The impact of pragmatic vs. prescriptive study designs on the outcomes of low back and neck pain when using mobilization or manipulation techniques: a systematic review and meta-analysis

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ABSTRACT

Objective: The purpose of this systematic review and meta-analysis was to examine the impact of pragmatic versus prescriptive study designs on the outcomes of low back and neck pain when using mobilization or manipulation techniques.

Methods: This study design was a systematic review and meta-analysis, which was performed according to the PRISMA guidelines. A search of MEDLINE and CINAHL complete databases was performed. Article titles and abstracts were reviewed to identify studies comparing mobilization and manipulation in low back or neck pain that met eligibility criteria. Validity of studies was examined using the Cochrane Risk of Bias tool. Data analysis was performed using RevMan 5.3. Forest plots were constructed after data were analyzed to determine effect sizes.

Results: Thirteen studies with a total of 1313 participants were included in the systematic review, and 12 studies with 977 participants in the meta-analysis. For most time-points prescriptive studies found manipulation to be superior to mobilization for both pain and disability. At no time-point did pragmatic designs find a difference between mobilization and manipulation for either pain or disability.

Discussion: When a pragmatic design was used, representing actual clinical practice, patients improved with both techniques with no difference between mobilization and manipulation. When clinicians were prescribed techniques, not representing true clinical practice, manipulation showed better outcomes than mobilization for pain and disability.

Level of Evidence: 1a

KEYWORDS

Manipulation; mobilization; prescriptive; pragmatic; manual therapy; pain; disability; spine

Introduction

Physical therapists often treat individuals with a variety of musculoskeletal conditions including mechanical low back pain (LBP) and/or cervical pain (CP) [1–3]. It has been reported that approximately 28.8% of the population 18 years and older will experience some form of low back pain within the last 3 months [4]. Additionally, 15.8% of the population will have experienced some form of neck pain within the last 3 months [4]. The 1-year incidence of neck pain has been reported to be between 10.4 and 21.3%, with higher incidence noted in office and computer workers [5]. In fact a recent systematic analysis found low back and neck pain to be one of the leading causes of disability in numerous countries around the world [6].

The cost of LBP continues to rise, ranking as the most expensive musculoskeletal ailment to manage. As of 2006, it is estimated that in the United States the total costs of low back pain exceeds 100 billion dollars yearly [7]. Approximately two-thirds of this is indirect costs, resulting from lost wages and productivity [7]. There is

an estimated 149.1 million lost workdays due to low back pain [8]. In terms of neck pain, between 11 and 14.1% of workers each year will be limited in their activity due to their symptoms [9]. One study from the Netherlands determined the total cost to treat cervical pain to be €485 million, which currently equates to about 520 million US dollars [10]. As the prevalence and costs of LBP and neck pain management continue to rise, debate remains among the medical community on the most effective way to reduce pain and disability as well as the societal burden associated with these disorders.

There are many conservative treatment approaches used to manage mechanical spine pain. Among those, interventions including manual therapy, therapeutic exercise, and modalities are most common [11]. Manual therapy, including manipulation and mobilization, appears to be one of the most common treatment choices applied by physical therapists for the management of these conditions. Research has shown that manual therapy and exercise is effective in treating non-specific spinal pain [1,12,13]. However, evidence

from studies has been conflicting [14,15] so it is unclear whether spinal manipulation or mobilization is superior to the other in the management of these conditions.

In addition to the controversies surrounding which technique is superior [16], it is also unclear if clinician decision-making impacts outcomes [17]. Two studies have explored the therapist equipoise and have found associations between the clinician's preferred technique and the patient reported outcomes. Interestingly, a recent trial compared two different forms of mobilization (one therapist selected and one in which the mobilization was standardized) and the results showed similar outcomes for pain and disability between groups, but at a 6-month follow-up, the group receiving therapist selected mobilization reported greater perceived well-being [18]. Further complicating issues is a meta-analysis by Kent et al. [19] that investigated if clinician treatment choice improves the outcomes of manual therapy for nonspecific LBP. Although few quality studies existed, Kent et al. found that roughly two-thirds of the included RCTs had clinician choice of treatment, and that there was no significant difference favoring the studies that allowed for clinician choice as opposed to those that did not [19].

Study designs that allow for clinician choice are often referred to as pragmatic while study designs that prescribe exactly which technique to use and levels to target are known as prescriptive. Pragmatic study designs attempt to examine the effectiveness of interventions as they would be applied in a typical clinical setting [20,21]. This often involves broader inclusion criteria with less focus on internal validity, and often comparing effectiveness of two competing treatments. Pragmatic trials involve a population that closely mirrors what a clinician would typically see in practice and frequently allows for clinical decision-making in the plan of care. Prescriptive study designs typically have narrow inclusion criteria, stronger internal validity, and specifically dosed interventions [21–23]. This design is optimal in maximizing ideal controlled circumstances rather than clinical reality. Prescriptive designs are focused on determining the specific effects of isolated treatments. It is plausible that the two study designs could find opposing results when directly comparing two interventions. To the best of our knowledge, to date there have been no systematic reviews or meta-analysis comparing the effects of manipulation and mobilization between prescriptive and pragmatic designs. Therefore, the purpose of this systematic review and meta-analysis is to examine the impact of pragmatic versus prescriptive study designs on the outcomes of low back and neck pain when using mobilization or manipulation techniques.

Methods

We performed this systematic review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [24].

Literature search

An electronic literature search was conducted between 1 December 2016 and 20 December 2016 in MEDLINE and CINAHL complete databases from their dates of inception to December of 2016. A combination of search terms was used to identify possible relevant articles. Search terms included mobilization, manipulation, low back pain, cervical pain, clinician choice, disability, and pain. Nine different combinations of these terms were used to complete the literature search which included: mobilization, low back pain; mobilization, manipulation; mobilization, manipulation, low back pain; mobilization, manipulation, low back pain, clinician choice; mobilization, manipulation, low back pain, clinician choice, disability; mobilization, manipulation, low back pain, clinician choice, disability, pain; mobilization, manipulation, cervical pain, clinician choice, disability; mobilization, manipulation, cervical pain, clinician choice, disability, pain; mobilization, manipulation, and cervical pain. Reference lists from identified articles were hand searched for any other potentially eligible studies. Additionally, corresponding authors of relevant articles were contacted by email and asked if they could identify any additional articles that had not been identified through the database searches (Figure 1).

Study selection

Six researchers completed the database searches independently and reviewed all article titles and abstracts to identify potentially relevant articles. All reviewers needed to reach a consensus for a study to be included in the systematic review and meta-analysis. Articles also needed to satisfy all of the following inclusion criteria: written in English; randomized clinical trials; compared mobilization versus manipulation in isolation; included patients with low back pain or neck pain; and used an outcome measure of pain and/or disability (Figure 1). Mobilization was defined as low-velocity spinal mobilization and manipulation was defined as high-velocity, low amplitude, thrust manipulation (HVLAT).

Eligible studies were classified as prescriptive or pragmatic based on the criteria used by Kent et al. To be classified as pragmatic, clinicians needed to be able to choose the technique and spinal levels to be treated. If both of these criteria were not met, the study was classified as prescriptive [19].

Data extraction

Data extraction was compiled using a standard form modified from a previous systematic review and meta-analysis [25]. Data included consisted of participants, sample size, interventions, follow-up period, outcome measure, adverse events, and main results.

Figure 1. Flowchart of included articles.

Risk of bias assessment tool

The methodological quality of each study was determined using the Cochrane risk of bias tool [26]. This tool uses five different items (selection bias, performance bias, detection bias, attrition bias, and reporting bias) to examine the validity of studies. The items are rated on a three-point scale to assess risk of bias (0 = high risk, 1 = unclear risk, 2 = low risk) with a maximum score of 16 points and lower scores indicating a higher risk of bias.

Similar to a previously published systematic review and meta-analysis we calculated a percentage score for

each study [25]. For example, if a study scored 11/16 points that would receive a risk of bias score of 68.8%. We also used a cut off of 69% for indicating high and low risk of bias [25].

Data analysis

The primary outcomes for this systematic review were pain and disability. We performed the meta-analyses using RevMan 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) for

different follow-up periods similar to a recent systematic review; immediate (within 5 min of the application of the intervention), 1–6 days, 4 weeks, 5–11 weeks, and 3–6 months. For analysis of continuous data we selected to use the standardized mean differences (SMD) with the 95% confidence interval (95% CI) since it is more generalizable [27] and allows for the assessment of outcomes that used different scales. The random effects model was used to account for variability between studies and its effect on the intervention. The I^2 statistic was used to measure the heterogeneity between trials [28]. According to Higgins and colleagues, an I^2 value of 25% represents a small, 50% moderate, and 75% large, degree of heterogeneity [29]. Effect size was interpreted using Cohen's criteria for pooled estimates. Cohen described 0.2 as small, 0.5 as moderate, and 0.8 as large effect sizes [30].

Results

Of the 29,384 potential studies identified during the original search, 13 studies were deemed relevant after screening titles, abstracts, and full article reviews. No additional articles were provided by any of the corresponding authors who were emailed asking if they were aware of any other articles that could potentially fit out eligibility criteria. Figure 1 shows the PRISMA flow diagram of the search strategy and results in addition to reasons for exclusion. No additional studies were identified through hand searching reference lists or contacting the corresponding author on each study. A total of 13 studies with a combined total of 1313 participants were included in the systematic review with 12 studies and 977 participants included in the meta-analysis. Of the three authors we contacted requesting additional data to complete the analysis, one author [31] did not provide adequate data to develop forest plots as the corresponding author was unable to identify the original data-set.

Study characteristics

Data included consisted of participants, sample size, interventions, follow-up period, outcome measure, adverse events, and main results can be found in Table 1.

Outcome measures

All 13 studies used a Visual Analog Scale (VAS) or Numeric Pain Rating Scale (NPRS) to measure pain-related outcomes. A total of seven studies reported outcome measures on disability [14,15,31–35] including the Neck Disability Index (NDI), Neck Bournemouth Questionnaire (NBQ), and the Oswestry Disability Index (ODI).

Prescriptive approach

Of the 13 total studies, 8 (61.5%) examined the effects of mobilization versus manipulation in a prescriptive

treatment design where the clinician did not have choice or clinical decision-making and included a total of 579 subjects. 7 prescriptive studies (467 subjects) examined mobilization versus manipulation when treating mechanical neck pain [32–33,37–39]. One study (112 subjects) examined mobilization versus manipulation when treating mechanical lower back pain [15].

Pragmatic approach

Of the 13 total studies, 5 (38.5%) examined the effects of mobilization versus manipulation in a pragmatic treatment design where the clinician had choice and clinical decision-making and included a total of 734 subjects. A total of 4 studies (585 subjects) examined mobilization versus manipulation when treating mechanical neck pain [31,34,40,41]. Additionally, 1 study (149 subjects) examined mobilization versus manipulation when treating mechanical lower back pain [14].

Risk-of-bias appraisal

The mean risk of bias scores of prescriptive studies was greater than pragmatic studies. The mean $\pm$ SD score on the Cochrane risk of bias tool across all eight prescriptive studies was 67.97% $\pm$ 8.48%. Six studies [15,33,35–38] had a score of at least 69% (11/16), indicating a moderate to low risk of bias. The other two studies [32,39] scored less than 69%, indicating high risk of bias (Figure 2).

The mean $\pm$ SD score on the Cochrane risk of bias tool across all five pragmatic studies was 53.75% $\pm$ 16.30%. Two studies [32,41] had a score of at least 69% (11/16), indicating a moderate to low risk of bias. The other three studies [31,34,41] scored less than 69%, indicating high risk of bias (Figure 2).

None of the studies had low risk of bias for all eight categories due to the impossibility to blind the providers to type of manual therapy provided. Only three studies [35–37] were able to blind the participant due to the intervention characteristics. In 7 of the 13 studies [15,31,33,36–40], blinding of the assessor was successfully reported. Selective reporting bias (incomplete outcome data) was present in 10 of the 13 studies [15,31–35,37,39–41]. Figure 3 represents bias and risk of bias across studies for each individual prescriptive and pragmatic study.

Primary analyses

Prescriptive outcomes for pain and disability

A total of 8 studies out of 13 (61.5%) compared pain outcomes in those treated with manipulations or mobilizations using a prescriptive approach. In studies reporting immediate outcomes, the SMD (0.45, 95% CI; 0.16, 0.74) demonstrates that manipulation was superior to mobilization in regards to an improvement in pain. Studies that reported findings within 1–6 days (SMD; 1.14, 95%

Table 1. Characteristics of the included studies using prescriptive and pragmatic intervention.

Study	Participants	Intervention	Follow-up Period	Outcome Measure	Results Between Groups
PRESCRIPTIVE STUDIES					
Cassidy et al. [36]	<i>n</i> = 100 subjects with report of unilateral neck pain with referral into trapezius muscle (16 < 1 week, 34.1 weeks-6 months, 50 > 6 months) Group 1 (<i>n</i> = 52): mean $\pm$ SD age, 34.5 $\pm$ 13 years Group 2 (<i>n</i> = 48): 37.7 $\pm$ 12.5 years <i>n</i> = 112 subjects with report of low back pain with or without symptoms into the lower extremity; median length of symptoms, (interquartile range), 45 (27, 60); 57 male, 55 female; mean $\pm$ SD age, 40.4 $\pm$ 11.5 years Group 1 (<i>n</i> = 37): 43.7 $\pm$ 10.4 years Group 2 (<i>n</i> = 38): 37.1 $\pm$ 11.5 years Group 3 (<i>n</i> = 37): 40.1 $\pm$ 12 years	Group 1 (<i>n</i> = 52): Manipulated (rotational) cervical to symptomatic level Group 2 (<i>n</i> = 48): Mobilized muscle energy technique with stretching to hypertonic cervical musculature Group 1 (<i>n</i> = 37): Supine thrust manipulation (non-specific lumbar) and spinal ROM exercise (2 sessions week 1), exercise regime (one session weekly for 3 weeks) Group 2 (<i>n</i> = 38): Side-lying thrust manipulation (non-specific lumbar) and spinal ROM exercise (2 sessions week 1), exercise regime (one session weekly for 3 weeks) Group 2 (<i>n</i> = 38): Side-lying thrust manipulation (non-specific lumbar) and spinal ROM exercise (2 sessions week 1), exercise regime (one session weekly for 3 weeks) Group 3: (<i>n</i> = 37): Non-thrust technique (2 Hz oscillatory P-A mobilization L4&L5) and spinal ROM exercise (2 sessions week 1), exercise regime (one session weekly for 3 weeks)	Within 5 min following intervention 1 week, 4 week, 6 months	Pain Intensity (NPS) Subjective Disability Report (ODQ) Pain Intensity (NPS)	Difference in pain intensity between groups: 6.8, <i>P</i> = 0.05 Difference in disability between groups 1&3: 1 week, 11.45, <i>P</i> < 0.001; 4 weeks, 14.23, <i>P</i> < 0.001; 6 months, 5.97, <i>P</i> < 0.027 Difference in disability between groups 2&3: 1 week, 7.94, <i>P</i> = 0.003; 4 weeks, 12.73, <i>P</i> < 0.001; 6 months, 6.81, <i>P</i> = 0.004 No statistically significant difference in disability between groups 1&2 reported Difference in pain intensity between groups 1&3: 1 week, 2.07, <i>P</i> < 0.001; 4 weeks, 1.79, <i>P</i> = 0.002; 6 months, 0.58, <i>P</i> = 0.018 Difference in pain intensity between groups 2&3: 1 week, 1.46, <i>P</i> < 0.001; 4 weeks, 1.32, <i>P</i> = 0.002; 6 months, 0.39, <i>P</i> = 0.29 No statistically significant difference in pain intensity between groups 1&2 reported Difference in disability between groups: 10.03 (95% CI: 5.3, 14.7), <i>P</i> < 0.001 Difference in pain intensity between groups: 2.03 (95% CI: 1.4, 2.7), <i>P</i> < 0.001
Cleland et al. [27]					
Cleland et al. [28]	<i>n</i> = 60 subjects with mechanical neck pain with or without upper extremity symptoms between the ages of 18 and 60; 27 male, 33 female; mean $\pm$ SD age, 43.3 $\pm$ 12.7 years Group 1 (<i>n</i> = 30): 42.7 $\pm$ 13.9 years Group 2 (<i>n</i> = 30): 43.8 $\pm$ 11.5 years <i>n</i> = 107; 34 males, 73 females with mechanical neck pain between the superior nuchal line and first thoracic spinal process Group 1 (<i>n</i> = 56): mean $\pm$ SD age, 41.5 $\pm$ 11.9 years Group 2 (<i>n</i> = 51): 42.7 $\pm$ 13.9 years	Group 1 (<i>n</i> = 30): Non-thrust mobilization/manipulation (30 sec grade III/IV central P-A mob each, T3-T6) Group 2 (<i>n</i> = 30): Thrust mobilization/manipulation (supine upper thoracic (T1-T4) and middle thoracic (T5-T8)) Group 1 (<i>n</i> = 56): HVLA thrust manipulation (R and L supine C1-C2, supine T1-T2) Group 2 (<i>n</i> = 51): Non-thrust mobilization (prone grade IV P-A unilateral oscillatory mobilization 30 sec R&L, 30 sec prone grade IV P-A central oscillatory mobilization T1-T2)	2-4 days following intervention 48 h following intervention	Subjective Disability Report (NDI) Pain Intensity (NPS) Subjective Disability Report (NDI) Pain Intensity (NPS)	Difference in disability between groups: 8 (95% CI: 5.9, 10.2), <i>P</i> < 0.001 Difference in pain intensity between groups: 2.0 (95% CI: 1.5, 2.5), <i>P</i> < 0.001

(Continued)

Table 1. (Continued).

Study	Participants	Intervention	Follow-up Period	Outcome Measure	Results Between Groups
Lopez-Lopez et al. [32]	<i>n</i> = 48 subjects 18–65 years of age with history of neck pain within the superior nuchal line and first thoracic spinous process with more than 12 weeks of evolution without radicular symptoms; 6 male, 42 female Group 1 (<i>n</i> = 15): mean $\pm$ SD age, 35.4 $\pm$ 8.0 years Group 2 (<i>n</i> = 16): 36.0 $\pm$ 9.9 years Group 3 (<i>n</i> = 17): 37.8 $\pm$ 8.6 years	Group 1 (<i>n</i> = 15) HVLA technique (supine HVLA manipulation to hypomobile cervical zygapophyseal joints until cavitation noted, max of 2 attempts Group 2 (<i>n</i> = 16) Mobilization (prone grade III P-A unilateral oscillatory mobilization over hypomobile cervical segments, 3 periods of 2 min)	Immediately following intervention	Pain intensity (VAS)	A statistically significant difference in pain intensity between groups was reported, <i>P</i> = 0.04
Pérez et al. [33]	<i>n</i> = 61 subjects 20–65 years of age with pain in the posterior cervical spine persisting at least 12 weeks without radicular symptoms to head, trunk, or arms; 35 male, 26 female Group 1 (<i>n</i> = 19): mean $\pm$ SD age, 36.2 $\pm$ 8.9 years Group 2 (<i>n</i> = 21): 35.6 $\pm$ 10.3 years Group 3 (<i>n</i> = 21): 37.8 $\pm$ 9.1 years	Group 1 (<i>n</i> = 19) HVLA technique (supine HVLA manipulation to hypomobile cervical segments in hypomobile planes of motion, max of 2 thrusts) Group 2 (<i>n</i> = 21) Mobilization (prone P-A unilateral oscillatory mobilization to hypomobile cervical segments, 2 min, 3 times)	Immediately following treatment, 1 month, month, 3 month	Subjective Disability Report (NDI) Pain Intensity (VAS)	No statistically significant difference in disability between groups reported No statistically significant difference in pain intensity between groups reported
Salom-Moreno et al. [34]	<i>n</i> = 52 subjects 18–60 years of age with idiopathic mechanical neck pain persisting for at least 6 months with no radicular symptoms; 30 male, 22 female Group 1 (<i>n</i> = 27): mean $\pm$ SD age 32 $\pm$ 7 years Group 2 (<i>n</i> = 25): 34 $\pm$ 9 years	Group 1 (<i>n</i> = 27) Thrust manipulation (supine, HVLA manipulation to T3–T6 until cavitation noted, max of 2 attempts) Group 2 (<i>n</i> = 25) Non-thrust mobilization (prone grade III–IV P-A central oscillatory mobilization to T3–T6 segments, 20 second bouts, 2 min total)	10 min following intervention	Pain Intensity (NPS)	Difference in pain intensity between groups: 1.4 (95% CI: 0.8–2.1), <i>P</i> < 0.001
Suvarnato et al. [35]	<i>n</i> = 39 subjects with either unilateral or bilateral chronic mechanical pain in the posterior neck and/or shoulder region; 10 male, 29 female Group 1 (<i>n</i> = 13): mean $\pm$ SD age, 35.33 $\pm$ 10.96 years Group 2 (<i>n</i> = 13): 37 $\pm$ 12.59 years Group 3 (<i>n</i> = 13): 39.91 $\pm$ 11.52 years	Group 1 (<i>n</i> = 13): Manipulation (prone 'screw thrust' high velocity thrust technique to zygapophyseal joints T6–T7) Group 2 (<i>n</i> = 13): Mobilization (grade III unilateral P-A mobilization on both sides of zygapophyseal joints of T6–T7 R&L, 1 min each)	Immediately following intervention, 24 h	Pain Intensity (VAS)	Difference in pain intensity between groups: immediately following intervention, .85 (CI: 7.84–9.54), <i>P</i> < 0.05; 24 h, 1.94 (CI: 7.84–11.72), <i>P</i> < 0.05
PRAGMATIC STUDIES					
Cook et al. [26]	<i>n</i> = 149 subjects 18 years of age or older with mechanically producible LBP; 70 males, 79 females Group 1 (<i>n</i> = 76): mean age $\pm$ SD, 46.1 $\pm$ 14.5 years Group 2 (<i>n</i> = 73): 50.3 $\pm$ 15.1 years	Group 1 (<i>n</i> = 76): Thrust manipulation (technique to affected lumbar segment, including sidelying rotational and/or supine ASIS thrust) Group 2 (<i>n</i> = 73): Non-thrust manipulation (technique to affected lumbar segment, including central P-A, unilateral P-A, and sidelying rotational mobilization)	Following treatment #2, at discharge (group 1: mean $\pm$ SD days in care, 33.8 $\pm$ 26.2 days; group 2: mean $\pm$ SD days in care, 37.6 $\pm$ 33.4 days)	Subjective Disability Report (ODI) Pain Intensity (NPS)	No statistically significant difference in disability between groups reported No statistically significant difference in pain intensity between groups reported

Gemmell et al. [38]	<p>$n = 47$ subjects 18–64 years of age with neck pain persisting between 4 and 12 weeks; 10 males, 37 females</p> <p>Group 1 ($n = 16$): mean $\pm$ SD age, 46.9 $\pm$ 9.1 years</p> <p>Group 2 ($n = 15$): 43.8 $\pm$ 13.0 years</p> <p>Group 3 ($n = 16$): 46.8 $\pm$ 11.8 years</p>	<p>Group 1 ($n = 16$): Manipulated (HVLTAT techniques to restricted cervical and upper thoracic segments) 2x/week for 3 weeks or until symptom free</p> <p>Group 2 ($n = 15$): Mobilized (supine grade III P-A and transverse oscillatory low grade passive movement to articular pillar and and spinous process of one or more restricted upper thoracic or cervical segments) 2x/week for 3 weeks)</p>	Immediately following final treatment, 3 month, months, 12 months	Subjective Disability Report (NBQ)	No statistically significant difference in disability between groups reported
Griswold et al. [30]	<p>$n = 20$ subjects 18–70 years of age with primary complaint of reproducible non-specific neck pain between the superior nuchal line and first thoracic spinous process; 9 males, 11 females</p> <p>Group 1 ($n = 7$): mean $\pm$ SD age, 37.4 $\pm$ 15.7 years</p> <p>Group 2 ($n = 13$): 41.2 $\pm$ 14.6 years</p>	<p>Group 1 ($n = 7$): Manipulated (HVLA thrust to the most symptomatic segment of both the cervical and upper thoracic spine)</p> <p>Group 2 ($n = 13$): Mobilized (applied to the most symptomatic cervical and thoracic segments)</p>	Following second treatment (3–4 days), at discharge (36–41 days)	Subjective Disability Report (NDI) Pain Intensity (NPS)	No statistically significant difference in disability between groups reported No statistically significant difference in pain intensity between groups reported
Hurwitz et al. [31]	<p>$n = 336$ subjects with report of neck pain from upper thoracic spine to occiput and the surrounding musculature; 105 male, 231 female</p> <p>Group 1 ($n = 171$): mean $\pm$ SD age, 45.7 $\pm$ 11.8 years</p> <p>Group 2 ($n = 165$): 45.7 $\pm$ 12.2 years</p>	<p>Group 1 ($n = 171$): Manipulation: with and without heat and with and without NMES. Subjects assigned to one of the spinal mobilization groups received at least 1 controlled dynamic thrust, applied with high-velocity and low-amplitude with minimal extension and rotation directed at one or more restricted upper thoracic and/or cervical spine joint segment within patient tolerance</p> <p>Group 2 ($n = 165$): Mobilization: with and without heat and with and without NMES. Subjects assigned to one of the spinal mobilization groups received one or more movements of low velocity and variable amplitude directed to one or more restricted upper thoracic and/or cervical spine joint segments</p>	2 week, 6 week, 3 month, 6 months	Subjective Disability Report (NDI) Pain Intensity (NPS)	Difference in disability intensity between groups: 2 week, 1.03 (95% CI: -0.002–2.08); 6 week, .92 (95% CI: -0.032–2.17); 3 month, .05 (95% CI: -1.33–1.44); 6 months, 0.46 (95% CI: -0.089–1.82) Difference in pain intensity between groups: 2 week, .14 (95% CI: -0.055–0.26); 6 week, .23 (95% CI: -0.26–0.72); 3 month, 0.05 (95% CI: -0.46–0.56); 6 months, 0.01 (95% CI: -0.52–0.54)
Leaver et al. [37]	<p>$n = 182$ subjects 18–70 years of age with neck pain between the superior nuchal line and first thoracic spinous process persisting less than 3 months; 64 male, 118 female</p> <p>Group 1 ($n = 91$): mean $\pm$ SD age, 38 $\pm$ 10.3 years</p> <p>Group 2 ($n = 91$): 39.7 $\pm$ 11.1 years</p>	<p>Group 1 ($n = 91$): Manipulated (HVLTAT manipulation technique applied to the upper cervical spine)</p> <p>Group 2 ($n = 91$): Mobilized (low velocity oscillatory passive movement applied to the upper cervical spine)</p>	Pain: 2 week, 12 weeks Disability: 4 week, 12 weeks	Subjective Disability Report (NDI) Pain Intensity (NPS)	No statistically significant difference in disability between groups reported No statistically significant difference in pain between groups reported

Notes: NPS = Numeric Pain Rating Scale, ODI = Oswestry Disability Questionnaire, NDI = Neck Disability Index; NBQ = Neck Bourneymouth Questionnaire; VAS = Visual Analog Scale.

Figure 2. Risk of bias mean scores across pragmatic and prescriptive studies.

CI; 0.83, 1.45), and 1–4 weeks (SMD; 1.02, 95% CI; 0.77, 1.27) also presented data that favored manipulations over mobilizations. However, data reported during 5–11 weeks showed no statistically significant difference between the two methods (SMD; 0.16, 95% CI; –0.48, 0.81). At longer term follow-up (3–6 month range), manipulations again proved to be more effective (SMD; 0.41, 95% CI; 0.06, 0.77) than mobilizations for reducing pain. Forest plots for pain when mobilization and manipulation were prescriptive can be found in Figure 4.

A total of four studies included in this meta-analysis reported disability scores when clinician's treatment was standardized. The results suggest that there was no difference between prescriptive manipulation and mobilization at the immediate (SMD; –0.19, 95% CI; –0.81, 0.43), and 5–11-week follow-up (SMD; –0.21, 95% CI; –0.83, 0.41). However manipulation had a significant effect on decreasing disability scores compared to prescriptive mobilizations at 1–6 days (SMD; 1.31, 95% CI; 0.97, 1.64), 1–4 weeks (SMD; 0.85, 95% CI;

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of outcome assessment (detection bias)	Blinding of participants	Blinding of providers	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Prescriptive Studies								
Cassidy et al.	+	-	-	-	+	?	-	+
Cleland et al. (2009)	+	+	-	-	+	?	+	+
Cleland et al. (2007)	+	+	-	-	?	?	+	+
Dunning et al.	+	+	-	-	+	?	+	+
Lopez-Lopez et al.	+	+	+	-	?	?	+	+
Perez et al.	+	+	+	-	+	+	-	+
Salom-Moreno et al.	+	+	+	-	+	?	+	?
Suvarnato et al.	+	+	-	-	+	+	+	?
Pragmatic Studies								
Cook et al.	+	+	-	-	?	+	+	+
Gemmell et al.	+	+	-	-	?	-	-	-
Griswold et al.	+	?	-	-	?	?	-	+
Hurwitz et al.	+	?	-	-	?	?	+	+
Leaver et al.	+	+	-	-	+	?	+	+

Figure 3. Risk of bias across pragmatic and prescriptive studies.
Note: + low risk of bias, - high risk of bias, ? unclear risk of bias.

0.58, 1.11), and 3–6 months (SMD; 0.46, 95% CI; 0.11, 0.80) (Figure 5).

Pragmatic outcomes of pain and disability

A total of 5 studies out of 13 (38.5%) compared outcomes for pain when individuals with neck or low back pain were treated with manipulation or mobilization using a pragmatic approach. Overall, there was no statistically significant difference between mobilizations or manipulations at any of the designated time frames. The SMDs were 0.26 (95% CI; -0.66, 1.18), -0.05 (95% CI; -0.34, 0.25), 0.01 (95% CI; -0.29, 0.32), 0.11 (95% CI; -0.19, 0.40) 0.38 (95% CI; -0.33, 1.09) at 1–6 days, 1–4 weeks, 5–11 weeks, 3–6 months, and 7–12 months, respectively, as shown by Figure 6.

Of the 13 studies reviewed, only 3 (23.1%) pragmatic studies reported disability scores. Figure 7 demonstrates that there was no statistically significant difference between mobilizations or manipulations at, 1–6 days (SMD; 0.43, 95% CI; -0.50, 1.36), 1–4 weeks (SMD; -0.06, 95% CI; -0.35, 0.24), 5–11 weeks (SMD; -0.04, 95% CI; -0.34, 0.26), or 3–6 months (SMD; -0.03, 95% CI; -0.33, 0.26).

The one pragmatic study by Hurwitz et al. [31] that was not included in the meta-analysis found no difference between manipulation and mobilization for pain or disability.

Discussion

This systematic review and meta-analysis was performed to investigate the difference in disability and pain outcomes within individuals with back and neck pain when mobilization and manipulation techniques were performed in either a prescriptive or pragmatic fashion in both the short and long terms. Thirteen CTs were identified including 8 which used a prescriptive design [15,32,33,35–39], and 5 which used a pragmatic approach [14,31,34,40,41]. The results of this meta-analysis suggest that when using a prescriptive approach comparing mobilization to manipulation to treat pain and disability, the outcomes favored manipulation. However, when a pragmatic approach to using manual therapy was performed in the respective studies, mobilization and manipulation were found to be equivalent. Additionally, when considering the 95% CIs around the point estimate for effect size at each time point, we noticed no overlap for pain at 1–6 days (95% CI; 0.83, 1.45 vs. 95% CI; -0.34, 0.25), 1–4 weeks (95% CI; 0.77, 1.27 vs. 95% CI; -0.29, 0.32), and disability at the 1–4 week follow-up (95% CI; 0.58, 1.11 vs. 95% CI; -0.35, 0.24). This further suggests that when applied in a prescriptive fashion manipulation has a superior outcome in reducing pain and disability compared to when both are applied in a pragmatic fashion for both pain and disability at 1–4 weeks and pain 1–6 days. However, the overlap in the 95% CI for pain and disability in the 3–6-month follow-up suggests there may be no actual difference between the outcomes of pragmatic and prescriptive study designs.

A number of reasons can explain the findings of the systematic review and meta-analysis. A number of differences exist between prescriptive and pragmatic studies such as inclusion criteria, different levels of focus on internal and external validity including the method of treatment delivery. The pragmatic approach is more representative of actual clinical care and demonstrates that when clinicians are allowed to use their decision-making and expertise, manipulation and mobilization have similar outcomes. In contrast, when clinician choice is removed, as in the prescriptive approach, which is not a true representation of actual clinical practice, a moderate effect size was observed in favor of manipulation. However, this type of study design is not actually representative of the method in which clinicians currently practice and in such the results may not be generalizable to actual clinical practice.

The included prescriptive studies had less risk of bias than the pragmatic approaches suggesting higher levels of internal validity. This may be reflective of the design nuances associated with pragmatic trials, which

Figure 4. Prescriptive mobilization vs. manipulation pain outcomes.

Figure 5. Prescriptive mobilization vs. manipulation disability outcomes.

are Phase III in orientation, are designed to reflect a true clinical practice setting, and devote greater attention to external validity. Mechanistically, under controlled situations, it does appear that manipulation has greater

benefit than mobilization for pain reduction. Indeed, one could argue that under less control (in pragmatic studies) some of the effect of manipulation may be lost through the interactions germane to a normal clinical setting (e.g.

Figure 6. Pragmatic mobilization vs. manipulation pain outcomes.

Figure 7. Pragmatic mobilization vs. manipulation disability outcomes.

attrition of patients, compliance, technique dosage and response) resulting in no difference between treatment techniques. It is worth noting that the prescriptive study results may also be reflective of sampling bias. For example, Cleland et al. [15] only selected subjects for inclusion criteria if they satisfied a clinical prediction rule [43]. We view these findings as two of the most interesting results of the systematic review, which require further investigation.

Strengths and limitations of the review

Strengths of this review include contacting corresponding authors on studies we included in this review to determine if we had missed any potentially relevant studies. We also used the previously validated Cochrane Risk of Bias Tool in assessing internal validity of the included research and statistical pooling of all but one of the identified relevant studies. However, due to the nature

of our question, this review does carry some limitations. First, we only searched two databases. It is possible that other databases might have revealed other studies relevant to the current systematic review. Also, a limited number (13) of available RCT's comparing manipulation to mobilization techniques with a low risk of bias score were available as it is impossible to blind the provider of the specific technique performed. We also were unable to include the Hurwitz et al. [31] study in the forest plots as adequate data were not provided in the article. Additionally, we included studies from various manual practitioners (e.g. physical therapy, chiropractors) and the literature search criteria included only English articles, which means we may not have captured additional studies in differing languages.

Conclusion

The results of this systematic review and meta-analysis suggest studies that used a prescriptive approach found manipulation to be superior to mobilization at most time points for individuals with neck and mechanical back pain. However, this design type is not entirely representative of actual clinical practice and removes any clinical decision-making which potentially could impact the effectiveness of either mobilization or manipulation. When clinicians had a choice in the segment targeted and technique used there was no significant difference in pain and disability outcome scores between patients treated with manipulation and mobilization. This suggests that when mobilization is performed in the exact same fashion as it would be in actual clinical practice it may be just as useful a technique as manipulation.

Disclosure statement

No potential conflict of interest was reported by the authors.

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