

Review Article

Efficacy of spinal manipulation and mobilization for low back pain and neck pain: a systematic review and best evidence synthesis

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Abstract

BACKGROUND CONTEXT: Despite the many published randomized clinical trials (RCTs), a substantial number of reviews and several national clinical guidelines, much controversy still remains regarding the evidence for or against efficacy of spinal manipulation for low back pain and neck pain.

PURPOSE: To reassess the efficacy of spinal manipulative therapy (SMT) and mobilization (MOB) for the management of low back pain (LBP) and neck pain (NP), with special attention to applying more stringent criteria for study admissibility into evidence and for isolating the effect of SMT and/or MOB.

STUDY DESIGN: RCTs including 10 or more subjects per group receiving SMT or MOB and using patient-oriented primary outcome measures (eg, patient-rated pain, disability, global improvement and recovery time).

METHODS: Articles in English, Danish, Swedish, Norwegian and Dutch reporting on randomized trials were identified by a comprehensive search of computerized and bibliographic literature databases up to the end of 2002. Two reviewers independently abstracted data and assessed study quality according to eight explicit criteria. A best evidence synthesis incorporating explicit, detailed information about outcome measures and interventions was used to evaluate treatment efficacy. The strength of evidence was assessed by a classification system that incorporated study validity and statistical significance of study results. Sixty-nine RCTs met the study selection criteria and were reviewed and assigned validity scores varying from 6 to 81 on a scale of 0 to 100. Forty-three RCTs met the admissibility criteria for evidence.

RESULTS: Acute LBP: There is moderate evidence that SMT provides more short-term pain relief than MOB and detuned diathermy, and limited evidence of faster recovery than a commonly used physical therapy treatment strategy.

Chronic LBP: There is moderate evidence that SMT has an effect similar to an efficacious prescription nonsteroidal anti-inflammatory drug, SMT/MOB is effective in the short term when compared with placebo and general practitioner care, and in the long term compared to physical therapy. There is limited to moderate evidence that SMT is better than physical therapy and home back exercise in both the short and long term. There is limited evidence that SMT is superior to sham SMT in the short term and superior to chemonucleolysis for disc herniation in the short term. However, there is also limited evidence that MOB is inferior to back exercise after disc herniation surgery.

Mix of acute and chronic LBP: SMT/MOB provides either similar or better pain outcomes in the short and long term when compared with placebo and with other treatments, such as McKenzie therapy, medical care, management by physical therapists, soft tissue treatment and back school.

FDA device/drug status: not applicable.

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Acute NP: There are few studies, and the evidence is currently inconclusive.

Chronic NP: There is moderate evidence that SMT/MOB is superior to general practitioner management for short-term pain reduction but that SMT offers at most similar pain relief to high-technology rehabilitative exercise in the short and long term.

Mix of acute and chronic NP: The overall evidence is not clear. There is moderate evidence that MOB is superior to physical therapy and family physician care, and similar to SMT in both the short and long term. There is limited evidence that SMT, in both the short and long term, is inferior to physical therapy.

CONCLUSIONS: Our data synthesis suggests that recommendations can be made with some confidence regarding the use of SMT and/or MOB as a viable option for the treatment of both low back pain and NP. There have been few high-quality trials distinguishing between acute and chronic patients, and most are limited to shorter-term follow-up. Future trials should examine well-defined subgroups of patients, further address the value of SMT and MOB for acute patients, establish optimal number of treatment visits and consider the cost-effectiveness of care. © 2004 Elsevier Inc. All rights reserved.

Keywords:

Low back pain; Cervical vertebrae; Manipulation/orthopedic; Randomized controlled trials; Comparative study; Review literature; Meta-analysis; Chiropractic; Osteopathy medicine; Manipulation/spinal

Background context

More than 50 mostly qualitative, nonsystematic reviews have been published since 1979 addressing the role of spinal manipulation and mobilization in the treatment of back and neck pain (NP) [1]. A majority of these reviews, including most of the systematic reviews [2–7], have concluded that spinal manipulation is an efficacious treatment for low back pain (LBP) [1]. However, most reviews restricted their positive conclusions to patients with acute LBP [1].

A number of scales and checklists have been developed to assess the quality of randomized clinical trials (RCTs) [8]. In general, positive or negative trial outcomes have been accepted at face value without consideration of the magnitude of the differences among interventions. A shortcoming of this approach is exemplified by reevaluations of individual RCTs on the efficacy of spinal manipulation, where it was found that the data supported conclusions that were in conflict with those of the original publications [9].

Our reevaluation of the literature follows from a previous systematic review of reviews [1], in which the authors observed that the vast majority of the reviews of spinal manipulation for LBP were of inadequate methodological quality. Furthermore, the authors identified a need to develop standards of quality for systematic reviews in general, which was emphasized in an accompanying editorial by Moher and Olkin [10]. The methodology used in this review is intended as a step in that direction. Using a stringent best evidence synthesis method, we reviewed the literature and contrasted our findings with other recent systematic reviews on the efficacy of spinal manipulation and mobilization for back and neck pain [11,12].

Purpose

The purpose of this review is to reassess the efficacy of spinal manipulative therapy (SMT) and mobilization (MOB)

for the management of LBP and NP, with special attention to applying more stringent criteria for study admissibility into evidence and for isolating the effect of SMT and/or MOB.

Methods

Data selection

SMT is defined as the application of high-velocity, low-amplitude manual thrusts to the spinal joints slightly beyond the passive range of joint motion [13]. MOB is defined as the application of manual force to the spinal joints within the passive range of joint motion that does not involve a thrust. A literature search for all RCTs evaluating the therapeutic efficacy of SMT and/or MOB for LBP and NP was performed accessing MEDLINE (1966 to end of 2002), Embase (1974 to end of 2002), CINAHL and the chiropractic reference systems CRAC and MANTIS. Articles in English, Danish, Swedish, Norwegian and Dutch reporting on randomized trials were identified by a comprehensive search of computerized and bibliographic literature databases. The search strategy was based on combinations of the main keywords: manipulation, spinal; low back pain; cervical vertebrae; manipulation/orthopedic, randomized controlled trials, comparative study, review literature, chiropractic and osteopathy.

Study selection

Each study had to have 10 or more subjects receiving SMT and/or MOB to be included in this review. The main outcome measures had to be explicitly patient oriented (eg, patient-rated pain, global improvement, low back or neck disability, recovery time, work loss, medication use and functional health status). Additionally, citation tracking of

references in relevant publications was used, including the nonindexed chiropractic, osteopathic, physical therapy and medical journals. Abstracts from proceedings and unpublished trials were not included.

Data abstraction and synthesis

A best evidence synthesis incorporating explicit information about outcome measures, interventions and magnitude of treatment differences and their associated p values was used to evaluate treatment efficacy [12,14,15]. Two authors (MH and GB) independently extracted and recorded relevant data from each article. Statistical pooling was considered to be an adjunct to the systematic review and not the primary goal.

Data presentation

All original data on outcomes were normalized to a 0–100 percentage-point scale whenever possible. Between-group differences are reported in the text in percentage points on the 100-point scale.

Categorization of low back and neck pain

Studies were classified into six categories: acute LBP, chronic LBP, mix of acute and chronic LBP, acute NP, chronic NP, and mix of acute and chronic NP. For the purpose of this review, acute was defined as a duration of less than 6 weeks, and chronic as a duration of 6 weeks or longer.

Categorization of short-term and long-term outcomes

Short-term follow-up was defined as outcomes evaluated up to 3 months after the initial study treatment. Long-term follow-up was defined as outcomes evaluated more than 3 months after onset of study therapy.

Assessment of methodological quality of RCTs

A critical evaluation list of eight methodological items and their operational definitions (see Appendix) was used to assess methodological quality and represents a modification of previously used instruments [16,17]. The quality scores for this review were well correlated ($r=0.80$) with scores from a 14-item scoring system used in a previous review [18]. The quality score items included concealment of treatment allocation, blinding of patients, blinding of provider and control of attention bias, blinding of assessor and influence by study personnel, similarity of study groups at baseline, dropouts accounted for, missing data accounted for and intention-to-treat analysis. Two reviewers performed the methodological scoring of the RCTs independently (MH and GB). Differences in scores were resolved by consensus between the two reviewers. Two other authors of this review scored the trials for which GB was the primary author. The reviewers could not be blinded to study results because of their familiarity with the literature. The validity scores

of the individual RCTs were used as part of the evidence determination.

Assessment of the level of evidence of efficacy

The criteria for determining the level of evidence of efficacy was adapted from the Agency for Health Care Policy and Research's guidelines for acute low back pain [19]. Our system evaluated the evidence by taking into account the following: 1) the type of comparison intervention (established efficacious treatment, commonly used therapy or placebo), 2) methodological quality as expressed by validity scores, 3) the number of studies and 4) statistical significance of study findings. Four categories were used to describe evidence levels: strong, moderate, limited and inconclusive. All eligible RCTs were considered regardless of their results. Statistical pooling of two or more trials was considered if they were homogeneous in terms of patient population, interventions, outcomes and follow-up time points. For determination of the outcome of each RCT, we prioritized patient-rated pain, disability and improvement.

The assessment of efficacy depended on the type of comparison intervention. To be declared evidence of efficacy, a study was required to show that SMT and/or MOB had at least a similar magnitude of effect compared with an established efficacious treatment or was superior to a placebo or a commonly used therapy. To be declared evidence of inefficacy, a study had to show that SMT was inferior to an established efficacious treatment, commonly used therapy or showed an effect similar or inferior to a placebo intervention or no-treatment control. For the purpose of this review, adequate statistical power was defined as at least 80% power to detect a group difference in effect size of 0.5 and an alpha level of .05. A group difference in effect size of <0.5 or <10 percentage points on the primary outcome measure was defined as representing a similar effect. Methodological quality and statistical significance were then considered to determine the evidence level, as defined in Table 1. Studies with strong, moderate, or limited evidence are tabulated in the evidence of efficacy summary tables. Studies with only inconclusive evidence were omitted from these tables (i.e., underpowered studies with statistically insignificant findings or studies with validity scores <20).

There is one additional assessment of evidence. When SMT is found to have similar effect to a commonly used therapy without established efficacy, neither efficacy nor inefficacy can be established. Furthermore, no study tested equivalence. Therefore, we called this case evidence of similarity of effect to distinguish the evidence from efficacy, inefficacy and equivalence.

Exclusion from evidence

An RCT was excluded from evidence synthesis under the following conditions: 1) the main outcome measure was not rated by the patient; 2) quantitative information on the main outcome was lacking; 3) the trial was designed to test

Table 1
Definition of levels of evidence

Level of evidence of efficacy or inefficacy	Requirements		
	Number of RCTs with validity score ≥ 50	Number of RCTs with validity score 20 to 49	Statistically significant results
A. Strong			
1.	≥ 2	—	Yes*
2.	≥ 2	—	No†
B. Moderate			
1.	1	—	Yes*
2.	1	—	No†
C. Limited			
1.	—	≥ 1	Yes*
2.	—	≥ 1	No†
3.	1	—	No‡
4.	—	≥ 2	No‡
D. Inconclusive/conflicting			
1.	Minimal standards for classification as limited evidence were not met.		
2.	Preponderance of evidence was conflicting, in terms of number and quality of eligible RCTs.		

* For efficacy: superior in effect to placebo, no treatment, established efficacious treatment or commonly used therapies. For inefficacy: inferior in effect to established efficacious treatment, commonly used therapy, placebo or no treatment.

† Studies must be adequately powered. For efficacy: similar in effect to established efficacious treatment. For inefficacy: similar in effect to placebo or no treatment. For similarity: similar in effect to therapy not established as efficacious.

‡ For efficacy: superior in effect to placebo, no treatment, efficacious treatment or commonly used therapies. For inefficacy: inferior in effect to established efficacious treatment, commonly used therapy, placebo or no treatment.

RCTs=randomized clinical trials.

the immediate postintervention effect of a single therapeutic session without a follow-up period; 4) SMT and/or MOB was combined with other therapies not allowing us to isolate its unique contribution to the overall treatment effect.

Results

Low back pain

We identified 46 LBP trials of SMT/MOB. Of these, 31 studies with a total of 5,202 participants met the inclusion criteria. SMT was investigated in 25 trials, MOB in 3 trials and a combination in 3 trials. Chiropractors in 14 trials, medical doctors in 7 trials, physical therapists in 6 trials and osteopaths in 4 trials provided SMT/MOB. Comparison therapies included acupuncture, back school, bed rest, corset, diathermy, education advice, electrical modalities, exercise, heat, injections, massage and trigger point therapy, medication, no treatment, placebo, physical therapy, sham SMT and ultrasound. The number of treatments varied from 1 to 24, and outcomes were measured from immediate posttreatment to 3 years after commencement of therapy. Among the studies in evidence, 6 trials (N=662) evaluated acute LBP,

11 trials (N=1,472) assessed chronic LBP and 14 trials (N=3,068) investigated a mix of acute and chronic LBP patients. The methodological qualities of the LBP RCTs are shown in Table 2. The 15 LBP studies excluded from evidence and the reasons for ineligibility are summarized in Table 3. The primary exclusion criterion was the inability to isolate a unique contribution of SMT/MOB to the treatment effect.

The LBP RCTs were divided into three subcategories: acute, chronic and a mix of acute and chronic. They were too dissimilar in terms of patient characteristics, outcome measures, time points and type of treatment comparisons to allow for statistical pooling. Whenever RCT group differences did not show statistical significance, they were termed nonsignificant.

Acute low back pain

Fifteen RCTs were identified. Six remained in evidence (Table 4) [20–25], and 9 were excluded [26–34] (Table 3).

Table 2
Methodological quality scores for low back pain trials in evidence

First author	Year	Validity items								Validity % score
		1	2	3	4	5	6	7	8	
Andersson [60]	1999	p	+	-	-	p	+	p	p	50
Bronfort [61]	1989	-	-	-	-	p	-	+	+	31
Bronfort [42]	1996	+	+	-	p	+	+	+	+	81
Burton [43]	2000	+	p	-	-	+	-	-	p	38
Cherkin [55]	1998	+	+	-	-	+	-	-	+	50
Coxhead [35]	1981	-	p	-	-	p	-	-	+	25
Doran [64]	1975	-	p	-	-	p	-	-	+	25
Evans [70]	1978	-	p	-	-	p	-	-	p	19
Farrell [25]	1982	-	-	-	-	p	+	-	p	25
Gibson [48]	1985	-	p	p	p	p	p	-	p	38
Giles [63]	1999	p	p	-	-	p	p	-	p	31
Glover [23]	1974	-	p	-	-	p	+	+	+	50
Godfrey [22]	1984	-	-	-	-	p	-	-	+	19
Hadler [20]	1987	-	+	-	p	+	+	+	+	69
Hemmilä [45]	1997,	-	+	-	-	+	+	+	+	63
	2002									
Herzog [46]	1991	-	-	-	-	p	-	-	-	6
Hoehler [65]	1981	-	-	+	-	p	-	-	p	25
Hsieh [54]	2002	p	+	-	-	+	+	p	+	63
Hurwitz [144]	2002	-	+	-	-	+	+	+	+	63
Koes [39,40]	1992	p	p	+	-	p	-	p	+	50
MacDonald [24]	1990	p	-	-	-	p	+	p	p	38
Mathews [21]	1987	p	p	+	-	p	-	p	+	19
Meade [56,57]	1990,	p	-	-	-	p	+	p	p	31
	1995									
Pope [37,38]	1994	p	+	-	-	p	-	-	+	38
Postacchini [66]	1988	p	-	-	-	-	-	-	-	6
Skargren [58,59]	1997	+	p	-	-	+	p	-	+	50
Timm [47]	1994	p	-	-	-	p	-	-	+	25
Triano [36]	1995	-	+	p	p	p	-	-	-	31
Waagen [41]	1986	p	-	+	p	+	-	-	p	44
Wreje [67]	1992	-	-	-	p	p	-	-	-	13
Zylbergold [62]	1981	-	-	-	-	p	+	+	p	38

+ = yes, - = no, p = unclear/partly.

See Appendix for operational definitions of validity items.

Table 3

Randomized trials of spinal manipulation and mobilization for low back pain excluded from evidence

First author	Year	Duration	Quality score	Reason for exclusion from evidence
Arkuszewski [49]	1986	c	13	Outcomes not rated by patients
Bergquist-Ullman [26]	1977	a	38	Unique contribution of manipulation to treatment effect could not be isolated
Blomberg [27]	1992	a	44	Unique contribution of manipulation to treatment effect could not be isolated
Delitto [28]	1993	a	31	Unique contribution of manipulation to treatment effect could not be isolated
Erhard [29]	1994	a	44	Unique contribution of manipulation to treatment effect could not be isolated
Gemmell [30]	1995	a	56	Comparison of two manipulation types; unique contribution confounded immediate posttreatment outcome for single session of manipulation
Helliwell [31]	1987	a	31	Less than 10 individuals per treatment group
Kinalski [68]	1989	?	13	Outcomes not rated by patients
Ongley [50]	1987	c	88	Unique contribution of manipulation to treatment effect could not be isolated
Rasmussen [32]	1979	a	38	Outcomes not rated by patients
Rupert [69]	1985	a/c	19	Inadequate information about main outcome
Seferlis [33]	1998	a	19	Unique contribution of manipulation to treatment effect could not be isolated
Sims-Williams [51]	1978	c	44	Unique contribution of manipulation to treatment effect could not be isolated
Sims-Williams [52]	1979	c	44	Unique contribution of manipulation to treatment effect could not be isolated
Waterworth [34]	1985	a	31	Unique contribution of manipulation to treatment effect could not be isolated

a=acute; c=chronic; a/c=mix of acute and chronic; ?=information not available.

Hadler et al. [20] (validity score [VS], 69) showed that one session of SMT was superior to one session of MOB. Glover et al. [23] (VS, 50) found one session of SMT to be superior to detuned diathermy 1 week after treatment. MacDonald and Bell [24] (VS, 38) found that SMT was nonsignificantly better than low back education in a subgroup of patients 1 week after the start of treatment. Farrell and Twomey [25] (VS, 25) showed that patients receiving SMT recovered faster than patients receiving a combination of diathermy, exercise and ergonomic instruction. Mathews et al. [21] (VS, 19) found that patients with LBP accompanied by sciatica improved faster with SMT than with heat after 2 weeks of treatment. Godfrey et al. [22] (VS, 19) found SMT combined with low-level electrical stimulation was nonsignificantly better in terms of pain reduction than low-level electrical stimulation alone after 2 weeks.

Evidence of efficacy

There is moderate evidence that SMT has better short-term efficacy than spinal mobilization and detuned diathermy. There is limited evidence that SMT has better short-term efficacy than a combination of diathermy, exercise and ergonomic instruction (Table 5).

Chronic low back pain

Fifteen RCTs on chronic LBP were identified, of which 11 evaluated SMT and/or MOB in isolation (Table 6) [35–48]. Four RCTs were excluded from evidence (Table 3) [49–52].

Bronfort et al. [42] (VS, 81) showed that the combination of SMT and exercise was similar in effect to the combination of nonsteroidal anti-inflammatory drugs (NSAIDs) and exercise. Hemmilä et al. [45] (VS, 63) found that SMT resulted in greater short- and long-term disability reduction

than home back exercise or physical therapy (PT). SMT was superior to PT for pain in the long term. Koes et al. [39,40] (VS, 50) showed SMT/MOB to have an advantage over general medical practice and placebo for severity of main complaint and perceived global improvement in the long term. Burton et al. [43] (VS, 38) showed that SMT had a higher short-term reduction in pain and disability for disc herniation than chemonucleolysis. Pope et al. [37,38] (VS, 38) found SMT superior to transcutaneous electrical nerve stimulation (TENS) in pain improvement. Waagen et al. [41] (VS, 38) reported an advantage of SMT over placebo in pain reduction after 2 weeks of treatment. Gibson et al. [48] (VS, 38) found detuned diathermy better than SMT/MOB and active diathermy. Baseline dissimilarity between groups rendered the results of this trial questionable. Triano et al. [36] (VS, 31) showed SMT had more short-term pain and disability reduction than sham SMT. Coxhead et al. [35] (VS, 25), showed SMT was superior to traction, exercise, corset and no treatment in the short term. Timm [47] (VS, 25) found MOB resulted in slightly more short-term disability reduction than PT and no-treatment control. Exercise resulted in more disability reduction than MOB. Herzog et al. [46] (VS, 6) found no significant short-term differences between SMT, back education and exercise in pain and disability reduction.

Evidence of efficacy

There is moderate evidence that SMT with strengthening exercise is similar in effect to prescription NSAIDs with exercise for pain relief in both the short and long term. There is moderate evidence that SMT/MOB is superior to physical therapy and to home exercise for reducing disability in the long term. There is moderate evidence that SMT/MOB is superior to general practice medical care and to placebo in the short term, and superior to physical therapy in the

Table 4
Randomized trials of spinal manipulation and mobilization for acute low back pain

First author (quality score)	Year	Study groups (n)	Treatments (n)	Results*
Acute LBP Farrell [25] (25)	1982	G1: SMT/MOB-PT (24) G2: diathermy, exercise, ergonomics (24)	<9	Pain: G2 vs G1: after first treatment 07; 1 week, -01; 3 weeks, 00 Recovery (difference in % of patients symptom free): status in <15 days G2 vs G1: 2 weeks, 38 [†]
Glover [23] (50)	1974	G1: SMT-MD and 4 detuned diathermy (43) G2: detuned diathermy (placebo) (41)	5	Pain improvement: G2 vs G1: after first treatment, 12; 3 days, -06; 7 days, -05 (all patients)
Godfrey [22] (19)	1984	G1: SMT-MD/DC & low elect stim (48) G2: min mass and low electro stim (42)	4	G2 vs G1: after first treatment, 31 [†] ; 3 days, 19; 7 days, 15 (subgroup: LBP <7 days duration [n=20])
Hadler [20] (69)	1987	G1: SMT-MD (26) G2: MOB-MD (28)	4	Pain improvement (difference in % of patients rating marked improvement): G2 vs G1: 2 weeks, 15 Disability improvement (% of patients rating marked improvement): G2 vs G1: 2 weeks, 00
MacDonald [24] (38)	1990	G1: SMT-DO and LBP education/advice (49) G2: LBP education/advice (46)	1 1	Disability: G2 vs G1: 3 days, 22 ⁺ ; 6 days, 09; 9 days, 10; 12 days, 03 (patients with pain duration of 2–4 weeks) 50% Disability reduction: reached more rapidly in G1 than G2 [†]
Mathews [21] (19)	1987	G1: SMT-PT (165) G2: heat (126)	5 5	Disability improvement: G2 vs G1: 1 week, -06; 2 weeks, 00; 3 weeks, 02 (all patients) G2 vs G1: 1 week, -03; 2 weeks, -12; 3 weeks, -13 (subgroup 1–13 days duration) G2 vs G1: 1 week, 13; 2 weeks, 08; 3 weeks, 01 (subgroup 14–28 days duration) G2 vs G1: 1 week, 08; 2 weeks, 03; 3 weeks, 08 (subgroup >28 days duration)
			<10 6	Pain (difference in % of patients recovered): G2 vs G1: 2 weeks, 08 (subgroup with simple LBP) G2 vs G1: 2 weeks, 13 [†] (subgroup with leg pain) Pain (difference in % patients relapsed), G2 vs G1: 1 year, 00

* Between-group differences in percentage points unless otherwise specified. Positive score indicates advantage for Group 1 (G1).

[†] p<.05 for unadjusted pairwise comparisons.

DC=chiropractor; DO=osteopathic doctor; MD=medical doctor; MOB=spinal mobilization; PT=physiotherapist; SMT=spinal manipulative therapy.

long term for patient improvement. There is limited evidence in the short term for the following: that in terms of pain/disability reduction, SMT/MOB is superior to physical therapy, home back exercise, TENS, traction/exercise/corset, no treatment and placebo; also in the short term, that SMT is superior to sham SMT and chemonucleolysis and that MOB is inferior to exercise for disc herniation (Table 7).

Mix of acute and chronic low back pain

Sixteen trials were identified. Fourteen met the criteria for admissibility (Table 8) [53–67]. Two trials were excluded (Table 3) [68,69].

Hurwitz et al. [53,144] (VS, 63) found SMT almost identical to medical care for pain and disability in the short and long term. Adding the use of physical modalities to SMT

Table 5
Evidence of efficacy for acute low back pain

SMT and/or MOB	Comparison intervention	Primary outcome(s)	Short term		Long term	
			Direction of effect*	Evidence level	Direction of effect*	Evidence level
SMT	Spinal mobilization [20] Detuned diathermy [23]	Disability	Superior	Moderate	No evidence	No evidence
SMT	Combination of diathermy, exercise and ergonomic instruction [25]	Time to recovery	Superior	Limited	No evidence	No evidence

* Effect of SMT and/or MOB in relationship to comparison intervention.

MOB=spinal mobilization; SMT=spinal manipulation therapy.

Table 6
Randomized trials of spinal manipulation and mobilization for chronic low back pain

First author (quality score)	Year	Study groups (n)	Treatments (n)	Results*
Bronfort [42] (81)	1996	G1: SMT-DC and strength exercise (71)	20	Pain: G2 vs G1: 5 weeks, 02; 3 months, 08; 1 year, 08 (adjusted differences)
		G2: NSAID & strength exercise (52)	20	
Burton [43] (38)	2000	G3: SMT-DC and stretch exercise (51) (cannot isolate effect of SMT with G3)	20	Disability: G2 vs G1: 5 weeks, 02; 3 months, 06 (adjusted differences)
		G1: SMT-DO (20) G2: Chemonucleolysis (20)	6–18 m=11	
Coxhead [35] (25)	1981	Factorial design, all combinations of: 1. SMT-PT, back school, diathermy 2. Traction, back school, diathermy 3. Exercise, back school, diathermy 4. Corset, back school, diathermy	5–10	Pain: Main effect of SMT vs no SMT: 4 weeks, 10 [†] Improvement (difference in % patients rating themselves better): Main effect of SMT vs no SMT: 4 weeks, 9; 4 months, 5
Gibson [48] (38)	1985	G1: SMT/MOB-DO (41)	4	Pain (reported here as pain improvement): G2 vs G1: 2 weeks, 00; 4 weeks, -03; 12 weeks, 02 (between-groups statistics not possible) G3 vs G1: 2 weeks, -10; 4 weeks, -07; 12 weeks, -20 (severity at baseline not comparable)
		G2: diathermy active (34)	12	
		G3: detuned diathermy (34)	12	
Hemmilä [44,45] (63)	1997,	G1: MOB-bonesetter (45)	m=8	Disability improvement: G2 vs G1: 6 weeks, 10; 3 months, 02; 6 months, 10 [†] ; 1 year, 08 G3 vs G1: 6 weeks, 10; 3 months, 04; 6 months, 12 [†] , 1 year, 12 [†]
	2002	G2: PT (35) G3: exercise (34)	m=10	
Herzog [46] (6)	1991	G1: SMT-DC (19)	10	Pain improvement G2 vs G1: 4 weeks, -08 Disability improvement G2 vs G1: 4 weeks, 00
		G2: back education and exercise (18)	10	
Koes [39,40] (50)	1992	G1: SMT/MOB-PT (36)	14	Main complaint improvement: G2 vs G1: 6 weeks, 04; 12 weeks, 05; 12 months, 13 [†] G3 vs G1: 6 weeks, 14 [†] ; 12 weeks, -03 G4 vs G1: 6 weeks, 14 [†] ; 12 weeks, 07 Physical function improvement: G2 vs G1: 6 weeks, 05; 12 weeks, 09; 12 months, 07 G3 vs G1: 6 weeks, 10; 12 weeks, -01 G4 vs G1: 6 weeks, 16 [†] ; 12 weeks, 10
		G2: Massage, exercise, heat, PT (36)	6	
		G3: MD, analgesic/anti-inflammatory rest, exercise, posture (32)	—	
		G4: detuned PT modalities (40)	—	
Pope [37,38] (38)	1994	G1: SMT-DC (70)	9	Pain improvement: G2 vs G1: 3 weeks, 07 G3 vs G1: 3 weeks, 15 [†] G4 vs G1: 3 weeks, 08 Disability: G2 vs G1: 3 weeks, 30 [†] (subgroup, n=63) G3 vs G1: 3 weeks, 20 [†] (subgroup, n=63) G4 vs G1: 3 weeks, 09 [†] (subgroup, n=63)
		G2: massage (36)	9	
		G3: TENS (28)	3+	
		G4: corset (30)	1	
Timm [47] (25)	1994	G1: MOB-PT (50)	24	Disability: G2 vs G1: 8 weeks, 05 G3 vs G1: 8 weeks, -18 [†] G4 vs G1: 8 weeks, -17 [†] G5 vs G1: 8 weeks, 05
		G2: hot packs, TENS, ultrasound (50)	24	
		G3: low-tech exercise (50)	24	
		G4: high-tech exercise (50)	24	
		G5: no treatment control (50)	24	
Triano [36] (31)	1995	G1: SMT-DC (70)	12	Pain: G2 vs G1: 2 weeks, 06; 4 weeks, 08 G3 vs G1: 2 weeks, 06; 4 weeks, 02 Disability: G2 vs G1: 2 weeks, 12 [†] ; 4 weeks, 07 G3 vs G1: 2 weeks, 06; 4 weeks, 02
		G2: sham SMT-DC (70)	12	
		G3: back education (69)	12	
Waagen [41] (44)	1986	G1: SMT-DC (11)	m=5	Pain G2 vs G1: After first treatment, 06; 2 weeks, 17 (statistical significance is indeterminate)
		G2: sham SMT-DC (18)	m=4	

* Between-group differences in percentage points unless otherwise specified. Positive score indicates advantage for Group 1 (G1).

[†] p<.05 for unadjusted pairwise comparisons.

DC=chiropractor; DO=osteopathic doctor; m=mean; MD=medical doctor; MOB=spinal mobilization; PT=physiotherapist; SMT=spinal manipulative therapy; TENS=transcutaneous electrical nerve stimulation.

Table 7
Evidence of efficacy for chronic low back pain

SMT and/or MOB	Comparison intervention	Primary outcome(s)	Short term		Long term	
			Direction of effect*	Evidence level	Direction of effect*	Evidence level
SMT (with strengthening exercise)	Prescription NSAID (with strengthening exercise) [42]	Pain	Similar	Moderate	Similar	Moderate
SMT/MOB	Physical therapy [39,40]	Improvement	Inconclusive	Inconclusive	Superior	Moderate
SMT/MOB	Detuned modalities [39,40] GP management [39,40]	Improvement	Superior	Moderate	No evidence	No evidence
SMT	Sham SMT [36]	Disability	Superior	Limited	No evidence	No evidence
SMT (Lay bonesetters)	Physical therapy or home back exercise [45]	Disability	Superior	Limited	Superior	Moderate
SMT	Chemonucleolysis for confirmed disc herniation [43]	Pain, disability	Superior	Limited	Inconclusive	Inconclusive
SMT/MOB	Placebo [35,39,41] No treatment [35]	Pain	Superior	Limited	No evidence	No evidence
	TENS [37] Traction, exercise and corset [35]					
MOB	High and low tech back exercise after disc herniation surgery [47]	Disability	Inferior	Limited	No evidence	No evidence

* Effect of SMT and/or MOB in relationship to comparison intervention.

GP=general practitioner; MOB=spinal mobilization; NSAID=nonsteroidal anti-inflammatory drug; SMT=spinal manipulative therapy; TENS=transcutaneous electrical nerve stimulation.

did not improve any outcomes. Hsieh et al. [54] (VS, 63) found a nonsignificant advantage for SMT over myofascial therapy and for back school over SMT in terms of pain and disability reduction. Cherkin et al. [55] (VS, 50) found a short-term advantage of SMT over a booklet, and no difference between SMT and McKenzie therapy for pain in the short term. Skargren et al. [58,59] (VS, 50) showed equal effectiveness for SMT and PT in terms of pain and disability reduction in the short and long term. Andersson et al. [60] (VS, 50) found a small but nonsignificant short-term benefit of SMT over standard medical care for pain and no difference for disability. Meade et al. [56,57] (VS, 31) showed a small, significant advantage of SMT over hospital outpatient management for disability in the short and long term. Bronfort [61] (VS, 31) showed that SMT was nonsignificantly better than medical general practice in improvement and sick leave, both in the short and long term. Zylbergold and Piper [62] (VS, 38) found that SMT and heat were nonsignificantly better than flexion exercise and heat for pain and disability. Giles and Müller [63] (VS, 31) found nonsignificantly more pain and disability reduction favoring SMT after 3 to 4 weeks of treatment compared with acupuncture and medication. Doran and Newell [64] (VS, 25), showed that SMT resulted in greater improvement than physiotherapy, corset or analgesics after treatment. No important differences were seen subsequently. Hoehler et al. [65] (VS, 25) found a nonsignificant but greater pain reduction for SMT than placebo massage. A significantly higher proportion in the SMT group reported effective treatment. Evans et al. [70] (VS, 19) found a substantially higher proportion of patients receiving SMT than patients receiving analgesics rated treatment effective. The advantage in pain reduction for SMT was nonsignificant. Wreje et al. [67] (VS, 13) found that one session of SMT produced a lower number of sick-leave days than friction massage. Postacchini [66] (VS, 6) showed greater global improvement for SMT than for placebo ointment. Other comparisons had ambiguous results.

Evidence of efficacy

There is moderate evidence that SMT is superior to an information booklet for pain reduction in the short term, but similar in the long term. There is also moderate evidence in the short and long term that SMT is similar to the following for pain and/or disability: McKenzie therapy, medical care with instruction in exercise, soft tissue therapy, physical therapy and back school. SMT is similar to medical care in the short term. There is limited evidence of short- and long-term superiority of SMT over hospital outpatient care for pain and disability. There is limited evidence of short-term superiority of SMT over medication and placebo massage (Table 9).

Neck pain

We identified 23 NP trials of SMT/MOB. Of these, 12 studies with a total of 1,172 participants met the inclusion criteria. SMT was investigated in 7 trials, MOB in 4 trials and a combination in 1 trial. Therapy was provided by a doctor of chiropractic in 5 trials, a medical doctor in 2 trials, a physical therapist in 4 trials and a manual therapist in 1 trial. Comparison therapies included acupuncture, collar, education, electrical exercise, heat, modalities, medication, no treatment, physical therapy, placebo and rest. The number of treatments varied from 1 to 24, and outcomes were evaluated from immediately after the first treatment to 1 year after commencement of therapy. Among the studies in evidence, 2 trials (N=82) evaluated acute NP, 5 trials (n=444) assessed chronic NP and 5 trials (n=646) investigated a mix of acute and chronic LBP patients. The methodological qualities of the NP RCTs are shown in Table 10. The 11 NP studies excluded from evidence and the reasons for ineligibility are summarized in Table 11. The primary exclusion criterion was the inability to isolate a unique contribution of SMT/MOB to the treatment effect.

Table 8

Randomized trials of spinal manipulation and mobilization for a mix of acute and chronic low back pain

First author (quality score)	Year	Study groups (n)	Treatment (n)	Results*
Andersson [60] (50)	1999	G1: SMT-DO (83) G2: usual care, MD (72)	12 12	Pain improvement: G2 vs G1: 12 weeks, 06 Disability improvement: G2 vs G1: 12 weeks, 01
Bronfort [61] (31)	1989	G1: SMT-DC (11) G2: drugs, injections, PT, advice (10)	7 8	Improvement (difference in % of patients rating $\geq 75\%$ improvement): G2 vs G1: 1 month, 06; 3 months, 37; 6 months, 26 Work loss (difference in % of patients with work loss <8 days): G2 vs G1: 6 months, 25
Cherkin [55] (50)	1998	G1: SMT-DC (133) G2: McKenzie exercise, PT (122) G3: educational booklet (66)	1–9 m=7 1–9 m=5	Bothersomeness: G2 vs G1: 4 weeks, 04; 12 weeks, 07; 1 year, 03 G3 vs G1: 4 weeks, 12 [†] ; 12 weeks, 12 [†] ; 1 year, 10 Disability: G2 vs G1: 4 weeks, 02; 12 weeks, 04; 1 year, 00 G3 vs G1: 4 weeks, 05; 12 weeks, 05; 1 year, 07
Doran [64] (25)	1975	G1: SMT-MD (116) G2: physiotherapy (114) G3: corset (109) G4: analgesics (113)	6 ? 1 ?	Improvement (difference in % of patients rating moderate to complete relief): G2 vs G1: 3 weeks, 12, 6 weeks, –02, 3 months, 09 G3 vs G1: 3 weeks, 15, 6 weeks, –12, 3 months, –09 G4 vs G1: 3 weeks, 15, 6 weeks, 07, 3 months, –02
Evans [70] (19)	1978	G1: SMT-MD (17) G2: analgesics (15)	3 3	Pain improvement: G2 vs G1: 3 weeks, 07 Improvement (difference in % of patients rating treatment effective/ highly effective): G2 vs G1: 3 weeks, 42 [†]
Giles [63] (31)	1999	G1: SMT-DC (32) G2: acupuncture (18) G3: medication (19)	6 6	Pain improvement: G2 vs G1: 4 weeks, 33 (median scores) G3 vs G1: 4 weeks, 28 Disability improvement: G2 vs G1: 4 weeks, 09 (median scores) G3 vs G1: 4 weeks, 09
Hoehler [65] (25)	1981	G1: SMT-MD (56) G2: soft tissue placebo massage (39)	? ?	Pain (difference in % of patients rating moderate to severe pain): G2 vs G1: at discharge, 12; 3 weeks after discharge, 27 Improvement (difference in % of patients reporting that treatment was effective): G2 vs G1: at discharge, 02; 3 weeks after discharge, 20 [†]
Hsieh [54] (56)	2002	G1: SMT-DC (49) G2: back school (48) G3: myofascial therapy (51) G4: SMT-DC and myofascial therapy (52)	9 3 9 9	Pain: G2 vs G1: 3 weeks, –05; 6 months, –01 G3 vs G1: 3 weeks, 05, 6 months, 06 G4 vs G3: 3 weeks, 07 [†] , 6 months, 08 (advantage for G4 over G3) Disability: G2 vs G1: 3 weeks, –01; 6 months, 01 G3 vs G1: 3 weeks, 06; 6 months, 07 G4 vs G3: 3 weeks, 09 [†] ; 6 months, 06 (advantage for G4 over G3)
Hurwitz [144] (69)	2002	G1: SMT-DC and exercise instruction (169) G2: care, MD, including exercise instructions (170) (2 other groups identical to G1 and G2 but with PT modalities)	1–21 m=6 1–23 m=4	Pain: G2 vs G1: 2 weeks, 00; 6 weeks, 02; 6 months, 02 Disability: G2 vs G1: 2 weeks, 01; 6 weeks, 02; 6 months, 03
Meade [56,57] (31)	1990 1995	G1: SMT-DC (384) G2: PT, SMT-PT (357)	9 6	Pain improvement: G2 vs G1: 6 weeks, 03 [†] , 6 months, 04 [†] ; 1 year, 02; 2 years, 04 [†] ; 3 years, 03 [†] Disability improvement: G2 vs G1: 6 weeks, 02; 6 months, 03 [†] ; 1 year, 02; 2 years, 03 [†] ; 3 years, 03 [†]
Postacchini [66] (19)	(1988)	G1: SMT-DC? (87) G2: drugs (81)	11–17 10–15	Global improvement (pain, disability, finger-floor distance and SLR): G2 vs G1: 3 weeks, 08; 2 months, –01; 6 months, –01 (acute); 3 weeks, 03; 2 months, –04; 6 months, 00 (chronic)

(continued)

Table 8
Continued

First author (quality score)	Year	Study groups (n)	Treatment (n)	Results*
		G3: massage and diathermy (78) G4: bed rest (29) G5: back school (50) G6: placebo ointment (72)		G4 vs G1: 3 weeks, 08; 2 months, 11; 6 months, 12 (acute) G3 vs G1: 3 weeks, 10; 2 months, 08; 6 months, 07 (acute); 3 weeks, -06; 2 months, -06; 6 months, -07 (chronic) G5 vs G1: 3 weeks, 07; 2 months, -03; 6 months, -13 (chronic) G6 vs G1: 3 weeks, 19 [†] ; 2 months, 12; 6 months, 07 (acute); 3 weeks, 09; 2 months, 08; 6 months, 12 (chronic) (statistical significance for most contrasts is indeterminate)
Skargren [58,59] (50)	1997	G1: SMT-DC (138) G2: physiotherapy (115)	m=7 m=8	Pain improvement: G2 vs G1: after treatment, 04; 6 months, 00; 1 year, 00 Disability: improvement G2 vs G1: after treatment, 03; 6 months, 01; 1 year, 00
Zylbergold [62] (38)	1981	G1: SMT-PT and heat (8) G2: flexion exercise, heat (10) G3: ergonomic instruction (10)	8 ? ?	Pain improvement: G2 vs G1: 1 month, 10 G3 vs G1: 1 month, 18 Disability improvement: G2 vs G1: 1 month, 09 G3 vs G1: 1 month, 06
Wreje [67] (13)	1992	G1: SMT-MD (23) G2: friction massage (23)	1 1	Pain G2 vs G1: 3 weeks, 10 (day); -20 (night); -30 (stairs) (data incomplete) Work loss (median days sick leave): G2 vs G1: 3 weeks, 07 [†] (data incomplete)

* Between-group differences in percentage points unless otherwise specified. Positive score indicates advantage for Group 1 (G1).

[†] p<.05 for unadjusted pairwise comparisons.

DC=chiropractor; DO=osteopathic doctor; m=mean; MD=medical doctor; PT=physiotherapist; SMT=spinal manipulative therapy; ?=information not available.

The NP RCTs were divided into three subcategories: acute, chronic and a mix of acute and chronic. They were too dissimilar in terms of patient characteristics, outcome measures, time points and type of treatment comparisons to allow for statistical pooling. Whenever RCT group differences did not show statistical significance, they were termed nonsignificant.

Acute neck pain

Five trials involving MOB or SMT were identified. Two met the criteria for admissibility (Table 12) [71,72], and three trials were excluded (Table 11) [73–75].

Nordemar and Thorer [71] (VS, 44) found a regimen with MOB was nonsignificantly better than the regimen without MOB in the short term for pain. MOB was no better than TENS.

Table 9
Evidence of efficacy for a mix of acute and chronic low back pain

SMT and/or MOB	Comparison intervention	Primary outcome(s)	Short term		Long term	
			Direction of effect*	Evidence level	Direction of effect*	Evidence level
SMT (with instruction in exercise)	Medical care with instruction in exercise [144]	Pain, disability	Similar	Moderate	Similar	Moderate
SMT/MOB	Myofascial soft tissue treatment or back school [54]	Pain, disability	Similar	Moderate	Similar	Moderate
SMT	McKenzie therapy [55]	Pain	Similar	Moderate	Similar	Moderate
SMT	Informational booklet [55]	Pain	Superior	Moderate	Similar	Moderate
SMT (as main part of chiropractic management)	Management by physical therapists [58,59]	Pain, disability	Similar	Moderate	Similar	Moderate
SMT	Standard medical care [60]	Pain, disability	Similar	Moderate	No evidence	No evidence
SMT (as main part of chiropractic management)	Hospital outpatient management including SMT [57]	Small advantage in disability and pain	Superior	Limited	Superior	Limited
SMT	Medication [64], placebo, massage [65]	Pain improvement	Superior	Limited	No evidence	No evidence

* Effect of SMT and/or MOB in relationship to comparison intervention.

MOB=spinal mobilization; SMT=spinal manipulative therapy.

Table 10
Methodological quality scores for neck pain trials in evidence

First author	Year	Validity items								Validity % score
		1	2	3	4	5	6	7	8	
Brodin [84]	1982	p	p	p	–	p	–	–	p	31
Bronfort [76]	2001	+	+	–	–	+	+	+	+	75
David [79]	1998	+	–	–	–	p	p	–	p	31
Giles [63]	1999	p	p	–	–	p	–	–	p	25
Hoving [82]	2001	+	+	–	–	+	+	p	+	69
Howe [72]	1983	–	p	–	–	p	–	–	p	19
Hurwitz [83]	2002	+	+	–	–	+	p	p	+	63
Jordan [78]	1998	p	p	–	–	+	–	–	p	31
Koes [39,40]	1992	p	p	+	–	p	–	p	+	50
Nordemar [71]	1981	–	–	–	–	p	+	+	+	44
Skargren [58,59]	1997,98	p	p	–	–	+	p	–	+	44
Sloop [77]	1982	–	–	+	p	p	–	–	p	31

+ = yes, – = no, p = unclear/partly.

See Appendix for operational definitions of validity items.

Howe et al. [72] (VS, 19) observed a higher proportion of patients receiving SMT experienced short-term pain improvement after the first treatment than a no-treatment control.

Evidence of efficacy

The evidence was inconclusive for acute NP in the short term. There were no trials with long-term outcomes in evidence (Table 13).

Chronic neck pain

Five trials met the criteria for admissibility in the treatment for chronic NP [39,40,76–79] (Table 14). Two trials [80,81] were excluded from evidence (Table 11).

Bronfort et al. [76] (VS, 75) found that high-technology rehabilitative exercise produced more long-term pain reduction than SMT. Koes et al. [39,40] (VS, 50) found SMT/MOB superior to massage and to medical care for physical functioning in the short term. Jordan et al. [78] (VS, 31) found small, nonsignificant differences between spinal manipulation, intensive exercise and physical therapy in the

short and long term. Sloop et al. [77] (VS, 31) showed a nonsignificant advantage of SMT over placebo in the short term for pain reduction and improvement. David et al. [79] (VS, 31) reported nonsignificantly higher reduction in pain for MOB than acupuncture in the short and long term; disability was similar.

Evidence of efficacy

There is moderate evidence for the following: that SMT/MOB is superior to general practice medical care and physical therapy in the short term for improving physical functioning; that SMT is at most similar to high-technology rehabilitative exercise in the short term and long term; that SMT/MOB is similar in effect to detuned modalities in the short term (Table 15).

Mix of acute and chronic neck pain

Five trials were included in evidence (Table 16) [58,63,82–84]. Six trials were excluded (Table 11) [85–90].

Hoving [82] (VS, 69) found that patients receiving MOB had faster improvement and less pain than patients receiving physical therapy or general practice care in the short and long term. Hurwitz et al. [83] (VS, 63) found essentially no differences between the effect of SMT and MOB in terms of pain and disability reduction in the short and long term. Skargren et al. [58] (VS, 44) showed that physical therapy resulted in greater pain reduction than SMT in the short and long term. Brodin [84] (VS, 31) found greater short-term pain reduction for a combination therapy including MOB than for a combination therapy including massage or for analgesics alone. Giles and Müller [63] (VS, 25) found SMT produced nonsignificantly more pain and disability improvement in the short term than acupuncture or analgesic medication.

Evidence of efficacy

There is moderate evidence that MOB is superior to PT for pain control in the short and long term and superior to

Table 11
Randomized trials of spinal manipulation and mobilization for neck pain excluded from evidence

First author	Year	Duration	Quality score	Reason for exclusion from evidence
Cassidy [85]	1992	a/c	44	Immediate posttreatment outcome for single session of manipulation
Fitz-Ritson [81]	1995	c	50	Unique contribution of manipulation to treatment effect could not be isolated
Kogstad [86]	1978	a/c	38	Unique contribution of manipulation to treatment effect could not be isolated
McKinney [73]	1989	a	31	Unique contribution of manipulation to treatment effect could not be isolated
Mealy [74]	1986	a	19	Unique contribution of manipulation to treatment effect could not be isolated
Parkin-Smith [88]	1998	?	19	Comparison of two manipulation types; unique contribution confounded
Provinciali [75]	1996	a	25	Unique contribution of manipulation to treatment effect could not be isolated
Schalkwyk [89]	2000	?	19	Comparison of two manipulation types, unique contribution confounded
Sterling [80]	2001	c	31	Immediate posttreatment outcome for single session of manipulation
Vasseljen [87]	1995	a/c	44	Unique contribution of manipulation to treatment effect could not be isolated
Wood [90]	2001	?	19	Comparison of two manipulation types; unique contribution confounded

a=acute; c=chronic; a/c=mix of acute and chronic; ?=unknown.

Table 12
Randomized clinical trials of spinal manipulation and mobilization for acute neck pain

First author (quality score)	Year	Study groups (n)	Treatments (n)	Results*
Howe [72] (19)	1983	G1: SMT-MD (26) G2: No treatment (26)	1–3	Pain improvement (% of patients) G2 vs G1: after first treatment, 62 [†] , 1 week, 14; 3 weeks, 18
Nordemar [71] (44)	1981	G1: MOB-PT and analgesic, education, rest, collar (10)	6	Pain: G2 vs G1: 1 week, -1; 6 weeks, 00; 3 months, 00 G3 vs G1: 1 week, 09; 6 weeks, 00; 3 months, 00
		G2: TENS and analgesic, education, rest, collar (10)	6	
		G3: Analgesics, education, rest, collar (10)	6	

* Between-group differences in percentage points unless otherwise specified. Positive score indicates advantage for Group 1 (G1).

[†] p<.05 for unadjusted pairwise comparisons.

G1=group 1; G2=group 2; G3=group 3; MD=medical doctor; MOB=spinal mobilization; PT=physiotherapist; SMT=spinal manipulative therapy; TENS=transcutaneous electrical nerve stimulation.

medical care in the short term. There is also moderate evidence that SMT and MOB are similar in the short and long term. There is limited evidence that SMT is inferior to PT in the short and long term. There is also limited short-term evidence that MOB is superior to some medical regimens (Table 17).

Sensitivity analysis

A sensitivity analysis was conducted to evaluate the effect of changing the quality scores required for each level of evidence in Table 1. We assessed the effect of ± 10 points in the 100-point quality scale. For LBP, lowering the required score would have added 4 studies with limited evidence of efficacy for SMT. Raising the score from 50 to 60 would have reduced the level of evidence from moderate to limited for 7 of 9 LBP studies. For NP, lowering the score would have introduced limited evidence of efficacy of MOB for acute NP and added to the moderate evidence of SMT efficacy for a mix of acute/chronic NP. Raising the cutoff score would have reduced moderate evidence for chronic NP to limited evidence. Overall, sensitivity analysis showed that changing the rules of evidence would have produced little impact on the conclusions of our review.

Discussion

Our review is an attempt to improve on the methodology of existing systematic reviews, as suggested by Assendelft et al. [1]. We decided that studies with confounded treatment effects could not support the efficacy of the target

therapies. Consequently, combination-therapy studies had to isolate the unique contribution of SMT and/or MOB to the overall treatment effect to be admitted into evidence. Patient-oriented outcomes, such as pain or disability, were required for all studies. An effort was made to transform the relevant outcomes to a common scale of percentage points, allowing a standardized comparison across different studies.

We chose to evaluate the evidence of efficacy based on the best evidence synthesis method [11,12] rather than a formal meta-analysis of all available RCTs. A number of meta-analytical methods have been advocated for combining clinical trials [91–94], but there is limited consensus regarding decision rules for statistical pooling of study results [95,96]. It is recognized by several authors that one of the most important limitations of published meta-analyses is inadequate control for clinical heterogeneity (important differences in treatments, outcome measures and clinical characteristics of patients) of included studies [14,95–97]. Because clinical heterogeneity was found to be a major issue in the RCTs that formed the basis for our efficacy determination, we decided not to perform a statistical pooling of trial results. However, if current efforts (eg, by the Cochrane Collaboration [98]) are successful in further developing the methodology, statistical pooling of clinically heterogeneous studies may be feasible in the future.

Systematic reviews on effectiveness of SMT/MOB

There are now more randomized controlled clinical trials on spinal manipulation for the management of LBP than for any other treatment method. Several systematic reviews of studies evaluating spinal manipulation for back pain have

Table 13
Evidence of efficacy for acute neck pain

SMT and/or MOB	Comparison intervention	Primary outcome(s)	Short term		Long term	
			Direction of effect*	Evidence level	Direction of effect*	Evidence level
MOB	TENS [71], Analgesics [71]	Pain	Inconclusive	Inconclusive	No evidence	No evidence
SMT	No treatment [72]	Pain	Inconclusive	Inconclusive	No evidence	No evidence

* Effect of SMT and/or MOB in relationship to comparison intervention.

MOB=mobilization; SMT=spinal manipulative therapy; TENS=transcutaneous electrical nerve stimulation.

Table 14
Randomized clinical trials of spinal manipulation and mobilization for chronic neck pain

First author (quality score)	Year	Study groups (n)	Treatments (n)	Results*
Bronfort [76] (75)	2001	G1: SMT-DC (64)	24	Pain: G2 vs G1: 5 weeks, -06; 11 weeks, -07; 3 months, -12 [†] ; 6 months, -06; 1 year, -07 (area under the curve favors G2 from 0–52 weeks [†]) Disability: G2 vs G1: 5 weeks, -03; 11 weeks, -03; 3 months, -05; 6 months, -03; 1 year, -04
		G2: high-tech exercise (63)	24	
		G3: SMT, low-tech exercise (64)	24	
David [79] (31)	1998	G1: MOB-PT. (13)	?	Pain: G2 vs G1: 6 weeks, 10; 6 months, 10 Disability: G2 vs G1: 6 weeks, 02; 6 months, 03
		G2: acupuncture (17)	?	
Jordan [78] (31)	1998	G1: SMT-DC (40)	12	Pain improvement: G2 vs G1: after treatment, 03; 4 months, -03; 1 year, 10 (median scores) G3 vs G1: after treatment, 03; 4 months, -03; 1 year, 03 Disability: improvement G2 vs G1: after treatment, -03; 4 months, -07; 1 year, 00 (median scores) G3 vs G1: after treatment, 03; 4 months, -03; 1 year, 00
		G2: physical therapy incl. MOB (39)	12	
		G3: intensive exercise (40)	12	
Koes [39,40] (50)	1992	G1: SMT/MOB-PT (21)	14	Main complaint improvement: G2 vs G1: 6 weeks, 00; 12 weeks, 08; 12 months, 06 G3 vs G1: 6 weeks, 17; 12 weeks, 15 G4 vs G1: 6 weeks, 04; 12 weeks, 15 Physical function improvement: G2 vs G1: 6 weeks, 09; 12 weeks, 14 [†] ; 12 months, 06 G3 vs G1: 6 weeks, 11; 12 weeks, 19 [†] G4 vs G1: 6 weeks, 03; 12 weeks, 04
		G2: massage, exercise, heat, PT (13)	6	
		G3: analgesic/anti-inflammatory, rest, exercise, posture (17)	?	
		G4: detuned PT modalities (14)	?	
Sloop [77] (31)	1982	G1: SMT-MD and amnesic dose diazepam (21)	1	Pain: G2 vs G1: 3 weeks, 13 Improvement (difference in % of patients reporting improvement): G2 vs G1: 3 weeks, 29
		G2: amnesic dose diazepam (18)	1	

* Between-group differences in percentage points unless otherwise specified. Positive score indicates advantage for Group 1 (G1).

[†] p<.05 for unadjusted pair-wise comparisons.

DC=chiropractor; MD=medical doctor; MOB=spinal mobilization; PT=physiotherapist; SMT=spinal manipulative therapy; ?=information not available.

been published since 1985. Most of the reviews have assessed and factored in the methodological quality or validity of the RCTs. However, weighting the credibility of trial results using these quality scores remains controversial, and no single approach for incorporating quality scores in the

determination of the evidence has been accepted (eg, methods suggested by Detsky et al. [99]). There is some evidence suggesting that nonrandomized, unblinded trials, cases series and trials with historical controls tend to overestimate the magnitude of a difference or an effect [100,101].

Table 15
Evidence of efficacy for chronic neck pain

SMT and/or MOB	Comparison intervention	Primary outcome(s)	Short term		Long term	
			Direction of effect*	Evidence level	Direction of effect*	Evidence level
SMT	High tech rehabilitative exercise [76]	Pain	Inferior/similar	Moderate	Similar	Moderate
SMT/MOB	GP management [39,40]	Physical function	Superior	Moderate	No evidence	No evidence
SMT/MOB	Physical therapy [39,40]	Physical function	Superior	Moderate	Inconclusive	Inconclusive

* Effect of SMT and/or MOB in relationship to comparison intervention.

GP=general practitioner; MOB=spinal mobilization; SMT=spinal manipulative therapy.

Table 16
Randomized clinical trials of spinal manipulation and mobilization for a mix of acute and chronic neck pain

First author (quality score)	Year	Study groups (n)	Treatments (n)	Results*
Brodin [84] (31)	1982	G1: MOB-PT and analgesics, information (23) G2: Analgesics, light massage, inform (17–25) G3: Analgesics (23)	9 9 ?	Pain (difference in % of patients with no/slight pain): G2 vs G1: 4 weeks, 24 [†] G3 vs G1: 4 weeks, 22 [†]
Giles [63] (25)	1999	G1: SMT-DC (23) G2: acupuncture (15) G3: medication (12)	6 6	Pain improvement: G2 vs G1: 4 weeks, 10 (median scores) G3 vs G1: 4 weeks, 13 Disability improvement: G2 vs G1: 4 weeks, 04 (median scores) G3 vs G1: 4 weeks, 10
Hoving [82] (69)	2001	G1: MOB-MT (40) G2: usual care, MD (40) G3: PT including massage, exercise, stretching (39)	≤6 ≤3 ≤12	Pain improvement: G2 vs G1: 7 weeks, 16 [†] ; 13 weeks, 06; 1 year, 01 G3 vs G1: 7 weeks, 13 [†] ; 13 weeks, 04; 1 year, 11 [†] Success (difference in % patients recovering): G2 vs G1: 7 weeks, 34 [†] ; 13 weeks, 30 [†] ; 1 year, 15 G3 vs G1: 7 weeks, 19 [†] ; 13 weeks, 12; 1 year, 09
Hurwitz [83] (63)	2002	G1: SMT-DC (171) G2: MOB-DC (165) 2×2×2 factorial design SMT/MOB with and without heat and electric stimulation	? ?	Pain: G2 vs G1 (main effect): 2 weeks, 01; 6 weeks, -02; 3 months, -0; 6 months, -01 (adjusted differences) Disability: G2 vs G1 (main effect): 2 weeks, -01; 6 weeks, -01; 3 months, -01; 6 months, -01 (adjusted differences)
Skargren [58,59] (44)	1997	G1: SMT-DC (41) G2: PT (29)	m=7 m=8	Pain improvement: G2 vs G1: after treatment, -12 [†] ; 6 months, -12; 1 year, -17 [†] Disability: improvement G2 vs G1: after treatment, -02; 6 months, -03; 1 year, -04

* Between-group differences in percentage points unless otherwise specified. Positive score indicates advantage for Group 1 (G1).

[†] p<.05 for unadjusted pairwise comparisons.

DC=chiropractor; G1=group 1; G2=group 2; G3=group 3; m=mean; MOB=spinal mobilization; MT=manual therapist; SMT=spinal manipulative therapy; ?=information not available.

Yet, there is little evidence that quality scores assigned to RCTs are good predictors of the magnitude and direction of outcomes of therapy [102]. Most research methodologists are in agreement that quality is important [103] but are unclear as to how much quality really matters.

The first attempt at statistical pooling of clinical trial results was performed by Ottenbacher and Di Fabio [2], who

calculated effect sizes for pain and flexibility in 92 subcomparisons within nine trials on SMT for LBP, 2 of which were nonrandomized. He concluded that there was only limited empirical support for the efficacy of SMT.

In 1991, Koes et al. [16] published a systematic review of back and neck pain and concluded that, even though some results were promising, the efficacy of spinal manipulation

Table 17
Evidence of efficacy for a mix of acute and chronic neck pain

SMT and/or MOB	Comparison intervention	Primary outcome(s)	Short term		Long term	
			Direction of effect*	Evidence level	Direction of effect*	Evidence level
MOB	Physical therapy [82]	Pain	Superior	Moderate	Superior	Moderate
MOB	Management by family physicians [82]	Pain	Superior	Moderate	Inconclusive	Inconclusive
SMT	MOB [83]	Pain, disability	Similar	Moderate	Similar	Moderate
SMT (as main part of chiropractic management)	Physical therapy (management by physical therapist) [58,59]	Pain	Inferior	Limited	Inferior	Limited
MOB (with analgesics, light massage, information)	Analgesics, light massage, information [84]	Pain	Superior	Limited	No evidence	No evidence

* Effect of SMT and/or MOB in relationship to comparison intervention.

MOB=spinal mobilization; SMT=spinal manipulative therapy.

had not been convincingly demonstrated. They chose not to perform statistical pooling but to primarily look at trial results as reported by authors, and relate the methodological quality to negative and positive outcomes. They also concluded that the quality of the 34 trials on LBP was disappointingly low and much more attention needed to be paid to methodology in future trials. An update in 1996 of the Koes et al. review involving three additional trials did not change their conclusions [104].

Anderson et al. [4] performed effect size pooling for 23 LBP trials, 5 of which were nonrandomized, and concluded that SMT was consistently more effective than a number of comparison therapies. A sensitivity analysis including only the studies with relatively high-quality scores yielded a slightly lowered pooled estimate of effect size. Similarly, Di Fabio [3] found that the published clinical trials did provide evidence of efficacy of spinal manipulation for treatment of acute LBP.

In a more detailed and critical evaluation, Shekelle et al. [5] concluded that spinal manipulation had been demonstrated to be of short-term benefit in certain patients, particularly those with uncomplicated acute LBP. They based this conclusion on a meta-analysis (statistical pooling) of a subset of seven clinical trials, which had data on recovery at 3 weeks. The overall pooled estimate showed a 17% higher likelihood of recovery in favor of spinal manipulation. However, a substantial number of trials were excluded from the meta-analysis because most of the published RCTs at the time used continuous outcomes that could not be collapsed into dichotomous outcomes used in the meta-analysis (ie, recovered/not recovered). The reviews by Andersen et al. [4] and Shekelle et al. [5] formed the major basis for the conclusions regarding the efficacy of spinal manipulation in the acute low back problems guidelines developed by the Agency for Health Care Policy and Research in the United States [19].

Two reviews by Assendelft et al. [17,105] (1992 and 1996) have focused entirely on trials addressing the efficacy of SMT for patients with LBP in which the SMT was delivered by chiropractors. The result of the second review, an update of the first involving a total of eight RCTs, was that no convincing evidence of efficacy of chiropractic SMT for either chronic or acute LBP could be demonstrated. The authors considered performing statistical pooling but decided that it was not possible because of the heterogeneity of the trials [17].

The most comprehensive systematic review involving an array of different treatments for LBP was reported by van Tulder et al. [7] in 1997. They assessed the methodological quality of the trials and used specific evidence-based rules to determine the presence and strength of evidence of efficacy. They concluded that for acute LBP, there was limited evidence to suggest that spinal manipulation is better than placebo, physical therapy, exercise and short-wave diathermy. For chronic LBP, they found strong evidence that spinal manipulation was better than placebo and moderate evidence

that it was better than the treatment offered by a general practitioner, massage, bed rest and analgesics.

Also in 1997, Bronfort [106,107] published a systematic review of the efficacy of spinal manipulation emphasizing the magnitude of treatment effects compared with other treatments in determining the strength of evidence. He elected to ignore the conclusions by the authors of the individual RCTs and to focus on the data only. He reached a conclusion similar to that of Van Tulder et al. [7], finding evidence of short-term efficacy for spinal manipulation in patients with both acute and chronic LBP. Currently, a Cochrane review by Assendelft and Shekelle [108] is in process that addresses the efficacy of spinal manipulation for both acute and chronic LBP.

The methodological differences among systematic reviews have the potential to generate varying conclusions regarding the efficacy of spinal manipulation. Surprisingly, the conclusions regarding SMT for acute LBP have been relatively consistent, with one exception. The majority of the reviews indicated some evidence supporting the short-term efficacy of SMT for acute LBP, whereas Koes et al. [104] found the evidence inconclusive. For chronic LBP, the results of the systematic reviews have been more mixed, with the earlier reviews finding inconclusive evidence and later reviews finding moderate to strong evidence in support of SMT. Table 18 summarizes the systematic reviews that have addressed SMT for LBP.

Four systematic reviews have assessed the efficacy of SMT and MOB in NP conditions [3,16,109,110]. Koes et al. [16] found no convincing evidence of efficacy of SMT in NP patients based on the review of five trials. Di Fabio [3] also found no evidence of efficacy. Hurwitz et al. [110] reviewed three RCTs on acute NP [71,73,74] and concluded that there was a short-term benefit of cervical MOB. In contrast, we excluded two of the studies [73,74] contributing to this conclusion because the unique treatment effects of MOB could not be isolated. Furthermore, Hurwitz et al. [110] performed a meta-analysis of three subacute/chronic NP trials [40,72,77]. They concluded that SMT and/or MOB

Table 18
Summary conclusions for systematic reviews of spinal manipulation for low back pain based on all available randomized clinical trials at the time of review

First author, year	Low back pain	
	Acute	Chronic
Ottensbacher, 1985 [2]	+	?
Di Fabio, 1992 [3]	+	?
Anderson, 1992 [4]	+	*
Shekelle, 1992 [5]	+	?
Koes, 1996 [16,104]	?†	?
van Tulder, 1997 [7]	+	+
Bronfort, 1997 [106,107]	+	+

*=no differentiation made between acute and chronic conditions.

†=evidence of spinal manipulation efficacy in subgroups.

+ =conclusions in favor of spinal manipulation efficacy; ?=inconclusive evidence of spinal manipulation efficacy.

showed a clinically important short-term advantage over muscle relaxants and usual medical care. We decided to refrain from statistical pooling of the trials on the grounds of clinical heterogeneity. Despite the methodological differences, the findings of Hurwitz et al. are consistent with our results. Finally, Aker et al. [109] concluded that conservative treatment of SMT and MOB in combination with other therapies is efficacious for NP. In their discussion, they state that their analysis did not allow for the isolation of the unique effect of the target therapies.

In a review of reviews on treatment for NP, Hoving et al. [111] showed that there was poor concordance among reviews including effectiveness of SMT and MOB. Many of the reviews displayed major methodological flaws. The authors concluded that there is a paucity of evidence from primary studies on NP, and hence, more research is needed to allow systematic reviews to formulate stronger conclusions.

Clinical practice guidelines

Since 1990, national health-care agencies, advisory groups or family medicine groups in North America, Europe, Israel, New Zealand and Australia have developed official national LBP guidelines (see Table 19). The number of RCTs has increased during this time, and different criteria have been used for prioritizing and incorporating scientific evidence in the development of these documents. It is therefore not surprising that the recommendations vary substantially. The New Zealand [112] and original British guidelines [113] relied primarily on the conclusions of the US guidelines. The Dutch [114] guidelines are based on a mixture of evidence and opinion, the Australian guidelines [115] on a nonsystematic review of the literature, and the Israeli guidelines [116] on the results of the systematic review by Koes et al. published in 1996 [16,117]. The US [19], the updated British [118]

and the newly published Norwegian guidelines [119] followed explicit rules for determining and weighting the scientific evidence. None of these last three mentioned guidelines have assessed the efficacy for chronic LBP, but all conclude that there is efficacy for and recommend the use of spinal manipulation in the treatment of acute LBP. Of the guidelines that have addressed the treatment of both acute and chronic LBP, the Finnish [120], Swiss [121] and German [122] advocate the use of SMT only in the acute phase. The Danish MTV report published in 1999 [123] recommends SMT as a treatment option for both acute and chronic LBP. The Swedish guidelines published in 2000 [124] also concluded that there is scientific evidence to support the use of SMT for short-term relief of both acute and chronic LBP. Currently, the European countries are working together to coordinate and produce updated European evidence-based guidelines for both acute and chronic LBP. As of mid-2002, the recommendations for acute LBP are in the process of being published.

Conclusions about the strength of evidence from systematic reviews and clinical guidelines are largely dependent on the evidence-classification system used by the authors. Because of the lack of consensus in this area [103], efforts are being made primarily by a rapidly growing international organization, the Cochrane Collaboration [125], to standardize methods guiding the conduct of systematic reviews. This organization is dedicated to the conduct of the highest quality systematic reviews of the effects of health care. As these standards evolve and get implemented, the validity of many of the systematic reviews and clinical guidelines in existence will likely be questioned and either abandoned or updated appropriately. Clinicians using guidelines are advised to become familiar with critical appraisal tools to help them in evidence-based clinical decision making [126,127].

Limitations

Clinicians should exercise caution in interpreting the results of individual RCTs on SMT and/or MOB. In spite of urgent calls for improved methodological quality of RCTs on spinal manipulation [105,128], it appears that even the most recently published RCTs have been of discouragingly low quality. Fifty-two (75%) of the 69 RCTs in this review exhibited relatively low quality (validity scores less than 50). Of the 43 trials accepted into evidence, 29 (67%) also had relatively low validity scores (6 to 44). Additionally, clinicians should be careful about generalizing the findings of systematic reviews to practice. Disparate patient populations are likely to be included in the reviews, and potentially important distinguishing characteristics, such as condition severity, are not always carefully defined. In addition, providers with different backgrounds and training apply diverse SMT/MOB therapeutic approaches.

Optimally, reviews should include all trials regardless of language [10]. Because of the languages spoken by the authors, this review was restricted to English, Scandinavian

Table 19

Summary conclusions from national clinical guidelines that include an assessment of the efficacy of spinal manipulation for low back pain

Country, year	Acute	Chronic
USA [19], 1994	+	NA
Holland [114], 1996	–*	+
Israeli [116], 1996	?	?
New Zealand [112], 1997	+	NA
Australia [115], 2000	–†	NA
Great Britain [118], 1999	+	NA
Switzerland [121], 1997	+	?
Denmark (MTV) [123], 1999	+	+
Germany [122], 2002	+	?
Sweden [124], 2000	+	+
Finland [120], 2001	+	?
Norway [119], 2001	+	NA

* Evidence of effectiveness but guideline group recommended against.

† No reason to prefer spinal manipulative therapy over other conservative options.

+ = recommends spinal manipulation as a treatment option; ? = evidence unclear; NA = not applicable (not part of the guideline).

and Dutch languages. Although an attempt was made to identify trials in other languages, this approach was not fully systematic and may have overlooked some relevant trials. However, none of the over 50 reviews previously reviewed by Assendelft et al. [1] included RCTs that were published in languages other than those addressed in this review.

Another possible limitation of the current review is publication bias [129]. No exhaustive effort was made to identify unpublished research, which is more likely to have negative outcomes [130–132]. This phenomenon is likely to be partly the result of lack of submission for and acceptance of negative trials for publication [132]. It is recognized that attempts to retrieve unpublished data from trials are also likely to be biased [131]. The best solution to this problem is to insist that journal editors make a policy of deciding on publication based on scientific quality and not on the outcome of the study. Also, to help prevent publication bias, prospective registration of all RCTs should be undertaken [130,132].

Specific conclusions regarding the strength of evidence from systematic reviews and practice guidelines vary substantially. This is not surprising given the differences in literature evaluation protocols regarding study inclusion criteria, subclassification of back and NP by duration of complaint and recurrence, methodological quality determination, rules for weighting evidence and statistical analysis. The validity scores of this review generally demonstrated modest correlation with the methodological scores of other systematic reviews on the topic ($r=0.41$ to 0.74) [7,16,110]. However, the five-point validity scale used in one review [109] was negatively correlated with our scores ($r=-0.26$). This means that substantial inconsistencies between quality scoring systems exist. In some cases, trials assigned low-quality scores in this review were assigned high scores in previous reviews. This disparity in review results is consistent with findings of other investigators in different clinical topic areas [103]. Until standardized methods to conduct systematic reviews are fully implemented (such as those being developed by the Cochrane Collaboration), there will continue to be disparity between even the highest-quality systematic reviews.

Trial results and treatment of individual patients

Interpretation of the results of RCTs has traditionally focused on the statistical significance, whereas the clinical importance of differences between treatments or control has frequently been ignored. Very little is known about what is considered by patients to be a minimal clinically important change in outcome measures, such as pain and disability. However, a key question needed to interpret the results of clinical trials is whether the measured standardized group difference in outcomes (effect size) is clinically important. Sometimes, the investigators arbitrarily stipulate the minimal clinically important difference. Usually, authors assume that if the mean difference between a treatment and

control is appreciably less than the smallest predetermined important change, then the treatment had little or no effect. Conversely, it is also assumed that if the observed mean difference between treatments is substantially larger than the smallest important change, most or all patients benefited from the treatment. This is not necessarily true.

Benefit depends not only on differences between group means, but also on the distribution of outcomes among patients within each treatment group. Members of an international clinical significance consensus group recently addressed this topic in a series of publications [133–135]. They concluded that no single approach to interpreting findings from RCTs and systematic reviews is perfect. Authors too often draw inappropriate conclusions when they declare treatment ineffectiveness based solely on presence or absence of statistical differences between a test treatment and a control. To inform decisions about management of the individual patients, it may be much more appropriate to think in terms of available treatment options that have shown a meaningful clinical effect rather than choosing or discarding specific therapies based on mean group differences of undefined clinical importance.

Side-effects and complications

In evaluating any therapy, weighing the potential risks against the potential benefits is a crucial issue. The adverse reactions associated with spinal manipulation can be divided into three categories. The first category consists of relatively common benign transient side effects, such as local muscle and joint soreness, which rarely lead to even short-term impairment in functional status [136]. The best source of information on these common side effects comes from several Scandinavian prospective studies [137], which show that the mild short-lasting muscle soreness occurs in up to half of patients treated. The second category consists of reversible serious complications, which are relatively uncommon, such as progression of neurological deficits resulting from lumbar disc herniation [136]. The third category consists of irreversible complications, which appear to be extremely rare. The risk of irreversible cauda equina syndrome is estimated to be as low as 1 in 100 million lumbar spine manipulations [5,138]. Additionally, misdiagnosis leading to delay in optimal treatment (eg, cancer presenting as a spinal pain syndrome) falls into this category. There are currently 46 RCTs published on spinal manipulation for LBP involving over 5,000 patients. No serious adverse events have been reported in these trials [107]. A systematic review of the literature to date on the second and third categories of complications consists mainly of single cases or a series of case reports totaling approximately 300 cases, of which the vast majority are related to manipulation of the cervical spine [139]. Individual estimates and the results of the retrospective surveys consistently suggest a risk of serious cerebrovascular complication of approximately 1 per 1 million cervical manipulations [140]. Overall, serious or severe

complications from spinal manipulation seem to be very rare. Although underreporting in the literature is a likely phenomenon, some reports may have wrongly attributed side effects to spinal manipulation [141]. Thus, the existing estimates are associated with substantial uncertainty and will only improve when more data become available from well-designed prospective studies [139].

Cost-effectiveness

Cost-effectiveness is defined as the cost associated with a specified clinical intervention per unit of a selected health outcome, such as pain reduction or improvement in disability and functional status [142]. One Canadian health economist considers the available evidence of cost-effectiveness of chiropractic SMT overwhelming compared with medical and other forms of therapy [143] and made recommendations to health policy makers that chiropractic inclusion in public health-care plans would result in substantial health-care cost savings in the area of LBP. This conclusion is almost exclusively based on analysis of retrospective and nonrandomized studies, which do not allow conclusions about clinical effectiveness. Cost comparisons have been performed alongside a few of the randomized studies. Based on retrospective cost estimations in the British Meade trial [57], the authors argued that the potential cost savings over a 3-year period were higher for patients with LBP managed by chiropractors than for patients managed by hospital outpatient departments [56,57]. In the trial by Cherkin et al. [55], the mean costs of care over a 2-year period were very similar for the physical therapy and chiropractic groups but about three times higher than for the booklet group. Skargren et al. [58] found no difference in the cost-effectiveness ratio between chiropractic and physical therapy in the management of neck and back pain in Sweden.

The most comprehensive cost-effectiveness analysis to date was performed by Hoving et al. [111]. The trial compared MOB, physical therapy and general practitioner care for a case mix of acute and chronic NP. MOB was more cost-effective than the other two interventions both in the short and long term. However, if the limitations of the existing studies addressing cost-effectiveness are carefully considered, and the premise that clinical efficacy and its relationship to cost is best addressed in prospective randomized studies, then, at present, the weight of evidence is still insufficient to make any clear conclusions regarding the relative cost-effectiveness of SMT in comparison with other health-care choices for LBP.

Conclusions

For acute LBP, there is moderate evidence that SMT provides more short-term pain relief than mobilization and detuned diathermy, and limited evidence of faster recovery than a commonly used physical therapy treatment strategy.

For chronic LBP, there is moderate evidence that SMT has an effect similar to an efficacious prescription NSAID, SMT/MOB is effective in the short term when compared with placebo and general practitioner care, and SMT/MOB is effective in the long term compared to physical therapy. There is limited to moderate evidence that SMT is better than physical therapy and home back exercise in both the short and long term. There is limited evidence that SMT is superior to sham SMT in the short term and superior to chemonucleolysis for disk herniation in the short term. There is limited evidence that MOB is inferior to back exercise after disc herniation surgery.

For a mix of acute and chronic LBP, SMT/MOB provides either similar or better pain outcomes in the short and long term when compared with placebo and with other treatments, such as McKenzie therapy, medical care, management by physical therapists, soft tissue treatment and back school.

For acute NP, there are few studies and the evidence is currently inconclusive.

For chronic NP, there is moderate evidence that SMT/MOB is superior to general practitioner management for short-term pain reduction but that SMT offers at most similar pain relief to high-technology rehabilitative exercise in the short and long term.

For a mix of acute and chronic NP, the overall evidence is not clear. There is moderate evidence that MOB is superior to physical therapy and family physician care, and similar to SMT in both the short and long term. There is limited evidence that SMT, in both the short and long term, is inferior to physical therapy.

Our data synthesis suggests that recommendations can be made with some confidence regarding the use of SMT and/or MOB as a viable option for the treatment of both LBP and NP. There have been few high-quality trials distinguishing between acute and chronic patients, and most are limited to shorter-term follow-up. Future trials should examine well-defined subgroups of patients, further address the value of SMT and MOB for acute patients, establish optimal number of treatment visits and consider the cost-effectiveness of care.

Appendix

Operational definitions of items included in the Critical Evaluation List for Randomized Clinical Trials

Scoring: The critical evaluation list contains eight items with three choices: yes (+), partial (P) and no (–). One point is awarded for a yes rating, a half point is assigned for a partial rating, and 0 points is given for a no rating. The quality score is determined by dividing the point total by 8 and multiplying the result by 100 to create a 100-point scale.

1. Similarity of baseline characteristics or adjusted effects reported

Yes: Comparability established by tabulating important predictor variables, including baseline value of outcome variables. If not comparable, adjusted between-groups effects computed (eg, analysis of covariance). P: Baseline comparability established for some but not all of the important predictor variables. No: Baseline comparability not established, and appropriate statistical adjustments not made or not possible.

2. Concealment of treatment allocation

Yes: The randomization process and allocation concealment established explicitly and appropriate. P: Incomplete description of randomization/concealment. No: Only randomization established.

3. Blinding of patients

Yes: Patient blinded to treatment. P: Patient partially blinded or blinding not clearly documented. No: Patient blinding not established.

4. Blinding of provider/attention bias

Yes: Provider blinded to treatment. P: Partial blinding achieved or documentation that provider enthusiasm/attention equivalent among groups. For example, two providers used such that a blinded provider interacts with the patient and an unblinded provider renders treatment. No: Provider not blinded and provider enthusiasm/attention not controlled.

5. Blinding of assessor/unbiased outcome assessment

Yes: Outcomes assessor blinded to treatment. For self-administered outcomes, patients not influenced by study personnel (eg, mailed questionnaire). P: Partial blinding or influence unclear. No: Assessor not blinded. For self-administered outcomes, patients likely influenced by providers or investigators during self-assessment.

6. Dropouts reported and accounted for in the analysis

Yes: Described for each group separately and impact on outcomes analyzed, or dropout rate less than 5%. P: Incomplete description/analysis. No: Not analyzed, or omission not justified.

7. Missing data reported and accounted for in the analysis

Yes: Described for each group separately and impact on outcomes analyzed, or missing data rate less than 5%. P: Incomplete description/analysis. No: Not analyzed, or omission not justified.

8. Intention-to-treat analysis/balanced cointervention

Yes: All patient data analyzed according to group of initial random allocation. In studies with documented full compliance with allocated treatments, no differential co-intervention between groups. P: Unclear from article whether intention-to-treat analysis was used and how. No: No intention-to-treat analysis used when applicable.

References

- [1] 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.
- [2] Ottenbacher K, Di Fabio RP. Efficacy of spinal manipulation/mobilization therapy. A meta-analysis. *Spine* 1985;10:833–7.
- [3] Di Fabio RP. Efficacy of manual therapy. *Phys Ther* 1992;72:853–64.
- [4] 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.
- [5] Shekelle PG, Adams AH, Chassin MR, Hurwitz EL, Brook RH. Spinal manipulation for low-back pain. *Ann Intern Med* 1992;117:590–8.
- [6] Lee KP, Carlini WG, McCormick GF, Albers GW. Neurologic complications following chiropractic manipulation: a survey of California neurologists. *Neurology* 1995;45:1213–5.
- [7] 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.
- [8] Moher D, Jadad AR, Nichol G, Penman M, Tugwell P, Walsh S. Assessing the quality of randomized controlled trials: an annotated bibliography of scales and checklists. *Controlled Clin Trials* 1995; 16:62–73.
- [9] Hoehler FK, Tobis JS. Appropriate statistical methods for clinical trials of spinal manipulation. *Spine* 1987;12:409–11.
- [10] Moher D, Olkin I. Meta-analysis of randomized controlled trials. A concern for standards. *JAMA* 1995;274:1962–4.
- [11] Spitzer WO. Meta-meta-analysis: unanswered questions about aggregating data. *J Clin Epidemiol* 1991;44:103–7.
- [12] Slavin RE. Best-evidence synthesis: an alternative to meta-analytic and traditional reviews. *Educ Res* 1986;15:5–11.
- [13] Haldeman S, Phillips RB. Spinal manipulative therapy in the management of low back pain. In: Frymoyer JW, Ducker TB, Hadler NM, Kostuik JP, Weinstein JN, Whitecloud TS, editors. *The adult spine: principles and practice*. New York: Raven Press, Ltd., 1991:1581–605.
- [14] Slavin RE. Best evidence synthesis: an intelligent alternative to meta-analysis. *J Clin Epidemiol* 1995;48:9–18.
- [15] Spitzer WO, Lawrence V, Dales R, et al. Links between passive smoking and disease: a best-evidence synthesis. A report of the Working Group on Passive Smoking. *Clin Invest Med* 1990;13:17–46.
- [16] Koes BW, Assendelft WJ, van der Heijden GJ, Bouter LM, Knipschild PG. Spinal manipulation and mobilisation for back and neck pain: a blinded review. *BMJ* 1991;303:1298–303.
- [17] Assendelft WJ, Koes BW, van der Heijden GJMG, 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.
- [18] Bronfort G. Efficacy of manual therapies of the spine: a critical appraisal and review of the literature. Amsterdam, The Netherlands: Thesis Publishers Amsterdam, 1997.
- [19] Bigos S, Bowyer O, Braen GR, Brown K, Deyo R, Haldeman S. Clinical Practice Guideline Number 14: acute low back problems in adults. Rockville, MD: Public Health Service, Agency for Health Care Policy and Research, US Department of Health and Human Services, December 1994. AHCPR publication 95–0642.
- [20] 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;12:703–6.
- [21] Mathews JA, Mills SB, Jenkins VM, et al. Back pain and sciatica: controlled trials of manipulation, traction, sclerosant and epidural injections. *Br J Rheumatol* 1987;26:416–23.
- [22] Godfrey CM, Morgan PP, Schatzker J. A randomized trial of manipulation for low-back pain in a medical setting. *Spine* 1984;9:301–4.
- [23] Glover JR, Morris JG, Khosla T. Back pain: a randomized clinical trial of rotational manipulation of the trunk. *Br J Industr Med* 1974; 31:59–64.
- [24] MacDonald RS, Bell CMJ. An open controlled assessment of osteopathic manipulation in nonspecific low-back pain. *Spine* 1990;15: 364–70.

- [25] Farrell JP, Twomey LT. Acute low back pain. Comparison of two conservative treatment approaches. *Med J Aust* 1982;1:160–4.
- [26] 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;170:1–117.
- [27] 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.
- [28] 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.
- [29] 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.
- [30] Gemmell 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.
- [31] Helliwell PS, Cunliffe G. Manipulation in low back pain. *Physician* 1987;187–8.
- [32] Rasmussen GG. Manipulation in treatment of low back pain. A randomized clinical trial. *Manuelle Med* 1979;1:8–10.
- [33] Seferlis T, Nemeth G, Carlsson AM, Gillstrom P. Conservative treatment in patients sick-listed for acute low-back pain: a prospective randomised study with 12 months' follow-up. *Eur Spine J* 1998;7:461–70.
- [34] 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.
- [35] 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.
- [36] Triano JJ, McGregor M, Hondras MA, Brennan PC. Manipulative therapy versus education programs in chronic low back pain. *Spine* 1995;20:948–55.
- [37] 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.
- [38] 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.
- [39] Koes BW, Bouter LM, van Mameren H, 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.
- [40] Koes BW, Bouter LM, van Mameren H, 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.
- [41] 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 Med* 1986;2:63–7.
- [42] 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.
- [43] Burton AK, Tillotson KM, Cleary J. Single-blind randomised controlled trial of chemonucleolysis and manipulation in the treatment of symptomatic lumbar disc herniation. *Eur Spine J* 2000;9:202–7.
- [44] 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.
- [45] Hemmilä HM, Keinänen-Kiukaanniemi S, Levoska S, Puska P. Long-term effectiveness of bone-setting, light exercise therapy, and physiotherapy for prolonged back pain: a randomized controlled trial. *J Manipulative Physiol Ther* 2002;25:99–104.
- [46] 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.
- [47] 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.
- [48] Gibson T, Grahame R, Harkness J, Woo P, Blaggrave P, Hills R. Controlled comparison of short-wave diathermy treatment with osteopathic treatment in non-specific low back pain. *Lancet* 1985;1:1258–61.
- [49] Arkuszewski Z. The efficacy of manual treatment in low back pain: a clinical trial. *Manual Med* 1986;2:68–71.
- [50] 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.
- [51] 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. *BMJ* 1978;2:1338–40.
- [52] Sims-Williams H, Jayson MI, Young SM, Baddeley H, Collins E. Controlled trial of mobilisation and manipulation for low back pain: hospital patients. *BMJ* 1979;2:1318–20.
- [53] Hurwitz EL, Morgenstern H, Harber P, et al. Second prize—the effectiveness of physical modalities among patients with low back pain randomized to chiropractic care: findings from the UCLA low back pain study. *J Manipulative Physiol Ther* 2002;25:10–20.
- [54] Hsieh CY, Adams AH, Tobis J, et al. Effectiveness of four conservative treatments for subacute low back pain: a randomized clinical trial. *Spine* 2002;27:1142–8.
- [55] Cherkin DC, Deyo RA, Battie 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.
- [56] 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.
- [57] 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.
- [58] 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.
- [59] 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;23:1875–84.
- [60] 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.
- [61] Bronfort G. Chiropractic versus general medical treatment of low back pain: a small scale controlled clinical trial. *Am J Chiro Med* 1989;2:145–50.
- [62] Zylbergold RS, Piper MC. Lumbar disc disease: comparative analysis of physical therapy treatments. *Arch Phys Med Rehabil* 1981;62:176–9.
- [63] Giles LGF, Müller R. Chronic spinal pain syndromes: a clinical pilot trial comparing acupuncture, a nonsteroidal anti-inflammatory drug, and spinal manipulation. *J Manipulative Physiol Ther* 1999;22:376–81.
- [64] Doran DM, Newell DJ. Manipulation in treatment of low back pain: a multicentre study. *BMJ* 1975;2:161–4.
- [65] Hoehler FK, Tobis JS, Buerger AA. Spinal manipulation for low back pain. *JAMA* 1981;245:1835–8.
- [66] Postacchini F, Facchini M, Paliieri P. Efficacy of various forms of conservative treatment in low back pain. A comparative study. *Neuro Orthop* 1988;6:28–35.

- [67] 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.
- [68] 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. *J Manual Med* 1989;4: 44–6.
- [69] Rupert RL, Wagnon R, Thompson P, Ezzeldin MT. Chiropractic adjustments: results of a controlled clinical trial in Egypt. *ICA Int Rev Chiro* 1985;58–60.
- [70] 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.
- [71] Nordemar R, Thorner C. Treatment of acute cervical pain—a comparative group study. *Pain* 1981;10:93–101.
- [72] Howe DH, Newcombe RG, Wade MT. Manipulation of the cervical spine—a pilot study. *J R Coll Gen Pract* 1983;33:574–9.
- [73] McKinney LA, Dornan JO, Ryan M. The role of physiotherapy in the management of acute neck sprains following road-traffic accidents. *Arch Emerg Med* 1989;6:27–33.
- [74] Mealy K, Brennan H, Fenelon GC. Early mobilization of acute whiplash injuries. *Br Med J Clin Res Ed* 1986;292:656–7.
- [75] Provinciali L, Baroni M, Illuminati L, Ceravolo MG. Multimodal treatment to prevent the late whiplash syndrome. *Scand J Rehabil Med* 1996;28:105–11.
- [76] Bronfort G, Evans R, Nelson B, Aker P, Goldsmith C, Vernon H. A randomized clinical trial of exercise and spinal manipulation for patients with chronic neck pain. *Spine* 2001;26:788–99.
- [77] Sloop PR, Smith DS, Goldenberg E, Dore C. Manipulation for chronic neck pain. A double-blind controlled study. *Spine* 1982;7: 532–5.
- [78] Jordan A, Bendix T, Nielsen H, Rolsted Hansen F, Host D, Winkel A. Intensive training, physiotherapy, or manipulation for patients with chronic neck pain. A prospective single-blinded randomized clinical trial. *Spine* 1998;23:311–9.
- [79] David J, Modi S, Aluko AA, Robertshaw C, Farebrother J. Chronic neck pain: a comparison of acupuncture treatment and physiotherapy. *Br J Rheumatol* 1998;37:1118–22.
- [80] Sterling M, Jull G, Wright A. Cervical mobilisation: concurrent effects on pain, sympathetic nervous system activity and motor activity. *Manual Therapy* 2001;6:72–81.
- [81] Fitz-Ritson D. Phasic exercises for cervical rehabilitation after “whiplash” trauma. *J Manipulative Physiol Ther* 1995;18:21–4.
- [82] Hoving JL. Neck pain in primary care: the effects of commonly applied interventions. Institute for Research in Extramural Medicine (EMGO Institute) of the Vrije Universiteit, The Netherlands, 2001.
- [83] Hurwitz EL, Morgenstern H, Harber P, Kominski GF, Yu F, Adams AH. A randomized trial of chiropractic manipulation and mobilization for patients with neck pain: clinical outcomes from the UCLA neck-pain study. *Am J Public Health* 2002;92:1634–41.
- [84] Brodin H. Cervical pain and mobilization. *Manuelle Med* 1982; 20:90–4.
- [85] Cassidy JD, Lopes AA, Yong-Hing K. The immediate effect of manipulation versus mobilization on pain and range of motion in the cervical spine: a randomized controlled trial. *J Manipulative Physiol Ther* 1992;15:570–5.
- [86] Kogstad OA, Karterud S, Gudmundsen J. Cervicobrachialgia. Et kontrollert forsok med konvensjonell behandling og manipulasjon. *Tidsskr Nor Laegeforen* 1978;98:845–8.
- [87] Vasseljen O, Johansen BM, Westgaard RH. The effect of pain reduction on perceived tension and EMG-recorded trapezius muscle activity in workers with shoulder and neck pain. *Scand J Rehabil Med* 1995;27:243–52.
- [88] Parkin-Smith GF, Penter CS. A clinical trial investigating the effect of two manipulative approaches in the treatment of mechanical neck pain: a pilot study. *J Neuromusculoskel System* 1998;6:6–16.
- [89] van Schalkwyk R, Parkin-Smith GF. A clinical trial investigating the possible effect of the supine cervical rotatory manipulation and the supine lateral break manipulation in the treatment of mechanical neck pain: a pilot study. *J Manipulative Physiol Ther* 2000;23:324–31.
- [90] Wood TG, Colloca CJ, Matthews R. A pilot randomized clinical trial on the relative effect of instrumental (MFMA) versus manual (HVLA) manipulation in the treatment of cervical spine dysfunction. *J Manipulative Physiol Ther* 2001;24:260–71.
- [91] Cooper HM, Rosenthal R. Statistical versus traditional procedures for summarizing research findings. *Psychol Bull* 1980;87:442–9.
- [92] Eddy DM, Hasselblad V, Shachter RD. The statistical synthesis of evidence: meta-analysis by the confidence profile method. Orlando, FL: Academic Press, 1992:35–108, 351–366.
- [93] Hedges LV, Olkin I. Statistical methods for meta-analysis. Orlando, FL: Academic Press, 1985:2–46, 286–306.
- [94] Rosenthal R. Meta-analytic procedures for social research. Beverly Hills, CA: Sage Publications, 1984:6–82.
- [95] Feinstein AR. Meta-analysis: statistical alchemy for the 21st century. *J Clin Epidemiol* 1995;48:71–9.
- [96] Cook DJ, Sackett DL, Spitzer WO. Methodologic guidelines for systematic reviews of randomized control trials in health care from the Potsdam Consultation on Meta-Analysis. *J Clin Epidemiol* 1995; 48:167–71.
- [97] Victor N. The challenge of meta-analysis: discussion. Indications and contra-indications for meta-analysis. *J Clin Epidemiol* 1995;48:5–8.
- [98] Bombardier C, Esmail R, Nachemson AL, Back Review Group Editorial Board. The Cochrane Collaboration Back Review Group for Spinal Disorders. *Spine* 1997;22:837–40.
- [99] Detsky AS, Naylor CD, O'Rourke K, McGeer AJ, L'Abbe KA. Incorporating variations in the quality of individual randomized trials into meta-analysis. *J Clin Epidemiol* 1992;45:255–65.
- [100] Chalmers TC, Celano P, Sacks HS, Smith H. Bias in treatment assignment in controlled clinical trials. *N Engl J Med* 1983;309: 1358–61.
- [101] Miller JN, Colditz GA, Mosteller F. How study design affects outcomes in comparisons of therapy. II: Surgical. *Stat Med* 1989;8: 455–66.
- [102] Emerson JD, Burdick E, Hoaglin DC, Mosteller F, Chalmers TC. An empirical study of the possible relation of treatment differences to quality scores in controlled randomized clinical trials. *Controlled Clin Trials* 1990;11:339–52.
- [103] Moher D, Jadad A, Tugwell P. Assessing the quality of randomized controlled trials: current issues and future directions. *Int J Technol Assess Health Care* 1996;12:195–208.
- [104] Koes BW, Assendelft WJJ, van der Heijden GJMG, Bouter LM. Spinal manipulation for low back pain. An updated systematic review of randomized clinical trials. *Spine* 1996;21:2860–73.
- [105] Assendelft WJ, Koes BW, van der Heijden GJ, Bouter LM. The efficacy of chiropractic manipulation for back pain: blinded review of relevant randomized clinical trials. *J Manipulative Physiol Ther* 1992;15:487–94.
- [106] Bronfort G. Efficacy of spinal manipulation and mobilisation for low back and neck pain: a systematic review and best evidence synthesis PhD thesis. In: Efficacy of manual therapies of the spine. Amsterdam, The Netherlands: Thesis Publishers Amsterdam, 1997: 117–46.
- [107] Bronfort G. Spinal manipulation: current state of research and its indications. *Neurologic Clin North Am* 1999;17:91–111.
- [108] Assendelft W, Shekelle P. Spinal manipulation for low back pain (protocol for a Cochrane Review). Oxford: Update Software, 2002.
- [109] Aker PD, Gross AR, Goldsmith CH, Peloso P. Conservative management of mechanical neck pain: systematic overview and meta-analysis. *BMJ* 1996;313:1291–6.
- [110] Hurwitz EL, Aker PD, Adams AH, Meeker WC, Shekelle PG. Manipulation and mobilization of the cervical spine. A systematic review of literature. *Spine* 1996;21:1746–60.

- [111] Hoving JL, Gross AR, Gasner D, et al. A critical appraisal of review articles on the effectiveness of conservative treatment for neck pain. *Spine* 2001;26:196–205.
- [112] ACC and the National Health Committee. New Zealand acute low back guide. Wellington, NZ: Ministry of Health, 1997.
- [113] Waddell G, Feder G, McIntosh A, Hutchinson A. Clinical guidelines for the management of acute low back pain. London: Royal College of General Practitioners, 1996:1–35.
- [114] Faas A, Chavannes AW, Koes BW, et al. NHG-Standard 'Lage-Rugpijn.' *Ned Huisarts Wet* 1996;39:18–31.
- [115] Bogduk N. Evidence based clinical guidelines for the management of acute low back pain. Draft. Australia: National Health and Medical Research Council, 2000.
- [116] Borkan J, Reis S, Werner S, Ribak J, Porath A. Guidelines for treating low back pain in primary care. The Israeli Low Back Pain Guideline Group. *Harfuah* 1996;130:145–51.
- [117] Koes BW, Assendelft WJJ, van der Heijden GJMG, Bouter LM. Spinal manipulation and mobilization for low-back pain: an updated systematic review of randomized clinical trials. In: van Tulder MW, Koes BW, Bouter LM, eds. *Low Back Pain in Primary Care: effectiveness of diagnostic and therapeutic interventions*. Amsterdam: EMGO Institute, 1996:149–70.
- [118] Waddell G, McIntosh A, Hutchinson A, Feder G, Lewis M. Clinical guidelines for the management of acute low back pain. *Low Back Evidence Review*. London: Royal College of General Practitioners, 1999.
- [119] Norwegian low back guidelines. Akutte korsryggsmerter. Tverrfaglige kliniske retningslinjer. Oslo: The Norwegian Back Pain Network, Communication unit, Ullevål Hospital, 2002.
- [120] Malmivaara A, Kotilainen E, Laasonen E, et al. Clinical practice guidelines of the Finnish Medical Association Duodecim. Diseases of the low back. 2001.
- [121] Keel P, Weber M, Roux E, et al. *Kreuzschmerzen: Hintergründe, prävention, behandlung*. Basisdokumentation. Bern: Verbindung der Schweizer Ärzte (FMH), 1998.
- [122] *Handlungsleitlinie-Rückenschmerzen*. Empfehlungen zur Therapie von Rückenschmerzen, Arzneimittelkommission der deutschen Ärzteschaft. (Treatment guideline—backache. Drug Committee of the German Medical Society). *Z Arztl Fortbild Qualitätssich* 1997;91:457–60.
- [123] Manniche C. Low-back pain: frequency, management and prevention from an HTA perspective. The Scientific Board DIHTA, editor. Copenhagen: Danish Institute for Health Technology Assessment, 1999.
- [124] Nachemson A, Jonsson E, Englund L, et al. Neck and back pain: the scientific evidence of causes, diagnosis, and treatment. In: Nachemson AL, Jonsson E, editors. Philadelphia: Lippincott Williams and Wilkins, 2000.
- [125] Bero L, Rennie D. The Cochrane Collaboration. Preparing, maintaining, and disseminating systematic reviews of the effects of health care. *JAMA* 1995;274:1935–8.
- [126] Hayward RS, Wilson MC, Tunis SR, Bass EB, Guyatt G. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. Are the recommendations valid? *JAMA* 1995;274:570–4.
- [127] Wilson MC, Hayward RS, Tunis SR, Bass EB, Guyatt G. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. B. What are the recommendations and will they help you in caring for your patients? *JAMA* 1995;274:1630–2.
- [128] Koes BW, Bouter LM, van der Heijden GJ. Methodological quality of randomized clinical trials on treatment efficacy in low back pain. *Spine* 1995;20:228–35.
- [129] Dickersin K. The existence of publication bias and risk factors for its occurrence. *JAMA* 1990;263:1385–9.
- [130] Dickersin K. Why register clinical trials?—revisited. *Controlled Clin Trials* 1992;13:170–7.
- [131] Dickersin K, Chan S, Chalmers TC, Sacks HS, Smith H. Publication bias and clinical trials. *Controlled Clin Trials* 1987;8:343–53.
- [132] Rosenthal R. The "file drawer problem" and tolerance for null results. *Psychol Bull* 1979;86:638–41.
- [133] Glasziou P, Guyatt GH, Dans AL, Dans LF, Straus S, Sackett DL. Applying the results of trials and systematic reviews to individual patients. *Evidence-Based Med* 1998;3:165–6.
- [134] Guyatt GH, Juniper EF, Walter SD, Griffith LE, Goldstein RS. Interpreting treatment effects in randomised trials. *BMJ* 1998;316:690–3.
- [135] Guyatt GH, Osoba D, Wu AW, Wyrwich KW, Norman GR. Methods to explain the clinical significance of health status measures. *Mayo Clin Proc* 2002;77:371–83.
- [136] Dvorak J, Kranzlin P, Muhleman D, Walchli B. Musculoskeletal complications. In: Haldeman S, editor. *Principles and practice of chiropractic*. Norwalk: Appleton and Lange, 1992:549–77.
- [137] Senstad O, Leboeuf-Yde C, Borchgrevink C. Frequency and characteristics of side effects of spinal manipulative therapy. *Spine* 1997;22:435–41.
- [138] Haldeman S, Rubinstein SM. Cauda equina syndrome in patients undergoing manipulation of the lumbar spine. *Spine* 1992;17:1469–73.
- [139] Assendelft WJ, Bouter LM, Knipschild PG. Complications of spinal manipulation: a comprehensive review of the literature. *J Fam Pract* 1996;42:475–80.
- [140] Terrett AGJ, Kleynhans AM. Cerebrovascular complications of manipulation. In: Haldeman S, editor. *Principles and practice of chiropractic*. Norwalk: Appleton and Lange, 1992:579–98.
- [141] Powell FC, Hanigan WC, Olivero WC. A risk/benefit analysis of spinal manipulation therapy for relief of lumbar or cervical pain. *Neurosurgery* 1993;33:73–8.
- [142] Conrad DA, Deyo RA. Economic decision analysis in the diagnosis and treatment of low back pain. A methodologic primer. *Spine* 1994;19:2101S–6S.
- [143] Manga P, Angus D, Papadopoulos C, Swan W. The effectiveness and cost effectiveness of chiropractic management of low-back pain. Ottawa, ON, Canada: Pran Manga and Associates, 1993.
- [144] Hurwitz EL, Morgenstern H, Harber P, et al. A randomized trial of medical care with and without physical therapy and chiropractic care with and without physical modalities for patients with low back pain: 6-month follow-up outcomes from the UCLA low back pain study. *Spine* 2002;27:2193–204.