Review Article

Spinal Manipulation: A Systematic Review of Sham-Controlled, Double-Blind, Randomized Clinical Trials

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Abstract
For many years, spinal manipulation has been a popular form of treatment. Yet the debate about its clinical efficacy continues. The research question remains: Does spinal manipulation convey more than a placebo effect? To summarize the evidence from sham-controlled clinical trials of spinal manipulation as a treatment of various conditions, and to assess the methodological quality of these studies, a comprehensive search strategy was designed to locate all sham-controlled, double-blind, randomized trials of spinal manipulation as a treatment of any medical condition. Data were extracted from these trials and validated by two independent reviewers in a standardized fashion. All trials were critically analyzed and their methodological quality evaluated. Eight studies fulfilled the pre-defined inclusion/exclusion criteria. Three trials (two on back pain and one on enuresis) were judged to be burdened with serious methodological flaws. The results of the three most rigorous studies (two on asthma and one on primary dysmenorrhea) do not suggest that spinal manipulation leads to therapeutic responses which differ from an inactive sham-treatment.This analysis demonstrates that sham-controlled trials of spinal manipulation are sparse but feasible. The most rigorous of these studies suggest that spinal manipulation is not associated with clinically-relevant specific therapeutic effects. J Pain Symptom Manage 2001;24:879–889

Key Words
Alternative medicine, chiropractic, spinal manipulation, efficacy, placebo

Introduction

Chiropractic has been defined as a system of healthcare founded in 1895 by Daniel David Palmer. Traditionally, it has been based on the belief that the nervous system is the most important determinant of a person's state of health. Much of chiropractic relies on the theory that nerve interference caused by spinal misalignments ("subluxations") is the primary or underlying cause of most forms of ill health. Many chiropractors claim that correcting misalignments restores health and that regular spinal adjustments are essential to maintain well-being.[1,2] One technique used (not exclusively) by chiropractors to achieve spinal adjustment is spinal manipulation (SM). SM involves high

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velocity thrusts with either a long or short lever-arm, usually aimed at reducing pain and improving range of motion.

The debate concerning whether or not SM constitutes an efficacious treatment continues (e.g., Ernst and Assendelft[3]). An influential report[4] and meta-analysis[5] arrived at a positive overall conclusion and was instrumental in leading to the wide acceptance of SM as a treatment for low back pain. These analyses, however, included trials that were not of high scientific rigor. In particular, they did not differentiate between specific and non-specific effects of SM. "The possibility of spontaneous or placebo-driven improvement in chronic illness dictates that studies of the efficacy of treatment regimens be adequately controlled, randomized, and blinded."[6] Only sham-controlled trials will tell us whether the clinical effects of SM are more than a placebo effect, a question that seems important, not the least for meaningful risk/benefit and cost/benefit analyses of SM. This systematic review was aimed at summarizing all sham-controlled, double-blind, randomized clinical trials of SM with a view to answering the question, is SM associated with effects beyond placebo?

Methods

The following databases were searched, each from their inception to the end of 1998: Medline, Embase, CISCOM, Amed, and Cochrane Library. Furthermore, other experts (n = 9), chiropractic organizations (n = 16), the published bibliography of an ongoing Cochrane Review[7] and our own extensive files were consulted. The keywords used were: *chiropractic, spinal manipulation, spinal adjustments, osteopathy*, and *controlled clinical trials*. The bibliographies of all articles thus located were screened for further relevant papers. There is good evidence to suggest that this search strategy was, in fact, comprehensive.[8]

Initially, all clinical trials of SM (published in any language) were considered. Studies which were not sham-controlled[9–15] and not double-blind[16–18] were subsequently excluded. Trials of treatment packages including more than just SM interventions[19–21] and studies of spinal mobilization,[22–24] a therapeutic intervention distinct from SM, were also excluded. These strict inclusion criteria meant that some studies[10] were excluded even if they were sham-controlled. Trials were included regardless of whether SM was performed by chiropractors or other healthcare professionals.

For the purpose of this analysis, sham-controlled was defined as an intervention adopted for the control group which mimicked true SM but was deemed by the investigators to be inactive. Trials using other "placebo" interventions such as detuned physiotherapy equipment[9] were excluded. Double-blind was defined as blinding of both the patient and the evaluator as to treatment allocation; in such studies the therapist had, of course, to be unblinded. Our initial intention had been to assess trials according to the condition treated. Since only very few studies were located, this plan had to be abandoned.

All trials meeting the above-mentioned criteria were read in full by both authors (both are experienced at conducting systematic reviews; one has additional expertise in SM and the other in statistics). Information on trial methodology, treatment schedule, outcome measures and significance of results was validated and extracted independently by both authors in a standardized way (Tables 1 and 2). The inclusion of "deblinding" was deemed important since the risk of patient deblinding in such trials seems high, and patient deblinding would, in turn, introduce the very source of bias that sham-controls were aimed at excluding.

Methodological quality was assessed using the Jadad score[25] which ranges between a minimum of 0 and a maximum of 5. As this score is confined to randomization, blinding, and description of dropouts, further aspects of trial methodology and validity were considered. Disagreements between the authors were settled through discussion. Assessments were purely qualitative; statistical pooling (i.e., meta-analysis) of the data was not possible mainly because the studies related to different medical conditions and therefore no common endpoint was identifiable.

Results

Eight trials complied with the above-mentioned criteria and were included in this review.[6,26–31] Their key characteristics are summarized in Table 1 and further methodological details are provided in Table 2. In all of these

studies, SM had been performed by chiropractors (even though other professions were not an exclusion criterion, see above).

Researchers from the US Palmer College of Chiropractic randomized 19 patients with chronic low back pain (LBP) into one group receiving a standardized set of chiropractic adjustments and a control group receiving sham adjustments "using minimal force".[26] After two weeks of treatment, there were significant improvements in the actively treated group in terms of pain measured by visual analogue scale (VAS). No such differences were noted in the sham group. Spinal mobility improved significantly in the treated group compared with the control group. The authors conclude that, "both subjectively and objectively, chiropractic therapy is more effective at relieving low back pain."[26] This conclusion may be unreliable since 1) a degree of 'de-blinding' took place through noticeable differences of the active and sham treatment (80% treated patients and 67% control patients thought they received active treatment); 2) sample size was small; 3) there was a substantial number (n = 10) of drop-outs; 4) no intent-to-treat analysis was undertaken; and 5) the statistical comparisons regarding pain were intra-group rather than between groups.

A group of students from the same institution randomized 46 children with primary nocturnal enuresis into two groups.[27] After a positive diagnosis of segmental dysfunction, one group received high velocity, short lever thrusts consistent with the Palmer Package Adjusting Technique. The control group received sham adjustments which consisted of using an 'activator' at non-tension setting administered to the examiner's own underlying contact point over the thoracic area. At the end of the 10 weeks' treatment period, significantly less bed-wetting was noted in the experimental compared to the control group. Unfortunately, a similar difference was already noted at baseline. The frequency of wet nights significantly decreased in the experimental group. However, the intra-group changes showed no significant difference when compared between groups. Nevertheless, the authors conclude that these results "strongly suggest the effectiveness of chiropractic treatment for primary nocturnal enuresis."[27] Whether this is true is debatable, since the adequate statistical test did not, in fact, yield a statistically significant result. This trial is flawed in several other ways: randomization, blinding, and the treatment schedule are inadequately described; the primary endpoint is of questionable validity (parent questionnaire); and there were 11 dropouts but no intent-to-treat analysis was performed.

Researchers from the U.S. National College of Chiropractic conducted a randomized controlled trial (RCT) with three parallel arms.[28] A total of 209 consecutive patients with untreated low back pain lasting seven weeks or longer received chiropractic, sham-chiropractic, or back pain education. Chiropractic treatment consisted of high velocity, low amplitude SM. Sham treatment consisted of high velocity, low force mimic adjustments. At the end of the two weeks' treatment period, the results of the Oswestry Disability Score significantly favored the chiropractic treatment, while VAS pain measurements failed to reach the level of statistical significance. The authors concluded, "there appears to be clinical value to treatment according to a defined plan using manipulation."[28] This conclusion might be challenged on several grounds. A degree of deblinding could have occurred. A high number of dropouts was noted—of the 209 patients, only 117 cases could be included in the analysis of the Oswestry Disability Score—yet no intent-to-treat analysis was performed. On several important points, the write-up of the study is far from clear.

A group from the Danish National University Hospital randomized 31 chronic asthma patients to receive either twice-weekly (for 4 weeks) chiropractic or sham treatments.[29] The trial followed a crossover design, with 2 weeks' washout periods. All patients remained on conventional treatment throughout. Chiropractic and sham treatments were carried out by two experienced chiropractors recommended by their national professional body. Active treatment consisted of high velocity, low amplitude thrusts directed to spinal segmented biomechanical dysfunction diagnosed by standard chiropractic tests. Sham treatment consisted of gentle manual pressure over a spinal contact point while the therapist's other hand released the drop section of the treatment bench to cause a sudden change of position. The design of this study was approved by the research com-

Table 1

Sham-Controlled, Double-Blind, Randomized Trials of Spinal Manipulation

First Author (Year)	Condition Treated	Sample Size	Active[a] Treatment (*n*)	Sham[a] Treatment (*n*)	Treatment Schedule	Primary Outcome Measure	De-blinding Checked?	Statistical Analysis	Drop outs/ Withdrawals	Main Results	Jadad Score[b]
Waagen (1986)	chronic LBP	19	standardized chiropractic adjustments (10)	sham-adjustment using minimal force (9)	2–3 treatments/ week for 2 weeks	1) function 2) pain (VAS)	yes	*t*-test, (Wilcoxon) paired-sample signed-rank test, and Mann-Whitney-U test, no sample size calculation	10	Global Index of Function significantly improved in active treatment compared with control	3
Reed (1994)	primary nocturnal childhood enuresis associated with spinal subluxations	46	high velocity, short lever adjustments (31)	sham-adjustments using an 'activator' (15)	treatments for 10 weeks scheduled for evaluation for spinal subluxation at a minimum of every 10 days	enuresis by parent questionnaire wet/dry calendar marked daily	yes	*t*-test, no sample size calculation	11	significant inter-group differences at baseline *and* end of study, post treatment significantly less than baseline for treatment group but comparison of change between groups was not significant	2
Triano (1995)	chronic LBP	209	high velocity, low amplitude manipulations to the lumbar spine and pelvis	sham-manipulations of low force	6 days/week for 2 weeks	Oswestry Disability Score, pain (VAS) Modified Zung Depression Index	no	repeated measures ANOVA	39 drop outs and 25 excluded because of confounding factors	significant inter-group differences in favor of chiropractic group for Oswestry score pain, *ns* Zung, *ns*	3
Nielsen (1995)	chronic asthma	31	high velocity, low amplitude thrusts at site of segmental dysfunction (31)	rapid change of position of patient without direct manipulative thrust (31)	twice weekly treatments for 4 weeks; 2 week washout then crossed over to alternative treatment for 4 weeks	lung function tests, symptom score, broncho-dilator use, bronchial reactivity	yes	repeated measures ANOVA, no sample size calculation	2	no significant differences between groups emotional discomfort (VAS) post intervention was significantly different from control and from its preintervention values	5
Peterson (1997)	phobia	20 community college students	high force short lever, manually assisted adjusting instrument (activator)	as active treatment but with zero force	baseline then phobogenic stimulus then intervention given and phobogenic stimulus again	pulse rate emotional discomfort (VAS)	no	ANOVA	2	pulse rates were not statistically significant between treatment and control groups emotional discomfort (VAS) postintervention was significantly different from control and from its preintervention value	4
Balon (1998)	childhood asthma	91	adjustments as judged optimal by chiropractor low-amplitude, high velocity directional push (45)	gentle palpation to the spine and distraction maneuver low-amplitude low velocity (46)	3 times weekly for 4 weeks, then twice weekly for 4 weeks, then weekly for 8 weeks	lung function tests, symptom score, broncho-dilator use, peak expiratory flow (PEV)	yes	analysis of covariance	10	no significant differences between groups	5

(*continued*)

Table 1
Continued

First Author (Year)	Condition Treated	Sample Size	Active[a] Treatment (*n*)	Sham[a] Treatment (*n*)	Treatment Schedule	Primary Outcome Measure	De-blinding Checked?	Statistical Analysis	Drop outs/ Withdrawals	Main Results	Jadad Score[b]
Hondras (1999)	primary dysmenorrhea	138	high velocity, short lever, low amplitude thrust (69)	low force mimic maneuver (LFM) (66)	day 1 of cycles 2, 3 and 4. Prophylactic treatment of 3 visits took place the week before cycles 3 and 4	pain (VAS) radioimmunoessay ($KDPGF_{2\alpha}$) Moos' Menstrual Distress Questionnaire (MDQ)	not formally but most women indicated they thought they had received a 'real' manipulation	*t*-test linear modeling	3	VAS—no statistically significant difference in pre to post treatment scores between the 2 groups. $KDPGF_{2\alpha}$—changes in pre to post treatment levels were not statistically different between groups. VAS, $KDPGF_{2\alpha}$, MDQ showed no treatment effects but VAS and MDQ showed linear time effects	5
Hawk (1999)	LBP	18	flexion-distraction technique for spinal adjustment (18)	mimic spinal adjustment with zero force (18)	2 treatments of 1 type within one week, 3–5 days wash-out period, 2 treatments of other type	pain (VAS), Global Well-Being Scale	apparently yes, but little details provided: 3 patients guessed correctly	only descriptive statistics	none	active treatment numerically superior to sham	2

[a]for details, see text
[b]Jadad score quantifies the likelihood of bias by addressing randomization, blinding, and dropouts.
LBP = low back pain; VAS = visual analogue scale; *ns* = not significant.

Table 2
Further Methodological Characteristics of all Included Trials

First Author (Year)	Power Analysis Performed	Clear Description of Study Subjects	Explicit Inclusion Exclusion Criteria	Clearly Defined Reproducible Intervention	Outcomes Clearly Defined	Outcomes Appropriate	Method to Assess Outcomes Adequate	Adverse Events Mentioned	ITT	Statistical Analysis Adequate
Waagen (1986)	no	yes, first-time patients aged 18–65 years presenting with chronic LBP (>3wks) with mild to moderate intensity	LBP chief complaint, naïve to chiropractic, no contra-indications (listed in Appendix 1 of paper)	sham: lumbar drop-piece on standard chiropractic table set to minimal tension. Adjustment simulated by gentle pressure over both posterior iliac spines such that lumbar section fell. Para-spinal soft tissue massage	function: active SLR rt active SLR lf passive SLR rt passive SLR lf lumbar flexion lumbar extension lateral flexion rt lateral flexion lf VAS for pain	yes	yes	no	no	function—no within group analysis presented VAS—no between group analysis presented
Reed (1994)	no	yes, children with primary nocturnal enuresis	excluded if: diurnal enuretic activity, history of UTI, anatomical abnormalities, surgical intervention, infrequent wetting, contraindication to spinal adjustment, medication or spinal manipulation in 4 weeks prior to study	sham adjustment consisting of using an activator at nontension setting administered to the examiner's own underlying contact point (i.e. thumb/finger) over the thoracic area	wet/dry measurements for duration of 10 week treatment period and 2 weeks after treatment completed exit interview with parents	yes	yes	no	no	yes
Triano (1995)	yes—power calculated at 55% (sample size of 67/group required for 80% power)	yes, new patients presenting with mechanical LBP, aged 18 or over, pain L1-L5 and sacroiliac joints lasting >50 days or 6 episodes in preceding 12 months, palpatory tenderness over 1 or more zygapophysial articulations	exclusions: pain and activity scores <5%, evidence of neuropathy, systemic disease, osteoporosis, fracture, osseous pathology of spine, medication on irregular schedule, other treatment to relieve LBP, workers compensation or litigation claims	high velocity, low amplitude (HVLA) spinal manipulation—patient positioning with paraspinal load to enhance axial spinal torsion. sham treatment high velocity low force (HVLF) moves patient away from provider bends both knees and applies load in mid-sagittal plane	primary: 1) VAS for pain intensity 2) Oswestry LBP Disability Questionnaire 3) Modified Zung Depression Index	yes	yes	no	no	yes
Nielsen (1995)	yes—set such that there was <20% chance of overlooking a difference of 10–15% between interventions No sample size calculations given	yes, patients attending National University Allergy Department Out-patient Clinic confirmed by FEV_1 or PEF, using inhaled β2-agonists at least 6 times/day 3 or more days/week corticosteroids (4 times/day)	18–45 years age with chronic asthma (similar to NIH definition). excluded if: pregnancy, concurrent clinically significant medical diseases, chiropractic in last 5 years, contraindications to manipulation, oral steroids, concurrent immunotherapy, abnormal chest radiograph	active: high velocity, low amplitude thrust by short lever technique directed to spinal segmental biomechanical dysfunction sham: gentle manual pressure over spinal contact point (no direct thrust to spine)—rapid change in position of patient very similar to active treatment	1) Lung function tests 2) Non-specific bronchial reactivity 3) Symptom score (VAS) 4) Diaries—use of inhalers, PEF, symptom scores	yes	yes	no side effects observed	no	yes
Peterson (1997)	no	no, students with the presence of a simple phobia as defined by DSM-III-R	explicit inclusion-exclusion criteria Excluded if: past experience with manual muscle testing, acquainted with examiner, pain or loss of strength in both shoulders, posttreatment with spinal manipulation for emotional distress	active: high force, short lever, manually assisted adjusting instrument (activator) with audible click sham: zero force, short lever manually assisted adjusting instrument with audible click	pulse emotional discomfort (VAS)	yes	not validated	no adverse effects	no	yes

(*continued*)

Table 2
Continued

First Author (Year)	Power Analysis Performed	Clear Description of Study Subjects	Explicit Inclusion Exclusion Criteria	Clearly Defined Reproducible Intervention	Outcomes Clearly Defined	Outcomes Appropriate	Method to Assess Outcomes Adequate	Adverse Events Mentioned	ITT	Statistical Analysis Adequate
Balon (1998)	yes—36 subjects in each group required for 80% power to detect an increase from baseline of at least 10% in morning PEF	yes, children 7–16 years with asthma (diagnosed by a physician) for more than 1 year and use of bronchodilator at least 3 times/week, recruited through advertising	presence of asthma confirmed by FEV_1, on medication for at least 6 months, evidence of vertebral subluxation on palpation as determined by chiropractor screening Excluded if: other lung disease, contraindications, previous chiropractic, unstable asthma, noncompliant	active: adjustments determined by chiropractor—low-amplitude, high velocity directional push sham: soft-tissue massage and gentle palpation applied to the spine and distraction maneuver, all low-amplitude low velocity contacts (i.e. hands on without adjustments)	primary: change from baseline in morning PEF measured before use of bronchodilator at 2 and 4 months, frequency PEF fell below 85% was compared between groups, secondary: changes in airway responsiveness, FEV_1, symptoms, inhaler use, oral corticosteroid use, quality of life and overall satisfaction	yes	yes	exacerbation of asthma	no	yes
Hondras (1999)	yes, 68 subjects in each group required for 80% power to detect effect sizes of 15 mm on the VAS and 20 pg/ml for plasma $KDPGF_{2\alpha}$ levels	yes, women 18–45 years with regular menstrual cycles accompanied by moderate to severe pain and with a diagnosis of primary dysmenorrhea	no signs of cervical dysplasia, no use of IUD or oral contraceptives, secondary dysmenorrhea excluded, chiropractic for low back pain preceding 6 months. Any contraindication to SMT pregnancy	active: high velocity, short lever, low amplitude thrust delivered to all clinically relevant vertebral levels from T10 to LS and sacroiliac joints sham: to minimize mechanical torque on the longitudinal axis of the spine associated with true manipulation thrust, high velocity, short lever, low amplitude thrust	pain (VAS) plasma concentration ($KDPGF_{2\alpha}$) Moos' Menstrual Distress Questionnaire (MDQ)	yes	yes	soreness in low back region SMT (3) LFM (2)	yes	yes
Hawk (1999)	no	no	none	no	yes, VAS for pain, Global Well-Being Scale	yes	yes	no	n.a.	no

ITT = intent-to-treat; LBP = low back pain; ? = of debatable validity; SLR = straight-leg-raising test; rt = right; lt = left; n.a. = not applicable.

mittee of the European Chiropractic Union, and a member of the Northwestern College of Chiropractic U.S. served as an advisor. Standard lung function tests, daily usage of medication, patient-rated asthma severity, and non-specific bronchial reactivity had been defined as main outcome variables. The results yield no statistically significant or clinically relevant inter-group differences in any of these parameters. When patients were asked which treatment they preferred, 19 opted for the active and 10 for the sham therapy. The authors conclude that their results do not support the hypothesis that chiropractic treatment is superior to sham as a treatment for chronic asthma. This study is well designed and seems to have been executed with care. However, because of its relatively small sample size, the study had a high chance of missing a true difference between the treatment and placebo groups.

Peterson, a chiropractor in private practice, published a small randomized control trial (RCT) with 18 college students suffering from phobias.[30] The participants were exposed to a picture of the object of their phobia (e.g., a spider). Subsequently the treatment group received a short-lever SM using an adjusting instrument (activator) modified by adding a double-headed transverse process tip. The force of the SM was "high" in this group, while the sham group received a similar treatment with the instrument's force set at zero. Following these interventions, participants were re-exposed to their frightening stimulus. The endpoints measured were pulse rate and subjective emotional response quantified by a visual analogue scale. Analyses of variance showed that there were no pre–post differences in heart rate but a significant decrease in emotional discomfort was reported in the experimental group. Generally this trial seems well designed; it is, however, burdened with several specific shortcomings, namely, small sample size and non-validated outcome measure.

A group of researchers from the Canadian Memorial Chiropractic College randomized 91 children suffering from asthma to receive either regular chiropractic or sham treatments for 16 weeks by one of 11 experienced chiropractors.[6] Active treatment consisted of SM deemed to be the optimal treatment for each individual according to prior chiropractic diagnosis. Sham treatments consisted of hands-on procedures without adjustments. In addition, all patients remained on usual medical care. Standard lung function tests, symptoms, and usage of medication had been defined as the main outcome variables. The results showed no differences between these groups in relation to any parameter. Patients were unable to distinguish active from sham therapy. The authors conclude "chiropractic spinal manipulation provided no benefit for asthmatic children."[6] This study was well designed and executed. Particular strong points are a proper sample size calculation, checks for de-blinding, the fact that active treatment was individualized according to the need of the patient as seen by experienced chiropractors, and the employment of a sufficiently large number of experienced chiropractors.

Hondras et al. conducted an RCT with women suffering from primary dysmenorrhea.[31] In this study, 138 patients received either SM (high velocity, short lever, low amplitude thrusts) during 4 cycles or sham treatment. The main outcome measurements were pain by VAS, a dysmenorrhea symptom score, and plasma levels of the hormone $KDPGF_{2\alpha}$. The results of this study show no significant differences in response between the two groups. This study has all the hallmarks of a rigorous trial including a sample size based on a power calculation, proper accounting for drop-outs, explicit inclusion/exclusion criteria, and mention of adverse effects.

A research team from a chiropractic research college conducted a two-period crossover trial with 18 volunteer staff suffering from acute or sub-acute low back pain.[32] The flexion-distraction method was used to perform spinal adjustments. A hand-held instrument (activator adjusting instrument) with the pressure gauge set at zero was employed for carrying out the sham treatments. In each treatment period of one week, 2 treatments were performed. The outcome measures were pain by VAS and the Global Well-Being Scale. Their results were not analyzed with test statistics. Both endpoints improved with both sham and real adjustments. However, the authors state that "there was a greater improvement in most cases with active treatment." Eight of 14 patients questioned felt that sham therapy was successful. Due to its small sample size and lack

of test statistics, this study is not interpretable in any definitive way.

Discussion

The small number of sham-controlled trials is disappointing but in itself meaningful (all but one trial[26] were published in the 1990s). This review is further limited by the small sample sizes of the primary investigations, the methodological weakness of some studies, and by the possibility of reviewer bias. Nevertheless, the above data collectively show that sham-controlled trials of SM are feasible. They also imply that the notion that SM has specific therapeutic effects in any medical condition or complaint is not supported by well-designed studies. Moreover, they demonstrate that SM is associated with a sizeable placebo effect, which arguably creates the necessity to test SM with sham-controlled clinical trials, particularly if the research question is aimed at identifying specific therapeutic effects.

Sham-controlled, double-blind RCTs are aimed at determining whether SM is efficacious beyond a placebo in effect.[6] Other types of placebo interventions (e.g., detuned ultrasound equipment) may be associated with placebo effects that differ from the ones associated with SM. Thus it seems that only sham-controlled trials with successful patient-blinding can adequately differentiate between the specific and non-specific effects of SM.

Of all 7 sham-controlled trials, 3 stand out in terms of methodological quality (Table 1 and 2), achieving the maximum of 5 points on the Jadad score.[6,28,31] The results of these studies indicate that sham-treatment is associated with a similar therapeutic response to that of real SM. In all three trials, there were clinical improvements in the experimental *and* control group but no significant differences between those groups. This suggests that, in these settings, the therapeutic effects were due to nonspecific (placebo) effects or the regression towards the mean.[33]

Interestingly, two of these studies relate to asthma[6,28] and one to primary dysmenorrhea.[31] Three sham-controlled trials of low back pain, which is by far the most important indication for SM,[3,5] were included.[26,27,32] In all cases, the authors drew positive conclusions from their data. However, serious methodological flaws cast serious doubts on these conclusions. An authoritative systematic review of *all* randomized (but not necessarily sham-controlled) trials also found "no convincing evidence of the effectiveness of chiropractic for acute or chronic low back pain."[34] More recent non–sham-controlled trials also show mixed results. Two studies failed to demonstrate that SM is more effective for low back pain than physiotherapy.[35,36] Other such studies, however, yielded more positive results.[37,38] Conclusions regarding the specific efficacy of SM for low back pain, therefore, must await adequately designed sham-controlled trials.

Even if the mechanism of action is that of a powerful placebo, SM might still be useful in clinical practice. Both the patient and the treating clinician are usually not critically concerned about mechanisms of action as long as there is clinical improvement. This argument is applicable only if the therapy under discussion is not associated with considerable risks.[39] The risks of SM are still under-researched. In the trials reviewed above, adverse effects were not mentioned in the weaker studies;[26–28] Nielsen et al. explicitly stated that no adverse events occurred,[29] Balon et al. only noted exacerbation of asthma symptoms,[6] and Hondras et al. found some minor soreness at the site of SM.[31] Two recent prospective investigations of adverse effects suggest that mild, transient adverse effects (mostly local or referred pain) occur in about 50% of all cases.[40,41] Serious complications of SM seem to be very rare. They include vertebral artery dissection (upper spinal manipulation) and cauda equina syndrome (lower spinal manipulation).[42,43] At present the incidence figures of such events are unfortunately impossible to determine, and estimates range from less than 1 in 20,000 to 1 in 1,000,000.[42] Some authors suggest that the published estimates are too low due to prevalent underreporting.[44,45] Unpublished data from the present authors show that underreporting of complications after SM is very close to 100%. In this context, it is relevant to mention that the incidence of serious complications due to nonsteroidal anti-inflammatory drugs is 100–400 times higher than that of SM.[46] It may be misleading to compare one therapy for which postmarketing surveillance systems exist against another for which comparable safety monitoring is absent.

Finally, the usefulness of any form of treatment would be determined by its costs. In the U.S., the annual cost for chiropractic services is substantial. Eisenberg et al.[47] estimated the total number of visits to U.S. chiropractors in 1997 at 192,000,000. If one estimates the average cost conservatively at US $50 to US $60, the resulting expenditure amounts to US $9,600 million to US $11,520 million per year. Several cost-benefit analyses exist, and some seem to favor SM over other treatment options.[48] Yet the matter is still controversial,[49] and one recent study concluded that the total costs of SM and physiotherapy in treating back and neck pain were not relevantly different.[50]

In conclusion, sham-controlled, double-blind RCTs of SM are feasible and represent an attempt to differentiate between specific and non-specific therapeutic effects. Few such studies exist and some of the existing ones are burdened with serious methodological shortcomings. The three most rigorous trials do not suggest that SM is associated with specific therapeutic effects.

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