Critique author	Linda Metzger

Bibliographic Data	
Authors	Haas M, Vavrek D, Peterson D, and et al.
Title	Dose-response and efficacy of spinal manipulation for care of chronic low back pain: a randomized controlled trial
PMID	24139233
Citation	The Spine Journal 14 (2014) 1106–1116
Other information if relevant	The trial was registered on ClinicalTrials.gov NCT00376350.

Methods	
Aim of study	To identify the dose-response relationship between visits to a chiropractor for spinal manipulation and chronic low back pain (cLBP) outcomes and to determine the efficacy of manipulation by comparison with a light massage control.
Design	Assessor single-blinded randomized controlled trial

Participants	
Population from which participants are drawn	Participants were recruited through craigslist, mailers, and local newspapers in the Portland, Oregon area. They were informed that the study was investigating 18 visits for different combinations of two manual therapies for cLBP.
Setting (location and type of facility)	This study took place at one of 9 Portland-area chiropractic clinics convenient to the participant. Care was provided by one of the 12 licensed chiropractors with 4 to 24 years of experience whose abilities were known to the authors.
Age	adults 18 years of age or older, mean age 41.3 years
Sex	195 men, 196 women, total 391 at baseline
Total number of participants for whom outcome data were reported	At 12 weeks, 356 (91%) participants were analyzed using intention-to-treat analyses, and at 24 weeks, 350 (89.5%) participants were analyzed. The number tested at follow-ups was not significantly different between groups.
Inclusion criteria	At least 18 years of age, have a current episode of cLBP of at least 3 months duration, some LBP on 30 days in the previous 6 weeks, and a minimum LBP index of 25 on a 100-point scale.
Exclusion criteria	Participants were excluded if they received manual therapy within the previous 90 days or for contraindications to study interventions, and complicating conditions such as active cancer, spine pathology, inflammatory arthropathies, autoimmune disorders, anticoagulant conditions, neurodegenerative diseases, pain radiating below the knee, organic referred pain, pregnancy, and disability compensation.
Other information if relevant	Groups were comparable on most baseline sociodemographic, clinical symptom characteristics, and outcome measure scores with the exception of smoking. The inclusion of smoking in the analysis produced no substantive changes in effect sizes. The mean duration of LBP was 11.8 years. The average participant experienced LBP 6 days per week and took medication for it twice per week. Participants were compensated for each treatment visit, mailed questionnaires, and phone interviews ($10–$20).

Intervention Groups

Group 1	
Group name	SMT 0 (control group)
Number in group	95 at baseline
Description of intervention	This group received 0 visits for spinal manipulative therapy (SMT) and 18 visits for light massage. Each visit was 15 minutes long (includes co-interventions) with a treating chiropractor. The **light massage control** consisted of 5 minutes of gentle effleurage and petrissage of the low back (lumbar and lower thoracic) paraspinal muscles, focused on the symptomatic areas. The massage used was gentler and of shorter duration than recommended for therapeutic massage practice. It was a minimalist intervention to control for touching the patient.
Duration of treatment period	All participants were assigned 18 treatment visits, 3 per week for 6 weeks.
Co-interventions if reported	For every visit, participants received a hot pack for 5 minutes to relax spinal muscles before 5 minutes of light massage. The visit was completed with 5 minutes of very low-dose pulsed ultrasound (20% duty cycle with 0.5 watts/cm^2) used as a quasi-sham.
Additional information if relevant	

Group 2	
Group name	SMT 6
Number in group	99 at baseline
Description of intervention	This group received 6 visits for spinal manipulative therapy (SMT) and 12 visits for light massage. Each visit was 15 minutes long (includes co-interventions) with a treating chiropractor. **Spinal manipulative therapy** consisted of manual thrust (high velocity, low amplitude) spinal manipulation in the lumbar and transition thoracic regions, predominantly in the side-posture position. Specific manipulations to be performed were determined at each visit by the chiropractor through ongoing evaluation of the participants including patient progress, self-reported and provocative pain, spinal range of motion, and palpation of the spine and paraspinal soft tissue. Manipulation was not performed at a visit, if the treating chiropractor failed to find any indication. See description above for light massage control intervention.
Duration of treatment period	All participants were assigned 18 treatment visits, 3 per week for 6 weeks.
Co-interventions if reported	For every visit, participants received a hot pack for 5 minutes to relax spinal muscles before 5 minutes of light massage or SMT. The visit was completed with 5 minutes of very low-dose pulsed ultrasound (20% duty cycle with 0.5 watts/cm^2) used as a quasi-sham.
Additional information if relevant	

Group 3	
Group name	SMT 12
Number in group	97 at baseline
Description of intervention	This group received 12 visits for spinal manipulative therapy (SMT) and 6 visits for light massage. Each visit was 15 minutes long (includes co-interventions) with a treating chiropractor. See descriptions above for spinal manipulative therapy and light massage control intervention.
Duration of treatment period	All participants were assigned 18 treatment visits, 3 per week for 6 weeks.
Co-interventions if reported	For every visit, participants received a hot pack for 5 minutes to relax spinal muscles before 5 minutes of light massage or SMT. The visit was completed with 5 minutes of very low-dose pulsed ultrasound (20% duty cycle with 0.5 watts/cm^2) used as a quasi-sham.
Additional information if relevant	

Group 4	
Group name	SMT 18
Number in group	100 at baseline
Description of intervention	This group received 18 visits for spinal manipulative therapy (SMT) and 0 visits for light massage. Each visit was 15 minutes long (includes co-interventions) with a treating chiropractor. See description above for spinal manipulative therapy.
Duration of treatment period	All participants were assigned 18 treatment visits, 3 per week for 6 weeks.
Co-interventions if reported	For every visit, participants received a hot pack for 5 minutes to relax spinal muscles before 5 minutes of SMT. The visit was completed with 5 minutes of very low-dose pulsed ultrasound (20% duty cycle with 0.5 watts/cm^2) used as a quasi-sham.
Additional information if relevant	

Co-Primary outcomes	
Outcome name and criteria for definition	1) The self-reported modified Von Korff pain and functional disability scales. The pain score is the average of three 11-point numeric rating scales converted to a 100-point scale: back pain today, worst back pain in the last 4 weeks, and average back pain in the last 4 weeks. The disability score is also the average of 3 scales: interference with daily activities, social and recreational activities, and the ability to work (outside or around the house).The minimal clinically important difference (MCID) in pain or disability between groups was a 10 out of 100 point difference.
Time points measured and/or reported	Baseline assessment and follow-up evaluation was by mailed questionnaire or blinded phone interview at 6, 12, 18, 24, 39, and 52 weeks after randomization. The primary end points were at 12 and 24 weeks.

Differences between groups	**Within group results:** All 4 groups demonstrated improved clinically meaningful outcomes in pain reduction and improvement in functional disability at the 12-weekendpoint. At the 12 week follow-up, the SMT 0 group reduced their pain score from baseline by 14.3 points, the SMT 6 group reduced by 18.3 points, the SMT 12 group reduced by 22.6 points, and the SMT 18 group reduced it by 20.1 points. At the 12 week follow-up, the SMT 0 group improved their functional disability score from baseline by 16.0 points, the SMT 6 group reduced by 20.0 points, the SMT 12 group reduced by 24.1 points, and the SMT 18 group reduced it by 21.8 points. These pain and disability improvements persisted in all groups up to 52 weeks after randomization. **Between group results:** At 12 weeks, the maximum pain difference between treatment and no-SMT control was observed for 12 SMT visits (adjusted mean difference (AMD) = 8.6, p=.002). At 24 weeks, there were no meaningful differences from the control (AMD < 2.5). At the 12-week primary end point, the greatest advantage for SMT over control for disability was also found for 12 SMT visits (AMD = 7.5, p=.011), and at the 24-week primary end point, there were no clinically meaningful effects (AMD <3.4). These results at the 12 week follow-up for pain and disability were statistically significant, but did not quite meet the authors predetermined minimal clinically important difference for a between group effect of 10 points. Overall, there were minimal differences between adjacent dose groups at all time points for pain and disability. There were no clinically meaningful differences in pain or disability profiles between 12 and 18 SMT visits.
Additional information if relevant (adverse effects, no. tested at follow-up, adherence	All groups showed strong adherence to care with 90% to 95% of participants attending all 18 study visits. Compliance with data collection was greater than 80% for all follow-up time points. Nine participants were completely lost to follow-up. There were no notable adverse events. Three persons reported seeking care for symptomatic relief of LBP exacerbation related to the study.
Additional information if relevant	Intention to treat analysis was conducted.

Secondary outcomes	
Outcome name and criteria for definition	The secondary outcome measures were pain unpleasantness, Physical and Mental Component Summary Scales of the short-form 12, Health State Visual Analog Scale from EuroQol, perceived pain and disability improvement, and the number of the following in the previous 4 weeks: days with pain and disability and medication use.
Time points measured	Baseline assessment and follow-up evaluation was by mailed questionnaire or blinded phone interview at 6, 12, 18, 24, 39, and 52 weeks after randomization. The primary end points were at 12 and 24 weeks.
Differences between groups	All 4 groups demonstrated improved secondary outcomes over the 6-week treatment period that also persisted for 52 weeks. The improvement in the no-SMT control group was of such magnitude that there were few sizable statistically significant differences between treatment and control groups.
Additional information if relevant	

Conclusions	
Key Conclusions Of Study Authors	- This study found based on the pain and functional disability primary outcomes, 12 sessions of SMT yielded the overall best, but modest, treatment effects (group differences). This was particularly noted in the short term at the 12-week primary end point. Group differences were negligible at the 24-week primary end point, and favored 18 SMT sessions to a small degree in the long term at 52 weeks. - The aim of this study was to find a saturation dose level for use in future studies. The results suggest overall that 12 sessions of spinal manipulation in 6 weeks from a chiropractor yielded the most favorable pain and functional disability improvement in the short-term for chronic nonspecific LBP. Mean participant improvement for this SMT-12 group was substantial at the end of 6 weeks and sustainable to 52 weeks. Approximately, half of patients would be expected to achieve 50% improvement in pain/disability. - In general, the data were consistent with a dose-response relationship being saturated at 12 sessions with little or no additional benefit attributable to additional SMT visits, even at 52 weeks. Analysis of the full-time profile supported no additional benefit overall of 18 over 12 sessions. In addition, responder analysis gave additional support for some advantage of 12 visits but only in the short term. - Twelve sessions of SMT is the current best estimate for use in comparative effectiveness trials. However, this recommendation is made with caution because the gradient of treatment effects across dose groups was too small to clearly distinguish 12 visits from adjacent dose levels. Even with 12 visits, the contribution of SMT to outcomes beyond that of a focused light massage delivered by a chiropractor (hands-on control) was at best modest at the 12-week primary end point and negligible at the 24-week primary end point. - The between-group differences of 8.6 in pain and 7.5 in disability scores at a primary end point (12 weeks) are certainly marginal, but it is not clear yet whether effects of this magnitude constitute a degree of clinical relevance. - The linear dose-response gradients for the primary outcomes were small in general, reaching approximately 2/100 scale points per six sessions of SMT at 12 and 52 weeks. - The effects across dose accumulate to a modest benefit of SMT above the hands-on control. - The light massage control was technically a comparison intervention rather than a true sham. The differences between SMT and the comparison control may be somewhat smaller in this study than it would be for a comparison with a true sham manipulation.

Risk of bias assessment		
Domain	Risk of bias Low High Unclear	Comments
Random sequence generation *(selection bias)*	Low	Randomization was conducted using computer-generated design-adaptive allocation to balance six baseline variables across groups.
Allocation concealment *(selection bias)*	Low	Allocation to study groups was concealed from all study personnel and participants by requiring entry of data into the computer program collected immediately before randomization.
Blinding of participants and personnel *(performance bias)*	High	Because of the nature of the interventions, it was not possible to blind participants or treatment provider.The lack of blinding does not prejudice the conclusions.
Blinding of outcome assessment *(detection bias)*	Low	Patient coordinators, who collected some outcomes by phone interview, remained blinded to group assignment throughout the study.
Incomplete outcome data *(attrition bias)*	Low	Compliance with data collection was greater than 80% for all follow-up time points. All participants lost to follow-up were included in the ITT analysis.
Selective outcome reporting? *(reporting bias)*	Low	The trial was registered with clinicaltrials.gov
Other bias		Intention to treat analysis was used.

Sponsorship if reported		
Study funding sources if reported	This study was funded by the National Center for Complementary and Alternative Medicine (NCCAM), National Institutes of Health (U01 AT001908). The contents of this publication are the sole responsibility of the authors and do not necessarily reflect the official views of NCCAM. The funding agency played no role in the study.	
Possible conflicts of interest for study authors	No Conflicts.	
Notes:		

Comments by DOWC staff

- The findings of this study showed that 12 sessions of spinal manipulation in 6 weeks from a chiropractor yielded the most favorable pain and functional disability improvement compared to a hands-on control in the short-term (12 weeks) for chronic nonspecific LBP. Eighteen sessions of spinal manipulation was not more beneficial than 12 sessions for the treatment of chronic LBP.

- The adjusted mean difference (AMD) in pain at 12 weeks between a control group receiving 18 sessions of light massage and a group receiving 12 sessions of spinal manipulation and 6 sessions of light massage (SMT 12) was 8.6 points. The AMD between the control group and a group receiving 6 sessions of spinal manipulation and 12 sessions of light massage (SMT 6) was 4.5 points. It behooves us to consider whether an additional 6 sessions of spinal manipulation is worth an additional decrease of 4.1 pain points in patients with chronic LBP.

- The results support a beneficial effect of all 4 interventions for treating chronic LBP pain and disability. All 4 groups demonstrated improved clinically meaningful outcomes in pain reduction and disability improvement over the 6-week treatment period that persisted for 52 weeks. The fact that there was little difference in pain and disability scores between adjacent SMT dose groups makes it difficult to recommend one treatment dose over another.

- The between-group differences of 8.6 in pain and 7.5 in disability scores for the SMT 12 group versus the control group at a primary end point (12 weeks) are certainly marginal, and they do not meet the authors predetermined minimal clinically important difference for a between group effect of 10 points. Most of the between group (dose) differences at the various time points are nonsignificant and smaller than 7.5 points. This suggests that there is no clinically important difference between different amounts of spinal manipulation and that spinal manipulation provides little clinical superiority compared to a hands-on control.

- Since the community recruited participants were not typically seeking or receiving care for their back pain problems, it is unclear whether the conclusions can be generalized to those who are seeking care for their back pain.

- The study's design was excellent in controlling for the non-specific effects of added provider attention and bias. Since all groups had 18 visits of hands-on therapy thereby controlling the number of visits, the time with the participant, the effects of touching the patient, patient-provider interaction, and intervention credibility, the potential risk of attention bias was eliminated.

- Study strengths included the use of an RCT design, a large sample size with adequate statistical power to detect clinically meaningful effects, trial registration, a pre-specified protocol, defined primary outcomes, design features known to minimize bias such as assessor blinding and concealed allocation, an intention-to-treat analysis, a low drop-out rate at 12 weeks, long-term follow-up (52 weeks) beyond the end of treatment, and high compliance to treatment.

- The main limitation of the study was lack of blinding of providers and patients.

Assessment by DOWC staff	
Overall assessment as suitability of evidence for the guideline ☐ High quality ☒ Adequate ☐ Inadequate	This adequate quality study provides some evidence that 12 sessions of spinal manipulation in 6 weeks from a chiropractor yields the most favorable pain reduction and functional disability improvement compared to a hands-on control in the short-term (12 weeks) for chronic nonspecific LBP, but there was little difference in pain and disability scores and no clinically important differences between adjacent spinal manipulation dose groups, making it difficult to recommend one treatment dose over another.
If inadequate, main reasons for recommending that the article not be cited as evidence	

Additional references if relevant
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