Spinal manipulation, medication, or home exercise with advice for acute and subacute
neck pain: A randomized controlled trial

Gert Bronfort, DC, PhD*; Roni Evans, DC, MS; Alfred V. Anderson, DC, MD;
Kenneth H. Svendsen, MS; Yiscah Bracha, MS; Richard H. Grimm, MD, MPH, PhD

Author Affiliations:
From Northwestern Health Sciences University, Minneapolis, MN; Pain Management and
Rehabilitation Center, Minneapolis, MN; Berman Center for Outcomes and Clinical Research at
the Minneapolis Medical Research Foundation, Minneapolis, MN

*Corresponding author responsible for publication and reprints

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Abstract

Background: Mechanical neck pain is a common condition, afflicting an estimated 70% of all individuals at some time in their lives. Very little research exists to guide the choice of therapy for acute and subacute neck pain.

Objective: To determine the relative efficacy of spinal manipulation therapy, medication, and home exercise with advice for acute and subacute neck pain in both the short and long term.

Design: Randomized controlled trial

Setting: 1 university research center, 1 pain management clinic in Minnesota

Patients: 272 persons, 18-65 years of age with non-specific neck pain 2-12 weeks duration

Interventions: 12 weeks of spinal manipulation therapy (SMT), medication (MED), or home exercise with advice (HEA)

Measurements: The primary outcome was patient-rated pain measured at 2, 4, 8, 12, 26, and 52 weeks post-randomization. Secondary measures were self-reported disability, global improvement, medication use, satisfaction, general health status (SF-36 physical and mental health scales), and adverse events. Blinded evaluation of neck motion was performed at 4 and 12 weeks.

Results: For pain, there was a statistically significant advantage of SMT over MED after 8, 12, 26, and 52 weeks (p<=0.01). HEA was superior to MED at 26 weeks (p=0.02). No important
differences in pain were found between SMT and HEA at any time point. Results for most of the secondary outcomes were similar to the primary outcome.

**Limitations:** Inability to blind patients and providers. No specific criteria for defining clinically important group differences were pre-specified or available from the literature.

**Conclusion:** For patients with acute and subacute neck pain, spinal manipulation was more effective than medication management in both the short and long term. However, a few instructional sessions of home exercises with advice resulted in outcomes similar to those of spinal manipulation at most time points.

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**ClinicalTrials.gov Identifier:** NCT00029770
Introduction

Neck pain is a prevalent condition, with nearly three quarters of individuals experiencing it at some time in their lives. (1,2) It is one of the most commonly reported symptoms in primary care settings, (3,4) resulting in millions of ambulatory healthcare visits each year and rising healthcare costs. (5-8) While not life threatening, neck pain can have a negative effect on productivity and overall quality of life. (1,9-11)

Spinal manipulation is a manual therapy commonly applied by chiropractors, physical therapists, osteopaths, and other healthcare providers for neck pain conditions. (12) Similarly, home exercise programs and medications are widely used to manage neck pain. (13) Recent Cochrane reviews report insufficient evidence to assess the effectiveness of commonly used medications or home exercise programs for the treatment of acute neck pain. (13,14) Similarly, the evidence for spinal manipulation is also limited, with only low quality evidence supporting its use for neck pain of short duration. (15)

The purpose of this randomized trial was to test the hypothesis that spinal manipulation therapy (SMT) is more effective than medical care (MED) and home exercise with advice (HEA) for acute and subacute neck pain.

Methods

Setting

The trial was conducted from 2001 to 2007 in Minneapolis, Minnesota. All eligibility screening, randomization, and short term data collection activities occurred at a university affiliated
research center; long term data collection took place by mail. Spinal manipulation and
instruction in home exercise were provided at a university affiliated outpatient clinic. Medical
treatment was provided at a pain management clinic. The study was approved by the
institutional review boards of Northwestern Health Sciences University and Hennepin County
Medical Center. Written informed consent was obtained from all participants.

Participants

Participants were recruited using targeted mailings to neck pain patients registered with Blue
Cross/Blue Shield Minnesota and through newspaper and radio advertisements. Interested
individuals were screened for eligibility at two baseline appointments by clinicians blinded to the
randomization schedule. Inclusion criteria were 18 to 65 years of age, primary complaint of
mechanical, non-specific neck pain (equivalent to grades I and II classification according to the
Neck Pain Task Force (16,17)), 2–12 weeks duration of current neck pain episode, and neck
pain score of 3 or greater on a 0–10 numerical rating scale. Participants were asked to refrain
from seeking additional treatment for neck pain by non-study healthcare providers during the
12-week intervention phase.

Exclusion criteria were cervical spine instability, fracture, neck pain referred from peripheral
joints or viscera, progressive neurological deficits, existing cardiac disease requiring medical
treatment, blood clotting disorders, diffuse idiopathic hyperostosis, inflammatory or destructive
tissue changes of the cervical spine, infectious disease or other severe disabling health
problems, substance abuse, pregnant or nursing women, previous cervical spine surgery, and
pending or current litigation. In addition, participants were excluded if they had received any of
the study treatments within the last three months.
Randomization and Interventions

Randomization using permuted blocks of different sizes (18) took place at the second baseline appointment. The randomization schedule was prepared off-site by the study statistician prior to participant enrollment and was concealed from the investigators, treatment providers, and research staff using consecutively numbered, sealed, opaque envelopes. As patients became eligible, envelopes were opened in consecutive order by a research staff member in the presence of the patient.

The intervention protocol was tested in a previous pilot study by our research team. (19) Maximum treatment duration was 12 weeks. Treatment providers were trained in the study intervention protocols and were required to document treatment activities in a standardized clinical record. These records were routinely monitored by research staff to ensure protocol adherence.

Spinal Manipulation Therapy (SMT) Group

Six chiropractors with a minimum of 5 years experience served as the primary providers of treatment. Visits lasted 15–20 minutes and included a brief history and examination of the cervical and thoracic spine. The primary focus of treatment was spinal manipulation of areas of the spine with segmental hypomobility using diversified techniques including low amplitude spinal adjustments (a high velocity type of joint thrust manipulation) and mobilization (a low velocity type of joint oscillation). (20) The specific spinal level to be treated and the number of treatment sessions over the 12 week period was left to the discretion of the provider based on manual palpation of the spine and associated musculature, as well as the patient’s response to treatment. (21) Adjunct therapy common to clinical practice included limited light soft tissue
massage, assisted stretching, and hot and cold packs to facilitate the manipulation treatment.

Advice to stay active or modify activity was recommended as needed.

**Medication (MED) Group**

A licensed medical physician provided care to participants in the MED group with the focus of treatment on prescription medication. Visits lasted 15–20 minutes and included a brief history and examination. The first line of therapy was nonsteroidal anti-inflammatory drugs (NSAIDs) and/or acetaminophen. (22,23) Patients who did not respond to the first line of therapy, as well as those intolerant to NSAIDs, were prescribed narcotic medications. Muscle relaxants were also used. Advice to stay active or modify activity was issued as needed. The choice of medications and number of visits was made by the physician based on the patient’s history and response to treatment.

**Home Exercise with Advice (HEA) Group**

Home exercise with advice was provided in two one-hour sessions, 1–2 weeks apart at the university-affiliated outpatient clinic. Six therapists provided instruction to patients. The primary focus was simple self-mobilization exercise (gentle controlled movement) of the neck and shoulder joints, including neck retraction, extension, flexion, rotation and lateral bending motions, as well as scapular retraction, with no resistance. The delivery method was one-on-one and the program was individualized in terms of the patient’s abilities, tolerance, and activities of daily living. Patients were instructed to do 5–10 repetitions of each exercise, up to 6–8 times per day. A booklet (24) and laminated cards of prescribed exercises were provided. Sessions were supplemented with information regarding the basic anatomy of the cervical spine and advice including postural instructions and practical demonstrations of lifting, pushing, pulling, and other daily actions.
Outcomes and Measurements

We collected patient demographic and clinical characteristics at the initial baseline appointment through self-report questionnaires, clinical history, and physical examination. Self-reported outcomes (e.g., pain) were measured six times during the 12-week treatment period (at two baseline appointments and 2, 4, 8, and 12 weeks post-randomization). In addition, self-report outcomes were collected twice during the post-treatment period (at 26 and 52 weeks) via mailed questionnaire. All self-report questionnaires were completed by patients independently free of investigator, study staff, or treatment provider influence. Patients were asked in each questionnaire if anyone attempted to influence their responses. Objective measures of cervical spine motion were measured at 4 and 12 weeks by seven trained examiners masked to treatment assignment. (25) Blinding was maintained by systematically instructing patients not to reveal treatment information and by ensuring examiners had no exposure to activities in the outpatient clinics.

We chose patient-rated pain, a priori, as the primary outcome measure, using the 11-box numerical rating scale: 0 (no symptoms) to 10 (highest severity of pain). (26-29) Secondary outcomes included the Neck Disability Index (NDI), (30) global improvement, (31-33) medication use, (34) satisfaction with care, (25,34) the Medical Outcomes Study Short Form 36-item Health Survey (SF-36 D), (35), and cervical spine motion (CA6000). (36,37)

Prior to randomization, patients were asked in the self-report questionnaire how they expected their neck pain to change in response to treatment. Response choices were: much better, better, no change, worse, and much worse. Patients were also asked to report additional healthcare use by non-study providers in the self-report questionnaires at all time points.
Patients were posed standardized questions at each treatment visit to assess side effects since the last visit; responses were documented in the clinical record.

**Statistical Analyses**

The sample size calculation was based on an ability to detect a 0.8 point difference between the highest and lowest of the group means in patient-rated neck pain (the primary outcome) at the end of 12 weeks of treatment. This difference was informed by previous neck pain trials conducted by our group (19,25) and the ability to detect a small-medium effect size. The standard deviation (SD) used was 1.8 (pain scale: 0-10) based on our pilot study and estimates from the literature. (25,38) With a power of 0.90 and a 3-group design tested at an alpha level of 0.05 (two-tailed test), 75 participants per group were required (SPSS SamplePower® 1.0, International Business Machines Corp., Armonk, New York). We allowed for a loss to follow up rate of up to 15%. Therefore, we aimed to recruit 90 patients per group for a total of 270 participants.

In primary analyses, we evaluated changes in neck pain between baseline and week 12 and performed longitudinal analyses using week 2, 4, 8, and 12 data (short term outcome). In secondary (exploratory) analyses of both primary and secondary outcomes, we evaluated changes in patient-rated outcomes between baseline and weeks 2, 4, 8, 12, 26, and 52, and performed longitudinal analyses using weeks 2, 4, 8, 12, 26, and 52 (long term outcome). Both types of analyses were conducted using linear mixed models analysis (MIXED procedure in SAS 9.1®, SAS Institute Inc., Cary, NC) with baseline values as outcomes. (39-42) Clinical and demographic variables showing group differences at baseline were used as covariates in the analysis if they were at least moderately correlated with changes in outcomes. (43,44)

The study database was prepared by data managers blinded to study allocation.
The intention-to-treat principle was adhered to by including all participants with baseline data in the analyses regardless of loss to follow up.

To protect against increased risk of Type I errors, we used Fisher’s (protected) least significant difference test. (45,46)

The mixed model analysis included all patients that had at least baseline assessments. In the event of missing data, the reasons were explored and the pattern of the missing data was determined to select the best method of data imputation. The original analyses were then repeated with data fully imputed (using the MI procedure SAS 9.1) as sensitivity analyses to assess the impact of the missing data. (47-51)

No pre-specified thresholds for clinically important group differences were set since they have not been established in the literature. To facilitate interpretation of the magnitude of group differences, responder analyses were conducted for pain reduction by group (absolute risk reduction) of 50%, 75%, and 100% (including 95% CIs) at the end of the treatment phase and at week 26 and 52 follow-up. (52-55)

Role of Funding Sources

The trial was funded by the National Institute of Health’s National Center for Complementary and Alternative Medicine (grant R01 AT000707). The funding source had no role in the study design, collection, analysis, data interpretation, or writing of this report.
Results

A total of 504 individuals were evaluated for eligibility, of whom 272 were randomized: 90 to the MED group, 91 to SMT, and 91 to HEA. A summary of patient recruitment, participation, and attrition across the length of the study is summarized in Figure 1.

Demographic and clinical characteristics of the randomized participants are summarized in Table 1. Potentially important between-group differences were noted for sex, duration of neck pain, pain during the night, and expectation of change in neck pain.

Table 2 provides details of the three different study interventions.

Primary Outcomes

There were statistically significant differences in patient-rated pain improvement with SMT compared to medical therapy at 12 weeks (0.94 (0.37 to 1.51) greater reduction in pain from baseline with SMT than with medical therapy on a 0-10 pain scale; p=.001) and in longitudinal analyses incorporating pain ratings every two weeks from baseline to 12 weeks (0.55 (0.10- to 1.00) greater reduction in pain with SMT than with medical therapy; p=0.017); and at 12 weeks a statistically significantly higher absolute proportion of patients in the SMT group experienced reductions of pain of at least 50% (Table 3). Differences between patient-rated pain improvement with SMT and with home exercise were smaller and not statistically significant; differences with home exercise and medical therapy were also not statistically significant, although a higher absolute proportion of patients performing home exercise experienced reductions of pain at 12 weeks of at least 75% compared to those receiving medical therapy.
Findings from longer term analyses were comparable: patient-rated pain improvement favored SMT over medical therapy, but not SMT over home exercise or home exercise over medical therapy at 26 and 52 weeks compared to baseline. A higher absolute proportion of SMT compared to medical therapy patients experienced reductions of pain of at least 50% at 26 but not 52 weeks; there were no differences in those proportions at any time in comparisons of SMT and home exercise, and a higher absolute proportion of home exercise compared to medical therapy patients experienced reductions of pain of at least 75% at 26 but not 52 weeks.

Adjustment for baseline imbalances in sex, cause of pain, and depression did not change the group differences in pain outcomes.

**Secondary Outcomes**

Most of the secondary outcomes showed a similar pattern of group difference to the primary outcomes. (For all secondary outcomes results, see Appendix Tables 1-4.) SMT was superior to medical therapy at the end of treatment and during follow-up in terms of global improvement, patient satisfaction, and SF-36-assessed physical but not mental function; SMT was also superior to medical therapy in measures of long-term medication use (1.26 (0.53 to 1.99) fewer days per week of medication use at 1 year; p<0.001).

The SMT and HEA groups performed similarly to one another on most of the secondary outcomes. An advantage of SMT over HEA was observed for satisfaction with care in both the short and long term.

Home exercise with advice was superior to medical therapy in both the short and long term for satisfaction with care, and in long-term medication use (1.00 (0.27 to 1.73) fewer days per week use at 1 year; p=0.008).
Changes in cervical spine motion after 4 and 12 weeks are shown in Appendix Table 4. Overall, the greatest changes in cervical spine motion were observed in the HEA group. Results of the group differences in 3-dimensional cervical spine motion patterns will be reported elsewhere.

Of all participants, one indicated that someone tried to influence his responses; as this was a week 52 questionnaire collected by mail independent of study staff; this is unlikely to be of consequence.

**Missing Data Analysis**

Among the 272 participants randomized, 219 (80.5%) provided data on neck pain at every visit. We considered loss to follow up to be nonrandom from 12 participants: those who never commenced treatment (6 in MED) and those who decided to stop participation in the study after they received treatment (2 in MED, 1 in SMT; 3 in HEA). We first imputed values to the missing responses of these 12 participants by using the mean percentage reduction from baseline at all time points specific to the group they belonged. Then we imputed the rest of the missing data during treatment and the two post-treatment follow up time points using the SAS multiple imputation strategy, based on the assumption that the data were missing at random. The results of analyses with imputed values changed the estimates of group differences very little and all statistically significant differences remained the same.

**Non-Study Treatments**

During the 12-week intervention, 4 participants reported visits to other healthcare providers for their neck pain (MED n=3, HEA n=1). By week 52, about equal numbers of individuals in each treatment group sought additional healthcare use following completion of the study treatment phase (SMT n=18, MED n=14, HEA n=17).
Adverse Events

No serious adverse events were reported in the study. Expected, non-serious adverse events, or side effects, typical to treatments did occur and were all transient in nature, requiring little or no change to activity levels. Forty percent of the SMT group and 46% of the HEA group reported adverse events, primarily musculoskeletal pain. Less frequent were paresthesia, stiffness, headache, and crepitus (see Appendix Table 5). Sixty percent of individuals in the MED group reported side effects, the most common being gastrointestinal symptoms and drowsiness. Less commonly reported were dry mouth, cognitive disturbance, rash, congestion and disturbed sleep.

Discussion

In the absence of available criteria for what constitute clinically important group differences, several factors should be considered in aggregate. This includes the statistical significance of the results of the primary efficacy analysis, as well as results of the responder analyses and the secondary outcomes analyses. Additionally, the durability of treatment effect, the safety and tolerability of the interventions, and patient’s ability and willingness to comply must be taken into account. (56)

In this trial comparing spinal manipulation to medical therapy and home exercise for the treatment of acute and subacute neck pain, spinal manipulation appeared more effective than medical therapy using a variety of measures of neck pain and function. However, spinal manipulation demonstrated no apparent benefits over home exercise. Spinal manipulation and home exercise led to similar short and long term outcomes, but participants receiving medical therapy seemed to fare worse, continuing to have higher use of pain medication for neck pain.
throughout the trial’s entire observation period. Noteworthy is the performance of the HEA group, which has the potential for cost savings over spinal manipulation and medication interventions.

The potential for side effects is a factor that patients and clinicians consider when making treatment decisions. While the frequency of reported side effects was similar among the three groups (41-58%), the nature of the side effects differed, with patients in the SMT and HEA groups reporting predominantly musculoskeletal events, and those in the MED group reporting side effects more systemic in nature. Importantly, patients in the MED group reported higher level of medication use after the intervention phase.

Most patients had subacute neck pain lasting more than four weeks, beyond the time when pain is likely to resolve spontaneously, and there is evidence that half of nonspecific neck pain patients continue to have neck pain a year after the original complaint. (57) Although the trial did not incorporate a placebo arm, it is unlikely that the observed results are due to natural history alone.

To date, there have been very few clinical trials assessing the effectiveness of noninvasive interventions for acute and subacute neck pain not associated with whiplash. Consequently, there is no established and evidence-informed first line of therapy for this type of neck pain. (12,13)

We searched MEDLINE, EMBASE, CINAHL, and The Cochrane Library (using the terms spinal manipulation and neck pain) to identify all randomized trials published from 1960 to 2011 evaluating spinal manipulation therapy for acute or subacute neck pain. We found three trials. (58-61) Our trial is most comparable to the trial by Hoving et al, (58,59) in which 75% of patients had neck pain less than 12 weeks duration. Six weeks of manual therapy (mainly spinal
mobilization) was compared to usual medical care (advice, home exercise, and medication).

These authors found manual therapy to be superior to medical care, with reductions in pain and disability similar to what we observed at 8 weeks but less than what we observed at 12 weeks.

In another study by Pool et al, (60) 6 weeks of manual therapy (up to 6 sessions) was compared to 6 weeks of a behavioral-graded activity program (maximum of 18 sessions of 30 minutes each). At 3 months, the behavioral-graded activity program demonstrated slightly larger reductions in pain and disability than manual therapy; however, the magnitude of improvements in the behavioral program was similar to that found for SMT in our trial. One trial by Cleland et al (61) found thrust mobilization/manipulation more effective than non-thrust manual treatment in subacute neck pain patients. When considered in the context of the existing evidence, the results of our trial suggest spinal manipulation/mobilization and instruction in home exercises constitute viable treatment options for the management of acute and subacute mechanical neck pain.

**Strengths and Limitations**

Our study has several strengths, including a rigorous concealed randomization procedure, use of recommended reliable outcome measures, masked objective outcomes assessors, and long term post-randomization follow up (6 and 12 months.) A limitation of this study is that it was not possible for patients and providers to be blinded due to the nature of the treatments received and delivered. Another limitation was the lack of available criteria for the definition of a clinically important group difference for the different outcomes. Further, the study does not differentiate between the specific effects of treatment and the contextual, or non-specific, effects including patient-provider interactions and expectations. Rather, this study was intended to be pragmatic in nature, answering clinical questions regarding commonly used treatment approaches approximating how they are delivered in practice.
Conclusion

For patients with acute and subacute neck pain, spinal manipulation was more effective than management with medication in both the short and long term; however, a few sessions of supervised instruction in home exercises with advice resulted in outcomes similar to those of spinal manipulation at most time points.

Authors’ Contributions

Conception and design: Bronfort, Evans, Grimm, Bracha
Statistical Analysis: Bracha, Svendsen
interpretation of data: Bronfort, Bracha, Svendsen, Evans
Drafting of the article: Bronfort, Evans
Critical revision of the article for important intellectual content: Bronfort, Evans, Bracha, Svendsen, Grimm, Anderson
Final approval of the article: Bronfort, Evans
Provision of study materials or patients: Bronfort, Grimm, Anderson
Statistical expertise: Bracha, Svendsen, Grimm
Obtaining of funding: Bronfort, Evans, Grimm, Bracha
Administrative, technical or logistic support: Bronfort, Evans
Collection and assembly of data: Bronfort, Evans

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Summary of Financial Conflicts of Interest Disclosures

Gert Bronfort:
Dr. Bronfort’s employer, Northwestern Health Sciences University, received funding through a restricted grant provided by the National Center for Complementary and Alternative Medicine (NCCAM) to perform the study described in this manuscript. Dr. Bronfort currently serves as a non paid member of the National Advisory Council for Complementary and Alternative Medicine.

Roni Evans:
Dr. Evans’ employer, Northwestern Health Sciences University, received funding through a restricted grant provided by NCCAM to perform the study described in this manuscript. She has no other financial or nonfinancial relationships, conditions, or circumstances that present potential conflict of interest.

Al Anderson:
Dr. Anderson did not receive payment for the submitted work. He has no other financial or nonfinancial relationships, conditions, or circumstances that present potential conflict of interest.

Yiscah Bracha:
Ms. Bracha’s employer at the time, Berman Center for Outcomes and Clinical Research, at the Minneapolis Medical Research Foundation, received funding through a subcontract with Northwestern Health Sciences University (funding provided through NCCAM). She has no other financial or nonfinancial relationships, conditions, or circumstances that present potential conflict of interest.

Ken Svendsen:
Mr. Svendsen received payment as a consultant. He has no other financial or nonfinancial relationships, conditions, or circumstances that present potential conflict of interest.

Richard Grimm:
Dr. Grimm’s employer, Berman Center for Outcomes and Clinical Research at the Minneapolis Medical Research Foundation, received funding through a subcontract with Northwestern Health Sciences University (funding provided through NCCAM). He serves as a paid Chair of a Data Safety and Monitoring Board for Pfizer and as a consultant for Pfizer, Merck, and Takeda. Dr. Grimm has grants pending with Roche and the National Institutes of Aging and has accepted honoraria from Merck and Takeda for speaking engagements.

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**Reproducible Research Statement**

**Protocol:** Available to interested readers by contacting Dr. Bronfort at gbronfort@nwhealth.edu.

**Statistical Code:** Available to interested readers by contacting Dr. Bronfort at gbronfort@nwhealth.edu.

**Data:** Not available
Current postal addresses for all authors

Gert Bronfort, DC, PhD
Wolfe-Harris Center for Clinical Studies
Northwestern Health Sciences University
2501 W 84th St
Bloomington MN 55431

Roni Evans, DC, MS
Wolfe-Harris Center for Clinical Studies
Northwestern Health Sciences University
2501 W 84th St
Bloomington MN 55431

Alfred V. Anderson, DC, MD
Medical Pain Management
5775 Wayzata Blvd, Suite 110
Saint Louis Park, MN
55416

Kenneth H. Svendsen, MS
900 Forest Ave
Birmingham, MI 48009

Yiscah Bracha, MS
Division of Health Policy and Clinical Effectiveness
Cincinnati Children's Hospital
3333 Burnet Ave, MLC 5040
Cincinnati, OH 45229

Richard H. Grimm, MD, MPH, PhD
Berman Center for Outcomes & Clinical Research
825 S 8th St, Suite 440
Minneapolis MN 55404
References


Table 1. Baseline demographic and clinical characteristics (SD)

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<th></th>
<th>SMT</th>
<th>MED</th>
<th>HEA</th>
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<tr>
<td>Number of participants</td>
<td>91</td>
<td>90</td>
<td>91</td>
</tr>
<tr>
<td>Age (years)</td>
<td>48.3 (15.2)</td>
<td>46.8 (12.2)</td>
<td>48.6 (12.5)</td>
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<td>Gender (% female)</td>
<td>58.2</td>
<td>72.2</td>
<td>65.9</td>
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<td>Married/living with someone (%)</td>
<td>60.4</td>
<td>73.3</td>
<td>60.4</td>
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<td>College graduate (%)</td>
<td>55.0</td>
<td>48.9</td>
<td>52.8</td>
</tr>
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<td>Current smoker (%)</td>
<td>13.2</td>
<td>14.4</td>
<td>17.6</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>27.6 (5.8)</td>
<td>27.9 (6.6)</td>
<td>26.4 (6.1)</td>
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<tr>
<td>Duration of neck pain (weeks)</td>
<td>7.0 (3.2)</td>
<td>7.4 (3.0)</td>
<td>6.8 (3.2)</td>
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<tr>
<td>Frequency of neck pain</td>
<td>3.5 (0.9)</td>
<td>3.3 (0.9)</td>
<td>3.7 (0.9)</td>
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<tr>
<td>(0=none of the time; 5=all of the time)</td>
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<td>Pain radiation to upper extremity (%)</td>
<td>24.2</td>
<td>20.0</td>
<td>23.3</td>
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<tr>
<td>Awake at night because of neck pain (%)</td>
<td>49.5</td>
<td>65.6</td>
<td>61.5</td>
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<td>Reported cause of neck pain:</td>
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<td></td>
<td></td>
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<tr>
<td>- Trauma</td>
<td>29.7</td>
<td>22.2</td>
<td>16.5</td>
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<tr>
<td>Auto accident (%)</td>
<td>8.8</td>
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<tr>
<td>Leisure time accident (%)</td>
<td>16.5</td>
<td>12.2</td>
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<tr>
<td>Job accident (%)</td>
<td>4.4</td>
<td>2.2</td>
<td>2.2</td>
</tr>
<tr>
<td>- No apparent cause (%)</td>
<td>45.1</td>
<td>48.9</td>
<td>50.5</td>
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<tr>
<td>- Did not recall (%)</td>
<td>5.5</td>
<td>8.9</td>
<td>6.6</td>
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<tr>
<td>- Other (e.g., repetitive motion, stress, sleep position) (%)</td>
<td>19.8</td>
<td>20.0</td>
<td>26.4</td>
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<tr>
<td>Depression (CES-D) score (0-100)</td>
<td>14.3 (12.7)</td>
<td>15.3 (11.0)</td>
<td>12.7 (9.6)</td>
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<td>Expectation of change in pain</td>
<td>1.5 (0.7)</td>
<td>1.8 (.6)</td>
<td>1.9 (0.6)</td>
</tr>
<tr>
<td>(1=much better; 5=much worse)</td>
<td></td>
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SMT=Spinal Manipulation Therapy; MED=Medication; HEA=Home Exercise with Advice
Table 2. Details of treatment interventions

<table>
<thead>
<tr>
<th>Treatment group (number of patients who received treatment)</th>
<th>Mean number of visits (range)</th>
<th>Specific aspects of intervention</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMT (91)</td>
<td>15.3 (2-23)</td>
<td>Cervical SMT</td>
<td>90 (99%)</td>
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<tr>
<td></td>
<td></td>
<td>Thoracic SMT</td>
<td>56 (62%)</td>
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<tr>
<td></td>
<td></td>
<td>Soft tissue</td>
<td>79 (87%)</td>
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<tr>
<td></td>
<td></td>
<td>Assisted stretch</td>
<td>61 (67%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hot packs</td>
<td>38 (42%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cold packs</td>
<td>61 (67%)</td>
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<tr>
<td></td>
<td></td>
<td>Prescription medication</td>
<td>0</td>
</tr>
<tr>
<td>MED (84)</td>
<td>4.8 (1-8)</td>
<td>NSAID, opioid analgesic, and muscle relaxant</td>
<td>76 (90%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NSAID and opioid analgesic</td>
<td>3 (4%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NSAID and muscle relaxant</td>
<td>2 (2%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Opioid analgesic and muscle relaxant</td>
<td>1 (1%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Muscle relaxant only</td>
<td>1 (1%)</td>
</tr>
<tr>
<td>HEA (91)</td>
<td>2 (1-2)</td>
<td>Exercise instruction</td>
<td>91 (100%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Education (spinal anatomy, etc)</td>
<td>91 (100%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Self care advice (pain management, etc)</td>
<td>91 (100%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Instructions for ADLs (lifting, etc)</td>
<td>88 (97%)</td>
</tr>
<tr>
<td></td>
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<td>Prescription medication</td>
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</table>

SMT=Spinal Manipulation Therapy; MED=Medication; HEA=Home Exercise with Advice; NSAID=nonsteroidal anti-inflammatory drug; ADLs=activities of daily living
### Table 3. Between-group differences for changes from baseline in patient-rated pain

<table>
<thead>
<tr>
<th></th>
<th>SMT (n=91)</th>
<th>MED (n=90)</th>
<th>HEA (n=91)</th>
<th>Change in SMT minus change in MED</th>
<th>P value</th>
<th>Change in SMT minus change in HEA</th>
<th>P value</th>
<th>Change in HEA minus change in MED</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>5.27 (1.57)</td>
<td>4.93 (1.49)</td>
<td>5.05 (1.64)</td>
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<tr>
<td>Week 2</td>
<td>3.77 (1.86)</td>
<td>3.62 (1.97)</td>
<td>3.47 (2.12)</td>
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</tr>
<tr>
<td><strong>Week 2 – Week 0</strong></td>
<td>1.51 (1.15 to 1.86)</td>
<td>1.28 (0.92 to 1.65)</td>
<td>1.57 (1.22 to 1.93)</td>
<td>0.22 (-0.35 to 0.79)</td>
<td>0.44</td>
<td>-0.07 (-0.63 to 0.50)</td>
<td>0.82</td>
<td>0.29 (-0.28 to 0.86)</td>
<td>0.32</td>
</tr>
<tr>
<td>Week 4</td>
<td>2.93 (2.02)</td>
<td>2.89 (1.83)</td>
<td>2.80 (2.15)</td>
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</tr>
<tr>
<td><strong>Week 4 – Week 0</strong></td>
<td>2.31 (1.90 to 2.73)</td>
<td>1.68 (2.35 to 2.69)</td>
<td>1.85 (2.69)</td>
<td>0.30 (-0.27 to 0.87)</td>
<td>0.30</td>
<td>0.05 (-0.52 to 0.61)</td>
<td>0.87</td>
<td>0.25 (-0.32 to 0.83)</td>
<td>0.39</td>
</tr>
<tr>
<td>Week 8</td>
<td>2.01 (1.88)</td>
<td>2.39 (1.80)</td>
<td>2.22 (2.22)</td>
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<tr>
<td><strong>Week 8 – Week 0</strong></td>
<td>3.24 (2.80 to 3.67)</td>
<td>2.13 (2.88 to 3.33)</td>
<td>2.73 (3.69)</td>
<td>0.73 (0.16 to 1.30)</td>
<td>0.012</td>
<td>0.38 (-0.18 to 0.95)</td>
<td>0.185</td>
<td>0.35 (-0.22 to 0.92)</td>
<td>0.23</td>
</tr>
<tr>
<td>Week 12</td>
<td>1.50 (1.70)</td>
<td>2.08 (1.65)</td>
<td>1.74 (1.84)</td>
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<tr>
<td><strong>Week 12 – Week 0</strong></td>
<td>3.75 (3.41 to 4.16)</td>
<td>2.81 (3.10 to 3.74)</td>
<td>3.31 (2.88 to 3.74)</td>
<td>0.94 (0.37 to 1.51)</td>
<td>0.001</td>
<td>0.44 (-0.13 to 1.00)</td>
<td>0.130</td>
<td>0.50 (-0.07 to 1.08)</td>
<td>0.087</td>
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<td><strong>Short Term</strong></td>
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<tr>
<td>Week 26</td>
<td>1.90 (2.24)</td>
<td>2.33 (1.86)</td>
<td>1.77 (2.09)</td>
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<tr>
<td><strong>Week 26 – Week 0</strong></td>
<td>3.30 (2.83 to 3.77)</td>
<td>2.52 (2.06 to 2.98)</td>
<td>2.31 (2.73 to 3.69)</td>
<td>0.78 (0.20 to 1.36)</td>
<td>0.009</td>
<td>0.09 (-0.49 to 0.67)</td>
<td>0.76</td>
<td>0.69 (0.10 to 1.28)</td>
<td>0.021</td>
</tr>
<tr>
<td>Week 52</td>
<td>1.60 (1.53)</td>
<td>2.14 (1.85)</td>
<td>1.92 (2.34)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Week 52 – Week 0</strong></td>
<td>3.57 (3.13 to 4.00)</td>
<td>2.70 (2.20 to 3.20)</td>
<td>3.07 (2.46 to 3.69)</td>
<td>0.87 (0.27 to 1.47)</td>
<td>0.005</td>
<td>0.49 (-0.10 to 1.08)</td>
<td>0.101</td>
<td>0.37 (-0.22 to 0.97)</td>
<td>0.22</td>
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<tr>
<td><strong>Long Term</strong></td>
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<td>Week 12</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>≥ 50%</td>
<td>82.2%</td>
<td>69.0%</td>
<td>77.0%</td>
<td>13.2% (0.5% to 25.8%)</td>
<td></td>
<td>5.2% (-6.7% to 17.1%)</td>
<td></td>
<td>8.0% (-5.3% to 21.2%)</td>
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</tr>
<tr>
<td>≥ 75%</td>
<td>56.7%</td>
<td>33.3%</td>
<td>48.3%</td>
<td>23.3% (9.0% to 37.7%)</td>
<td></td>
<td>8.4% (-6.3% to 23.1%)</td>
<td></td>
<td>14.9% (0.4% to 29.5%)</td>
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</tr>
<tr>
<td>100%</td>
<td>32.2%</td>
<td>13.1%</td>
<td>29.9%</td>
<td>19.1% (7.1% to 31.2%)</td>
<td></td>
<td>2.3% (-11.3% to 16.0%)</td>
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<td>16.8% (4.8% to 28.8%)</td>
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</tr>
<tr>
<td>Week 26</td>
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</tr>
<tr>
<td>≥ 50%</td>
<td>75.0%</td>
<td>59.0%</td>
<td>71.6%</td>
<td>16.0% (1.7% to 30.3%)</td>
<td></td>
<td>3.4% (-10.1% to 16.9%)</td>
<td></td>
<td>12.6% (-2.1% to 27.3%)</td>
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<tr>
<td>≥ 75%</td>
<td>53.6%</td>
<td>30.8%</td>
<td>49.4%</td>
<td>22.8% (8.0% to 37.6%)</td>
<td></td>
<td>4.2% (-11.1% to 19.4%)</td>
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<td>18.6% (3.7% to 33.6%)</td>
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</tr>
<tr>
<td>100%</td>
<td>36.9%</td>
<td>19.2%</td>
<td>34.6%</td>
<td>17.7% (4.2% to 31.2%)</td>
<td></td>
<td>2.3% (-12.3% to 17.0%)</td>
<td></td>
<td>15.3% (1.8% to 28.9%)</td>
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<tr>
<td>Week 52</td>
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</tr>
<tr>
<td>≥ 50%</td>
<td>81.8%</td>
<td>69.0%</td>
<td>69.6%</td>
<td>12.8% (-1.0% to 26.6%)</td>
<td></td>
<td>12.2% (-1.1% to 25.5%)</td>
<td></td>
<td>0.6% (-14.2% to 15.4%)</td>
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</tr>
<tr>
<td>≥ 75%</td>
<td>53.2%</td>
<td>38.0%</td>
<td>49.4%</td>
<td>15.2% (-0.7% to 31.1%)</td>
<td></td>
<td>3.9% (-11.8% to 19.6%)</td>
<td></td>
<td>11.3% (-4.4% to 27.1%)</td>
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<tr>
<td>100%</td>
<td>27.3%</td>
<td>16.9%</td>
<td>36.7%</td>
<td>10.4% (-2.9% to 23.6%)</td>
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<td>-9.4% (-24.0% to 5.1%)</td>
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<td>19.8% (6.1% to 33.6%)</td>
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</tr>
</tbody>
</table>

Values are means (standard deviations) for individual time point data and means (95% Confidence Interval) for both within group change from baseline and between group comparisons.

*Group differences based on weeks 2, 4, 8, and 12 data; †Group differences based on weeks 2, 4, 8, 12, 26, and 52 data

SMT=Spinal Manipulation Therapy; MED=Medication; HEA=Home Exercise with Advice

Pain: 0-10 scale (0=no neck pain, 10=the worst neck pain possible)
<table>
<thead>
<tr>
<th></th>
<th>Wk 12 Change in Neck Pain</th>
<th>Pnx26bl</th>
<th>Pnx52bl</th>
<th>BL1 and BL2 Mean CESD</th>
<th>DURATION in weeks</th>
<th>BL1 Q2 (Patient's Gender)</th>
<th>BL1 Q3 (Mental Status)</th>
<th>BL1 Q17 (Pain worse with coughing or sn)</th>
<th>BL1 Q23 (Neck pain wake you up at night)</th>
<th>BL1 Q4 (How much schooling)</th>
<th>Expectation in Assigned Group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Wk 12 Change in Neck Pain</strong></td>
<td></td>
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<tr>
<td>Pearson Correlation</td>
<td></td>
<td>-0.52**</td>
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<tr>
<td>Sig. (2-tailed)</td>
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<td>0.00</td>
<td>0.03</td>
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</table>

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).

---

<table>
<thead>
<tr>
<th></th>
<th>Wk 12 Change in Neck Pain</th>
<th>Pnx26bl</th>
<th>Pnx52bl</th>
<th>BL1 and BL2 Mean CESD</th>
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<th>BL1 Q4 (How much schooling)</th>
<th>Expectation in Assigned Group</th>
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<tr>
<td><strong>Wk 12 Change in Neck Pain</strong></td>
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<td>Spearman's rho</td>
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<td>-0.64**</td>
<td>-0.61**</td>
<td>-0.14**</td>
<td>0.05**</td>
<td>-0.03</td>
<td>-0.01</td>
<td>-0.18**</td>
<td>-0.200**</td>
<td>-0.232**</td>
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<td>0.00</td>
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</tbody>
</table>

** Correlation is significant at the 0.01 level (2-tailed).
* Correlation is significant at the 0.05 level (2-tailed).