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Outcomes of Usual Chiropractic; Harm (OUCH). A randomised controlled trial

Bruce F. Walker¹ DrPH, Jeff J. Hebert¹ PhD, Norman J. Stomski¹ PhD, Brenton R. Clarke² PhD,
Ross S. Bowden² M.Mathematics, Barrett Losco¹ M.Chiropractic, Simon D. French³ PhD.

1. School of Health Professions, Murdoch University
2. School of Engineering and Information Technology, Mathematics & Statistics, Murdoch University
3. Centre for Health, Exercise and Sports Medicine, University of Melbourne

Corresponding Author

NJ Stomski, Murdoch University, 90 South St Murdoch, 0893606038,
N.Stomski@murdoch.edu.au

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Study Design: Blinded parallel group randomised controlled

Objective: Establish the frequency and severity of adverse effects from short term usual chiropractic treatment of the spine when compared to a sham treatment group.

Summary of Background Data: Previous studies have demonstrated that adverse events occur during chiropractic treatment. However, as a result of design limitations in previous studies, particularly the lack of sham-controlled randomised trials, understanding of these adverse events and their relation with chiropractic treatment, is suboptimal.

Methods: We conducted a trial to examine the occurrence of adverse events resulting from chiropractic treatment. It was conducted across 12 chiropractic clinics in Perth, Western Australia. The participants comprised 183 adults, aged 20-85, with spinal pain. Ninety two participants received individualized care consistent with the chiropractors' usual treatment approach; 91 participants received a sham intervention. Each participant received two treatments.

Results: Completed adverse questionnaires were returned by 94.5% of the participants after appointment one and 91.3% after appointment two. Thirty three per cent of the sham group and 42% of the usual care group reported at least one adverse event. Common adverse events were increased pain (sham 29%; usual care 36%), muscle stiffness (sham 29%; usual care 37%), headache (sham 17%; usual care 9%). The relative risk was not significant for either adverse event occurrence (RR= 1.24 95% CI 0.85 to 1.81); occurrence of severe adverse events (RR= 1.9; 95% CI 0.98 to 3.99); adverse event onset (RR= 0.16; 95% CI 0.02 to 1.34); or adverse event duration (RR=1.13; 95% CI 0.59 to 2.18). No serious adverse events were reported.

Conclusions: A substantial proportion of adverse events following chiropractic treatment may result from natural history variation and non-specific effects.

Key words: back pain; neck pain; adverse effects; chiropractic; manipulation, spinal; randomized controlled trial; clinical trial; placebo effects; nocebo effects

Level of Evidence: 2

We examined the frequency and severity of adverse effects from short term usual chiropractic treatment of the spine. The relative risk was not significant for adverse event occurrence; occurrence of severe adverse events; adverse event onset; or adverse event duration. A substantial proportion of these events result from non-specific effects.

- 1) Adverse events resulting from chiropractic are common.
- 2) Most adverse events resulting from chiropractic are benign and transitory.
- 3) A substantial proportion of adverse events resulting from chiropractic appear to be due to non-specific effects.

Introduction

Chiropractic therapy is commonly used to manage musculoskeletal conditions in high income countries.^{1,2} The occurrence of adverse events resulting from chiropractic treatment is of considerable interest to chiropractors and the general public. Most adverse events associated with chiropractic treatment are mild, short lasting, and typical of musculoskeletal condition symptoms.³⁻¹¹ However, due to a lack of appropriately designed studies, particularly sham-

controlled trials, there are differences in views about what constitutes a chiropractic treatment related adverse event.

The occurrence of adverse events following chiropractic treatment has been examined in one randomised controlled trial,³ five prospective single arm studies,⁴⁻⁸ and three retrospective studies.⁹⁻¹¹ These studies reported that 34% to 61% of participants experienced at least one adverse event.⁴⁻⁸ Most events were benign, transient, and typically consisted of increased pain, muscle stiffness, tiredness, headache, and radiating discomfort.⁴⁻⁸ Less common events were dizziness, nausea, tinnitus, and impaired vision. More serious adverse events associated with chiropractic treatment, including disc injury, cauda equina syndrome, fracture and stroke, have been reported but the rate has not been robustly established.^{9,11-13}

Predictors of adverse events have been identified in four previous studies of chiropractic treatment.^{6,8,14,15} These predictors included female sex,^{6,8} age (27-46 years),¹⁵ high-velocity manipulation (compared to low-velocity mobilisation),¹⁵ first treatment session,⁶ medication use,¹⁵ and more than one region treated or only thoracic spine treated,¹⁵ treatment including cervical rotation,⁸ work status,⁸ and general practitioner visit in previous six months.⁸ Notably, none of the identified predictors have been found to influence adverse events consistently across studies.

Several limitations constrain the findings of previous studies. In the prospective studies, the chiropractors providing treatment also administered the questionnaires, which possibly resulted in underreporting of adverse events.⁴⁻⁸ In addition, recall bias may also have led to an underestimation of adverse events in the retrospective studies.¹⁶ Moreover, all previous studies lacked a sham intervention, which may have resulted in an overestimation of adverse events as some events could have been associated either with natural history or non-specific effects.

Therefore the estimates of adverse events resulting from the specific effect of treatment are not known. What is known is that adverse events following chiropractic treatment of spinal pain range from trivial to catastrophic. Given these facts plus the limitations of previous studies, additional research is required to develop a more accurate safety profile of chiropractic treatment.

We assessed whether common adverse events differed between participants who received usual chiropractic treatment or a sham intervention for spinal pain. We also captured information about the types, severity, onset, and duration of adverse events.

Methods

Study Design

The complete protocol for this study has been published elsewhere and it was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12611000542998).¹⁷ We conducted this parallel-group randomised controlled trial over three months between August 2012 and October 2012 in twelve Western Australia metropolitan chiropractic centres. Participants were allocated either to: 1) a sham group including typical interaction with the practitioner, or 2) a usual care group providing individualised chiropractic treatment. Participants and outcome assessors were blinded to group allocation. All participants provided demographic and clinical characteristics at entry to the trial, adverse events were evaluated two days after each of the two treatments, and blinding was assessed at two week follow-up.

Recruitment

Participants were recruited from newspaper advertisements. All included participants were 18 years or older; English literate; had non-specific spinal pain (neck, mid-back, or low back pain)

of a least one week duration; and scored at least three on the Numerical Rating Scale for pain,¹⁸ and 12 on the Functional Rating Index.¹⁹

We excluded participants who felt they would be unable to tolerate any intervention potentially delivered in usual chiropractic, including: manipulation; mobilisation; traction; soft tissue massage; and physical modalities.

We also excluded participants who had: spinal pain related to cancer or infection; spinal fracture; spondyloarthropathy; known osteoporosis; progressive upper or lower limb weakness; symptoms of cauda equina syndrome or other significant neurological condition; disc herniation; cardiovascular disease; uncontrolled hypertension; cognitive impairment; blood coagulation disorder; previous spinal surgery; previous history of stroke or transient ischaemic attacks; pacemaker or other electrical device implanted; a current compensation claim.

Intervention Components

Each participant was assigned to either a sham group or usual chiropractic group, whereupon two treatments were delivered with approximately one week between treatments. The chiropractors delivering either the sham or usual chiropractic treatment attended a training session that provided instruction about the trial and how to undertake their respective treatments. To be eligible, all chiropractors need to practice within the Western Australian metropolitan region and were required to be registered with the Chiropractic Board of Australia

Sham Group: the practitioners in this group comprised four registered chiropractors who administered at each visit a) de-tuned ultrasound,²⁰ b) an Activator instrument,²¹ a hand held device that delivers a low impulse, wound to lowest output and administered on the back randomly through a tongue depressor to disperse any remaining force and c) a randomly placed hand on the spine while ultrasound was administered to give a “hands on” experience.

Usual Care: the practitioners in this group consisted of eight registered chiropractors, who provided individualized chiropractic care consistent with their usual treatment approach. The only condition that may have influenced the chiropractors' usual treatment approach was a request to adhere to Australian imaging guidelines.²²

Randomisation

A statistician used a random number generator to create a permuted block randomisation list with variable block sizes of eight to twelve. The group assignment was placed in sequentially numbered, opaque, sealed, envelopes. Staff not administering baseline or outcomes measures opened the envelope and allocated participants to the groups.

Informed Consent and Blinding

Murdoch University's Human Research Committee granted ethics approval for the study (2011/109). All participants provided written informed consent. Research staff administering baseline measures and outcome measures were also blinded to group allocation.

Outcome Assessment

Our primary outcome was adverse event occurrence. We inquired about occurrence of adverse events by using a questionnaire that was informed by previous research.⁴⁻⁸ The occurrence of an adverse event was assessed by an item stating "Did you experience any new unwelcome symptoms or an increase of your presenting symptoms during the first 48 hours (two days) after treatment?"(yes/no). Further details about any adverse events were obtained by four open and four close-ended questions about increased pain, muscular stiffness, headache, and radiating discomfort. Each question enquired about the intensity (11-point Numerical Rating Scale), onset

(five categorical responses ranging from less than 10 minutes to more than 24 hours), and duration (five categorical responses ranging from less than one hour to more than two days). Participants completed the adverse event questionnaire two days after each appointment and returned it by postal mail. The period between the appointment and completion of the questionnaire was selected to allow sufficient time for the manifestation of adverse events.

Statistical Analysis

Our *a priori* sample size estimation was based on detecting a 20% difference in the occurrence of adverse events between the two treatment groups. Assuming an alpha level of 0.05 and a two-tailed hypothesis, recruiting 180 participants (90 per group) would provide 80% power to detect a difference of at least this magnitude. We believed a 20% difference to be a conservative estimate as previous studies have shown that about half of those who receive chiropractic treatment experience adverse events,⁴⁻⁸ whereas in a previous study the de-tuned ultrasound adverse event rate was less than 10%.²⁰

All data were reported descriptively. We classified adverse event intensity as: NRS 1-3 = mild; NRS 4-6 = moderate; NRS 7-10 = severe. Missing data were handled with multiple imputation.²³ We undertook intention to treat and available case analyses. We calculated relative risk (RR) statistics with 95% confidence intervals for the following outcomes: adverse event occurrence, severe adverse event occurrence (severe or not severe), adverse event duration (more or less than 24 hours), and time to onset of adverse event (more or less than 24 hours). When more than one adverse event was reported, the most intense adverse event was identified by the highest NRS score and used for all analyses. Blinding was evaluated by using the Bang Index.²⁴

Results

Study Population

Participants

We screened 272 potential participants, of whom 198 satisfied selection criteria. Between August to September 2012, 183 participants were randomised to either a sham intervention group (n=91) or usual care group (n=92). Participant flow through the study is displayed in Figure 1.

At baseline there were no important differences in demographic details or clinical characteristics, apart from the higher percentage of women in the usual care group (42% compared to 31%).

Participant baseline demographic details and clinical characteristics are displayed in Table 1.

The vast majority of patients (98%) had experienced spinal pain for more than three months.

Three quarters had experienced spinal pain for more than 5 years (75% in sham group; 73% in usual care). The overwhelming majority indicated it had been more than 1 year since last experiencing a 4-week pain free period (89% in sham group; 98% usual care group), and over two thirds indicated it had been more than 1 year since their last 1 week pain free period (71% in sham group; 68% in usual care group).

Chiropractors

In total, 8 chiropractors (5 males) delivered usual care and 4 chiropractors (2 males) provided the sham intervention. Chiropractors had on average 12.6 (SD 2.3) years clinical experience, whereas chiropractors in the sham group had on average 3.6 (SD 1.1) years clinical experience.

About three quarters of the chiropractors had obtained their qualifications from Australian universities (8/11). All chiropractors were registered and practiced fulltime.

Type of Therapies Used in Usual Care Group

Details about therapies used are displayed in Table 2.

Adverse Events: Types, Severity, Onset and Duration

Adverse events

In total, 33% of the sham group, and 42% of the usual care group reported at least one adverse event after either appointment.

The types, onset, and duration of adverse events are displayed in Tables 3-5. Most participants who experienced an adverse event reported more than one event (71% in sham group; 77% usual care group). In total, 198 adverse events were reported (92 in sham group; 106 in the usual care group). Common adverse events were increased pain (29% in sham group; 36% usual care group), muscle stiffness (29% in sham group; 37% usual care group), headache (17% in sham group; 9% usual care group), and radiating discomfort (15% in sham group; usual care group 15%). Less common adverse events, each of which accounted for less than 5% of adverse events in the respective groups, included dizziness, muscle spasm, fatigue, sleeplessness, and joint swelling. The RR for experiencing an adverse event was not significant (RR= 1.24; 95% CI 0.85 to 1.81).

Across both appointments adverse event intensity was most commonly moderate in the sham group (50%; n=46/92), and in the usual care group either moderate (37%; n= 39/106) or severe (37%; n=39/106). The rate of severe adverse events was not different between the groups (RR= 1.9; 95% CI 0.98 to 3.99).

Across both appointments, 79% of the adverse events reported in the sham group (73/92), and 84% in the usual care group (89/106), occurred within 24 hours. The RR for adverse event onset was not significant (RR= 0.16; 95% CI 0.02 to 1.34).

For duration and across both appointments, 51% of the adverse events in the sham group (47/92), and 41% in the usual care group, persisted for less than 24 hours (44/106). The RR for adverse events duration was not significant (RR=1.13; 95% CI 0.59 to 2.18).

The intention to treat and available case analyses provided consistent results with one exception. Regarding the occurrence of serious adverse events, the relative risk estimates were 2.02 (95% CI 1.01 to 4.07) in the available case analysis and 1.97 (95% CI 0.98 to 4.0) in the intention to treat analysis.

Blinding

The proportion of participants who identified the assigned treatment was 67% for the sham group and 85% for the usual care group. Bang Index values showed that 25% of the sham group (95% CI 10% to 40%) and 61% of the usual care group (95% CI 48% to 74%) guessed correctly beyond what would be expected by chance.²⁴

Discussion

This was the first study to use a sham controlled design to examine adverse events following chiropractic treatment. A substantial proportion of adverse events experienced during chiropractic care for spinal pain may be the result of natural symptom fluctuation or from non-specific effects. Adverse events were common in both the usual chiropractic care and sham

groups but no important differences were seen between the groups, and no serious adverse events were reported. However, while very similar, the estimates of severe adverse event risk arising from the intention to treat and available case analyses resulted in conflicting conclusions. Although the intention to treat approach was our primary analysis, we cannot rule out the possibility of increased risk of severe adverse event occurrence with chiropractic treatment compared to sham therapy. The adverse event rate reported by the usual care group in this study was consistent with rates reported by previous studies (42% compared to 34%-61%).⁴⁻⁸ Moreover, the finding that most adverse events were benign and transitory is also consistent with other chiropractic studies.⁴⁻⁸ The proportion of adverse events in these previous studies due to other effects such as natural history or non-specific effects remains indeterminable because none of the studies used a sham arm. However, the results of our study suggest that many adverse events experienced following chiropractic treatment result from either natural history variation or non-specific effects. Some may view these results as evidence that chiropractic treatment is essentially an entirely benign intervention, but it more likely reflects that our study was underpowered to detect a statistically significant difference between groups.

Studies of interventions other than manual therapies have also associated non-specific effects with adverse events.²⁵⁻²⁷ Interestingly, some studies demonstrated that the adverse events reported by participants in either the placebo or sham arm mirror the adverse events in the active intervention arm.²⁸⁻³² This association has been attributed in part to the effect of patient expectancy, which typically depends on details about possible adverse events conveyed either through information sheets, consent forms or the investigators' behaviour.²⁵⁻³² Other studies have shown that a strong aversion to experience an adverse event, coupled with a sense of helplessness about avoiding it, may evoke negative emotions and subsequent reductions in

beneficial non-specific effects.³³ It then seems likely that an expectation of adverse events coupled with not wanting to experience adverse events may promote non-specific effects that contribute to adverse events.³³

Careful consideration should be given to how the information from this study is presented to patients. As numerous studies have shown, disclosing information about the risks of adverse events increases the likelihood of adverse events occurring.²⁵⁻³² Conversely, framing information about adverse events in positive terms (noting that most patients did not experience an adverse event), rather than negative terms (detailing the minority who experienced an adverse event), can lead to a lower adverse event rate.^{34,35} In light of this, we recommend that a form of words be developed for chiropractic patients that accurately reflects the results of our study about potential common adverse events without unnecessarily engendering fear.

Conducting this study under typical clinical conditions enhances the external validity of our findings. However, this study was powered to detect a 20% difference in adverse events, therefore we were underpowered to detect the magnitude of between group differences observed in our sample of participants. In terms of internal validity, we did not measure either anxiety or depression, and it should be noted that it is possible that differing levels of anxiety or depression may have influenced the participants' experience of adverse events in either group. However, there were no important differences between groups in the psychosocial characteristics we assessed at baseline including the Pain Catastrophising Scale and Fear-Avoidance Beliefs Questionnaire. Nevertheless, it should be noted that it is possible that differing levels of anxiety or depression may have influenced the participants' experience of adverse events in either group. We endeavoured to blind study participants to group allocation but were unsuccessful. This was probably due to inherent difficulties in finding an adequate sham intervention to use in a

chiropractic trial, or indeed any type of randomised controlled trial.³⁶ The lack of blinding success may have influenced the reporting of adverse events. In particular, the adverse event rate may have been underreported in the sham group as the majority thought they were receiving an inactive intervention.

Finally, the chiropractors providing usual care were more experienced than chiropractors delivering the sham intervention. However, experience is unlikely to affect an inert sham intervention such as that delivered in this trial. It may be the case that the more experienced chiropractors had better interpersonal skills, which may have reduced the number of adverse events attributable to non-specific effects.

In conclusion, additional studies of larger and more diverse populations are warranted. Such studies should be powered to detect the magnitude of between group differences observed in this trial and include a wait list arm to account for natural variation in spinal pain.

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References

1. Walker BF, Muller R, Grant WD. Low back pain in Australian adults. health provider utilization and care seeking. *J Manipulative Physiol Ther.* Jun 2004;27(5):327-335.

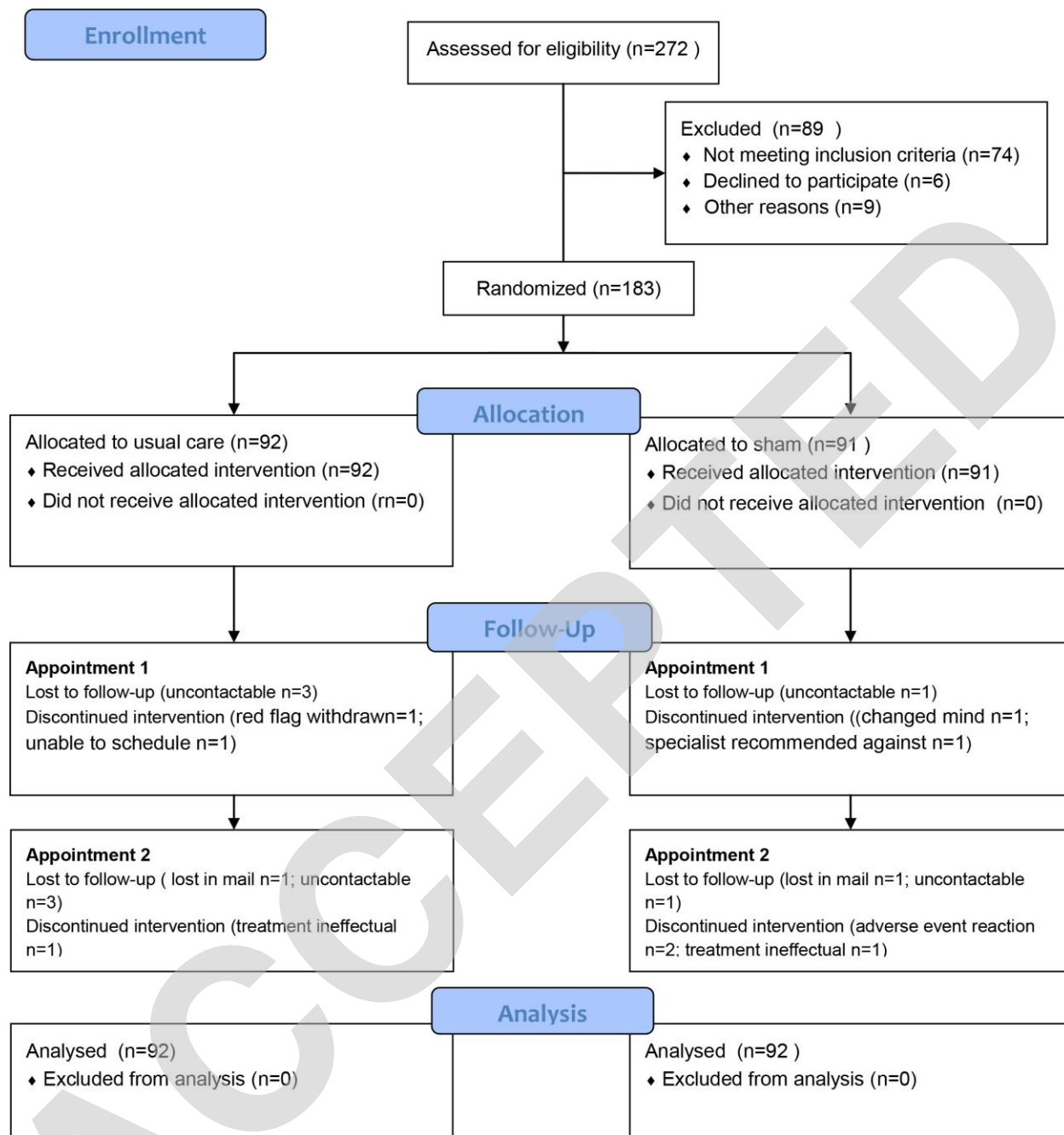
2. Lambeek LC, van Tulder MW, Swinkels IC, Koppes LL, Anema JR, van Mechelen W. The trend in total cost of back pain in The Netherlands in the period 2002 to 2007. *Spine*. 2011;36(13):1050-1058.
3. Hurwitz EL, Morgenstern H, Vassilaki M, Chiang LM. Adverse reactions to chiropractic treatment and their effects on satisfaction and clinical outcomes among patients enrolled in the UCLA Neck Pain Study. *J Manipulative Physiol Ther*. 2004;27(1):16-25.
4. Barrett AJ, Breen AC. Adverse effects of spinal manipulation. *Journal of the Royal Society of Medicine*. May 2000;93(5):258-259.
5. Cagnie B, Vinck E, Beernaert A, Cambier D. How common are side effects of spinal manipulation and can these side effects be predicted? *Man Ther*. 2004;9(3):151-156.
6. Leboeuf-Yde C, Hennius B, Rudberg E, Leufvenmark P, Thunman M. Side effects of chiropractic treatment: a prospective study. *J Manipulative Physiol Ther*. 1997;20(8):511-515.
7. Rubinstein S, Leboeuf-Yde C, Knol D, de Koekkoek T, Pfeifle C, van Tulder M. Predictors of Adverse Events Following Chiropractic Care for Patients with Neck Pain. *J Manipulative Physiol Ther*. 2008;31(2):94 - 103.
8. Senstad O, Leboeuf-Yde C, Borchgrevink C. Frequency and characteristics of side effects of spinal manipulative therapy. *Spine*. 1996;22(4):435-440.
9. Carey PF. A report on the occurrence of cerebral vascular accidents in chiropractic practice. *J Can Chiropr Assoc*. 1993;37:104-106.
10. Klougart N, Leboeuf-Yde C, Rasmussen LR. Safety in chiropractic practice. Part II: Treatment to the upper neck and the rate of cerebrovascular incidents. *J Manipulative Physiol Ther*. Nov-Dec 1996;19(9):563-569.

11. Rezai M, Cote P, Cassidy JD, Carroll L. The association between prevalent neck pain and health-related quality of life: a cross-sectional analysis. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*. Mar 2009;18(3):371-381.
12. Coulter ID, Hurwitz, E.L., Adams, H. The Appropriateness of Manipulation and Mobilization of the Cervical Spine. *RAND*. 1996.
13. Hebert JS, N; French, S; Rubinstein, S. Serious Adverse Events and Spinal Manipulative Therapy of the Low Back Region: A Systematic Review of Cases. *J Manipulative Physiol Ther*. 2013;In Press.
14. Rubinstein SM, Leboeuf-Yde C, Knol DL, de Koekkoek TE, Pfeifle CE, van Tulder MW. Predictors of adverse events following chiropractic care for patients with neck pain. *J Manipulative Physiol Ther*. Feb 2008;31(2):94-103.
15. Hurwitz EL, Morgenstern H, Vassilaki M, Chiang LM. Frequency and clinical predictors of adverse reactions to chiropractic care in the UCLA neck pain study. *Spine (Phila Pa 1976)*. Jul 1 2005;30(13):1477-1484.
16. Hassan E. Recall Bias can be a Threat to Retrospective and Prospective Research Designs. *The Internet Journal of Epidemiology*. 2006;3(2).
17. Walker B, Losco B, Clarke B, Hebert J, French S, Stomski N. Outcomes of usual chiropractic, harm & efficacy, the ouch study: study protocol for a randomized controlled trial. *Trials*. 2011;12(1):235.
18. Katz J, Melzack R. Measurement of pain. *Surg Clin North Am*. 2010;79:231 - 252.

19. Feise RJ, Michael Menke J. Functional rating index: a new valid and reliable instrument to measure the magnitude of clinical change in spinal conditions. *Spine (Phila Pa 1976)*. Jan 1 2001;26(1):78-86; discussion 87.
20. Costa LO, Maher CG, Latimer J, et al. Motor control exercise for chronic low back pain: a randomized placebo-controlled trial. *Phys Ther*. 2009;89(12):1275-1286.
21. Methods A. <http://www.activator.com>.
22. Group AAMPG. Evidence-based management of acute musculoskeletal pain. *National Library of Australia* 2003.
23. Rubin DB. Multiple Imputation for Nonresponse in Surveys. *J. Wiley & Sons, New York*. 1997.
24. Bang N, Ni L, Davis C. Assessment of Blinding in Clinical Trials. *Control Clin Trials*. 2004;25(2):143 - 156.
25. Amanzio M, Corazzini LL, Vase L, Benedetti F. A systematic review of adverse events in placebo groups of anti-migraine clinical trials. *Pain*. 2009;146(3):261-269.
26. Barsky AJ, Saintfort R, Rogers MP, Borus JF. Nonspecific medication side effects and the nocebo phenomenon. *Jama*. 2002;287(5):622-627.
27. Colloca L, Miller FG. The nocebo effect and its relevance for clinical practice. *Psychosom Med*. Sep 2011;73(7):598-603.
28. Myers MG, Cairns JA, Singer J. The consent form as a possible cause of side effects. *Clin Pharmacol Ther*. 1987;42(3):250-253.
29. Lancman ME, Asconape JJ, Craven WJ, Howard G, Penry JK. Predictive value of induction of psychogenic seizures by suggestion. *Ann Neurol*. 1994;35(3):359-361.

30. Flaten MA, Simonsen T, Olsen H. Drug-related information generates placebo and nocebo responses that modify the drug response. *Psychosom Med.* 1999;61(2):250-255.
31. Luparello TJ, Leist N, Lourie CH, Sweet P. The interaction of psychologic stimuli and pharmacologic agents on airway reactivity in asthmatic subjects. *Psychosom Med.* 1970;32(5):509-513.
32. Mondaini N, Gontero P, Giubilei G, et al. Finasteride 5 mg and sexual side effects: how many of these are related to a nocebo phenomenon? *J Sex Med.* 2007;4(6):1708-1712.
33. Vase L, Robinson ME, Verne GN, Price DD. Increased placebo analgesia over time in irritable bowel syndrome (IBS) patients is associated with desire and expectation but not endogenous opioid mechanisms. *Pain.* 2005;115(3):338-347.
34. Miller FG, Colloca L. The placebo phenomenon and medical ethics: rethinking the relationship between informed consent and risk-benefit assessment. *Theor Med Bioeth.* 2011;32(4):229-243.
35. Edwards A, Elwyn G, Covey J, Matthews E, Pill R. Presenting risk information--a review of the effects of "framing" and other manipulations on patient outcomes. *J Health Commun.* 2001;6(1):61-82.
36. Boutron I, Estellat C, Guittet L, et al. Methods of blinding in reports of randomized controlled trials assessing pharmacologic treatments: a systematic review. *PLoS medicine.* Oct 2006;3(10):e425.

Figure Legend:



Flow of the patients through each stage of the study.

Tables

Table 1 Participant baseline demographics and clinical characteristics*.

Demographics	Usual Care Group (n=92)	Sham Group (n=91)
Mean (SD) age (years)	56.9 (14.6)	53.0 (14.3)
Women	39 (42.4)	28 (30.8)
Low Income	31 (34.4)	24 (27.2)
Middle/High Income	59 (65.6)	66 (72.8)
Did Not Complete Secondary School	25 (27.2)	25 (28.1)
Currently Smoke	26 (27.5)	25 (27.8)
Moderate/Heavy Alcohol Consumption	30 (32.6)	37 (40.7)
Clinical Characteristics	Usual Care Group (Mean (SD))	Sham Group (Mean (SD))
Numerical Rating Scale	5.3 (1.7)	5.2 (1.9)
Functional Rating Index	18.3 (5.3)	18.3 (5.6)
Pain Catastrophising Scale	14.3 (10.1)	16.2 (12.0)
Fear Avoidance Beliefs Questionnaire-Activity	13.9 (5.9)	14.1 (5.5)
Fear Avoidance Beliefs Questionnaire-Work	15.3 (10.7)	16.5 (11.5)

* Figures are number (percentage) unless stated otherwise.

Table 2 Types of therapies used across both appointments

Therapy	Applied to participants (%)
Manipulation	96.5
Soft Tissue Therapy	67.4
Range of Motion Exercise	51.1
Mobilisation	52.6
Strengthening Exercise	5.5
Traction	1.1
Heating Modalities	1.1

Table 3 Types of Adverse Events

Adverse Event	Severity					
	Minor		Moderate		Severe	
Treatment group	sham	chiro	sham	chiro	sham	chiro
Muscle stiffness (sham=27;chiro=39)	6	13	15	15	6	11
Increased pain (sham=27;chiro=38)	3	6	15	14	9	18
Headache (sham=16;chiro=10)	7	5	7	2	2	3
Radiating discomfort (sham=14;chiro=16)	5	4	4	8	5	4
Other* (sham=8;chiro=3)	1	0	5	1	2	2

Total (sham=92;chiro=106)	22	28	46	39	24	39
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*pain/stiffness: sham=3 chiro=0; gluteal strain: sham=2; chiro=0; joint swelling/pain: sham=2; chiro=0; dizziness: sham=2; chiro=1; disturbed sleep: sham=1; chiro=0; muscle spasm: sham=0; chiro=1.

Table 4 Onset of Adverse Events

Adverse Event	Onset			
	Less than 24 hours		More than 24 hours	
Treatment group	sham	chiro	sham	chiro
Muscle stiffness (sham=27;chiro=39)	22	33	5	6
Increased pain (sham=27;chiro=38)	24	31	3	7
Headache (sham=16;chiro=10)	10	9	6	1
Radiating discomfort(sham=14;chiro=16)	11	13	3	3
Other* (sham=8;chiro=3)	6	3	2	0
Total (sham=92;chiro=106)	73	89	19	17

*pain/stiffness: sham=3 chiro=0; gluteal strain: sham=2; chiro=0; joint swelling/pain: sham=2; chiro=0; dizziness: sham=2; chiro=1; disturbed sleep: sham=1; chiro=0; muscle spasm: sham=0; chiro=1.

Table 5 Duration of Adverse Events

Adverse Event	Duration					
	Less than 24 hours		24 to 48 hours		More than 48 hours	
	sham	chiro	sham	chiro	sham	chiro
Muscle stiffness (sham=27;chiro=39)	12	14	9	12	6	13
Increased pain (sham=27;chiro=38)	12	12	8	12	7	14
Headache (sham=16;chiro=10)	13	8	3	1	0	1
Radiating discomfort (sham=14;chiro=16)	7	9	2	2	5	5
Other* (sham=8;chiro=3)	3	1	0	2	5	0
Total (sham=92;chiro=106)	47	44	22	29	23	33

*pain/stiffness: sham=3 chiro=0; gluteal strain: sham=2; chiro=0; joint swelling/pain: sham=2; chiro=0; dizziness: sham=2; chiro=1; disturbed sleep: sham=1; chiro=0; muscle spasm: sham=0; chiro=1.