects already included at the study level. These additional random effects control for the correlation between effect sizes in a single study. We fit this model in SAS PROC MIXED statistical software, version 8.0 (SAS Institute, Inc., Cary, North Carolina) (35). The results from this sensitivity analysis were comparable to those from the primary analysis.

We present all effect sizes back-translated into clinically relevant values by using the 100-mm VAS scale for pain and the RDQ for function (assuming a standard deviation of 25 for the VAS and 6 for the RDQ). Results are presented for each combination of treatment and duration level, except those for which no data were observed.

Publication Bias

For each outcome, we graphically evaluated a funnel plot of the effect sizes for asymmetry resulting from the nonpublication of small, negative studies. Because graphical evaluation can be subjective, we also conducted an adjusted rank-correlation test (36) and a regression asymmetry test (37) to serve as formal statistical tests for publication bias. We drew these graphs and conducted these tests by using Stata statistical software, version 6.0 (34).

Appendix Figure. Flow chart of selected studies (based on the Quality of Reporting of Meta-Analysis [QUOROM] format).



From Moher et al. (83). Excluded studies ($n = 18$) could be excluded for more than one reason. CCTR = Cochrane Controlled Trials Register; RCT = randomized, controlled trial.

Appendix Table 1. Extended Evidence Table of Included Studies*

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Scores†	Modified Jadad List	Pure Jadad List
Glover et al. (41), 1974	Work medical center; duration of LBP not specified; radiation pattern not specified	Standardized co-intervention (served as placebo): de-tuned diathermy for 4 consecutive days I: Rotational manipulation by first author; profession of manipulator unclear (<i>n</i> = 43) R: No treatment (<i>n</i> = 41)	Pain (% relief); global improvement (3-point scale) (not reported); pressure pain (algometer) (not reported); straight-leg raising (degrees) (not reported) Follow-up: 3 days, 7 days; results of 1-month follow-up not reported	V1 + V2 + V3 – V4 + V5 – V6 – V7 + V8 + V9 + V10 – Total‡ 6	3	3
Doran and Newell (42), 1975	Hospital setting; acute, sub-acute, and chronic LBP; no radiation below knee	Standardized co-interventions: paracetamol, 2 tablets every 4 hours, as necessary, and postural advice I: Manipulation and mobilization at discretion of manipulator; profession of manipulator unclear (<i>n</i> = 98 at 3-week follow-up); number of treatments = average, 6.0; minimum, 2/week R1: Physiotherapy, according to usual practice, without manipulation (<i>n</i> = 104 at 3-week follow-up); number of treatments = average, 7.3; minimum, 2/week R2: Corset (type determined by hospital (<i>n</i> = 93 at 3-week follow-up) R3: No treatment (except standardized co-interventions)	Global improvement (6-point scale); spinal mobility (inspection) Follow-up: 3 weeks, 6 weeks, 3 months, 1 year	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 + V8 – V9 + V10 + Total 4	2	2
Bergquist-Ullman and Larsson (43), 1977	Industry; acute and subacute LBP (<8 weeks); no radiation below knee	I: Manipulation and mobilization according to Cyriax, Kaltenborn, Lewit, and Janda by PT; co-interventions: postural advice and strengthening exercises (<i>n</i> = 72); number of treatments = average, 4; maximum, 10 R1: Instructions and exercises (<i>n</i> = 70); number of treatments = 4 (in 2 weeks) R2: Placebo short waves (<i>n</i> = 75); number of treatments = average, 5; maximum, 10	Pain (pain index: range, 0–70); functional status (10 items, 4-point scale); spinal mobility (modified Schober); absenteeism (patient and insurance) Follow-up: 10 days, 3 weeks, 6 weeks, 1 year	V1 + V2 ? V3 – V4 – V5 – V6 – V7 ? V8 + V9 – V10 + Total 3	2	2
Evans et al. (44), 1978	Setting unclear; most likely hospital referrals; subacute and chronic LBP (>3 weeks); probably with and without radiation below knee	Standardized co-intervention; codeine phosphate, two 16-mg capsules, as necessary I: Rotational thrust manipulation to both sides by MD (<i>n</i> = 15 at 3-week follow-up); number of treatments = 3 (on weekly interval) R: No treatment (<i>n</i> = 17 at 3-week follow-up)	Pain (4-point scale); global improvement (4-point scale); spinal mobility (centimeters) Follow-up: 1, 2, and 3 weeks Crossover design, possible carry-over effect; therefore, only first 3 weeks results used in review	V1 + V2 ? V3 – V4 + V5 – V6 – V7 + V8 + V9 + V10 ? Total 5	2	2

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Score†	Modified Jadad List	Pure Jadad List
Sims-Williams et al. (45), 1978	General practice; duration unclear; radiation pattern unclear	I: Manipulation and mobilization according to Maitland by PT; co-interventions: traction, exercises, heat (<i>n</i> = 40 at 3-month follow-up); treatment = 5 during week 1 and then 3/week for 3 weeks; total number of treatments = 14 R: Detuned diathermy by PT (<i>n</i> = 43 at 3-month follow-up); treatment = 5 during week 1 and then 3/week for 3 weeks; total number of treatments = 14	Pain (6-point scale); spinal mobility (degrees); absenteeism (questionnaire) Follow-up: 1, 3, and 12 months	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 + V8 + V9 + V10 + Total 5	1	1
Rasmussen (46), 1979	Outpatient department; acute LBP; no radiation below knee	I: Rotational manipulation in pain-free direction by PT (<i>n</i> = 12 at follow-up) R: Short-wave diathermy (<i>n</i> = 12 at follow-up); number of treatments = 6 (3/week)	Pain (dichotomous); generic functional status (dichotomous); spinal mobility (Schober, dichotomous); absenteeism (not reported) Follow-up: 2 weeks	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 ? V8 + V9 + V10 + Total 4	2	2
Sims-Williams et al. (47), 1979	Outpatient department; duration unclear; radiation pattern unclear	I: Manipulation and mobilization according to Maitland by PT; co-interventions: traction, exercises, heat (<i>n</i> = 42 at 3-month follow-up); treatment = daily for 1 week and then 3/week for 3 weeks; total number of treatments = 14 R: Detuned diathermy by PT (<i>n</i> = 40 at 3-month follow-up); treatment = daily for 1 week and then 3/week for 3 weeks; total number of treatments = 14	Pain (6-point scale); spinal mobility (degrees); absenteeism (questionnaire) Follow-up: 1, 3, and 12 months	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 + V8 + V9 + V10 + Total 5	1	1

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Scores†	Modified Jadad List	Pure Jadad List
Coxhead et al. (48), 1981	Hospital outpatient department; duration of symptoms not specified; with and without radiation below knee	Factorial design: 4 interventions (I, R1, R2, R3), each yes or no, resulting in 16 combinations; numbers at randomization not given; each intervention given to half of randomly assigned patients (approximately $1/2 \times 334 = 167$) Standardized co-interventions: short-wave diathermy and 1/2-hour back school Frequency of treatment for all patients: daily for first week, decreasing frequency for next 3 weeks I: Manipulation according to Maitland by PT; average number of treatments = unclear R1: Traction, motor-driven Tru-Trac; average number of treatments = unclear R2: Exercises; average number of treatments = unclear R3: Corset, ready-made fabric	Pain (VAS); global improvement (3-point scale); absenteeism (% patients); medical consumption (% patients) Follow-up: 4 weeks, 4 months, and 16 months	V1 + V2 ? V3 - V4 4 V5 - V6 - V7 ? V8 + V9 + V10 + Total 5	3	3
Hoehler et al. (49–51), 1981	Hospital; acute, subacute, and chronic LBP; radiation pattern not specified	I: Rotational manipulation ($n = 56$); profession of manipulator unclear; number of treatments = not specified R: Soft tissue massage ($n = 39$); number of treatments = not specified	Pain (% very severe pain); spinal mobility (fingertip–floor); straight-leg raising (degrees) Follow-up: at discharge (timing unclear), 3 weeks after discharge (timing unclear)	V1 + V2 ? V3 - V4 ? V5 - V6 + V7 + V8 - V9 ? V10 ? Total 3	3	1
Zylbergold and Piper (52), 1981	Physiotherapy outpatient department; duration of symptoms not specified; no radiation below knee	I: Rotational mobilization by PT ($n = 8$); number of treatments = 8 (2/week) R1: Physiotherapy (moist heat, flexion exercises, home exercises) ($n = 10$); number of treatments = 4–6 (2–3/week for 2 weeks) R2: Home care (instructions, exercises) ($n = 10$); number of treatments = 4–6 (2–3/week for 2 weeks)	Pain (5-point scale); back pain-specific functional status (8 items, 5-point scale); spinal mobility (centimeters) Follow-up: 1 month	V1 + V2 ? V3 - V4 ? V5 ? V6 - V7 ? V8 ? V9 + V10 + Total 3	1	1
Farrell and Twomey (53), 1982	Setting unclear, acute LBP; radiation pattern unclear, but no neurologic signs	I: Manipulation and mobilization according to Stoddard and Maitland by PT ($n = 24$); treatment = 3/week for maximum of 3 weeks; number of treatments = average, 3.5 R: Microwave for 15 minutes and exercise ($n = 24$); treatment = 3/week for maximum of 3 weeks; number of treatments = average, 5.8	Pain (VAS); back pain-specific functional status (Bergquist-Ullman); spinal mobility (goniometer) Follow-up: 1 and 3 weeks	V1 + V2 ? V3 - V4 + V5 - V6 - V7 ? V8 + V9 + V10 + Total 5	1	1

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Score†	Modified Jadad List	Pure Jadad List
Godfrey et al. (54), 1984	Patients referred from primary care; acute LBP (<2 weeks); radiation pattern not specified	I: Rotational manipulation according to Maigne by DC or MD; co-intervention; soft tissue massage (n = 48); number of treatments = unclear R: Light massage by kin-ologist or faradic current (n = 42); number of treatments = unclear; if no improvement after treatment (n = 5), manipulation was performed	Pain (composite scale with pain, stiffness, and tenderness) (5-point scale); generic functional status (10 items); spinal mobility (fingertip–floor) Follow-up: 2 weeks; incomplete follow-up at 3 weeks (results not reported)	V1 + V2 ? V3 – V4 + V5 – V6 + V7 + V8 – V9 + V10 5 Total –	2	2
Gibson et al. (55), 1985	Hospital outpatient department; subacute and chronic LBP (>2 months); radiation pattern unclear	I: Manipulation and mobilization by DO (n = 41); number of treatments = 4 (on weekly interval) R1: Short-wave diathermy (n = 34); number of treatments = 12 (3/week for 4 weeks) R2: Detuned short-wave diathermy (n = 34); number of treatments = 12 (3/week for 4 weeks)	Pain (VAS); spinal mobility (centimeters); analgesic use (% patients); absenteeism (% patients) Follow-up: 2, 4, and 12 weeks	V1 + V2 ? V3 – V4 + V5 – V6 – V7 + V8 + V9 + V10 + Total 6	2	2
Waterworth and Hunter (56), 1985	General practice; acute LBP (<4 weeks); no radiation below knee	Standardized co-intervention: instructions I: Manipulation by PT; co-intervention: McKenzie exercise therapy (n = 40); number of treatments = 10 (daily for maximum of 2 weeks) R1: Difflusinal, 500 mg twice daily for 10 days (n = 37)	Pain (4-point scale); global improvement (4-point scale); spinal mobility (4-point scale) Follow-up: 4 and 12 days	V1 + V2 ? V3 – V4 + V5 – V6 – V7 – V8 + V9 + V10 – Total 4	2	2
Rupert and Ezzeldin (82), 1985	Hospital; acute, subacute, and chronic LBP; radiation pattern unclear Subgroup analysis for patients with acute LBP (<4 weeks) and subacute and chronic LBP (>4 weeks)	I: Manipulation by DC (n = ?); Number of treatments = 8 (3/week) R: Sham manipulation (n = ?); Number of treatments = 8 (3/week) R2: Drugs and bed rest (n = ?); Number of visits = 8 (3 treatments/week)	Pain (VAS); spinal mobility (fingertip–floor); straight-leg raising Follow-up: 3 weeks	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 ? V8 ? V9 + V10 ? Total 2	2	1
Waagen et al. (57), 1986	Chiropractic college; subacute and chronic LBP (>3 weeks); no radiation below knee	I: Manipulation by DC (n = 11); number of treatments = 4–6 (2–3/week for 2 weeks) R: Sham manipulation by DC (n = 18); number of treatments = 4–6 (2–3/week for 2 weeks)	Pain (VAS); spinal mobility (standardized scores); straight-leg raising Follow-up: 2 weeks	V1 + V2 – V3 – V4 + V5 – V6 + V7 – V8 + V9 ? V10 5 Total	4	2
Hadler et al. (58, 59), 1987	Primary care; acute LBP (<4 weeks); radiation pattern not specified	I: Long-lever high-velocity thrust manipulation by MD (n = 28); number of treatments = 1 R: Rotational mobilization by MD (n = 26); number of treatments = 1 Contrast is manipulation (I1) versus mobilization (I2)	Global improvement (7-point transition); back pain–specific functional status (Roland-Morris) Follow-up: 3, 6, 9, and 12 days Subgroup analysis: symptoms at <2 weeks and symptoms at 2–4 weeks	V1 + V2 ? V3 – V4 + V5 – V6 + V7 ? V8 + V9 + V10 + Total 6	3	2

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Score†	Modified Jadad List	Pure Jadad List
Mathews et al. (60), 1987	Outpatient department; acute and subacute LBP (<3 months); with and without restricted straight-leg raising	Standardized co-interventions: paracetamol, spinal corset (when indicated), instructions, and advice I: Rotational or thrust manipulation by PT (n = 165); number of treatments = unclear (most likely daily up to 2 weeks) R: Infrared heat (n = 126); number of treatments = unclear (3/week for 15 minutes each)	Pain (6-point scale); straight-leg raising (degrees); analgesic use (pill count) Follow-up: 2 weeks, 3 months, 6 months, 12 months	V1 + V2 ? V3 – V4 + V5 + V6 – V7 + V8 + V9 + V10 – Total 6	2	2
Ongley et al. (61), 1987	Outpatient department, recruitment by advertisement; chronic LBP (>1 year); with and without radiation below knee	Standardized co-interventions: paracetamol and flexion exercises I: Manipulation by MD; co-interventions: first visit, infiltration with lignocaine and triamcinolone followed by injection with proliferant (n = 42); number of treatments = 1 manipulation followed by weekly visits for co-intervention for 5 weeks; total of 6 visits R: Nonforceful manipulation by MD; co-interventions: first visit, infiltration with lignocaine followed by injection with saline (n = 40); number of treatments = 1 sham manipulation followed by weekly visits for co-intervention for 5 weeks; total of 6 visits In index group, potentially strong contribution of co-intervention (corticosteroid injection)	Pain (VAS; back pain-specific functional status (Roland and Waddell); spinal mobility (degrees) Follow-up: 1, 3, and 6 months	V1 + V2 + V3 – V4 – V5 – V6 + V7 + V8 + V9 + V10 + Total 7	4	3

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Score†	Modified Jadad List	Pure Jadad List
Postacchini et al. (62), 1988	Hospital outpatient department; acute (<4 weeks) and chronic (>9 weeks) LBP; with and without radiation below knee	I: Manipulation by chiropractor (<i>n</i> = 87 at follow-up); number of treatments for patients with acute LBP = 11 (daily for first week, then 2/week); number of treatments for patients with chronic back pain = 12 (2/week) R1: Diclophenac "full dose" (<i>n</i> = 81 at follow-up); duration of treatment = 2 weeks R2: Physiotherapy: massage, electrotherapy, infrared, etc. (<i>n</i> = 78 at follow-up); number of treatments = 15 (daily for 3 weeks) R3: Bed rest (<i>n</i> = 29 at follow-up); duration of treatment = 6–8 days R4: Back school (<i>n</i> = 50 at follow-up); number of treatments = 4 in 1 week R5: Placebo gel (<i>n</i> = 73 at follow-up); duration of treatment = 1 or 2 weeks	Pain (4-point scale); back pain-specific functional status (10 items); spinal mobility (fingertip–floor); abdominal muscle strength Follow-up: 3 weeks, 6 weeks, and 6 months Unequal numbers because not all interventions applied on the different patient groups (acute-chronic)	V1 + V2 ? V3 – V4 + V5 – V6 – V7 ? V8 ? V9 + V10 – Total 3	2	2
Kinalski et al. (63), 1989	Rehabilitation center; duration of LBP not specified; radiation pattern not specified	I: Manipulation according to Janda, Lewit, and others; profession of manipulator unclear (<i>n</i> = 61); number of treatments = not specified; duration of treatment = 9.75 days R: Physiotherapy (heat, infrared, traction, interference currents) (<i>n</i> = 50); number of treatments = not specified; duration of treatment = 20.7 days	Pain (4-point scale); spinal mobility (Thomayer sign; 4-point scale); muscle strength (4-point scale) Follow-up: unclear, possibly at end of treatment	V1 + V2 ? V3 – V4 ? V5 ? V6 – V7 ? V8 ? V9 – V10 ? Total 1	1	1
Bronfort (64), 1989	Primary care; acute, subacute, and chronic LBP; with and without radiation below knee	Standardized co-intervention: ergonomic instruction I: Manipulation by DC (<i>n</i> = 10); number of treatments = average, 7.0 R: Medical treatment, including physiotherapy, analgesics, injections, and bedrest (<i>n</i> = 11); number of treatments = average, 7.7	Global measure of improvement (6-point scale); symptoms (% patients), analgesic use (% patients), absenteeism (% patients) Follow-up: 1, 3, and 6 months	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 + V8 + V9 ? V10 + Total 4	2	2
MacDonald and Bell (65), 1990	General practice; acute, subacute, and chronic LBP; radiation pattern unclear	Standardized co-intervention: occupational and posture advice, exercises I: Manipulation by DO (<i>n</i> = 50); number of treatments = unclear (time interval was 2/week) R: Clinic visits (<i>n</i> = 50); number of treatments = unclear	Pain (VAS); back pain-specific functional status (12 items); generic functional status (VAS) Follow-up: weekly for 3 months Subgroup analyses: symptoms at <2 weeks, symptoms at 2–4 weeks, and symptoms at >4 weeks	V1 + V2 ? V3 – V4 + V5 – V6 – V7 ? V8 + V9 + V10 + Total 5	1	1

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Score†	Modified Jadad List	Pure Jadad List
Herzog et al. (66), 1991	Chiropractic college; subacute and chronic LBP (>1 month) (sacroiliac disorder); no radiation below knee	I: Manipulation (sacroiliac) by chiropractor (<i>n</i> = 16 at follow-up); number of treatments = 10 (3/week) R: Back school by PT (<i>n</i> = 13 at follow-up); number of treatments = 10 (3/week)	Pain (VAS); back pain–specific functional status (Oswestry); sacroiliac mobility (Gillet test); gait analysis (scales) Follow-up: 3 weeks	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 + V8 – V9 + V10 – Total 3	2	2
Koes et al. (67–70), 1992	Primary care and advertisement; subacute and chronic LBP; no radiation below knee	I: Manipulation and mobilization according to directives of professional organization and performed by PT; number of treatments = average, 5.4; mean duration of treatment = 8.9 weeks R1: Physiotherapy (exercises, massage, heat, electrotherapy) (<i>n</i> = 66); number of treatments = average, 14.7; mean duration of treatment, 7.8 weeks R2: Detuned diathermy and ultrasonography (<i>n</i> = 64); number of treatments = average, 11.1; mean duration of treatment = 5.8 weeks R3: Visit general practitioner: advice, analgesics, exercises, bed rest, etc. (<i>n</i> = 61); number of treatments = 1	Pain (6-point scale); improvement in main symptom (10-point scale); global improvement (6-point scale); generic functional status (SIP); spinal mobility (degrees) Follow-up: 3, 6, 12, 26, and 52 weeks	V1 + V2 + V3 – V4 + V5 + V6 – V7 + V8 + V9 + V10 + Total 8	3	3
Pope et al. (71, 72), 1992	Chiropractic college; subacute and chronic LBP (3 weeks–6 months); no radiation below knee	I: Manipulation by DC (<i>n</i> = 70); number of treatments = 9 (3/week for 3 weeks) R1: Soft tissue massage (<i>n</i> = 37); number of treatments = 9 (3/week for 3 weeks) R2: Transcutaneous muscle stimulation (<i>n</i> = 28); treatment = 8 hours/day for 3 weeks; number of visits = 3/week R3: Corset (<i>n</i> = 29); duration of treatment = 3 weeks	Pain (VAS); back pain–specific functional status (Oswestry and Roland–Morris); spinal mobility (centimeters); fatigue test; extension force test Follow-up: 3 weeks	V1 + V2 + V3 – V4 ? V5 – V6 – V7 + V8 + V9 + V10 + Total 6	3	3
Wreje et al. (73), 1992	General practice; subacute and chronic LBP (sacroiliac symptoms) (<3 months); no radiation below knee	Standardized co-intervention: paracetamol, information on sick leave I: Sacroiliac mobilization by MD (<i>n</i> = 18 at follow-up); number of treatments = 1 R: Transverse frictions (<i>n</i> = 21 at follow-up); number of treatments = 1	Pain (VAS); absenteeism (days); analgesic use (pill count) Follow-up: 3 weeks	V1 + V2 ? V3 – V4 – V5 – V6 ? V7 ? V8 + V9 + V10 – Total 3	2	2

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Score†	Modified Jadad List	Pure Jadad List
Cramer et al. (74), 1993	Clinic chiropractic college; acute LBP; no radiation below knee	I: Side-lying manipulation by DC; co-interventions included electrical muscle stimulation and cold packs (<i>n</i> = 117); number of treatments = 3–5 in 10 days R: Detuned ultrasound, soft tissue massage, and cold packs by DC (<i>n</i> = 19); number of treatments = 3–5 in 10 days	Pain (VAS); back pain–specific functional status (Oswestry); nerve conduction (H_{max}/M_{max}) Follow-up: unclear, most likely 10 days	V1 + V2 ? V3 – V4 – V5 – V6 – V7 ? V8 + V9 + V10 + Total 4	1	1
Delitto et al. (75), 1993	Physiotherapy department; acute and subacute LBP (<7 weeks); with or without “leg symptoms”; radiation pattern unclear All randomly assigned patients were initially classified as fitting the McKenzie “extension–mobilization” category	I: Sacroiliac joint manipulation at first visit; profession of manipulator unclear; co-intervention: McKenzie extension exercises (<i>n</i> = 14); number of manipulations = 1 (total of 3 visits in 1 week) R: McKenzie flexion exercises (<i>n</i> = 10); number of flexion exercise treatments = 3 visits in 1 week	Back pain–specific functional status (Oswestry) Follow-up: 1 week	V1 + V2 – V3 – V4 – V5 – V6 – V7 ? V8 ? V9 + V10 + Total 3	2	
Blomberg et al. (11–15), 1994	Primary care; acute and subacute LBP (<3 months) with and without radiation below knee	I: Manipulation and mobilization according to Kaltborn, Evjent, and Hamberg by one MD; co-interventions: muscle stretching, auto-traction (15%), steroid injection (54%) (<i>n</i> = 48); number of treatments by MD = average, 2.8; by PT = average, 2.0 R: Standardized conventional activating treatment (many types) by MDs and PTs (<i>n</i> = 53); number of treatments by MD = average, 3.8; by PT = average, 8.6	Pain (VAS); back pain–specific functional status (VAS, 15 questions); generic functional status (VAS, 27 items); spinal mobility; absenteeism (health insurance data); drug use Follow-up: 1, 2, and 4 months By telephone (11-point scales): pain, disability, recovery, and drug use (pill count) Telephone follow-up: 3, 7, 14, 21, and 90 days	V1 + V2 + V3 – V4 + V5 + V6 – V7 + V8 + V9 – V10 + Total 7	2	2
Erhard et al. (76), 1994	Physiotherapy department; acute and subacute LBP (<3 months) with or without “leg symptoms”; radiation pattern unclear	I: Sacroiliac joint manipulation at first visit and repeated, if indicated; co-intervention: flexion and extension exercises (<i>n</i> = 12) by persons in various professions, including DC and PT; number of manipulation treatments = 1–2 (total of 3 visits in 1 week) R: McKenzie extension exercises (<i>n</i> = 12); number of treatments = 3 visits in 1 week	Back pain–specific functional status (Oswestry) Follow-up: 1 and 4 weeks	V1 + V2 ? V3 – V4 + V5 – V6 – V7 ? V8 – V9 + V10 – Total 3	3	3

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Score†	Modified Jadad List	Pure Jadad List
Timm (77), 1994	Industry, post-laminectomy; chronic LBP (>6 months); no radiation below knee	I: Large-amplitude, low-velocity manipulation according to Maitland by PT (<i>n</i> = 50); number of treatments = 24 (3/week) R1: Physiotherapy (hot packs, ultrasound, TENS (<i>n</i> = 50); number of treatments = 24 (3/week) R3: High-tech McKenzie exercises (<i>n</i> = 50); number of treatments = 24 (3/week) R4: No treatment (<i>n</i> = 50)	Back pain–specific functional status (Oswestry); spinal mobility (Cybex, Schober) Follow-up: 8 weeks	V1 + V2 ? V3 – V4 ? V5 – V6 – V7 ? V8 ? V9 + V10 + Total 3	2	2
Meade et al. (78, 39), 1995	Outpatient physiotherapy departments and chiropractic clinics; acute, subacute, and chronic LBP with and without radiation below knee	I1: Manipulation by DC; co-interventions: exercises (9%), traction (2%), corset (2%) (<i>n</i> = 378); number of treatments = 9.1 I2: Physiotherapy by PT, including manipulation and mobilization according to Maitland (72%), manipulation according to Cyriax (12%), traction (25%), corset (4%), exercises (30%); number of treatments = 6.3 Contrast index group 1 and index group 2 mainly comparison of two manipulative regimens	Pain (proportion at 1 year; back pain–specific functional status (Oswestry); spinal mobility (centimeters), drug use (proportion); straight-leg raising (degrees))	V1 + V2 + V3 – V4 – V5 + V6 – V7 ? V8 + V9 – V10 + Total 5	1	1
Triano et al. (79), 1995	Chiropractic college; subacute and chronic LBP (>50 days); no radiation below knee	I: Manipulation by DC (<i>n</i> = 47 at follow-up); number of treatments = 12 (daily for 2 weeks) R1: Sham manipulation (<i>n</i> = 39 at follow-up); number of treatments = 12 (daily for 2 weeks) R2: Back education program (<i>n</i> = 43 at follow-up); number of treatments = 12 (daily for 2 weeks)	Pain (VAS); back pain–specific functional status (Oswestry); depression (Zung) Follow-up: 2 and 4 weeks	V1 + V2 + V3 – V4 ? V5 – V6 + V7 + V8 – V9 + V10 – Total 5	4	3
Bronfort et al. (80), 1996	Primary care, advertisement; subacute and chronic LBP (>6 weeks); no radiation below knee	I1: Thrust manipulation by DC; co-intervention: strengthening exercises (<i>n</i> = 17); number of treatments = 10 in 5 weeks I2: Thrust manipulation by DC; co-intervention: stretching exercises (<i>n</i> = 51); number of treatments = 10 in 5 weeks R: Naproxen, two 500-mg tablets twice daily for 5 weeks; co-intervention: strengthening exercises (<i>n</i> = 52) Index 1 and reference groups have equal co-intervention Randomization ratio (I1):(I2): R = 3:2:2	Pain (11-point scale); back pain–specific functional status (Roland–Morris); generic functional status (COOP–WONCA); spinal mobility (Schober); trunk strength (motion analyzer) Follow-up: 5 weeks, 11 weeks, 1 year	V1 + V2 + V3 – V4 + V5 + V6 – V7 + V8 – V9 + V10 + Total 7	2	2

Continued on following page

Appendix Table 1—Continued

Study (Reference), Year	Setting; Duration; Radiation Pattern	Interventions	Outcomes and Follow-up	CBPG Scores†	Modified Jadad List	Pure Jadad List
Hemmilä et al. (81), 1997	Primary care center and advertisement; subacute and chronic back pain (>7 weeks) with and without radiation below knee (18 patients with acute LBP were randomly assigned but not analyzed)	I: Bone-setting for folk-healer, mainly mobilization (<i>n</i> = 45); number of treatments = 8.1 in 6 weeks R1: Physiotherapy, mainly manual (no thrusts), thermal, electrotherapy by PT (<i>n</i> = 34); number of treatments = 9.9 in 6 weeks R2: Home exercises with individual instruction by PT (<i>n</i> = 35); number of treatments = 4.5 in 6 weeks	Pain (VAS); spinal mobility (Schober); side bending (degrees); extension (degrees); straight leg raising (degrees); pressure pain threshold level L5 (in N/m ²) Follow-up: 6 weeks, 3 months, and 6 months	V1 + V2 ? V3 – V4 – V5 + V6 – V7 + V8 + V9 + V10 + Total 6	3	3
Skargren et al. (8–10), 1997	Primary care centers; acute, subacute, and chronic LBP; no radiation below knee	I: Manipulation at discretion of DC, manipulation (98%) and mobilization (11%) (<i>n</i> = 179); number of treatments = 4.9 in average of 4.1 weeks R: Physiotherapy at discretion of PT, manipulation (2%) and mobilization (36%); also, traction, soft tissue treatment, McKenzie exercises (<i>n</i> = 144); number of treatments = 6.4 in average of 4.7 weeks	Pain (VAS); global improvement (7-point scale); back pain-specific functional status (Oswestry); generic functional status (6-point scale); medical consumption (questionnaire and log therapist); absenteeism (questionnaire) Follow-up: 6 months and 1 year	V1 + V2 ? V3 – V4 – V5 + V6 – V7 NA V8 ? V9 – V10 + Total 3	2	2
Cherkin et al. (7), 1998	Primary care patients from health maintenance organization; acute, subacute, and chronic LBP; no radiation below knee	I: Manipulation by DC, mainly thrusts (<i>n</i> = 122); number of treatments = average, 6.9 in 4 weeks R1: McKenzie exercise therapy by PT (<i>n</i> = 133); number of treatments = average, 4.6 in 4 weeks R2: Education booklet (<i>n</i> = 66)	Pain (11-point scale); back pain-specific functional status (Roland); medical consumption (registration and questionnaire) Follow-up: 4 weeks, 12 weeks, 52 weeks, and 104 weeks	V1 + V2 + V3 – V4 – V5 + V6 – V7 NA V8 + V9 – V10 + Total 5	1	1
Andersson et al. (16), 1999	Primary care patients from health maintenance organization; subacute and chronic LBP; few patients with radiation below knee	I: Osteopathic treatment by DO, including thrusts, muscle energy, articulation, and myofascial release (<i>n</i> = 83); number of treatments unclear; treatment done in a 12-week period R: Standard allopathic care, including medication, active physical therapy, ultrasound, diathermy, corset (<i>n</i> = 72); number of visits to health maintenance organization, 8 in a 12-week period; total number of treatments, including those from other therapists = unclear	Pain (VAS); back pain-specific functional status (Oswestry); spinal mobility (flexion and extension in degrees); straight-leg raising (degrees) Follow-up: 12 weeks	V1 + V2 + V3 – V4 – V5 + V6 – V7 + V8 + V9 + V10 + Total 7	3	3

* CBPG = Cochrane Back Pain Group; COOP-WONCA = Dartmouth Primary Care Cooperative Information Project Functional Health Assessment Charts/World Organization of National Colleges, Academies, and Academic Associations of General Practice/Family Physicians; DC = chiropractor; DO = osteopathic physician; I = index group; LBP = low back pain; MD = medical doctor; PT = physiotherapist; R = reference group; SIP = Sickness Impact Profile; TENS = transcutaneous electrical nerve stimulation; VAS = visual analogue scale.

† Validity items for the CBPG: V1, randomization; V2, allocation concealment; V3, blinding care provider; V4, control for co-interventions; V5, report of co-interventions for each group; V6, blinding patient; V7, blinding outcome assessor; V8, withdrawals and dropouts; V9, timing of outcome assessment comparable; V10, intention-to-treat analysis. Options for the validity items: + = positive; – = negative; ? = do not know; NA = not applicable.

‡ Validity score total is the addition of all items scored positive (range, 0–10); high score indicates good internal validity.

