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Effectiveness of Spinal Manipulation for Treatment of Chronic Non-Specific Low Back Pain: A Systematic Review and Meta-Analysis

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ABSTRACT

Objective: To estimate the extent to which spinal manipulation is effective for adult patients with chronic non-specific low back pain (CNSLBP)

Design: Systematic review and meta-analysis of randomized controlled trials.

Data sources: Ovid Medline, Ovid AMED, Ovid EMBASE, CINAHL, Index to Chiropractic Literature (ICL); Cochrane Library, PubMed, and Trip database.

Eligibility criteria for selecting studies: Randomized controlled trials examining the effect of spinal manipulation therapy (SMT) in adults (≥ 18 years) with chronic non-specific low back pain.

Review methods: Two reviewers independently selected studies, extracted data, and assessed risk of bias and quality of the evidence. The effect of SMT was compared with recommended therapies, non-recommended therapies, sham (placebo) SMT, and SMT as an adjuvant therapy. Main outcomes were pain and back specific functional status, examined as mean differences and standardized mean differences (SMD), respectively. Outcomes were examined at 6, 12, 18, 24 weeks and one year. Quality of evidence was assessed using GRADE. Risk of bias, statistical heterogeneity and precision was explored.

Results: Nine randomized controlled trials including a total of 1777 participants were identified, who were on average middle aged (18-65 years). The trials had considerable percentages of risk of bias. Moderate quality evidence suggested that the pooled estimate of pain intensity after one year and functional disability after 6 weeks of SMT is significantly effective (MD=-9.88, CI=-16.51, -3.24) and (MD=-7.59, CI=-8.47, -6.71) respectively. Regarding pain intensity, no statistically significant difference was recorded between experimental and control groups at 6 and 24 weeks after SMT (MD=1.16, CI=-15.25, 17.56, MD=-5.12, CI=-12.86, 2.63 respectively). Regarding functional disability, no significant difference was recorded between both groups at 18 and 24 weeks after SMT (MD=-4.05, CI=-18.47, 10.37, MD=-3.90, CI=-14.60, 6.80 respectively). Also, no significant difference was detected between both studied groups regarding physical and mental health at 12 weeks, 24 weeks and 1 year of SMT and mean satisfaction with SMT.

Conclusion: It is difficult from the included studies to conclude that spinal manipulation is superior to conventional treatment for CNSLBP in short term effect but adding spinal manipulation with other conventional therapies may be beneficial for long-term benefit. However, given the small number of studies included in this analysis, we should be cautious of making strong inferences based on these results. The research to date is still heterogeneous, and questions remain about optimal treatment duration, number of sessions, practitioners to be involved, and the kinds of patients who may benefit the most.

Keywords: Spinal manipulation, Low back pain, chiropractic, systematic review.

INTRODUCTION

Chronic Non-Specific Low Back Pain (CNSLBP) is defined as “pain, tension, soreness, and/or stiffness located between the costal margin and buttocks and lasts for longer than three months while particular causes of low back pain are unknown, accounting for <15% of all back pain cases” (Bogduk N et al. 2004). Low back pain (LBP) is one of the most common occupational disorder worldwide (Deyo RA et al. 2006 and Leroux I.et al.2005), a leading cause of disability (Vos T.al 2012) and a major cause of absenteeism (Druss BG et al.2002 and Asklof T et al.2015). LBP disability-adjusted life years increased from 58.2 million in 1990 to 83.0 million in 2010 (Hoy D et al.2014). The global point prevalence of LBP is 9.4% (8) and the life time prevalence is around 85% (Schmidt CO et al.1998 and Cassidy JD et al.2012). The direct costs of back pain in the United States in 2010 were $34 billion, (Gaskin DJ et al.2012) with additional indirect costs including lost workplace productivity estimated at $200 billion (Institute for Health Metrics and Evaluation; 2013).

Several factors complicate the treatment of CNSLBP, as most patients are reported to have no identifiable pathophysiologic cause for their pain (US Bone and Joint Initiative, 2018) and specific interventions for CLBP have little or no demonstrated efficacy (Meucci RD et al.2015). Adequate treatment of low back pain is therefore important for patients, clinicians, and healthcare policy makers. Chiropractic is widely used to treat low back pain and has been examined in numerous randomized controlled trials of varying methodological quality and size, with varying results (Airaksinen O et al.2006, Qaseem A et al.2017, Bons SCS et al.2017 and NICE guideline et al.2016).

Spinal manipulation (SM) is a commonly used form of manual therapy. It has been recommended by recently published clinical practice guidelines for LBP management (Barnes PM et al.2008 and Wolsko PM et al.2003). The mechanisms linking SM to LBP improvement are largely unknown (Chou R et al.2007 and Koes BW et al.2010). Evidence suggests that SM exerts a beneficial effect via multiple mechanisms including biomechanical, neurophysiological, cellular, and/or psychosocial components (Bialosky JE et al.2009, king, HH. et al.2011, Pickar JG et al.2012 and Gay CW, et al.2014). Spinal manipulation, a form of manual therapy commonly used in the US, (Barnes PM et al.2007 and Wolsko PM et al.2003) has been recommended by clinical guidelines for LBP management (Chou R et al.2007 and Koes BW et al.2010 Recommendations are based on evidence that SM demonstrates mild to moderate effectiveness, comparable to other non-invasive LBP treatment methods (Goertz CM et al.2012).

In some countries, SMT is recommended as a component of a broader treatment package including exercise, (NICE guideline et al.2016) whereas in others is not included or mentioned at all (Bons SCS et al.2017). The most recent guidelines suggest that SMT should be considered a second line or adjuvant treatment option, after exercise or cognitive behavioural therapy (Higgins JPT et al.2011). Not all clinical practice guidelines support SMT and variability exists between those which do suggesting a need for stronger evidence (Koes BW et al.2010). To resolve the issue of effectiveness, we conducted a systematic review and meta-analysis. This review therefore aimed to study the clinical effectiveness of standard spinal manipulation care for LBP in comparison to usual standard care provided by other healthcare providers.

Aim of the Study

The specific objective of this review is to estimate the extent to which spinal manipulation care is effective for adult patients with chronic non-specific low back pain compared to other conservative care approaches (e.g. medical care and physiotherapy without manipulation).

MATERIAL AND METHODS

Types of Studies

We included published randomized controlled trials (RCTs) with spinal manipulation interventions. We excluded studies reporting on spinal pain without separate results for LBP and studies examining specific pathologies (e.g., disc herniation, cancer, spondylolisthesis or compression fractures).

Types of Participants

Individuals with chronic non-specific low back pain aged 18 years and more have no spinal surgery or osteoporosis.

Types of Interventions

SMT consisting of manual high velocity, low amplitude, thrust manipulation.

Types of Outcome Measures

Primary outcomes: 1.Pain (e.g., visual analogue scale, numerical rating scale, McGill pain score); 2.Functional status (e.g. Roland-Morris questionnaire, Oswestry Disability Index)

Secondary outcomes: 1.Health related quality of life (e.g., SF-36, EuroQol); 2.Return to work (by means of number of days to return to work or proportion of patients at work); 3.Satisfaction of the participants with SMT.

Additional Criteria

Studies published in languages other than English, duplicate publications and studies without full text manuscript available (e.g. abstracts, conference proceedings, presentations) were excluded.

Search Methods for Identification of Studies

We identified trials through systematic searches of Ovid Medline, Ovid AMED, Ovid EMBASE, CINAHL, Index to Chiropractic Literature (ICL); Cochrane Library, PubMed, and Trip database.

Searching Other Resources

We checked the reference lists of all primary studies and reviewed articles for additional references.

DATA COLLECTION AND ANALYSIS

Selection of Studies

The titles and then the abstracts of potentially relevant articles read independently by two authors (ATE and NMR). Articles were rejected only if both review authors determined from the title or abstract that the article was not a randomized controlled trial. After reviewing the full articles, the studies that were not relevant to the review were excluded. Remaining records were independently checked by the same review authors. All papers that are thought to be of relevance were obtained and read by (ATE and NMR) independently. We recorded the selection process in detail to complete a PRISMA flow diagram (figure 1).

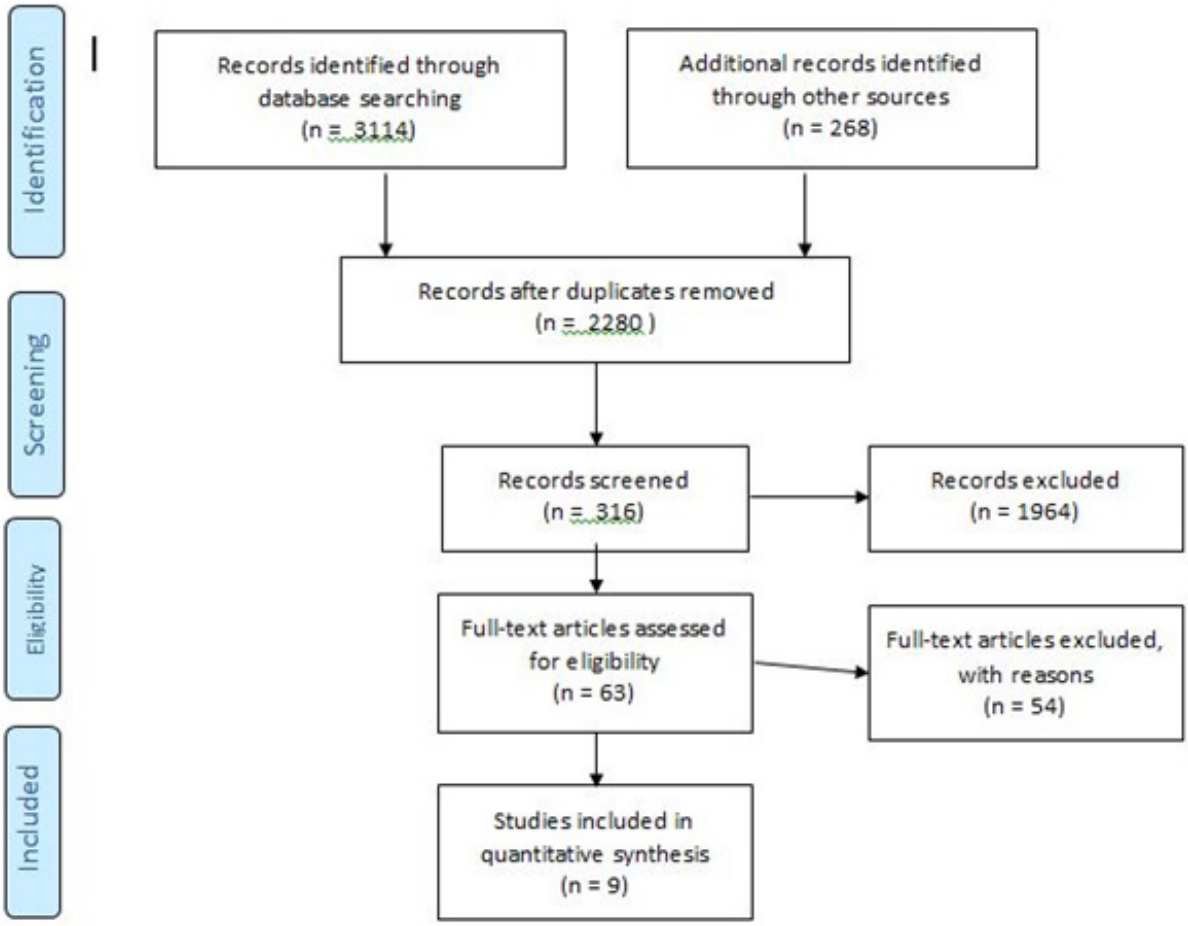

Figure 1: PRISMA flow diagram

Data Extraction and Management

We used a data collection form for study characteristics and outcome data. One author (ATE) extracted study characteristics from the included studies, as follows:

1. Methods: study design, total duration of study, study setting and date of the study.

2. Participants: number, mean age, gender, diagnostic criteria, inclusion and exclusion criteria.

3. Interventions: intervention and comparison.

4. Outcomes: primary and secondary outcomes specified and collected.

5. Notes: funding for trial and notable conflicts of interest of trial authors.

Assessment of Quality of Evidence

We assessed the quality of evidence of the primary outcomes using the GRADE approach (NICE guideline et al.2016) and presented the results in the “Summary of findings Table” available on request.

ID	Random sequence generation	Allocation concealment bias	Performance bias	Detection bias	Attrition bias	Reporting bias
Aura, et al., 2003 [30]	Low	Low	High	Unclear	Low	Low
Dougherty, et al., 2014 [31]	Low	Low	Low	Low	Low	Low
Geisser, et al., 2005 [32]	Unclear	Unclear	Unclear	Unclear	Low	Low
Jerrilyn, et al., 2017 [33]	Low	Low	High	Low	Low	Low
Meade, et al., 1990 [34]	Unclear	Low	Unclear	Unclear	Low	Unclear
Mitchell, et al., 2014 [35]	Low	Low	High	Low	Low	Unclear
Sarker, et al., 2019 [36]	Low	Low	Unclear	Unclear	Low	Low
Senna, et al., 2011 [37]	Unclear	Low	Low	Low	Unclear	Unclear
Ting Xia, et al., 2016 [38]	Low	Low	High	Low	Low	Low

Table 1: Risk of bias of included studies according to author's judgment.

Measures of Treatment Effect

We used Review Manager 5 (29) to manage the data and to conduct the analyses. We reported dichotomous outcomes as risk ratios (RRs) with 95% confidence interval (CI). For continuous outcomes, we calculated mean differences (MDs) with 95% CI when the studies used the same scale.

Unit of Analysis Issue

For studies with more than two intervention groups (multi-arm studies), we included only the directly relevant arms.

Dealing with Missing Data

We contacted investigators or study sponsors to verify key study characteristics and obtain missing numerical outcome data where possible.

Dealing with Heterogeneity

We used the I^2 statistic to measure heterogeneity among the trials in each analysis.

Subgroup Analysis

We summarized and analyzed all eligible studies in Review Manager 5 (29). (NMR and ATE) extracted the data; the first author entered all data and the second author checked all entries. We resolved disagreements by discussion. We undertook meta-analyses only where this is meaningful. We combined the data using a random-effects model.

RESULTS

Results of Search

We searched 3382 relevant articles and we identified 2280 articles after removal of duplicates. Then, abstracts were reviewed based on inclusion and exclusion criteria. So, 63 full-text articles were reviewed for eligibility, nine of them, met the inclusion criteria and included in the review. Details of the flow of studies are given in Prisma flow diagram (Figure 1).

Included Studies

Details of the characteristics of the included studies (methods, participants, interventions, comparison groups and outcome measures) are available on request.. The countries in which the studies were conducted varied. Five studies were conducted in the United States, (Paul E Dougherty et al.2014, Michael E. Geisser et al.2005 Jerrilyn A. Cambron et al.2017, Joel E Bialosky et al.2014, Christine M. Goertz et al.2016), one each in India, (Kanchan Kumar Sarker et al.2019), United Kingdom, (T W Meade et al.1990), Norway, (Olav Frode Aure et al.2003), and Egypt (Mohammed K. Senna et al.2011). All trials were published in English. In total, 1777 patients were examined. Study sample sizes ranged from 49 to 741 (median 110, interquartile range 90-221).

Outcome measures	MD/OR	95% CI	Number of partici-pants	Heterogeneity	Quality of evidence
Pain intensity after 6 weeks	1.16	-15.25, 17.56	565	I2= 99%, P=0.00001	Low
Pain intensity after 24 weeks	-5.12	-12.86, 2.63	464	I2 = 86%, p=0.00001	Low
Pain intensity after 1 year	-9.88	-16.51, -3.24	407	I2 = 83%, P=0.003	Moderate
Functional disability after 6 weeks	-7.59	-8.47, -6.71	505	I2 =73%, P=0.00001	Moderate
Functional disability after 18 weeks	-4.05	-18.47, 10.37	503	I2 =93%, P=0.00001	Low
Functional disability after 24 weeks	-3.9	-14.6, 6.8	464	I2 =90%, P=0.0001	Low
SF physical health after 12 weeks	1.63	-5.68, 8.93	317	I2 =95%,P=0.00001	Low
SF physical health after 24 weeks	2.1	-3.23, 2.81	437	I2 =94%, 0.00001	Low
Sf physical health after 1 year	4.97	-0.89, 10.83	257	I2 =93%, 0.00001	Very low
SF mental health after 24 weeks	-1.07	-3.41, 1.26	314	I2 =0%, P=0.57	Low
proportion of patients with severe pain after 1 year	0.32	0.03, 3.36	352	I2=89%, P=0.002	Low
roportion of patients with pain free after 1 year	1.23	0.83, 1.84	407	I2 =0%, P=0.83	Moderate
portion of patients with sick leaves after 1 year	0.32	0.11, 0.97	207	I2 =58%, P=0.12	Low
satisfaction with SMT	0.49	-0.66, 1.63	140	I2 =78%, P=0.03	Low

Table 2: Summary of the main outcome of the included trials.

Participants

The review included 1777 patients with chronic non-specific low back pain. The inclusion criteria included; ages 18 years and more, chronic low back pain more than 3 months, Pain intensity ≥ 4 in Numerical Rating scale/Visual Analogue Scale. None of the studies made a clear distinction between persistent low back pain or exacerbation of a chronic condition. Exclusion criteria included; safety concerns for receiving SMT, severe osteoporosis, prior spinal surgery, tumor, specific cause for LBP.

INTERVENTION

Details of the interventions explained in the characteristics of the included studies (table 1). The intervention was SMT consisting of manual high velocity, low amplitude, thrust manipulation. Comparators included the usual care normally available to patients with low back pain including a brief light massage, shorter and lighter than what would be considered appropriate in a therapeutic massage practice.

Risk of Bias in Included Studies

We present details of risk of bias for each of the included trials in the' Risk of bias 'table (Table 1) and (Figures 2 and 3). Overall, the studies included in this review were at some risk of bias. All studies had at least one domain with unclear or high risk of bias except (Dougherty et al, 2014). All the studies reported low risk for attrition bias except (Senna et al, 2011) which was unclear risk. Sex studies were low risk for reporting bias and three studies were unclear risk ((Meade et al, 1990), Mitchell et al, 2014 and (Senna et al, 2011)). All the studies recorded low risk for random sequence generation bias except three studies were unclear risk ((Geisser et al, 2005), (Meade et al, 1990) and (Senna et al, 2011)). All the studies were low risk for allocation concealment bias except one study was unclear risk (Geisser et al, 2005) (32). Five studies were low risk for detection bias and four studies were unclear risk (Aure et al, 2003, Geisser et al, 2005, Meade et al, 1990 and Sarker et al, 2019). Four studies were high risk for performance bias (Aura et al, 2003, Jerrilyn et al, 2017, Michell et al, 2014 and Ting Xia et al, 2016), three were unclear (Geisser et al, 2005, Meade et al, 1990 and Sarker et al, 2019) and two were low (Dougherty et al, 2014 and Senna et al, 2011).

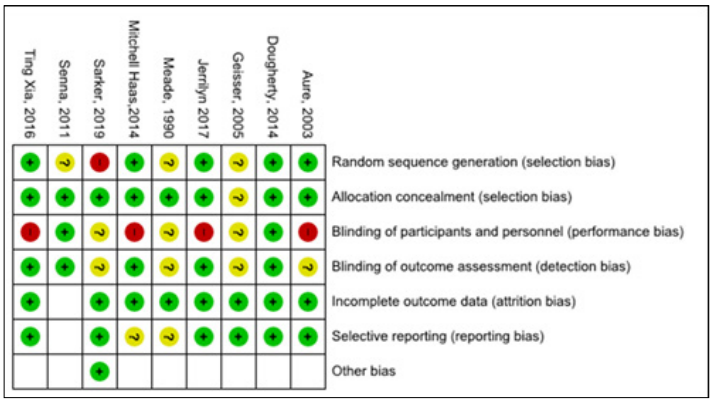

Figure 2: Risk of bias summary according to authors' judgment along included studies

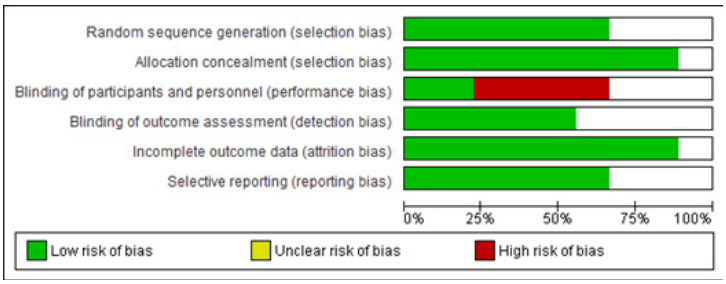

Figure 3: Risk of bias percentages according to Authors' judgment of included studies

EFFECT OF INTERVENTION

Primary Outcome

Summary of the main outcome of the included trials presented in table (2).

Pain intensity after 6 weeks of SMT: Pain intensity after 6 weeks of spinal manipulation therapy (SMT) was studied in 6 trials (Paul E Dougherty et al 2014, Michael E. Geisser et al. 2005, Jerrilyn A. Cambron et al. 2017, Joel E Bialosky et al 2014, Kanchan Kumar Sarker et al 2019, Mohammed K. Senna et al 2011) among 565 participants (Figure 4). Clinical improvement in pain intensity was recorded among experimental group in four trials, however, the pooled effect was not statistically significant (MD=1.16, CI=-15.25, 17.56). A statistically significant considerable heterogeneity between-trials was evident (I^2=99%, P<0.00001) indicating a considerable inconsistency among included trials in the estimate which may be due to differences in study participants regarding baseline of pain intensity besides variation in the method, duration and frequency of spinal manipulation sessions. Also, a wide confidence interval due to few number of studied participants indicating low precision. Test for funnel plot asymmetry was not applied because the included studies in the meta-analysis were less than 10 studies (Higgins JPT et al 2003).

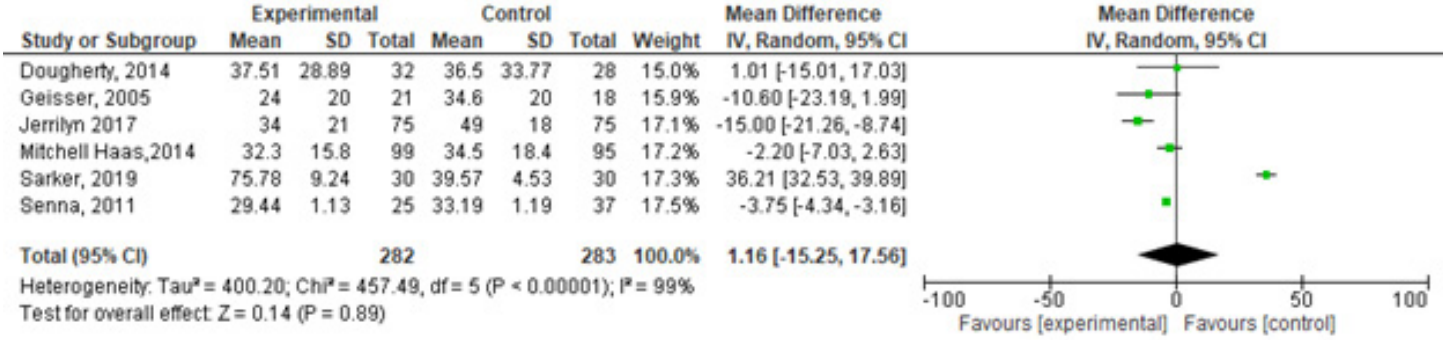

Figure 4: Forest plot of mean pain intensity among studied participants after 6 weeks of spinal manipulation

Pain intensity after 24 weeks of SMT: Pain intensity after 24 weeks of SMT was studied in 4 trials among 464 participants (Figure 5). Clinical improvement in pain intensity was recorded among experimental group in three trials. A reduction in the mean pain intensity after 24 weeks of SMT was evident (MD=-5.12), however, the pooled effect was not statistically significant (CI=-12.86, 2.63) with low precision (wide confidence interval). Also, a statistically significant considerable heterogeneity between-trials was evident (I^2=86%, P<0.00001) indicating a considerable inconsistency among included trials.

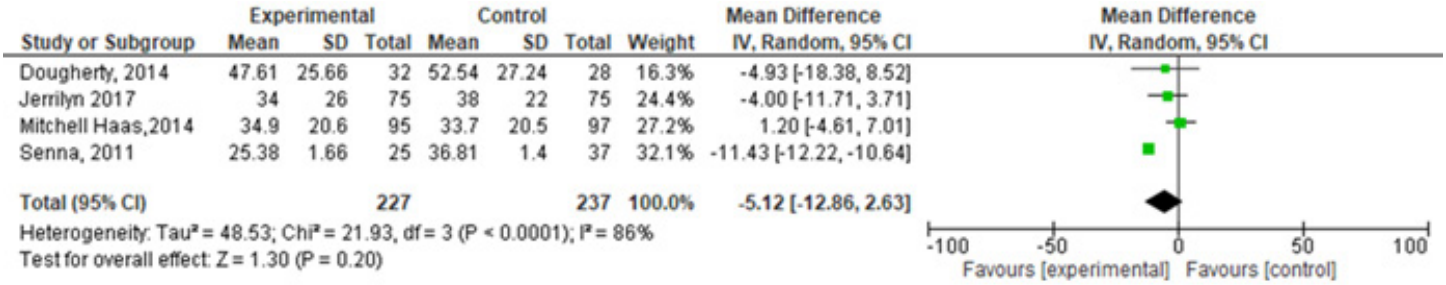

Figure 5: Forest plot of mean pain intensity among studied participants after 24 weeks of SMT.

Pain intensity after 1 year of SMT: Pain intensity after 1 year of SMT was studied in 3 trials among 407 participants (Figure 6). A statistically significant difference was recorded between experimental and control groups after 1 year SMT intervention with reduction in pain intensity (MD=-9.88, CI=-16.51, -3.24). However, a significant considerable heterogeneity between trials (I^2=83%, P=0.003) and low precision (wide confidence interval) were evident.

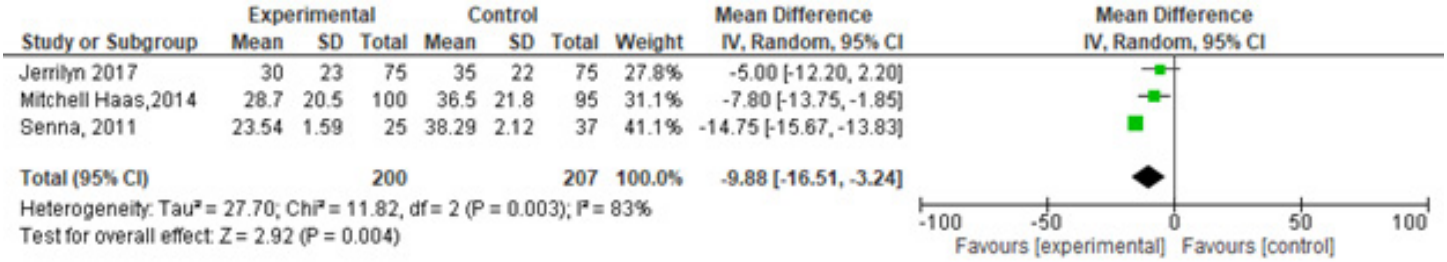

Figure 6: Forest plot of mean pain intensity among studied participants after 1 year of SMT.

Functional disability after 6 weeks of SMT: Functional disability after 6 weeks of SMT was studied in 5 trials among 505 participants (Figure 7). A statistically significant improvement in the mean functional disability between treatment and control groups after 6 weeks of SMT was recorded (MD=-7.59, CI=-8.47, -6.71). A significant substantial heterogeneity between trials was detected (I^2=79%, P=0.00001)

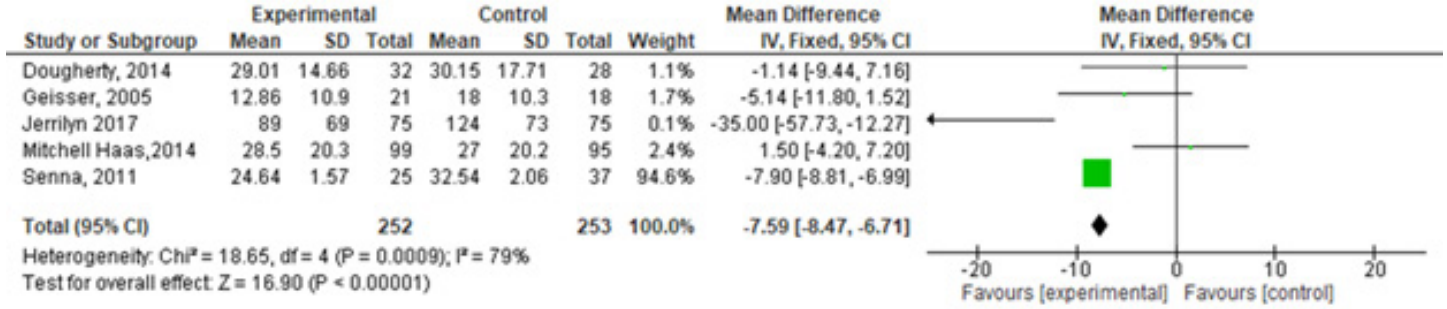

Figure 7: Forest plot of functional disability among studied participants after 6 weeks of SMT.

Functional disability after 18 weeks of SMT: Figure 8 presented Forest plot of functional disability among 457 participants in 5 trials after 18 weeks of SMT. No statistically significant difference was recorded between experimental and control groups (MD=-4.05, CI=-18.47, 10.37). A significant considerable between trials heterogeneity (I^2=93%, P=0.00001) and low precision (few participants) were detected.

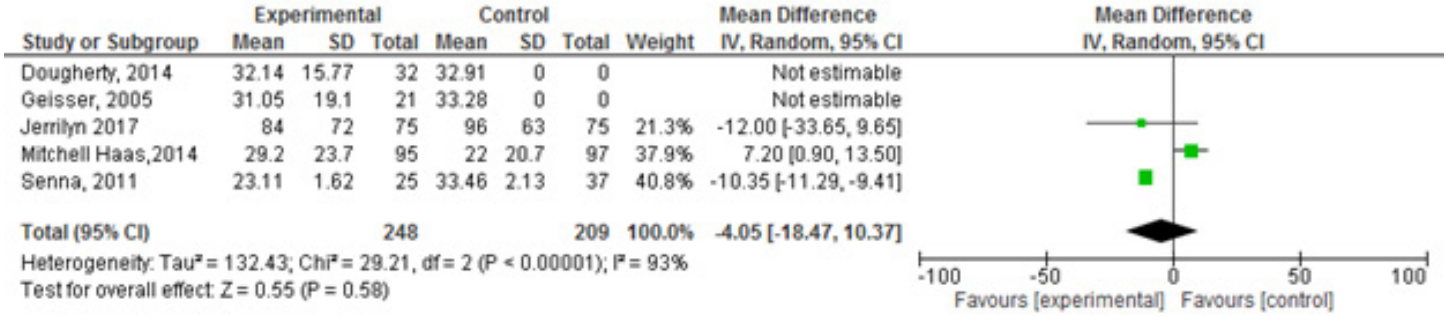

Figure 8: Forest plot of functional disability among studied participants after 18 weeks of SMT.

Functional disability after 24 weeks of SMT: Functional disability after 24 weeks of SMT was studied among 464 participants in 4 trials (Figure 9). No significant improvement in the functional disability was detected among experimental groups compared to control one after 24 weeks of SMT (MD=-3.90, CI=-14.60, 6.80). A significant considerable between trials inconsistency (I^2=90%, P=0.0001) and low precision (wide confidence interval) were recorded.

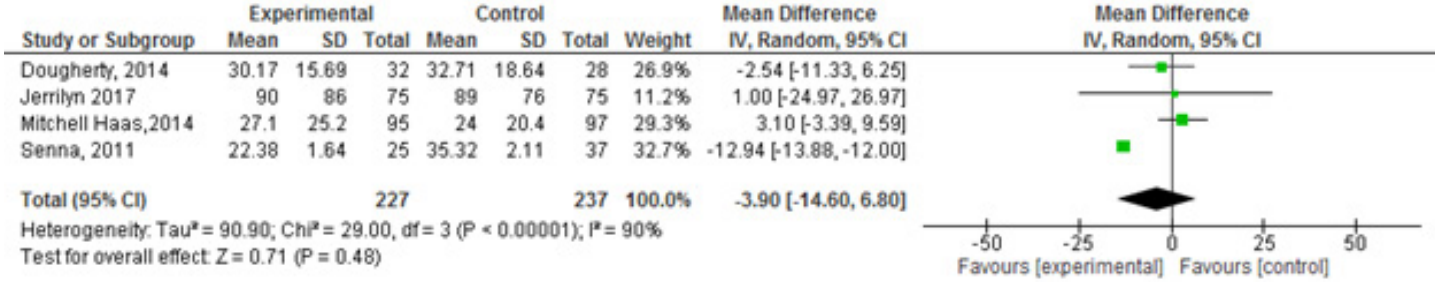

Figure 9: Forest plot of functional disability among studied participants after 24 weeks of SMT.

Secondary Outcome

SF physical health after 12 weeks of SMT: Physical health after 12 weeks of SMT was studied in 3 trials among 317 participants (Figure 10). No significant difference was recorded between experimental and control groups (MD=1.63, CI=-5.68, 8.93). A significant considerable between trials heterogeneity (I^2=95%, P=0.00001) and imprecision (wide confidence interval) were evident.

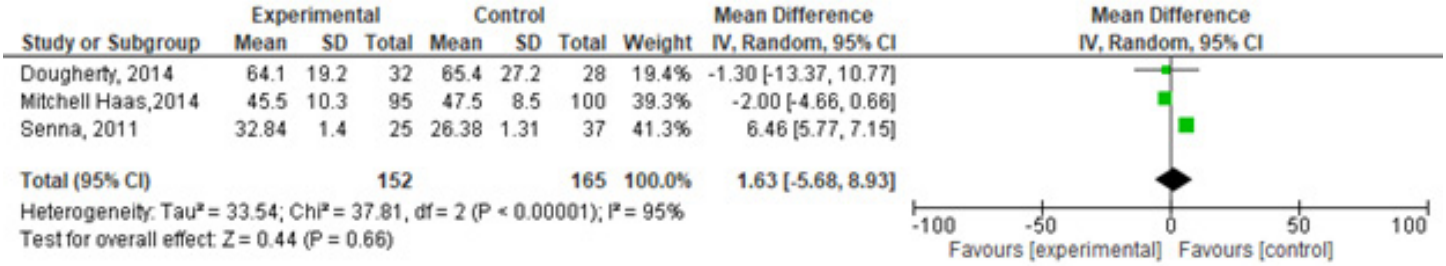

Figure 10: Forest plot of SF physical health among studied participants after 12 weeks of SMT.

SF physical health after 24 weeks of SMT: Explained the Forest plot of SF physical health among 437 participants in 4 trials after 24 weeks of SMT. No significant difference was detected between treatment and comparison groups (MD=2.10, CI=-3.23, 2.81). The figure also showed a significant considerable inconsistency between trials (I^2=94%, P=0.00001) and low precision (wide confidence interval) (Figure 11).

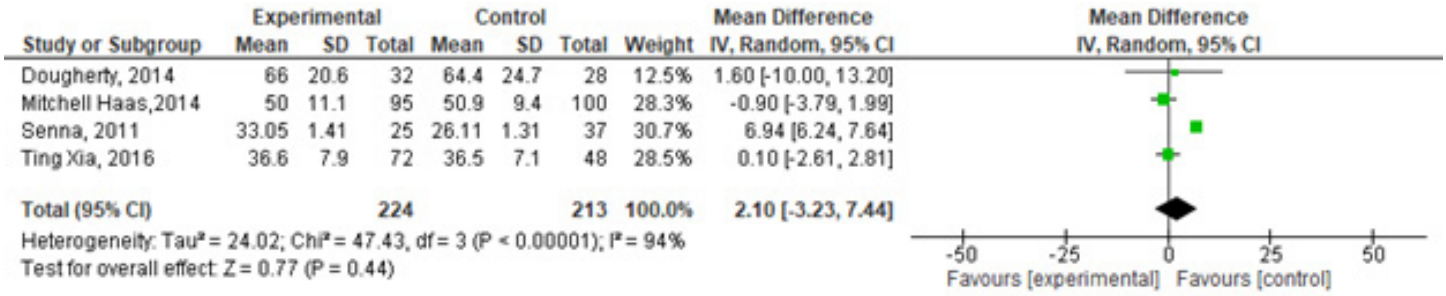

Figure 11: Forest plot of SF physical health among studied participants after 24 weeks of SMT..

SF physical health after 1 year of SMT: SF physical health after 1 year of SMT was studied in 2 trials only among 257 participants (Figure 12). No significant improvement of physical health was recorded among experimental group compared to control one (MD=4.97, CI=-0.89, 10.83). A significant considerable between trials heterogeneity (I^2=93%, P=0.0001) and low precision (participants less than 400) were demonstrated from the figure.

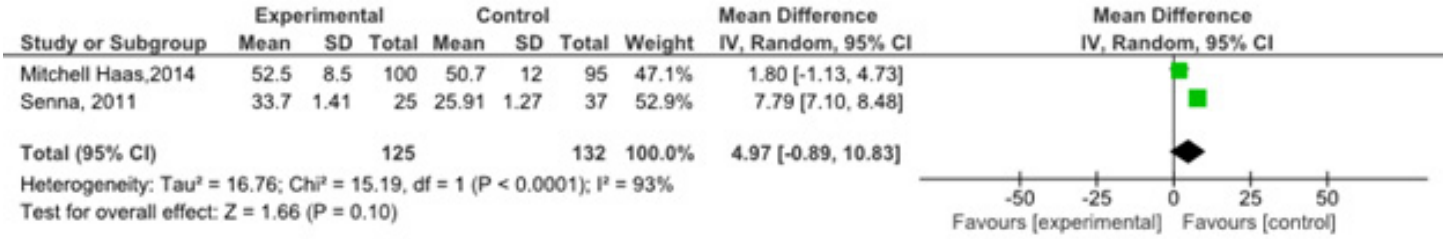

Figure 12: Forest plot of SF physical health among studied participants after 1 year of SMT.

SF mental health after 24 weeks of SMT: SF mental health was studied in 2 trials among 314 participants after 24 weeks of SMT (Figure 13). No significant improvement was detected among experimental group compared to control one (MD=-1.07, CI=-3.41, 1.26). No significant heterogeneity was recorded (I^2=0%, P=0.57).

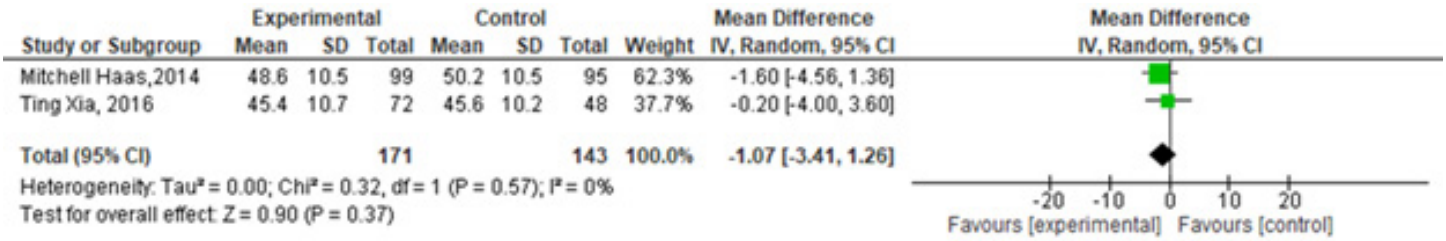

Figure 13: Forest plot of SF Mental health among studied participants after 24 weeks of SMT.

The proportion of patients with severe pain after 1 year of SMT: Forest plot of the proportion of patients with severe pain after 1 year of SMT was studied in 2 trials among 352 participants (Figure 14). No significant difference was recorded between experimental and control groups (OR=0.32, CI=0.03, 3.36). A significant considerable heterogeneity between the two trials (I^2=89%, P=0.002) and low precision were demonstrated.

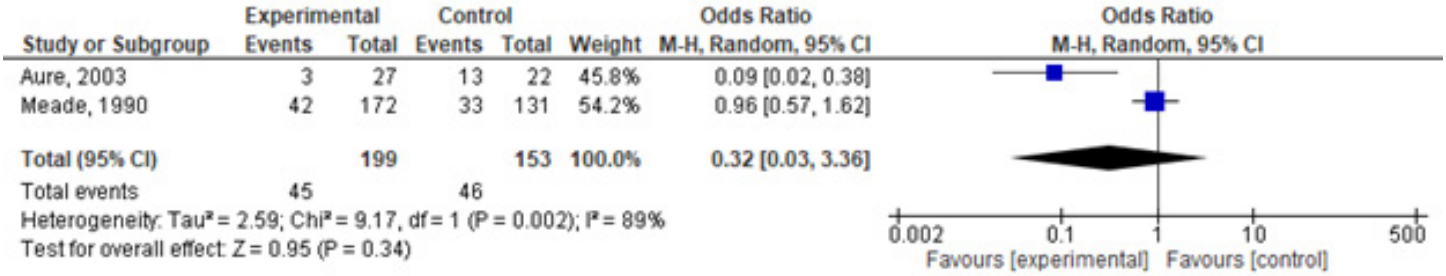

Figure 14: Forest plot of the proportion of patients with severe pain after 1 year of SMT.

The proportion of patients with pain free after 1 year of SMT: Forest plot of the proportion of patients with pain free after 1 year of SMT was studied in 2 trials among 407 participants (Figure 15). No significant difference was recorded between experimental and control groups with the experimental group was 23% more likely to be pain free compared to the control one (OR=1.23, CI=0.83, 1.84). No significant heterogeneity was recorded between the two studied trials (I^2=0%, P=0.83).

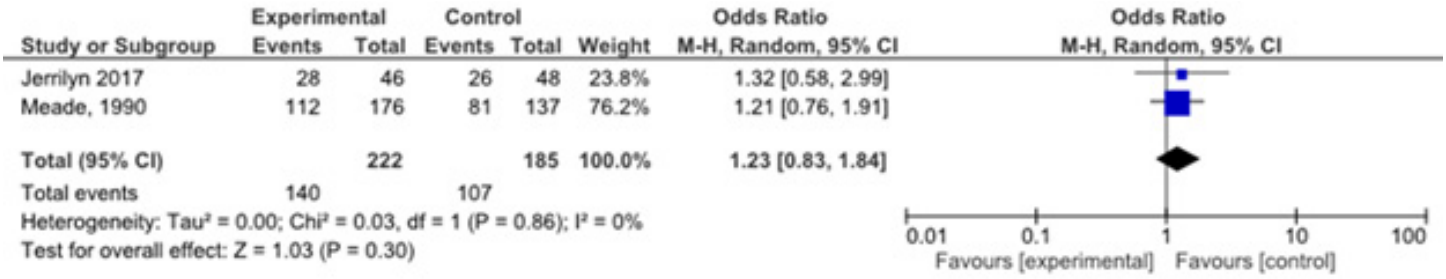

Figure 15: Forest plot of proportion of patients with pain free after 1 year of SMT.

The proportion of patients with sick leaves after 1 year of SMT: Forest plot of the proportion of patients with sick leaves after 1 year of SMT was studied in 2 trials among 207 participants (Figure 16). A statistically significant difference was reported between the experimental and control groups with the experimental group is 68% less likely to have sick leaves after 1 year of SMT compared to the control one (OR=0.32, CI=0.11, 0.97). A substantial insignificant heterogeneity was detected between the two trial (I^2=58%, P=0.12).

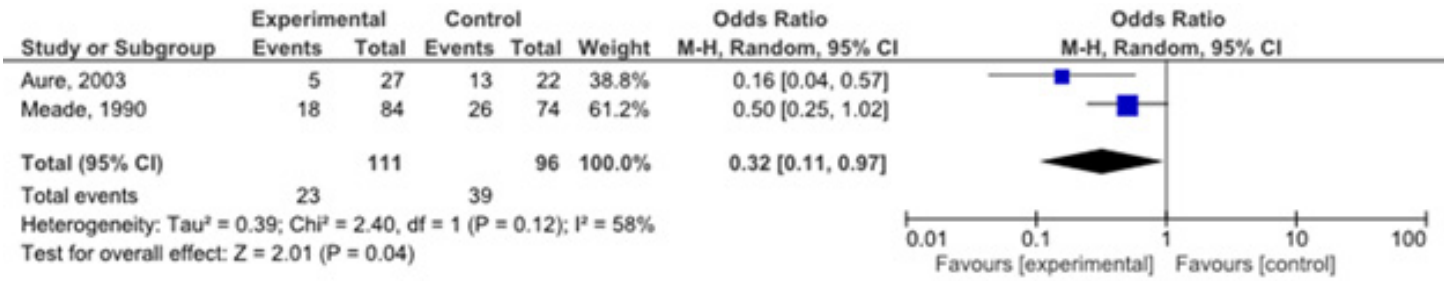

Figure 16: Forest plot of the proportion of patients with sick leaves after 1 year of SMT among studied participants.

The mean satisfaction of the participants with SMT: Forest plot of the mean satisfaction with the SMT was measured in 2 trials among 140 participants (Figure 17). No significant difference was recorded between experimental and control groups (MD=0.49, CI=-0.66, 1.63). A significant substantial heterogeneity was recorded between the two trial (I^2=78%, P=0.03).

Quality of Evidence

We assessed the quality of evidence in this review using GRADE approach (40). We considered the four recommended domains affecting study limitation including; risk of bias in the included studies, directness of the evidence, consistency across studies, and precision of the individual study estimates. Overall, the trials included in this review are randomized controlled trials with considerable percentages of risk of bias. Also, directness wasn't an issue in the review as all the included studies reported the effectiveness of SMT aimed at improving chronic low back pain. Regarding the pooled estimate of pain intensity after one year and functional disability after 6 weeks, we judged the quality of evidence to be moderate indicating moderate confidence that the evidence reflects the true effect, and further research is likely to change the estimate. We downgraded the evidence by one level because of substantial heterogeneity (I^2=83% and 73% respectively). Also, we judged the quality of evidence for the proportion of patients with pain free after one year to be moderate and we downgraded the evidence by one level due to low precision as the evidence come from two trials only (few numbers of included participants). Concerning the quality of evidence for the remaining outcome measures (except SF physical health after one year), we judged the quality of evidence to be low indicating low confidence that the evidence reflects the true effect, and further research is very likely to change the estimate. We downgraded the evidence by two levels because of considerable heterogeneity (indicated by high I^2) and imprecision (small sample size as few studies included in the analysis which was indicated by wide confidence interval). As regard SF physical health after one year, we judged the quality of evidence to be very low indicating that the estimate of the effect is very uncertain. We downgraded the evidence by three levels due to considerable heterogeneity and imprecision. We detected statistically significant heterogeneity in most of the meta-analyses, thus suggesting that the percentage of the variability in effect estimate is due to heterogeneity rather than to sampling error (chance) is important. The serious heterogeneity included in the review may be due to differences in study participants regarding baseline of pain intensity and variation in the intervention regarding method, duration and frequency of SMT sessions. The low precision may be attributed to the small sample size as only few studies were included in the analysis. Not to forget to mention, most of the outcome measures were subjective and reported by the participants.

DISCUSSION

The methodological quality of the RCT studies for spinal manipulation for chronic low back pain is adequate overall; however, studies remain heterogeneous in terms of sessions, duration, techniques involved with varying interventions and different practitioners with perhaps different training and backgrounds, controls or comparators being used across studies, and duration of chronicity of patients included. The staff, places, and facilities in which patients are receiving therapy are not well described. Spinal manipulation appears to be safe, based on what was reported in the literature. A small-moderate effect was found in favor of manipulation for patients with chronic low back pain, with pain duration of at least 3 months or more. This effect seems to increase over time at one year follow-up for reducing pain compared with other active comparators, namely exercise and physical therapy comparators. Manipulation was also shown to reduce disability. The quality of the body of evidence is moderate for both of these outcomes. There is currently a gap in the evidence concerning the efficacy of spinal manipulation compared with sham or no treatment on pain or disability in the population studied. Pooling across other subgroups was limited because there were too few sufficiently similar studies. In addition, we were not able to draw definitive conclusions about patients' HRQoL due to data limitations. Unlike the unimodal studies, which evaluated the results from the thrust or non-thrust interventions, the body of evidence from multimodal studies included a variety of interventions and integrated programs. For example, with exercise, individuals were allowed to choose their at-home routine or practitioners prescribed specific treatments. These types of programs may be attractive to patients because the programs may be similar to what would occur in real practice.

Overall Completeness and Applicability

The recommendations regarding manual therapies for chronic low back pain show some variation depending on country or region of origin. In most guidelines, manipulation is recommended or presented as a therapeutic option. In USA, recommendations exist in favor of manual therapies including manipulation and mobilization for chronic low back pain (Delitto A et al. 2012). The European Workgroup guidelines also recommend a referral for spinal manipulation therapy, including mobilization, for patients who are suffering from chronic back pain (Cowan P et al. 2008). However, other guidelines do not recommend it. It is not known why there are such inconsistencies across guidelines. Guidelines may have depended largely on panelists' interpretations, which have been based on insufficient or inconclusive evidence or reflected methodological flaws in the reported studies. Other factors that may influence guideline recommendations include local and national political variance or bias (Koes BW et al. 2010). Similar to the practice guidelines, recent systematic reviews have reported favorable evidence for treating chronic nonspecific low back pain using manipulation and mobilization, including chiropractic (Bronfort G et al. 2004 and Rubinstein SM et al. 2011), osteopathic manipulation therapy (Orrock PJ et al. 2013), and physical therapy (Ladeira CE et al. 2011). However, as with practice guidelines, these systematic reviews concluded that the scientific evidence is challenged by heterogeneity in the types of populations and interventions being studied, includes insufficient data to explore subgroup effects, and has methodological bias that can limit and complicate the interpretation of the results (Furlan AD et al. 2010). Most systematic reviews concluded that it is difficult to draw definitive conclusions regarding the risk-benefit of manual therapies in patients with chronic non-specific low back pain. We used the definitions of spinal manipulation based on Bronfort et al.2004 and Coulter et al.1996. Bronfort et al. 2004 identified 31 total low back pain trials. Of these, 11 trials (n=1,472) assessed chronic low back pain and 14 trials (n=3,068) investigated a mix of patients with acute and chronic low back pain. Because of heterogeneity across studies (i.e., too dissimilar in terms of patient characteristics, outcome measures, time points, and type of treatment comparisons), we did not include these studies. However, the results from Bronfort et al.2004 were generally in favor of spinal manipulation or mobilization for treating chronic low back pain. Bronfort et al. 2004 and Shekelle and Coulter 1997 suggested that recommendations for spinal manipulation may be made with some degree of confidence. They identified gaps in the current literature base that need to be filled in future work, such as the need for future trials to examine well defined subgroups of patients and further address the value of manipulation and mobilization to establish optimal number of treatment visits. Our review attempted to explore this, but research evidence remains lacking. We found that methodological flaws in the RCTs we analyzed-lack of power (low precision due to sample size) and some inconsistency-influenced our statistical analysis and the overall quality of the body of evidence. This review suggests that we can have moderate confidence in the estimate of the effect across the studies for each outcome evaluated and subgroup assessed, and the effect seems to increase over time, especially for manipulation therapy.

In the treatment of chronic nonspecific low back pain in adults, the quality of evidence varied suggesting that SMT does not result in clinically better effects for pain relief but does result in clinically better short-term improvement in function compared with non-recommended therapies, or sham, and when included as an adjuvant therapy. Moderate quality evidence suggests that spinal manipulative therapy results in similar outcomes to recommended therapies for short and intermediate pain relief.

Comparison with other Studies

Results of the present study are consistent with previous reviews (Bronfort G et al. 2004 and Rubinstein SM et al. 2011). Furthermore, our results are consistent with other recently published high quality systematic reviews (Jay K. et al. 2016 and Ian D Coulter et al. 2018) and guidelines that recommend SMT (Airaksinen O et al. 2006, Qaseem A et al. 2017 and Bons SCS et al. 2017). Previous studies evaluating thrust and non-thrust SM procedures for individuals with LBP have reported either an advantage for thrust SM procedures or similar effects between thrust and non-thrust SM. (Hadler NM et al.1987, Hondras MA et al. 2009 and Cook C et al. 2013) A study by Hurwitz et al (Hurwitz EL et al.1976) found that chiropractic care with and without physical modalities, and medical care with and without physical therapy, produced similar and significant improvements in low back pain. To this day, there is no consensus on the efficacy of SMT and its role in the care of CLBP. Some systematic reviews have reported quality evidence in support of SMT (Bronfort G et al.2008, Chou RHuffman LH et al.2007 and Rubinstein SM et al.2011), while others including the latest Cochrane review found SMT to be no better than other interventions (Rubinstein SM et al.2011). Results of systematic reviews, whether meta-analysis or best-evidence synthesis, may depend on the quantity of care used in the trials included in the reviews. Investigators have had virtually no evidence from dose-response trials to inform the number of SMT sessions provided.

Implications for Clinicians

SMT can be delivered as a standalone therapy, although it is typically offered within the constructs of a broader treatment package, together with exercise therapy or combined with usual care, as is recommended in recent national guidelines for low back pain. This is important because SMT is by nature a passive treatment. Therefore, to prevent inappropriate behaviour and to empower patients to take control of their condition it is vital that practitioners impart the proper message to their patients.

Strengths and Limitations

This systematic review had several strengths, including (1)

the use of a systematic, explicit, and transparent methodology, incorporating the evaluation of internal validity (risk of bias), external and model validity, meta-analysis according to patient reported outcomes, and GRADE framework applied to determine the overall quality of evidence for each critical outcome evaluated; and (2) an independent methodological review team to carry out each of the technical steps involved in the review phases. None of the study authors reported any conflict of interests.

The most important limitations are those related to most systematic reviews-namely, the limited number of studies with a low risk of bias, as well as ambiguity about the impact of publication bias. Furthermore, we could not resolve the problem related to statistical heterogeneity nor is this likely to be resolved in future reviews: studies of SMT are conducted in varied settings, among different populations, using several methods of recruitment and SMT techniques that are subsequently compared with various types of therapies. Finally, in most studies it was unclear if the research team was multidisciplinary, and whether it included clinicians involved in the treatment of patients, but perhaps most importantly, given that disclosure was often not reported, potential conflicts of interest cannot be ruled out.

Recommendations for Future Studies

Future trials of SMT for low back pain should include an economic evaluation; an analysis of the proportion of patients who achieved a specified level of pain relief (eg, percentage of those experiencing 50% pain improvement); a better description of the qualitative components of SMT, such as the context of the visit, patient beliefs, and preferences, and also quantitative components, such as factors that are likely to influence treatment. Future trials are not necessary, unless they contain a novel approach, are well conducted, and address any of these specific recommendations. Private or governmental agencies should refrain from funding small trials that are poorly conceived. Furthermore, it would be interesting to compare and evaluate whether spinal manipulation provided by specific type of practitioners is superb to Spinal manipulation therapy performed by others. For example, Chiropractic Manipulation Therapy (CMT) by a licensed Doctor of Chiropractic vs Osteopathic Manipulation Therapy (OMT) by a licensed Doctor of Osteopath vs. SMT done by all other providers i.e Physical therapists, Physiotherapists, Acupuncturists, Naturopaths etc.

CONCLUSION

There is moderate-quality evidence that SM (i.e., chiropractic) interventions may produce moderate reduction in pain intensity and reduce disability for patients compared with other active comparators such as exercise. The effect on disability seems to decrease over time at 3 and 6 months follow-up. Given the small number of studies with small sample size included in this analysis, we should be cautious of making strong inferences based on these results. More research is needed to assess other important patient reported outcomes in order to strengthen the evidence base regarding SM for reducing disability and increasing HRQoL for patients with chronic nonspecific low back pain. The research to date is still heterogeneous, and questions remain about optimal treatment duration, number of sessions, practitioners to be involved, and the kinds of patients who may benefit the most.

CONFLICT OF INTEREST

No any conflict of interest declared by authors

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