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Spinal manipulation and exercise for low back pain in adolescents: a randomized trial

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Abstract

Low back pain (LBP) is common in adolescence but there is a paucity of high quality research to inform care. We conducted a multicenter randomized trial comparing 12 weeks of spinal manipulative therapy (SMT) combined with exercise therapy (ET) to ET alone.

Participants were 185 adolescents aged 12–18 years with chronic LBP.

The primary outcome was LBP severity at 12, 26, and 52 weeks. Secondary outcomes included disability, quality of life, medication use, patient and caregiver-rated improvement and satisfaction. Outcomes were analyzed using longitudinal linear mixed effect models. An omnibus test assessing differences in individual outcomes over the entire year controlled for multiplicity.

Of the 185 enrolled patients, 179 (97%) provided data at 12 weeks and 174 (94%) at 26 and 52 weeks. Adding SMT to ET resulted in a larger reduction in LBP severity over the course of one year (P=0.007). The group difference in LBP severity (0–10 scale) was small at the end of treatment (mean difference=0.5; P=0.08), but was larger at weeks 26 (mean difference=1.1; P=0.001) and 52 (mean difference=0.8; P=0.009). At 26 weeks, SMT with ET performed better than ET alone for disability (P=0.04) and improvement (P=0.02). The SMT with ET group reported significantly greater satisfaction with care at all time points (P≤0.02). There were no serious treatment-related adverse events.

For adolescents with chronic LBP, spinal manipulation combined with exercise was more effective than exercise alone over a one-year period, with the largest differences occurring at six months. These findings warrant replication and evaluation of cost-effectiveness.

1. Introduction

The United States is in the midst of an unprecedented pain management crisis, with chronic pain impacting over ⅓ of the US population, and affecting more individuals than heart disease, diabetes, and cancer combined.[43] LBP is one of the most common and

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Conflicts of Interest

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burdensome of the pain conditions with an estimated 40–80% of individuals worldwide experiencing LBP at some point in their lives.[25; 31] LBP related disability has increased an alarming 42% over the past two decades, making it the leading cause of disability globally.[32] While there has been a long-standing belief that LBP is limited to adults, there is now substantial evidence to the contrary. In fact, research has shown that LBP develops with increasing frequency in adolescence, with prevalence rates reaching that of adults by the late teens.[10; 33; 34; 37] Importantly, adolescent LBP has been shown to be a strong predictor of adult LBP, which may have important negative implications for the lifetime course.[17; 28; 33] An additional concern is that 20%−40% of U.S. adolescent LBP sufferers receive an opioid prescription when they seek medical care.[24; 51] There is a heightened urgency to identify safe and effective non-pharmacological LBP treatments for all ages.[12]

In 2012, complementary healthcare approaches were used by one third of American adults [13] and 12% of children 4–17.[4] Spinal manipulative therapy (SMT) is the most common provider based complementary approach [4; 13] and is often used to treat LBP complaints. SMT consists of manual techniques including high velocity, low amplitude thrust procedures or low velocity, variable amplitude mobilization maneuvers. For LBP, SMT is applied to the lumbar vertebral or sacroiliac joints with the aim of restoring mobility and decreasing pain.[26] Recent guidelines for LBP in adults strongly recommended SMT as well as exercise prior to initiating pharmacologic treatment.[50] Rehabilitative exercise focused on teaching and encouraging patients how to manage their LBP, and potentially prevent future recurrences, is frequently combined with SMT as an important aspect of promoting patient self-efficacy.[15]

While there is fairly well established evidence regarding the effectiveness of commonly used conservative treatments like supervised exercise and SMT for adults with chronic LBP, [12; 52] there are few randomized trials focusing on adolescents with LBP.[10; 44]. Indeed, a systematic review of conservative treatments for LBP in children and adolescents was unable to locate any trials focused on SMT, and only three small studies [1; 20; 35] focused on exercise. Thus there is a critical need for more high quality RCTs to inform the responsible management of LBP in non-adult populations.[44]

To address the large research gaps for LBP management in adolescents, we performed a parallel-group, randomized controlled trial to test the comparative effectiveness of SMT plus exercise therapy (ET) versus ET alone for individuals 12–18 years of age with recurrent or chronic LBP. We chose exercise alone as a comparison intervention because of the encouraging preliminary evidence of effectiveness for adolescents with LBP and the potential to promote active pain coping behaviors.[44] The primary aim of this study was to test the hypothesis that the addition of SMT to exercise would be more effective than exercise alone at 12, 26, and 52 weeks in improving LBP pain severity. The impact on other important LBP related outcomes, including disability, quality of life, medication use, patient and caregiver-rated improvement and satisfaction, was also assessed.

2. Methods

A detailed description of the full study protocol was published previously.[53] The study was funded by the U.S. Department of Health and Human Services and was registered at clinicaltrials.gov (NCT01096628) This was a two-site, parallel-group randomized controlled trial that used allocation by rank-order minimization. Participants were recruited from March 2010 to December 2012, with follow-up data collection through December 2013. Institutional Review Boards at participating institutions (Northwestern Health Sciences University and University of Western States) approved the study protocol. Written patient assent and parent consent were obtained for participants 12–17 years of age and written consent was provided by participants who were 18 years of age. Primary and secondary outcomes were mostly self-reported, with the exception of blinded objective measures of spinal function and activity levels; all outcomes were collected independent of investigator influence. A Data Safety and Monitoring Board consisting of a medical physician, health services research scientist, and a statistician monitored the study.

2.1 Setting and participants

Study participants were recruited mainly from the general population using direct mail postcards, social media, paper and digital advertisements. Letters were also sent to local physicians and sport coaches requesting referrals. Screening, intervention and data collection took place at two clinical research centers in Minneapolis, Minnesota and Portland, Oregon. Interested parties were screened for eligibility initially by phone and at three subsequent in-person baseline evaluations. Inclusion criteria were: adolescents (12–18 years of age) with sub-acute recurrent or chronic, non-specific LBP (severity ≥ 3/10) with or without leg pain. Sub-acute recurrent LBP was defined as a current episode of 2–12 weeks duration with a history of at least one additional two-week episode of back pain in the past year. Chronic LBP was defined as duration of the current episode of ≥ 12 weeks. Participants were allowed to use over-the-counter medication as needed. Exclusion criteria were: SMT, ET, or changes in prescription pain medications within the past month, other concurrent provider-based treatment for LBP, contraindications to study treatment (e.g. clinical spinal instability, inflammatory arthropathies, etc.), benign joint hypermobility syndrome, and other serious physical or mental health conditions as determined by self-report and clinical exam and history.

2.2 Allocation

Assignment to study intervention was performed using a computerized dynamic allocation (rank-order minimization) system to balance participant characteristics of gender, age, LBP duration and severity between groups at each study site using a 1:1 allocation ratio. The first six participants at each site were randomly assigned using a computer-generated random allocation sequence secured in sealed, opaque, sequentially numbered envelopes to seed the dynamic allocation system. Randomization envelopes were also used as a backup if the dynamic allocation system was not available (e.g., internet service disruption). Allocation was concealed from investigators and all study personnel. The allocation program and envelopes were prepared by the study statistician prior to commencing enrollment independent of investigator influence.

2.3 Interventions

All study personnel were trained and certified to implement study protocols in an effort to ensure standardization within and across sites. Blinding of participants and treatment providers was not possible due to the physical nature of the interventions. The intervention period was 12 weeks. Chiropractors and exercise therapists were trained to deliver ET to both study groups. ET and SMT could have occurred in either order ie. ET either before or after SMT using protocols that our group has applied in previous studies of adults.[7; 8] Detailed descriptions of the interventions are provided in a previous publication.[53]

2.3.1 Exercise therapy (ET)—The goal of the ET program was to help adolescents manage their LBP and prevent future occurrences. The ET program included self-care education, supervised exercise and instructions for home exercise. Participants attended 8–16, 45 minute sessions with an exercise therapist or licensed chiropractor no more than 2 times per week. Treatment dose was determined based on patients' abilities and needs. Self-care education included patient-centered goal setting and emphasis on the importance of movement and activity, pain management, and spinal posture awareness with basic activities of daily living (e.g., sitting, getting out of bed and using a backpack). Participants were also provided printed instructions and photos for each exercise, along with a modified *Back in Action* book.[11] Each supervised exercise session began with a 5 minute light aerobic warm-up followed by stretching and strengthening exercises (bridge, abdominal crunches, quadruped, side bridge and back extensions). Participants began with exercises appropriate for their fitness level and progressed in difficulty by changing body position and/or labile surface (i.e. gym ball). They were provided instructions to perform the same exercises at home and to engage in 20–40 minutes of aerobic activity twice per week.

2.3.2 Spinal manipulation combined with exercise therapy (SMT+ET)—The goal of the combined SMT+ ET program was to enhance patients' ability to exercise by providing treatment to the lumbar vertebral or sacroiliac joints in an effort to increase mobility and decrease pain.[26] Participants attended 8–16, 10–20 minute study visits with experienced licensed chiropractors, no more than 2 times per week. SMT visits took place on the same day as ET sessions when possible, and could take place either before or after ET sessions. SMT dose, spinal levels treated, and technique were individualized to the patient based on the patient's prognosis, tolerance, and needs. A brief updated history and examination were conducted at each visit. High-velocity, low amplitude SMT was the preferred technique; however, low-velocity low amplitude SMT, mobilization, flexion-distraction manipulation, or drop-table assisted SMT could also be used. Up to a few minutes of ice or heat or light soft tissue massage were allowed to facilitate the SMT, if necessary. Participants in the SMT+ET group took part in the same exercise therapy program described above.

2.4 Outcomes

Participant demographic and clinical characteristics were collected during the baseline visits via a comprehensive health history and physical examination and self-report questionnaires. Self-reported outcomes were collected at the first two baseline visits and at 4, 8, 12, 26, and 52 weeks post-enrollment using questionnaires administered independent of staff or clinician

influence. Parent-reported outcomes were collected by questionnaires at 12, 26, and 52 weeks. Objective biomechanical outcomes were collected at baseline, 12, and 26 weeks post enrollment by examiners blinded to treatment assignment and independent of investigator influence. Individual qualitative interviews were also performed at 12 weeks exploring participants' perspectives.

2.4.1 Primary outcome—The primary outcome was self-reported typical level of LBP severity over the past week measured with the 11-box numerical rating scale (0= no pain, 10 = worst pain possible). The 11-box numerical rating scale performs similarly to the visual analogue scale in adult and pediatric populations.[30; 59]

2.4.2 Secondary outcomes—Secondary measures included patient-rated disability (18-item Roland-Morris Disability Questionnaire),[40; 55] quality of life (23-item PedsQL),[36; 56–58] improvement (9-point scale ranging from no symptoms,100% improvement, to as bad as it could be, 100% worse),[22] frequency of medication use for low back pain (days/week), and patient satisfaction with care (7-point scale, 1=completely satisfied, couldn't be better, 7=completely dissatisfied, couldn't be worse).[42] Healthcare utilization and home exercise compliance were also ascertained. Side effects and adverse events were queried on the self-report questionnaires using a list of expected events informed by past studies.[8; 41] Participants rated each adverse event using an 11-point bothersomeness scale (0 = not at all bothersome, 10= extremely bothersome). Further, participants were asked about any new or persisting events at each treatment visit. Parents/guardians were asked to rate their perception of the participating adolescent's improvement and satisfaction with care. In addition, the participant's expectation of 3-month improvement was assessed once immediately following treatment allocation using the same 9-point improvement scale listed above.

2.5 Sample size

The sample size calculation was based on the ability to detect an 8-percentage point mean difference in the primary outcome (LBP severity) at 12, 26, and 52 weeks. Assuming a SD of 1.4, based on a prior study within an adolescent LBP population, [35] and allowing for an attrition rate of 15%, 92 participants per group (184 total) were required to ensure 92% power at an alpha level of 0.01.

2.6 Statistical analysis

We used an intention-to-treat approach, analyzing all observed data from participants according to their allocated treatment assignment. Data analyses were performed in STATA, version 13.0 (StataCorp. 2013. Stata Statistical Software: Release 13. College Station, TX: StataCorp LP). The statistician was blinded to group allocation for all analyses.

All primary and secondary outcomes were analyzed using linear mixed effect models including fixed effects for time, treatment, and a time-by-treatment interaction, and a random intercept to account for within-subject correlation. The model included the baseline outcomes (when appropriate), site, and additional minimization variables (gender, age, LBP severity and duration) as covariates.

Primary outcome measure.—The primary outcomes were group differences in pain severity at weeks 12, 26, and 52 derived from the linear mixed effect model. Prior to conducting the analysis, the following strategy was agreed-upon by the statistician to control for multiple endpoints, but was not described previously in the protocol [53]. We used Fisher's protected least significant difference approach [38] to control for the repeated measures. An area under the curve minus baseline summary measure [3; 23] was used as the omnibus test to determine if the long-term pain profile (including baseline, 4, 8, 12, 26, and 52 weeks) was different between groups. The omnibus test needed to be significant (p-value ≤0.05) for group differences at 12, 26, and 52 weeks to be determined. A site-by-treatment-by-time interaction was included in the linear mixed effect model if significant ($P \leq 0.05$). Clinical and demographic variables were included as covariates if they were at least moderately correlated with change in outcomes.[49]

Secondary analyses of the primary outcome measure included group differences at weeks 4 and 8, the short-term profile (including baseline, 4, 8, and 12 weeks) and the long-term profile (including all time points). Additionally, responder analyses for no pain reduction, or pain reductions of 30% (minimal improvement), 50% (moderate improvement), 75%, and 100% (substantial improvement) were performed at weeks 12, 26, and 52.[48] Differences in proportions of responders between groups were calculated and 95% confidence intervals were analyzed using the Wilson method for risk differences. [45] Cumulative responder analysis graphs were created to display the proportion of responders for all possible levels of pain reduction.[21] Differences in cumulative response curves were assessed by determining the area under the response curve using the trapezoidal rule and 95% confidence intervals were calculated using bias-corrected bootstrapping with 1000 iterations.[9]

Secondary outcome measures—Secondary outcome measures analyzed for this manuscript included disability, improvement, medication days, quality of life, patient satisfaction, exercise compliance, and parent/guardian satisfaction and perceived improvement. Analyses of the secondary outcome measures included group differences at the relevant individual time points for all measures, in addition to short-term (including baseline, 4, 8, and 12 weeks) and long-term (including all time points) profiles for disability, medication days, and improvement. The same omnibus test approach used for the primary outcome was applied to the secondary outcomes to control for multiplicity. Non-parametric analyses (i.e. bootstrapping) were performed as a sensitivity analysis for models with non-normally distributed residuals [19]. Results of the objective biomechanical and qualitative data collection will be reported in separate manuscripts.

2.6.1 Missing Data & Sensitivity Analyses—Linear mixed effect model analyses provide unbiased estimates when data are missing at random [16]. The pattern and reasons for missing data were assessed to determine if sensitivity analyses were necessary for addressing data missing not at random. In addition, sensitivity analyses were conducted to assess the impact of treatment compliance and additional healthcare use (e.g. primary care, chiropractic, physical therapy, massage therapy, surgery) following the 12-week interventions. The impact of treatment compliance was assessed by a per-protocol analysis of participants who completed at least 8 intervention sessions. The impact of additional

healthcare use after the end of treatment (12 weeks) was assessed by including an indicator variable for additional healthcare use as a covariate.

3. Results

3.1 Baseline characteristics

A total of 457 participants were assessed for eligibility, of whom 185 were enrolled, 42 at the Oregon site and 143 at the Minnesota site (Fig 1). A total of 272 individuals were excluded from participating; 184 of these were unwilling to participate (reasons given included no longer interested, time commitment, preference for or against one or both interventions, and unspecified) and another 88 did not meet the other inclusion criteria. Allocation resulted in baseline comparability between groups. Table 1 summarizes the demographic and clinical characteristics of enrolled participants. Over two-thirds (69%) of participants were female. The duration of back pain was more than 1 year in 72% of the participants, the mean severity was moderate (5.3), and 11% had radiating pain to the leg. More than half (54%) reported having treatment for back pain in the past. Patients in the SMT+ET group had slightly higher expectations of improvement (1–9 scale) from their assigned treatment (mean=2.3, SD=0.7) compared to the ET alone group (mean=2.5, SD=0.8). Expectation of improvement was very weakly correlated with change in pain severity (r between −0.13 and −0.18) and was therefore not included as a covariate when analyzing the primary outcome measure.

3.2 Treatment frequency and adherence with the protocol

Overall, 91% of study participants attended their prescribed treatment visits: 96% in the SMT+ ET group and 87% in the ET alone group. The mean number of ET visits was 10.8 (SD=1.8; median=11.0) in the SMT+ ET group and 9.8 (SD=3.0; median=11.0) in the ET alone group. The mean number of SMT visits was 10.1 (SD=1.9; median=10) in the SMT+ ET group. Compliance with home exercise instruction was similar between groups and declined over time from around 2 days/week at the end of treatment to 1 day/week at one year. During the 12-week intervention, 5 participants reported visits to other healthcare providers for their LBP: 2 from the SMT+ ET group and 3 from ET alone. Between weeks 12 and 52, a total of 50 individuals sought additional healthcare: 21 in SMT+ ET (15 sought additional SMT) and 29 in ET alone (18 sought additional SMT).

3.3 Effectiveness assessments

3.3.1 Primary outcome measure.—The longitudinal omnibus test for pain showed SMT+ ET to be significantly superior to ET over the one-year period (P = 0.007). Based on the adjusted means for reduction in pain severity (0–10 scale), there was an advantage of 0.5 for SMT+ET over ET alone at the end of 12 weeks of treatment (P = 0.083), 1.1 at week 26 (P = 0.001), and 0.8 at week 52 (P = 0.009)(Table 2 & Figure 2). The SMT+ET group experienced significantly greater changes in the long-term profile of pain severity (P = 0.007), but not in the short-term profile (P=0.55) (Table 2).

3.3.2 Responder analysis of primary outcome.—On average, the difference in proportions for reduction of LBP severity across all possible thresholds for improvement

favored SMT+ET by approximately 7% at 12 weeks (95% CI −3% to 17%), 17% at 26 weeks (95% CI 8% to 27%), and 10% at 52 weeks (95% CI 0.1% to 20%). Detailed results from the responder analyses are provided in Table 3 and Figure 3. At 12 weeks, there were no differences between SMT+ET and ET alone for minimal (≥ 30%) or moderate (≥ 50%) reductions in LBP severity, but a larger proportion of participants in the SMT+ET group (10 to 15%) experienced substantial reductions in pain severity (≥ 75% or 100%). By week 26, an advantage was noted for SMT+ET across all levels of reduction in LBP severity, ranging from 14 to 25% greater proportions of participants. At week 52, approximately 10% more participants from the SMT+ET group reported minimal or moderate reductions in LBP severity, but these findings were not statistically significant. Smaller differences were also noted in proportions of patients experiencing a substantial reduction (≥ 75% or 100%) in LBP severity. In addition, more individuals in the ET only group reported no reduction or an increase in pain severity at weeks 26 and 52.

3.3.3 Secondary outcome measures.—Longitudinal profiles significantly favored SMT+ET for disability, improvement, and satisfaction over the long-term (Table 4). Quality of life and medication use did not significantly differ over the one-year period. Cross-sectional group differences for disability, improvement, medication use, and quality of life mainly favored the SMT+ET group, but most differences were not significant. However, at week 26, SMT+ET was superior to ET in terms of disability and improvement (Table 4). In addition, the SMT+ET group experienced significantly greater satisfaction with care than ET alone at weeks 12, 26 and 52. Both groups reported approximately 80% reduction in medication use at the end of treatment which was sustained during the entire follow-up period. (Table 4) Ratings by the parent/guardian showed a significant advantage for the combined group in the longitudinal profile for satisfaction, but not for improvement (Table 5).

3.3.4 Missing data & sensitivity analyses.—Among the 185 participants, 171 (92%) provided data on back pain at every time point, and 169 (86%) provided the secondary outcomes at every time point. A total of 4 participants in the SMT+ET group and 10 in the ET group did not provide primary outcome data at all time points and the pattern of missingness appeared to be non-random. We chose to perform two sensitivity analyses assessing the impact of missing data from these 14 individuals by imputing 1) the 10th percentile and 2) the 90th percentile by group for the primary outcome at each time point. [39] The estimated model coefficients from the sensitivity analyses based on the imputed data were of similar magnitude and in the same direction as the primary analysis and all statistically significant between group differences remained the same. The results from the per-protocol and additional healthcare use sensitivity analyses were very similar to the primary analysis with slight decreases in group differences, but no changes in statistical significance or the overall conclusions.

3.5 Adverse events.

Two serious adverse events (SAEs) occurred during the course of the trial. Both occurred in the SMT+ET group post intervention and were classified as unrelated to study interventions. One participant developed appendicitis and had an appendectomy. Another participant was

hospitalized due to renal issues related to type I diabetes. Minor self-limiting adverse events during the 12 weeks of intervention were reported with about equal frequency in both group (Table 6). The most commonly reported adverse events were unusual or increased soreness (51–54%) and different type of pain (31–34%).

4. Discussion

4.1 Summary of findings.

To our knowledge, this is the first adequately powered randomized trial to evaluate the effectiveness of promising non-pharmacologic interventions for adolescents with chronic LBP. We found that adding SMT to ET resulted in a larger reduction in the primary outcome of pain severity over the course of one year. Differences were small and not statistically significant at the end of treatment (week 12); however, differences were larger and statistically significant at the 6-month and one-year follow up. Similar results were observed for disability and improvement. These group differences cannot be explained by contamination in the post treatment follow-up with approximately the same number of participants in each group seeking additional healthcare for LBP in the 9 months post-treatment follow-up period. A sensitivity analysis demonstrated this additional healthcare use had no group differential impact on the post-treatment follow-up results.

The parent-rated improvement favored the SMT+ET group, and was statistically significant at week 52. Patient-rated satisfaction with treatment showed a statistically significant advantage for the SMT+ET group at all time points.

4.2 Clinical importance.

Determination of what constitutes a clinically important group difference has not been well standardized.[18] To facilitate interpretation of the outcome of this trial we considered several factors. This included the magnitude of group differences, proportion of responders, consistency of outcomes, durability of treatment effects, intervention safety and tolerability, and participant's adherence to treatment. [18] The magnitude of approximately 11 and 8 percentage points difference between groups in the primary outcome pain at week 26 and 52 respectively, translates into a moderate effect size in favor of the SMT+ET group which by most standards is considered clinically important.[5] This is supported by responder analysis results where differences in proportions for reduction of LBP severity across all possible thresholds for reduction in pain favored SMT+ET by approximately 17% and 10% at weeks 26 and 52, respectively. Although the differences in patient rated outcomes were small at some time points, they consistently favored the SMT+ET group after eight weeks of intervention and during the entire follow-up. Side effects were similar in both groups, mild and self-limiting, and occurred at a frequency comparable to adult populations.[60] Also, given the chronic nature of LBP in the adolescent participants in this study (mean duration approximately 2 years) it is noteworthy that both groups experienced an approximately 80% reduction in medication use at the end of treatment, which was further reduced during the one year follow-up period. These are important findings in light of growing concerns regarding the safety and effectiveness of pharmacologic treatments for managing pain. Further studies are needed to assess whether a similar advantage would be observed when

compared to no treatment or pharmacologic control groups. A similarly positive pattern was observed in parent-rated reports of satisfaction with care, and their perceptions of their child's improvement. When considering these factors in aggregate, we interpret the advantage of SMT+ET over ET alone to be of potential importance and worthy of additional research. Additionally, the healthcare and societal costs associated with SMT+ET and ET alone are also necessary to consider when interpreting the clinical importance of results. These will be addressed in a future manuscript.

Interestingly, in contrast to the ET alone group, the SMT+ET group continued to experience decreases in LBP severity after the end of treatment resulting in larger long-term group differences. The continued reduction in LBP severity may be due to the different, but related underlying mechanisms of action targeted by SMT and ET which appear to be complementary. The overall course of LBP severity within this sample of adolescents with chronic LBP receiving ET in combination with SMT was similar to findings from previous RCTs of adults with similar levels of baseline severity receiving similar treatment.[6; 46] Analyses of qualitative data collected alongside this trial might provide additional insights into the psychosocial factors that play a role in adolescents with LBP who receive these treatments. The qualitative findings will be addressed in a subsequent publication.

4.3 Comparison to other studies.

Systematic reviews on chronic LBP have found the most promise for NSAIDs, exercise, and spinal manipulation[12]; however, there has been extremely little research performed in younger populations. A recent systematic review of noninvasive and nonsurgical treatments for LBP in children and adolescents highlighted the need for more high quality RCTs focused on conservative treatment strategies to guide clinicians treating children and adolescents with LBP.[44] Specifically, the authors found no randomized trials focused on SMT for LBP management; however, they found three studies [1; 20; 35] focused on exercise that were promising. A meta-analysis of two studies comparing exercise to no treatment reported an improvement in pain severity of 2.9 points on a 0–10 scale after 2 to 3 months.[44] Since that review, a large RCT in 8 to 11 year olds concluded that adding regular exercise to education appears to reduce future episodes of LBP.[29] In addition, a small RCT in adolescents with acute LBP of mild intensity found preliminary evidence that the combination of SMT and exercise did not offer benefits relative to sham SMT and exercise.[54] Our study of adolescents with more chronic and moderately severe LBP is a much needed addition to the evidence base in the important and emerging area of pain management for adolescent sufferers. With sufficient power and use of standard recommended outcome measures, our study demonstrated that SMT with exercise provides potentially worthwhile long-term benefits for adolescents with LBP that is chronic in nature.

4.4 Strengths and limitations.

Our trial has several strengths, including adequate sample size, and a rigorous design intended to be primarily pragmatic but with substantial emphasis on internal validity. Systematic collection of side effects is also a strength. Limitations of the study include inability to blind patients and providers to the nature of the interventions. Further, we are unable to differentiate between specific and nonspecific treatment effects, such as patient-

provider interactions and the differential time and attention given to the combined SMT+ET group. Qualitative data collected as part of this trial examining participants' perspectives are expected to elucidate the impact of contextual effects associated with the interventions and will be reported in a future publication. Also, while we were unable to control for placebo and non-specific effects in this study, there is a strength to comparative effectiveness trials in that by comparing interventions that approximate how they would be delivered in practice, the findings may be more readily applicable to clinical practice.[14] Compliance with the prescribed treatment sessions was higher in the SMT+ET group (96%) compared to the ET alone group (87%). A sensitivity analysis demonstrated that treatment compliance did not impact the study conclusions. The rate of enrollment (185 enrolled of 457 screened) was slightly lower than studies performed on adults;[8] this is a potential limitation in attempting to generalize study results to non-research settings. Practical considerations of coordinating both patient and parent schedules likely play a role. However, baseline LBP severity of our participants is similar to what has been observed in other studies observing adolescents from a range of settings,[1; 2; 27; 35; 47] which mitigates generalizability concerns. Finally, this study was not designed to assess the effectiveness of SMT alone. Our rationale was based on existing evidence supporting the effectiveness of exercise, the potential for exercise to support patient self-efficacy, and a previous study we performed that demonstrated exercise and SMT result in similar outcomes for chronic LBP in adults.[8]

4.5 Implication for clinical practice.

Although adolescents with recurrent, sub-acute LBP were eligible, only 4% of participants met this criterion. The remaining participants (96%) had LBP that was chronic in nature. Consequently, the results of this study are most applicable to adolescents with LBP that is long-standing. Overall a supervised exercise program with the addition of spinal manipulation appears to be a promising treatment approach for chronic LBP in adolescents. Given the current limited evidence base to support management of LBP in adolescents, this has important implications for providers who use spinal manipulation and exercise in practice such as chiropractors, physical therapists and osteopaths, and other providers who refer to them.

4.6 Implications for future research.

There is still a dire need for more high-quality, adequately powered research studies to inform the management and the prevention of LBP in adolescents, especially those that focus on non-pharmacologic interventions. Future rigorously designed studies are needed to replicate this study, compare SMT and ET to commonly used medical interventions, and isolate the specific effects from placebo effects. Further, the cost effectiveness of these approaches requires investigation to fully inform their promotion for adolescents with LBP.

4.7 Conclusion.

For adolescents with chronic low back pain, spinal manipulation combined with exercise therapy was more effective than exercise alone over a one-year period, with the largest differences occurring at six months. These findings warrant replication and evaluation of cost-effectiveness.

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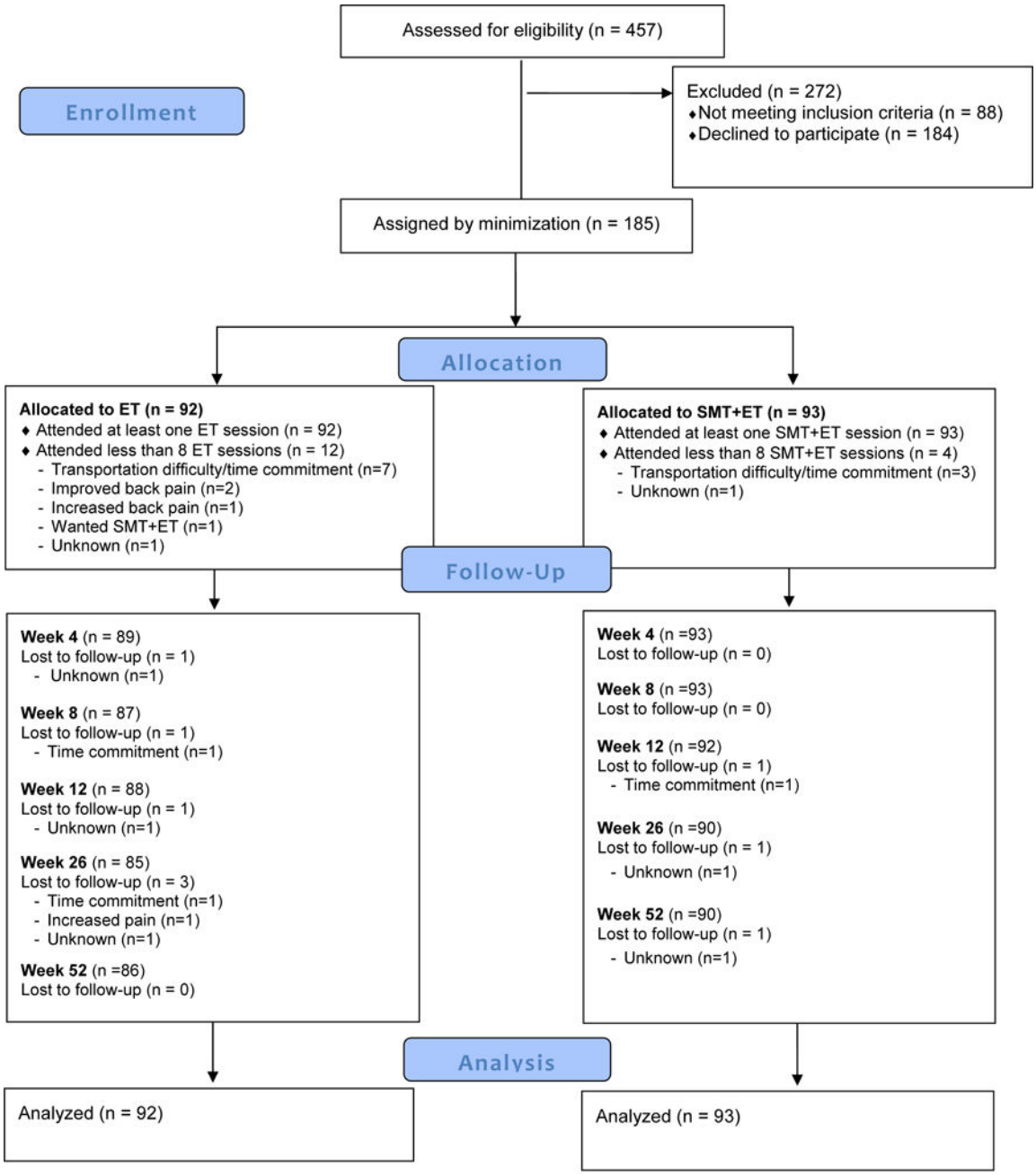
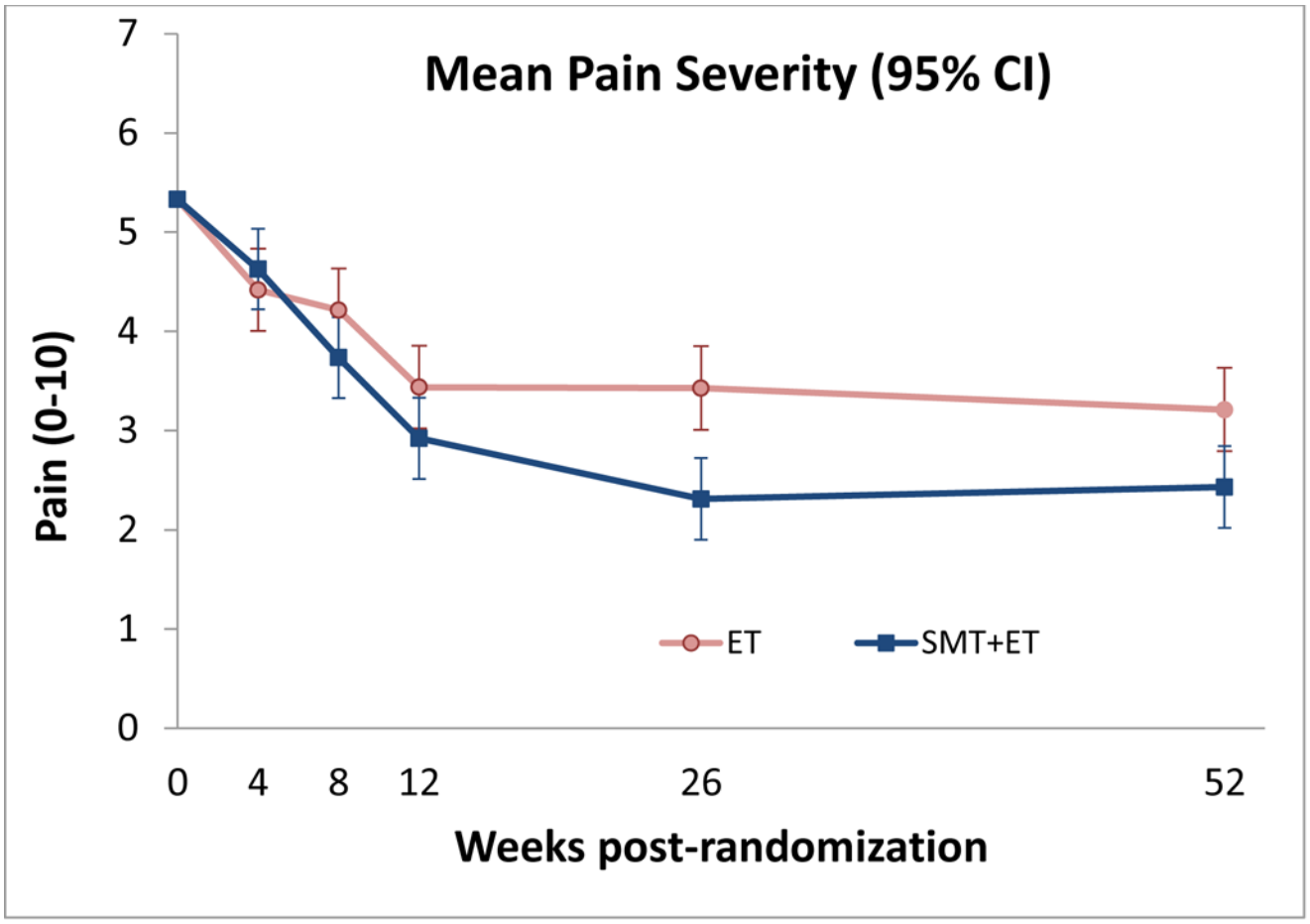


Figure 1.
Study flow diagram



Mean pain severity from model adjusting for minimization variables including baseline pain severity

Figure 2.
Mean pain severity over time

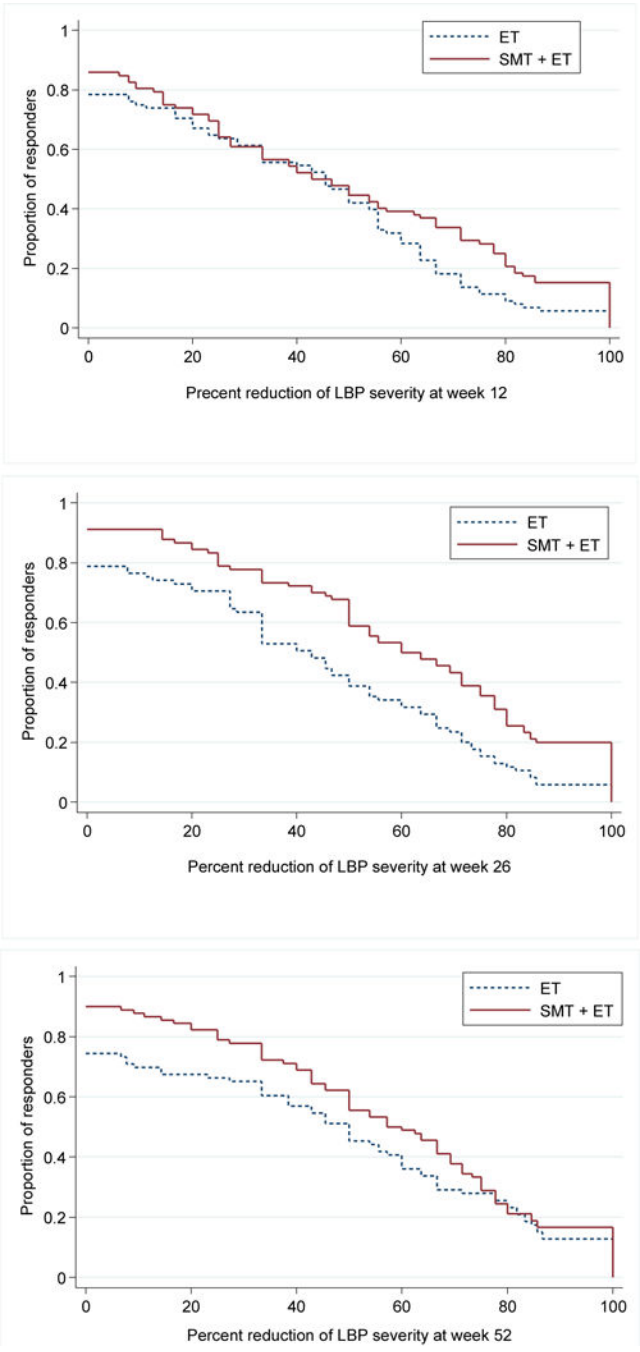


Figure 3.

Cumulative Responder Analyses – The y-axis displays the proportion of participants who reported a percent reduction in pain severity from baseline equal to or greater than the value on the x-axis.

Table 1.

Baseline demographics and clinical characteristics (mean (SD) unless otherwise noted).

Parameter	Treatment group	
	ET	SMT+ET
n	92	93
Age *	15.3 (1.8)	15.5 (1.6)
Female, n (%) *	62 (67.4%)	65 (69.9%)
BMI	23.0 (5.2)	23.5 (5.3)
Duration [weeks] *	110.3 (86.6)	108.6 (89.5)
-Median [25th to 75th percentiles]	104 [45.5 to 156]	104 [36 to 156]
Chronic (current episode ≥12 weeks), n (%)	90 (97.8%)	87 (93.55%)
Sub-acute/recurrent †, n (%)	2 (2.2%)	6 (6.45%)
Age of first episode	12.3 (2.3)	12.6 (2.5)
Prior treatment, n (%)	46 (50.0%)	53 (57.0%)
Depression, n (%)	11 (12.0%)	9 (9.7%)
Other pain, n (%)	44 (47.8%)	52 (55.9%)
Tobacco use, n (%)	5 (5.4%)	2 (2.2%)
Low back pain severity [0–10] *	5.3 (1.4)	5.3 (1.4)
Low back disability (Roland Morris) [0–18]	4.9 (3.2)	5.6 (3.2)
Pediatric quality of life (PedsQL) [0–100]	73.2 (12.8)	73.5 (11.2)
Medication use (days/week)	2.8 (1.5)	3.0 (1.3)
Expectation of improvement at the end of treatment (1–9)	2.5 (0.8)	2.3 (0.7)

† current episode 2 to <12 weeks with a previous 2 week episode in past year

* minimization variable

Table 2.

Primary outcome measure - Low back pain severity

	Treatment group		Group difference	
	ET	**SMT+ET**	**SMT+ET minus ET**	**P Value***
Low back pain severity [0–10]				
Mean at Week 0 (SD)	5.34 (1.35)	5.32 (1.43)		
Mean reduction at week 4 (95%CI)	0.93 (0.52 to 1.35)	0.72 (0.32 to 1.13)	−0.21 (−0.79 to 0.37)	0.477
Mean reduction at week 8 (95%CI)	1.14 (0.72 to 1.55)	1.62(1.21 to 2.02)	0.48 (−0.10 to 1.06)	0.106
Mean reduction at week 12 (95%CI)	1.91 (1.50 to 2.33)	2.43 (2.02 to 2.84)	0.52 (−0.07 to 1.10)	0.083
Short term response summary (Area under the curve minus baseline through week 12)	1.23 (0.88 to 1.58)	1.38 (1.04 to 1.73)	0.15 (−0.34 to 0.64)	0.55
Mean reduction at week 26 (95%CI)	1.92 (1.50 to 2.34)	3.04 (2.63 to 3.45)	1.12 (0.53 to 1.71)	<0.001
Mean reduction at week 52 (95%CI)	2.14 (1.72 to 2.56)	2.92 (2.51 to 3.33)	0.78 (0.19 to 1.37)	0.009
Long term response summary (Area under the curve minus baseline through week 52)	1.87 (1.51 to 2.22)	2.56 (2.21 to 2.91)	0.69 (0.19 to 1.19)	0.007

Mean values adjusted for minimization variables.

* Long term response summary serves as the omnibus test p-value. If p>.05, p-values for individual time points are not computed.

Table 3.

Responder analysis. Proportion of participants with at least 30, 50, 75, or 100% reduction in pain severity

	Treatment groups		Group differences
% pain reduction	**ET**	**SMT+ET**	**SMT+ET minus ET (95% CI)**
Week 12 *			
No reduction or increase	21.6%	14.1%	−7.5 (−18.7 to 3.8)
≥ 30%	61.4%	60.9%	−0.5 (−1.44 to 1.35)
≥ 50%	46.6%	47.8%	1.2 (−0.16 to 0.13)
≥ 75%	13.6%	29.4%	15.7 (3.7 to 27.2)
100%	5.7%	15.2%	9.5 (0.4 to 18.8)
Week 26 ^			
No reduction or increase	21.2%	8.9%	−12.3 (−23.0 to −1.7)
≥ 30%	63.5%	77.8%	14.2 (0.8 to 27.2)
≥ 50%	42.4%	67.8%	25.4 (10.7 to 38.7)
≥ 75%	17.7%	38.9%	21.2 (7.9 to 33.5)
100%	5.9%	20.0%	14.1 (4.1 to 24.1)
Week 52 †			
No reduction or increase	25.6%	10.0%	−15.6 (−26.7 to −4.3)
≥ 30%	65.1%	77.8%	12.7 (−0.7 to 25.5)
≥ 50%	51.2%	62.2%	11.1 (−3.5 to 25.0)
≥ 75%	27.9%	33.3%	5.4 (−8.1 to 18.7)
100%	12.8%	16.7%	3.9 (−6.8 to 14.4)

*Analysis included 88 participants in ET group and 92 in SMT+ET group

^Analysis included 85 participants in ET group and 90 in SMT+ET group

†Analysis included 86 participants in ET group and 90 in SMT+ET group

Table 4.

Participant-reported secondary outcome measures

	Treatment group		Group difference	
	ET	**SMT+ET**	**SMT+ET minus ET**	**P Value***
Low back disability (Roland Morris) [0–18]				
Mean at Week 0 (SD)	4.85 (3.15)	5.64 (3.24)		
Mean reduction at week 4 (95%CI)	0.69 (0.13 to 1.26)	0.46 (−0.09 to 1.02)	−0.23 (−1.03 to 0.56)	0.57
Mean reduction at week 8 (95%CI)	1.03 (0.46 to 1.60)	1.41 (0.85 to 1.96)	0.38 (−0.42 to 1.17)	0.36
Mean reduction at week 12 (95%CI)	1.78 (1.22 to 2.35)	2.33 (1.77 to 2.89)	0.54 (−0.25 to 1.34)	0.18
Short term response summary (Area under the curve minus baseline through week 12)	0.99 (0.17 to 1.81)	1.15 (0.34 to 1.97)	0.17 (−0.54 to 0.88)	0.65
Mean reduction at week 26 (95%CI)	2.41 (1.83 to 2.99)	3.24 (2.68 to 3.81)	0.84 (0.03 to 1.65)	0.04
Mean reduction at week 52 (95%CI)	2.87 (2.30 to 3.45)	3.51 (2.94 to 4.08)	0.64 (−0.17 to 1.45)	0.12
Long term response summary (Area under the curve minus baseline through week 52)	2.11 (1.33 to 2.88)	2.72 (1.95 to 3.49)	0.61 (0.004 to 1.21)	0.048
Improvement [1–9] †				
Mean at week 4 (95%CI)	3.83 (3.59 to 4.08)	3.85 (3.60 to 4.09)	0.01 (−0.33 to 0.36)	0.94
Mean at week 8 (95%CI)	3.46 (3.21 to 3.71)	3.20 (2.96 to 3.45)	−0.26 (−0.60 to 0.09)	0.15
Mean at week 12 (95%CI)	3.02 (2.77 to 3.27)	2.78 (2.54 to 3.03)	−0.24 (−0.59 to 0.11)	0.18
Short term response summary (Area under the curve through week 12)	3.53 (2.14 to 4.91)	3.38 (1.98 to 4.78)	−0.14 (−0.44 to 0.15)	0.34
Mean at week 26 (95%CI)	3.00 (2.74 to 3.25)	2.58 (2.33 to 2.83)	−0.41 (−0.77 to −0.06)	0.02
Mean at week 52 (95%CI)	2.99 (2.74 to 3.24)	2.73 (2.49 to 2.98)	−0.26 (−0.61 to 0.10)	0.16
Long term response summary (Area under the curve through week 52)	3.11 (1.73 to 4.49)	2.81 (1.42 to 4.21)	−0.29 (−0.57 to −0.02)	0.03
Medication use [days/week]				
Mean at Week 0 (SD)	2.79 (1.53)	2.96 (1.32)		
Mean reduction at week 4 (95%CI)	2.12 (1.87 to 2.37)	2.29 (2.05 to 2.54)	0.18 (−0.17 to 0.53)	
Mean reduction at week 8 (95%CI)	2.06 (1.80 to 2.31)	2.43 (2.19 to 2.68)	0.38 (0.02 to 0.73)	
Mean reduction at week 12 (95%CI)	2.26 (2.01 to 2.51)	2.46 (2.21 to 2.71)	0.20 (−0.15 to 0.55)	
Short term response summary (Area under the curve minus baseline through week 12)	2.34 (1.98 to 2.70)	2.60 (2.24 to 2.96)	0.26 (−0.04 to 0.56)	
Mean reduction at week 26 (95%CI)	2.27 (2.02 to 2.53)	2.40 (2.15 to 2.64)	0.12 (−0.24 to 0.48)	
Mean reduction at week 52 (95%CI)	2.35 (2.10 to 2.61)	2.53 (2.28 to 2.78)	0.18 (−0.18 to 0.54)	

	Treatment group		Group difference	
	ET	**SMT+ET**	**SMT+ET minus ET**	**P Value***
Long term response summary (Area under the curve minus baseline through week 52)	2.48 (2.13 to 2.83)	2.65 (2.30 to 3.01)	0.17 (−0.10 to 0.45)	0.22
Pediatric quality of life (PedsQL) [0–100]				
Mean at Week 0 (SD)	73.2 (12.8)	73.5 (11.2)		
Mean improvement at week 12 (95%CI)	7.56 (5.45 to 9.68)	8.90 (6.81 to 10.98)	1.33 (−1.64 to 4.31)	
Mean improvement at week 26 (95%CI)	8.64 (6.51 to 10.77)	11.36 (9.26 to 13.45)	2.72 (−0.27 to 5.71)	
Mean improvement at week 52 (95%CI)	9.81 (7.67 to 11.95)	11.82 (9.71 to 13.93)	2.02 (−0.99 to 5.02)	
Long term response summary (Area under the curve minus baseline through week 52)	8.70 (6.95 to 10.45)	10.67 (8.95 to 12.39)	1.97 (−0.48 to 4.43)	0.12
Satisfaction with care [1–7]^				
Mean at week 12 (95%CI)	2.37 (2.14 to 2.60)	2.00 (1.77 to 2.23)	−0.37 (−0.70 to −0.05)	0.02
Mean at week 26 (95%CI)	2.33 (2.10 to 2.56)	1.84 (1.61 to 2.07)	−0.49 (−0.81 to −0.16)	0.003
Mean at week 52 (95%CI)	2.32 (2.08 to 2.55)	1.92 (1.69 to 2.15)	−0.40 (−0.72 to −0.07)	0.02
Long term response summary (Area under the curve through week 52)	2.35 (1.99 to 2.71)	1.92 (1.56 to 2.28)	−0.43 (−0.71 to −0.15)	0.003

Mean values adjusted for minimization variables and baseline where indicated.

* Long term response summary serves as the omnibus test p-value. If p>.05, p-values for individual time points are not computed.

† 1 = 100% improvement

^ 1 = completely satisfied

Table 5.

Parent or guardian reported outcomes

Parameter	Treatment groups		Group differences	
Variable	**ET**	**SMT+ET**	**SMT+ET minus ET**	**P Value***
Improvement (1–9) †				
Mean at week 12 (95%CI)	3.31 (3.04 to 3.58)	3.02 (2.76 to 3.29)	−0.29 (−0.66 to 0.09)	
Mean at week 26 (95%CI)	3.16 (2.89 to 3.44)	2.99 (2.73 to 3.26)	−0.17 (−0.55 to 0.21)	
Mean at week 52 (95%CI)	3.29 (3.02 to 3.56)	2.90 (2.63 to 3.17)	−0.39 (−0.77 to −0.01)	
Long term response summary (Area under the curve through week 52)	3.22 (2.79 to 3.65)	2.95 (2.53 to 3.38)	−0.27 (−0.59 to 0.06)	0.11
Satisfaction (1–7)^				
Mean at week 12 (95%CI)	2.26 (2.05 to 2.47)	1.90 (1.69 to 2.10)	−0.36 (−0.65 to −0.07)	0.02
Mean at week 26 (95%CI)	2.26 (2.05 to 2.48)	2.02 (1.81 to 2.22)	−0.25 (−0.54 to 0.05)	0.10
Mean at week 52 (95%CI)	2.38 (2.17 to 2.59)	1.95 (1.75 to 2.16)	−0.43 (−0.72 to −0.13)	0.004
Long term response summary (Area under the curve through week 52)	2.20 (1.88 to 2.51)	1.87 (1.55 to 2.18)	−0.33 (−0.57 to −0.09)	0.007

Mean values adjusted for minimization variables

* 1 = 100% improve* Long term response summary serves as the omnibus test p-value. If p>.05, p-values for individual time points are not computed.

† 1 = 100% improvement

^ 1 = completely satisfied

Table 6.

Adverse events during the 12-week treatment*

	Treatment group				Group difference
	ET		SMT+ET		SMT+ET minus ET (95% CI)
	n † (%)	Median bothersomeness ^	n † (%)	Median bothersomeness ^	
Different type of pain	28 (31.1%)	4	32 (34.4%)	4	3.3% (−10.2 to 16.6)
Increased back pain severity	25 (27.8%)	4	20 (21.5%)	4	−6.3% (−18.6 to 6.2)
New or increased leg pain, numbness, or weakness	20 (22.5%)	3.5	16 (17.2%)	3.5	−5.3% (−16.9 to 6.3)
Unusual or increased soreness	45 (50.6%)	2.3	50 (53.8%)	2.2	3.2% (−11.1 to 17.3)
Skin irritation	5 (5.6%)	5	1 (1.1%)	7	−4.5% (−11.5 to 1.2)
More fatigue than usual	18 (20.2%)	3	21 (22.6%)	2.7	2.4% (−9.6 to 14.2)
Dizziness or lightheadedness	18 (20.0%)	3	13 (14.0%)	3	−6.0% (−17.0 to 4.9)
Upset stomach, nausea, or vomiting	12 (13.5%)	2	13 (14.0%)	4	0.5% (−9.8 to 10.7)
Changes in bowel or bladder habits	8 (8.9%)	3	2 (2.2%)	4.9	−6.7% (−14.6 to 0.1)

*Analysis included 90 participants in ET group and 93 in SMT+ET group

†Participants reporting at least one event during treatment, participants could report more than one event

^Bothersomeness on 0–10 scale; bothersomeness was averaged for participants with more than one of the same event during the 12 weeks of treatment