



The Effectiveness of Manual Therapy and Exercise Therapy in Treating Non-specific Neck Pain Patients

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Authors' contributions

This work was carried out in collaboration between all authors. Authors AAA, YHA and SAA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors S. S. Alanazi and AHA managed the analyses of the study. Authors AMA and S. S. Alshwaiman managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Background: Non-specific neck pain (NS-NP) is a common disabling condition. Pain, stiffness, tenderness and a restricted range of motion are the most common symptoms observed on the physical examination of an NS-NP patient. Manual therapy (MT) and exercise are treatments commonly used for this population. However, the effectiveness of those treatments in the short and long term is questionable.

Objectives: This systematic review aims to evaluate the effect of MT and/or exercise therapy on the pain and disability caused by NS-NP and to find the best available evidence from the literature.

Study Design: A systematic review of the literature (narrative synthesis).

Search Strategy: An inclusive search of different electronic databases (MEDLINE, CINAHL, PEDro, Science Direct and CENTRAL) was conducted to find the most relevant randomised

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controlled trials (RCTs) to satisfy the inclusion criteria of the review. The reference lists of relevant studies were also searched to find yet more relevant studies.

Means of Analysis: The methodological quality of the RCTs included was assessed using the PEDro scale. All the included trials were analysed qualitatively (narrative synthesis). The assessment of the methodology of each trial was conducted by a single reviewer.

Main Results: Twenty-five RCTs were eligible for inclusion in this review (13 trials for exercise therapy and 12 for MT). The total number of study participants was 3,422. The mean age of participants was 44. The mean sample size was 137. The methodological quality of the trials was high, except for two trials assessed as being of low quality (a score of 5 on the PEDro scale). This systematic review found strong evidence supporting the following interventions: strengthening exercises in the long term, and both HVLA thoracic manipulation and cervical mobilisation in the short term. Moderate evidence was found to support the following interventions: a combination of upper and middle thoracic manipulation and cervical mobilisation in the short term, a combination of cervical thrust manipulation and exercise in the intermediate term, neck stabilisation exercises in combination with physical therapy modalities in the intermediate term, and a combination of upper cervical and upper thoracic manipulation again in the short term.

Conclusion: Within the limitations of this systematic review, both MT and exercise therapy showed beneficial effects on NP pain and disability in the short term. However, the efficacy of MT on disability in the long term needs further investigation.

Keywords: Exercise therapy; manipulation; mobilisation; narrative synthesis; NS-NP; non-specific neck pain.

1. INTRODUCTION

Neck pain (NP) is a common musculoskeletal disorder and a major contributor to disability globally [1]. It is one of the four most commonly reported musculoskeletal disorders, being second only to lower back pain (LBP) [2,3]. [4] suggest that the majority of people may suffer from some degree of NP in their lifetime. Physical therapy is usually the first treatment of choice for patients with mechanical, idiopathic, insidious NP [5]. Manual therapy (MT) and exercise therapy, in particular, are considered the most common conservative interventions used in clinical settings with this population [5]. Yet, there is a lack of knowledge regarding the efficacy of those treatments for the NP population [6]. This systematic literature review presents results for the efficacy of MT and/or exercise therapy in the treatment of non-specific neck pain (NS-NP).

1.1 Effectiveness of Manual Therapy and Exercise in Previous Systematic Reviews

The effectiveness of the aforementioned interventions has been investigated in numerous systematic reviews [7,8,9,10,11,12,13,14, 15,16]. However, to date, there is only one systematic review that has directly compared exercise therapy with SMT effectiveness in the

same context [12]. Although numerous systematic reviews have been conducted to examine the effect of MT and exercise therapy on NS-NP, the trials included in those reviews involved patients with different conditions in addition to NS-NP, such as whiplash-associated disorders (WAD), radiculopathy and NP accompanied with other conditions (e.g. lower-back pain, shoulder pain, cervicogenic headache and dizziness) [6].

[12] conducted a systematic review with the aim of evaluating the efficacy of MT and exercise for NS-NP using a range of outcomes (pain, function/disability, quality of life, global perceived effect and patient satisfaction). Within that review, 17 randomised controlled trials were assessed for their methodological quality. The trials selected in that review compared MT and exercise to: a placebo; a waiting list/ no treatment control; an adjunct treatment; or another treatment. Ultimately, this review found high-quality evidence to suggest that the use of SMT or mobilisation in combination with exercise results in greater pain reduction in the short term than exercise alone, but no differences in the long run across multiple outcomes for (sub)acute/chronic NP. They also found moderate quality evidence supporting the use of SMT or mobilisation in combination with exercise rather than the use of SMT or mobilisation alone for chronic NP. However, the aforementioned study included a sample of patients with

radiculopathy and cervicogenic headache, which is beyond the scope of our review.

[15] conducted a systematic review to examine the efficacy of MT with or without exercise in the treatment of NS-NP using pain intensity and disability as outcome measures. Twenty-seven trials of cervical and thoracic manual therapies were included. The majority of the trials included involved NP patients of any duration. The main results of this review support the use of MT in the NS-NP population to reduce pain and improve function. This study also recommends the use of MT in combination with exercise. However, a weakness of this study is that most of the trials included in it investigated multimodal interventions, including MT. Only two trials compared single MT intervention with another intervention.

[1] conducted a Cochrane review to examine the efficacy of therapeutic exercises on the NS-NP population using a range of outcomes (pain, function, patient satisfaction, quality of life and global perceived effect). Twenty-one trials with different exercise forms were included. This review found that the use of neck stretching and strengthening exercises was beneficial for chronic MNP patients in the short and long term. This study also found no evidence for the efficacy of upper extremity strengthening exercises for NP. This review included only trials with a control group, which may increase the strength of its conclusion [17].

[11] conducted a Cochrane review to examine the impact of manipulation and mobilisation on pain, disability, patient satisfaction, quality of life and global perceived effect on the NS-NP population. Twenty-seven RCTs with 1,522 participants were included in this review. They found that cervical manipulation and mobilisation have comparable effects in terms of pain reduction and functional improvement. They also found that thoracic manipulation (either alone or combined with electrothermal modalities) may reduce pain and disability. This review included only RCTs, which may strengthen its findings [18].

[16] conducted a systematic review to evaluate and establish evidence for the effectiveness of manipulation and mobilisation in the treatment of NS-NP using the following outcomes: pain intensity, function, range of motion, global perceived improvement and pressure pain threshold. Five RCTs were included in this

review. This review, however, could not make a definitive statement regarding the efficacy of those interventions due to the limited number and poor methodological quality of the studies included.

However, all the aforementioned systematic reviews included trials with heterogeneous patient populations. To have better estimates of the efficacy of an intervention for NS-NP, the sample group of participants should focus strictly on NS-NP patients and exclude any other conditions (e.g. WAD, headache, dizziness, back pain, radiculopathy, and shoulder pain). That is because these conditions are not homogeneous in that they have different clinical presentations and are also believed to have different mechanisms and to respond differently to different interventions, a fact that might limit the conclusions of those RCTs [15].

1.2 Research Objectives

This review seeks to establish, from the available literature, whether MT (particularly upper spinal manipulation and mobilisation) and exercise therapy are effective interventions to treat NS-NP. The research objectives are as follows:

- 1) To evaluate the methodological quality of recently published articles, starting from 2000 and continuing up to 2013, on the efficacy of MT and/or exercise therapy for NS-NP.
- 2) To determine the short- and long-term effects of MT and therapeutic exercise, either in combination or individually, on pain intensity and disability among the population of NS-NP.

The focus of this review is on studies that have discussed MT and exercise therapy for NS-NP. Critical analysis of the current literature will help in identifying and expressing the best treatment approach that will help to inform clinical practice. By completion of this piece of research, a conclusion will be reached with regard to the efficacy of the various treatments for NP patients as well as a suggestion for the best approach to the treatment of NS-NP.

2. METHODS

2.1 Study Design

This study is a systematic literature review, which is a form of secondary study, to identify and

summarise the best contemporary available literature on the efficacy of MT and exercise therapy for NS-NP [19].

2.2 Search Strategy

The search strategy was designed to access all relevant published materials from electronic databases. The first stage was a limited search of the CINAHL and Medline databases to identify relevant keywords contained in the title, abstract and subject description. Then, terms identified in this way, in addition to their synonyms, were used for an extensive search of the literature. The final stage was to use reference lists and bibliographies from the identified studies in a further search for relevant studies. Full copies of potentially relevant papers were retrieved for assessment.

The following bibliographic databases were used to carry out the electronic search to identify potentially relevant papers: Ovid MEDLINE, CINAHL, CENTRAL (Cochrane Central Register of Clinical Trials), Science Direct and PEDro (Physiotherapy Evidence Databases). All the aforementioned electronic databases were searched from January 2000 to July 2013. A medical subject heading (MeSH) or keywords were utilised to make the search more accurate. Almost the same terms were used in an electronic search of all the databases, except for PEDro database which was searched separately. The search terms are presented in Appendix I (Tables 2.1 and 2.2).

2.3 Inclusion Criteria

Appropriate inclusion and exclusion criteria guided the selection of relevant papers. Moreover, in order to minimize selection bias, it is essential to restrict inclusion in the study to studies that have a defined diagnosis or specific characteristics to make the inclusion criteria as focused as specifically possible [20].

2.3.1 Types of participants

Clinical trials were included if they met the following criteria:

- Study sample consists of patients complaining of NS-NP or MNP of any duration (acute, subacute or chronic). Because there are different explanations of NP subgroups, the study sample was not restricted to specific subgroups of NP to

avoid problems that might arise as a result of this.

- The minimum age of participants (male or female) at the baseline is 18 years.
- Patients have received either MT or exercise treatment or a combination of both.

2.3.2 Types of trials

- This review considers only randomised controlled trials (RCTs). RCTs are considered to be the most vigorous methodology for investigating cause and effect relationships and the efficacy of intervention [21]. Furthermore, [18] describe a RCT as "the gold standard" in healthcare research, because of the ability of RCTs to determine the effectiveness of treatment intervention.
- Studies are published in the English language, but not limited to any particular country, from January 2000 until July 2013.
- Studies should aim to evaluate the effectiveness of SMT and/or exercise on patients suffering from NS-NP of any duration.
- A full copy of the study should be available for the review process.

2.3.3 Types of interventions

- Studies that examined the effects of MT (including cervical and thoracic manipulations or mobilisations) on NS-NP are included.
- Studies that investigated the effect of exercise therapy (such as specific neck exercises, shoulder exercises, active exercise, stretching, strengthening, postural, functional, stabilisation, and proprioception exercises) on NS-NP are included.

2.3.4 Types of comparisons

As one of the previously stated objectives is to find the best available evidence for the efficacy of MT and exercise on NP, all types of comparisons are considered when selecting trials. These include the following:

- a) Controls:
 - Sham or placebo;
 - No treatment or waiting list.

- b) Another treatment:
 - MT or exercise versus another intervention;
 - Exercise and/or MT plus another intervention versus that same intervention.
- c) Exercise and/or MT plus another intervention versus exercise or MT.
- d) A form of exercise versus another form of exercise.

2.3.5 Types of outcome measures

A study was included if it used the following primary outcome measures of interest:

- Pain intensity.
- Measures of function/disability (including but not limited to neck disability index, activities of daily living, return to work and sick leave).

These two outcomes were extensively used as primary outcomes to be measured in the literature.

2.4 Exclusion Criteria

Clinical studies failing to address the research objectives were rejected based upon the following criteria:

- A study was excluded if it involved subjects with any neurological symptoms, whiplash, radiculopathy, or cervicogenic headache, because their response to treatment is different [15].
- Any study not clearly stating the type of intervention used.
- Chiropractic or osteopathic studies that investigated instrumental spinal manipulation, because this review is focusing on manual therapies, as mentioned previously.
- Studies that investigated outcomes different from those outlined above.
- Any study design that was not an RCT (case studies, non-experimental studies and other designs, except clinical RCTs).
- Studies not published in English.

2.5 Studies Selection

Potentially relevant papers identified by the search strategy were examined for eligibility

against the inclusion and exclusion criteria. The selection of studies went through four stages. The first step was to identify the studies via a database search and a reference search. The second step was the removal of duplicates. Then, titles and abstracts were screened. The last step was a full assessment of articles in order to make a final decision regarding the inclusion of articles in the review. The steps are illustrated in Fig. 1 (see appendix III: PRISMA statement diagram). Each of the papers selected for this review offers relevant information about the efficacy of exercise therapy and MT for patients who are suffering from NS-NP.

2.6 Data Extraction

A description of the results of search strategies is provided according to the number of trials identified, and the sources from which they were obtained. Moreover, a list of excluded trials is also reported, plus the reasons for their exclusion (see Appendix II).

Details of the risk of bias assessment are also presented in a table (see Appendix I Table 4.1) and summarised within the literature review.

2.7 Minimisation of Bias in the Literature Review

There are numerous ways that bias can occur in the process of reviewing literature. In this review, every effort was made to eliminate all types of bias, including: publication bias, bias in the location of studies and biased inclusion criteria [22].

To eliminate publication bias, various electronic databases were used for the purpose of searching all available publications for articles, regardless of type. To eliminate bias in the location of studies, attention was paid to clear studies in similar environments or settings as far as possible. Finally, in order to avoid bias in inclusion criteria, studies were not chosen on the basis of their ability to support a specific point or conclusion. Rather, studies were selected if they were relevant to address the key points of this review.

2.8 Methods Assessing the Risk of Bias

In order to ensure that this review was carried out with minimal bias, an attempt was made to avoid any personal judgement of the chosen studies by using tools with objective criteria to

assess their quality and validity. Thus, the risk of bias when including trials was assessed using the PEDro scale and all trials were assessed by a single reviewer.

Each item of the PEDro scale was scored as either present (1) or absent (0) to reach a score out of 10 by summation. The first criterion of the PEDro scale was not added to the total score because it relates to external validity [23]. The validity and reliability of the PEDro scale were examined by [24] and [23]. Both studies reported that the PEDro scale is a valid and reliable scale suitable for use in assessing the methodological quality of trials. [23] suggest that the PEDro scale is sufficiently reliable to encourage its use in the systematic reviewing of physical therapy RCTs.

A few steps were followed to assess the risk of bias. Initially, each article was read and analysed separately. Then, for every criterion of the PEDro scale, every item was judged based on the opinion of the reviewer to reach a final score out of 11. Finally, the assessment of the articles was revised to make sure that every article was given an appropriate score. Each article scoring 6 or more was considered as having a low risk of bias, whereas those articles with a total score of 5 or less were considered to carry a high risk of bias [25].

2.9 Data Analysis

All data extracted from the selected trials were analysed qualitatively (narrative synthesis). Narrative synthesis uses non-statistical (subjective) methods to synthesise individual trial results [26]. This helps to make sense of the extracted data and their characteristics, as well as the final results of each study, in addition to significant similarities and differences identified in those studies. Data were tabulated in order to decide whether MT or exercise therapy were effective treatments for NS-NP patients. [27] acknowledge that “decisions about how data are to be grouped and tabulated should be based on the questions that the review is addressing”. The findings and conclusions of the studies, with regard to the effect of MT and exercise therapy on pain intensity and functional disability resulting from NS-NP, were analysed.

To facilitate a more valid recommendation, the quality of the evidence presented has to be taken into account when analysing study results [28]. According to [29], the level of evidence should be categorised into strong, moderate, limited,

conflicting and no evidence (see Appendix I (Tables 3.1 & 3.2)). Strong evidence is supported by consistent findings from various RCTs of high quality. Moderate evidence is supported by consistent findings from a variety of low quality RCTs or only one RCT of high quality. Limited evidence is supported by only one RCT of low quality. Conflicting evidence is supported by inconsistent findings from a number of RCTs [29]. This categorisation was strictly adhered to in the analysis of study findings.

3. RESULTS

3.1 Search Strategy Outcome

An electronic search of the MEDLINE, CINAHL, PEDro, CENTRAL and Science Direct databases produced 78 initially relevant studies. A search of the bibliographies and reference lists of the identified studies produced another 23 relevant studies. The total of identified studies was 93 after removing duplicates. Thirty-two articles were excluded as ineligible after reading their titles and abstracts. Then, the full texts of the included trials were assessed for their eligibility. This led to excluding 36 articles for various reasons (see Appendix II). Ultimately, 25 reports of RCTs were considered for inclusion in the body of this review for a methodological quality assessment. The results of search strategy are illustrated in Fig. 1 (see appendix III).

3.2 Characteristics of the Included Trials

All 25 included trials were heterogeneous in terms of sample size, intervention used, duration of the follow-up and methodological quality. And they all satisfy the inclusion criteria of this review.

The sample size of the included studies ranged from 24 to 393 and the mean of the sample sizes of the included trials was 137. The follow-up duration varied among the studies. Numerous studies reported their results based upon an immediate assessment post treatment. In contrast, a large number of the included trials employed an assessment period of up to 12 months after treatment. Other studies had a follow-up period of six months while some had a follow-up period of only one week. Only one study had a follow-up period of two years.

3.3 Characteristics of the Study Populations

All the included studies were similar in terms of the diagnosis of patients included in them (they

were either NS-NP or MNP). Nevertheless, there were differences in the age of participants. The vast majority of the included trials involved patients whose age ranged between 18 and 65 years. Five studies used a sample of patients with an age range of between 20 and 65 years. Two studies involved a sample of female office workers with an age of 25 years and over. One study involved patients aged between 23 and 44 years. One study involved patients with an age of over 55 years. The overall mean age of participants in the included trials was 44.

The duration of NP symptoms of participants in the included trials varied. However, the duration of symptoms in most of the included studies was three months and over. Such duration of pain can develop into chronicity for patients [30]. Other studies included patients with symptoms of less than three months' duration. The rest of the studies included NP patients of any duration. Therefore, a combination of acute, subacute and chronic NP patients was included in this review.

Generally, study participants were mixed by gender and race. However, the vast majority of participants were female, with an overall percentage of 72 per cent. Furthermore, the participants in the majority of the included trials were recruited from European countries, including the United Kingdom, the Netherlands, Spain, Sweden, Finland and Germany. Other studies participants were recruited from the United States of America, Hong Kong and Turkey.

3.4 Characteristics of the Interventions Used in the Included Trials

3.4.1 Manual therapy (MT)

The MT techniques used in the included trials involved high-velocity low-amplitude (HVLA) thoracic and cervical manipulation and low-velocity cervical passive mobilisation within or at the limit of joint ROM.

3.4.1.1 HVLA thoracic thrust manipulation

The technique used in most of the included trials was similar, with small variations. Some studies applied HVLA thoracic thrust manipulation, with the patient lying supine, by placing a pistol grip at the level immediately below the restricted segment and asking the patient to take a deep breath and perform an HVLA thrust during exhalation. One study used seated distraction

when doing thrust manipulation. One study used both of the aforementioned positions to treat the upper, middle and lower thoracic spine. Other studies did not state what technique was used for the manipulation.

3.4.1.2 HVLA cervical thrust manipulation

Mid-cervical and cervicothoracic junction manipulations were applied to patients in numerous studies. The technique of mid-cervical manipulation was performed with the patient in a supine position by applying contact using the index finger over the posterolateral aspect of C3 (cradle hold). Then, the head of patient was taken into side flexion with contralateral rotation to produce more tension in the tissue at the contact point, then applying HVLA thrust in an medial and upward direction toward the patient's contralateral eye. Cervicothoracic junction (C7-T1) manipulation was performed with the patient in a prone position with the head and neck rotated to the right. Then, the head and neck were taken into left side flexion to produce more tension in the soft tissue, followed by applying HVLA thrust toward the right side of the patient.

3.4.1.3 Non-thrust cervical mobilisation

Some studies used low-velocity passive cervical mobilisation at multiple levels within or at the limit of joint ROM to treat segmental mobility dysfunction and improve soft tissue function.

The number of treatment sessions varied between the studies. Many studies used one treatment session because they intended to measure the immediate effect of SMT. However, the number of repetitions within a treatment session was based on audible cavitation with a maximum of two attempts for each patient. Other studies used a maximum of six treatment sessions over six weeks. One study used one session per week for three weeks, while another study used two treatment sessions. A different study used 8 sessions over a four-week period and one used five treatment sessions. Other studies did not identify the number of treatment sessions assigned to the patient.

Generally, the treatment providers in all the included MT trials were physiotherapists. One study stipulated that all the treating therapists had had to complete a 60-hour postgraduate certification programme of practical training in the use of upper cervical and upper thoracic HVLA thrust manipulation.

3.4.2 Exercise therapy

The majority of the studies that investigated exercise used general stretching and strengthening exercises for the neck and upper. Some studies used a specific form of exercise such as Qigong exercises. The Qigong exercise programme consists of 14 groups of exercises. These exercise groups include general warming up, soft movements for the whole body, slow movement sequences in combination with breathing techniques and deep concentration. At the end of every session, the patient was asked to engage in relaxation, soft stretching and self-massage. One study used stabilisation exercises and the correction of posture. In this study, the patient was asked to sit in front of a mirror and find a neutral balanced position for the head and neck. Another study used the McKenzie method in addition to general exercise to provide the patient with knowledge of self-treatment in case of NP recurrence. This method of treatment is based on mechanical and symptomatic reactions on loading whereby patients receive individual treatment based upon their clinical presentation. Two studies used low-tech and high-tech rehabilitative exercises. The low-tech exercises started with warming up using a stationary bike and muscle stretching, followed by strengthening exercises for the upper limbs and dynamic neck extension, flexion and rotation exercises. The high-tech exercises were performed in similar manner but with greater intensity (load and repetitions).

The number of treatment sessions varied between the studies. Numerous studies used 12 treatment sessions. Others used 20 sessions. And some gave the patient two sessions a week for eight weeks. Others gave the patient three sessions a week for 12 weeks. One study used five sessions while another had 24 sessions over a period of 3 months. One study used ten group sessions, while another did not clearly state the number of treatment sessions.

All the included exercise therapy studies involved qualified physiotherapists giving and supervising the treatment sessions. The study of [31] stipulated that the physiotherapist had to have completed part C of the McKenzie education programme.

3.5 Outcome Measures Used in the Included Trials

All the included trials used pain and/or disability as outcome measures, as indicated in the

inclusion criteria. However, they utilised different tools to measure those outcomes. With regard to measurements of pain intensity, the vast majority of the studies used a numerical pain rating scale (NPRS). Other studies utilised a VAS. Both VAS and NPRS are valid instruments for measuring pain intensity [32,33]. However, according to [32], VAS is the most valid and cited form of pain measure.

The level of disability was measured in the included trials using different tools. However, NDI was the most popular measurement tool in those trials for measuring disability. NPQ was used in four of the included trials. Two studies used NPAD and one study designed a questionnaire with 8 questions to measure the level of disability. All the aforementioned disability measures have good psychometric properties [34]. However, NDI may be superior to the others. According to [32], NDI is the most valid of the tools reported. In addition, it has been revalidated in a wide range of studies for the purpose of NP patient evaluation [34].

3.6 Methodological Quality Assessment

3.6.1 Outcome of the risk of bias assessment

All the included trials were assessed for their methodological quality utilising the PEDro scale. The majority of the assessed articles were considered as having low risk of bias, with four articles scoring 6 out of 10, nine articles scoring 7 out of 10, nine articles scoring 8 out of 10 and two articles scoring 9 out of 10. One of the assessed articles scored 5 out of 10 and was thus considered as carrying high risk of bias. The outcome of the assessment of risk of bias is presented in table 4.1 (see Appendix I).

3.6.2 Randomisation and concealed allocation

All the included trials performed randomisation and concealed allocation except for four studies which lacked concealment of allocation.

3.6.3 Similarity of baseline characteristics

All the included trials had similar baseline characteristics.

3.6.4 Blinding of subject, therapist and assessor

Only three studies had sufficient blinding of subjects as to the allocation of treatment.

Therapist blinding was also inadequate in most of the studies with only two studies sufficiently blinded therapists to the allocation of treatment. However, the lack of blinding subjects or therapists in the majority of the included trials might be attributed to the difficulty of blinding subjects and therapists to treatment allocation in a physiotherapy setting [25]. In contrast, blinding of assessors was adequate in most of the included trials with only ten trials lacking blinding of the assessor.

3.6.5 Adequacy of follow-up

The vast majority of the trials had adequate follow-up. However, some studies had follow-up losses.

3.6.6 Intention to treat analysis

Only four studies paid inadequate intention to treatment analysis, whereas the rest of the included trials did pay adequate intention to treatment analysis.

3.6.7 Sufficiency of sample size

A few of the included studies had quite a limited sample size, only 24 or 36 participants. Furthermore, a large number of the included trials had an insufficient number of patients in their treatment groups (<70 per arm).

3.7 The Effect of Exercise Therapy on NS-NP

3.7.1 Exercise therapy versus varied comparisons

The study of [31], with a sample size of 77, long-term follow-up and a low risk of bias (PEDro score = 6) compared general exercise to McKenzie treatment and a control group (ultrasound at lowest intensity). This study found significant reductions in pain ($P<0.0001$) and disability ($P<0.01-0.001$) in all three groups during the treatment period (12 months) but no significant differences were found between the groups. This study could not provide definite evidence for treatment efficacy in patients with NP.

Another study, with a sample size of 180, long-term follow up and a low risk of bias (PEDro score= 7) compared strengthening exercises for the neck muscles with endurance exercises and a control group [35]. This study found that the

two training groups had significant reductions in pain and disability compared with the control group at the 12-month follow-up point ($P<0.001$). However, no significant differences were found between the two groups of exercises. The study concluded that both strengthening and endurance exercises are effective in reducing pain and disability in the long term.

The study of [36], with a sample size of 393, long-term follow-up and a low risk of bias (PEDro score = 8), compared dynamic muscle training and relaxation training to a control group. This study found no significant improvements in pain and disability over 12 months among the training groups compared with the control group. The study concluded that neither dynamic training nor relaxation could be effective for NP.

The study of [37], with a sample size of 60, long-term follow-up and a low risk of bias (PEDro score = 6), compared neck stabilisation exercises to isometric stretching exercises and electrotherapy modalities (TENS, ultrasound and IRR). This study found significant reductions in pain intensity in all groups at the 6-month follow-up point ($P<0.05$). The group that completed stabilisation exercises maintained this improvement at 9 and 12 months. The study also found a significant decrease in disability among the group doing stabilisation exercises over the treatment period ($P<0.05$). This study concluded that neck stabilisation exercises are superior to isometric exercises for treating NP.

3.7.2 Exercise therapy versus other treatments

The study of [38], with a sample size of 151, long-term follow-up and a low risk of bias (PEDro score = 6), compared a group on a neck and upper limb exercise programme (GET) to usual physiotherapy (UP) (MT, neural and muscle treatments, modalities, individualised exercise, advice and education). This study found that the group on GET saw a 1.5% improvement in the mean disability score while the group on UP saw an improvement in the mean disability score of 5.1%. However, treatment effects were found to be non-significant ($P=0.74$). The study of [39], with a sample size of 145, a 6-month follow-up and a low risk of bias (PEDro score= 7), compared a neck exercise programme (strengthening of the deep neck muscles) to IRR. In terms of disability, this study found that both groups saw a significant improvement in disability scores after 6 weeks of treatment

($P < 0.001$), and the exercise group was significantly better than the control group ($P = 0.03$). However, after 6 months of treatment, the differences between the two groups were found to be non-significant. With regard to pain intensity, there were more significant reductions in pain intensity after 6 weeks in the exercise group compared to the control group ($P = 0.01$). Those reductions in pain were maintained at 6 months ($P < 0.01$).

3.7.3 A combination of exercise therapy and SMT versus exercise therapy alone and SMT alone

Two studies were found, with a sample size of 191, long-term follow-up and a low risk of bias (PEDro score = 7) comparing SMT alone and high-tech rehabilitative exercises alone to a combination of SMT and low-tech exercises [40,41]. Both studies found significant reductions in pain intensity over the treatment period for the two exercise groups ($P = 0.02$). However, no significant improvements were found in disability ($P = 0.13$). Both studies concluded that rehabilitative exercises, whether alone or in combination with SMT, are more effective in reducing pain than SMT alone.

3.7.4 Qigong exercises versus various comparisons

Two studies were found comparing Qigong exercises (warming up, whole body soft movements combined with breathing techniques and deep concentration, followed by relaxation, soft stretching and self-massage) to standard exercises (stretching and strengthening) and no treatment [42,43]. The results of the two studies were different. The study of [43], with a sample size of 123, a 6-month follow-up and a low risk of bias (PEDro score = 7) demonstrated the superiority of Qigong exercises over no treatment in terms of pain intensity ($P = 0.002$), whereas the study of [42], with a sample size of 121, a 6-month follow-up and a high risk of bias (PEDro score = 5), found no significant difference between the Qigong exercises and no treatment groups ($P = 0.099$). Both studies reported that there was no significant difference between Qigong exercises and standard exercises ($P = 0.092$ and $P = 0.699$, respectively).

The study of [44], with a sample size of 122, a long-term follow-up and a low risk of bias (PEDro score = 7), compared Qigong exercises to standard exercises. This study found significant

improvements in pain and disability immediately after treatment in both groups. Those improvements were maintained at 6-month and 12-month follow-up points. However, no significant differences were found between the groups. This study concluded that both treatments are effective in reducing pain and disability in the long term.

3.7.5 Exercise therapy versus the same treatment in both arms

The study of [45], with a sample size of 101, a long-term follow-up and a low risk of bias (PEDro score = 7), compared a combination of strengthening and stretching exercises to stretching exercise alone. The study found no significant differences between the treatment groups in terms of pain and disability. However, there was a significant decrease in disability in both groups at the 12-month follow up point ($P < 0.001$). This study concluded that both training regimens may be effective in achieving long-term improvement.

3.7.6 A combination of exercise therapy and SMT versus exercise therapy alone and home exercises and advice

The study of [46], with a sample size of 270, a long-term follow-up and a low risk of bias (PEDro score = 8), compared low technology exercises with and without SMT to home exercises and advice. This study found significant differences between the groups in terms of pain and disability at the 12-week follow-up point in favour of exercises with and without SMT ($P = 0.001$). However, there were no significant differences between the groups at a 52-week follow-up point ($P > 0.05$). This study concluded that exercises with and without SMT are beneficial in the short term.

3.8 The Effect of MT on NS-NP

3.8.1 HVLA thoracic spine thrust manipulation versus placebo

Two studies were found comparing high-velocity low-amplitude (HVLA) thoracic-thrust manipulation to a placebo [47,48]. The placebo intervention used in both studies was similar in that both studies applied an open hand at the same level with no HVLA manoeuvre during exhalation. Both studies showed that thoracic - thrust manipulation reduces pain immediately after treatment. However, the study of [47], with a sample size of 101, a short-term follow-up and a

low risk of bias (PEDro score = 6), revealed that the change in VAS score between the experimental and control groups was not statistically significant ($P=0.961$). On the other hand, the study of [48], with a sample size of 36, a short-term follow-up and a low risk of bias (PEDro score = 8), showed that the difference in VAS change score between manipulation and placebo groups was significant in favour of the manipulation group ($P<0.01$).

3.8.2 HVLA thoracic spine thrust manipulation versus the same treatment in both arms

The study of [49], with a sample size of 45, a short-term follow-up and a low risk of bias (PEDro score = 9), compared thoracic thrust manipulation in combination with electro-thermal therapy (IRR and TENS) to the same electro-thermal therapy. The study of [50], with a sample size of 120, a 6-month follow-up and a low risk of bias (PEDro score = 8), examined thoracic thrust with same treatment carried out in both arms (IRR and advice). Both studies found significant reductions in pain among the experimental groups at all the assessment follow-up points (immediately post treatment ($P=0.001$), at 3 months ($P=0.002$) and 6 months ($P=0.004$)). With regard to disability, there were only significant reductions at the immediate post-treatment assessment points ($P<0.001$ and $P=0.016$, respectively).

The study of [51], with a sample size of 64, a short-term follow-up and a low risk of bias (PEDro score = 7), compared upper and middle thoracic thrust manipulation in combination with cervical mobilisation and exercises to cervical mobilisation and exercises. This study found significant reductions in pain and disability among the experimental group at a 1-week follow up point ($P<0.001$). This study concluded that thoracic thrust manipulation and cervical mobilisation in addition to exercises is an effective treatment for NP in the short term.

3.8.3 Cervical mobilisation versus various comparisons

Two studies were found, with a sample size of 183, a long-term follow-up and a low risk of bias (PEDro score = 8), comparing cervical mobilisation to active exercises (strengthening, postural, stretching, and relaxation exercises) and advice [52,53]. In terms of pain intensity, both studies found significant differences

between treatments groups at a 7-week follow-up point in favour of mobilisation ($P=0.01$). With regard to disability, small (not statistically significant) differences were found between treatment groups at a 7-week follow-up point in favour of mobilisation ($P=0.06$). At 13- and 52-week follow-up points, there were only small differences between the three treatment groups. Both studies concluded that mobilisation is an effective treatment for reducing NP in the short term.

3.8.4 Cervical thrust manipulation versus an alternative treatment

The study of [5], with a sample size of 80, a short-term follow-up and a low risk of bias (PEDro score = 9), compared HVLA cervical thrust manipulation to Kinesio taping. Over the one-week period of this study, similar decreases in pain and disability were found in both treatment groups. Those decreases were not considered to be statistically significant ($P=0.447$ for pain, $P=0.736$ for disability).

3.8.5 Spinal manipulation versus varied comparisons

The study of [54], with a sample size of 272, a long-term follow-up and a low risk of bias (PEDro score = 7), compared SMT (thrust and non-thrust) to medication, home exercises and advice. They found that SMT resulted in statistically significant reductions in pain (at 12-, 26- and 52-week follow-up points) compared to that of medication but not to home exercises ($P=0.001$). Similarly, significant reductions were found in disability in favour of SMT ($P<0.001$). This study concluded that SMT is more effective than medication in treating NP in both the short and long term.

3.8.6 Cervical and thoracic manipulation versus mobilisation

The study of [3], with a sample size of 107, a short-term follow-up and a low risk of bias (PEDro score = 8), compared cervical and thoracic thrust to no thrust manipulation. This study found significant reductions in pain (2.3 points on the PNRS compared to 4.4) and disability (10.8 points on the NDI compared to 18.4) at a 48-hour follow-up point in favour of thrust manipulation ($P<0.001$). This study concluded that a combination of upper cervical and upper thoracic thrust manipulation is more effective than mobilisation for a short-term effect.

3.8.7 Cervical thrust manipulation versus thoracic thrust manipulation

The study of [55], with a sample size of 24, a 6-month follow-up and a low risk of bias (PEDro score = 7), compared cervical thrust manipulation and exercise to thoracic thrust manipulation and exercises. This study found significant reductions in pain ($P \leq 0.003$) and disability ($P \leq 0.001$) among the cervical group at 1-week, 4-week and 6-month follow-up points from the start of treatment. This study concluded that a combination of cervical thrust manipulation and exercises is more effective than thoracic thrust manipulation and exercises in treating NP.

3.8.8 Cervical thrust manipulation versus cervical, cervico-thoracic and thoracic thrust manipulation

The study of [56], with a sample size of 82, a short-term follow-up and a low risk of bias (PEDro score = 8), compared cervical thrust manipulation to cervical, cervico-thoracic and thoracic thrust manipulation. In terms of pain intensity, this study found similar non-significant decreases in both groups ($P = 0.612$). In contrast, a significant reduction in disability was found in favour of the cervical, cervico-thoracic and thoracic groups ($P = 0.022$).

3.9 Excluded Trials

A total of 36 articles did not satisfy the inclusion criteria of the review. Most of the excluded articles failed to satisfy the outcome criterion [57,58,59,17,60,61,62,63,64,65,66,67]. Some of the excluded trials investigated NP with neurological symptoms [68,69,70]. Other studies were excluded because they looked at spinal pain (lumbar and cervical) [71,72,73]. Two studies were excluded because they aimed to examine the rate of change in neck-muscle strength after training [74,75]. Two other studies were excluded because they did not clearly state the age of the participants [76,77]. Other studies were related to chiropractic and osteopathy [78,79,80,81]. Two studies did not state which type of MT was used [82,83] (see appendix II).

4. DISCUSSION

4.1 Summary of Key Findings

Twenty-five RCTs were included in the body of this review. The total number of participants in studies of exercise therapy was 2,125, whereas

the total number of participants in MT studies was 1,297. The vast majority of participants in all the included trials were female and middle-aged. The vast majority of included trials were considered to be of high quality with only two articles of low quality. The majority of trials used NPRS and NDI as outcome measures for measuring pain intensity and disability. The included trials were generally heterogeneous in terms of participants' characteristics, sample size, intervention parameters and methodological quality.

With regard to the effect of exercise therapy on NS-NP, there is strong evidence to support the use of neck-muscle strengthening exercises to reduce pain and disability in NS-NP patients in the long term, based on VAS and NDI scores [31,35]. Furthermore, there is strong evidence that Qigong exercises are comparable in their effectiveness to standard exercises for reducing pain and disability in the long term based on VAS and NDI scores [44,43]. There is also strong evidence that a combination of exercise therapy and SMT is as effective as exercise therapy alone in reducing pain for NS-NP patients in the short term, based on NPRS scores [46,41]. There is moderate evidence that neck stabilisation exercises are more effective than isometric exercises in combination with physical therapy modalities for treating NS-NP in the intermediate term [37].

In terms of the efficacy of MT for NS-NP, there is strong evidence that HVLA thoracic thrust manipulation is effective in reducing pain immediately after treatment for NS-NP patients based on NPRS scores [49,50]. There is also strong evidence that cervical mobilisation is more effective in reducing pain than exercise and advice in the short term, based on NPRS scores [53,52]. There is moderate evidence that a combination of upper and middle thoracic thrust manipulations and cervical mobilisation is more effective in reducing pain and disability than cervical mobilisation alone in the short term, based on NPRS and NDI scores [51]. Moreover, there is moderate evidence that SMT (thrust and non-thrust) is more effective than medication in reducing pain and disability in the short and long term based on NPRS and NDI scores [54]. There is moderate evidence that a combination of upper cervical and upper thoracic thrust manipulation is more effective than mobilisation in reducing pain and disability in the short term, based on NPRS and NDI scores [3]. There is moderate evidence that a combination of cervical

thrust manipulation and exercises is more effective than thoracic thrust manipulation and exercises in NS-NP patients, based on NPRS and NDI scores [55]. There is conflicting evidence that HVLA thoracic thrust manipulation is more effective in reducing pain than a placebo in NS-NP patients when assessed immediately after treatment using VAS [47,48].

4.2 Quality of the Evidence

The blinding of therapists and subjects was a major methodological limitation inherent to the included studies. This was a limitation of studies assessing exercise therapy for NS-NP. In fact, none of the trials involving exercise therapy blinded the therapist, and only two MT trials blinded the therapist. Moreover, the blinding of subjects was only conducted in three of the MT trials. The blinding of subjects is important to minimise expectation bias and to help ensure that treatments are equally credible [1]. However, it is nearly impossible to blind a physiotherapist so as to prevent identification of the allocated group of his/her patient, especially in studies related to exercise [10,25]. Furthermore, [16] suggest that "MT treatments are difficult to study in a double-blinded manner (i.e. therapists and patients blinding) and studies assessing the relative effectiveness of different manual therapies may have lower scores because blinding cannot be achieved using current designs".

There are other important issues that might affect confidence in the results of the included trials, such as the adequacy of sample size. Sixty per cent (15/25) of the trials had small sizes (<70 per arm) [1]. This might lead to underestimation of an important existing effect [84]. Concealment of treatment allocation is another issue and was inadequate in four of the included trials (16%). Concealed allocation is an important element in RCTs for eliminating selection bias [85]. The lack of concealment of treatment allocation threatens the validity of the conclusion in RCTs [86].

4.3 Level of Agreement and Disagreement with Previous Systematic Reviews

While this systematic review found strong evidence for there being no difference between using a combination of SMT and exercises and exercise therapy alone, [12] found strong evidence from three high quality trials supporting the use of SMT in combination with exercise over the use of exercise therapy alone. However, they

found no differences in a long-term follow-up. These findings are consistent with the findings of [87] and [7]. Furthermore, [9] found moderate evidence that SMT showed significant improvements among NS-NP patients when compared to a placebo in the short term, whereas this systematic review has found conflicting evidence proving that, and both studies investigated NP of any duration (acute and chronic).

In contrast, [8] found similar results in their review in that they found moderate to high quality evidence supporting the use of SMT (thrust or non-thrust) over medication for chronic NP in the short and long term. [15] also obtained similar results regarding proving the superiority of SMT over medication in improving pain and disability in the long term. The latter study also found similar results with regard to the efficacy of thoracic thrust manipulation in reducing pain immediately after treatment. In terms of the efficacy of exercise, similar results were obtained by [88,10], who found strong evidence supporting the use of dynamic strengthening exercises for the neck muscles in NS-NP patients. Likewise, [1] found low quality evidence for the beneficial effects of using strengthening exercises for treating NS-NP in the short and long term.

4.4 Limitations and Strengths of this Review

4.4.1 Limitations of this review

There are various factors that may limit the conclusion drawn by this review. One of the factors is the lack of experience in conducting a systematic review. This may be seen in the author's search for literature and identifying the main authors on this topic. Thus, some important trials might be not included, which may affect the conclusion to the review. The author may also have missed certain steps in the search strategy. Specifically, this systematic review has included only published trials. So, it may be prone to a degree of publication bias [89]. Furthermore, this review has not investigated non-English language trials which may be seen as language bias [90]. However, the high cost of professional translation of necessity led to omitting non-English trials. In addition, this review has included only a few trials (7 out of 25 trials) that compared the effect of MT and exercise therapy with control groups (placebo or sham treatment). In fact, comparing MT or exercise to no treatment is very important to establish a firm foundation for the effect of these interventions [1]. [17] suggest

that comparing a placebo or no treatment to another intervention provides a clear answer of the effectiveness of any treatment. Control groups are also important to differentiate between the real effect of treatment and the placebo effect, which cannot be eliminated, especially in MT trials [91]. However, many authors avoid using placebo controls in their trials for ethical considerations [92]. The included trials were assessed for their methodological quality by a single reviewer. This also may limit the validity of the systematic review [93]. The small sample sizes in some of the included trials may also have underestimated the effect of interventions [57]. Even though the majority of the trials used PNRS and NDI for measuring pain and disability, there were some variations in the outcome measures, which ultimately affect the standardisation. The standardisation of outcome measures used by different trials is important in seeking to achieve effective comparisons for different interventions [94].

4.4.2 Strengths of this review

Fortunately, this review does however have some important advantages, which relate to its methodology. A comprehensive search of the available electronic databases was conducted. This is important to minimise bias in a systematic review [95]. This systematic review has addressed a clearly focused question and stated clear objectives. It includes a variety of studies from different settings. In addition, the trials in this review were included based on their ability to answer the review questions, and they all have an appropriate design. All the included trials were similar in terms of their populations and the fact that they had clear objectives. This review involves only RCTs, which is an appropriate study design to answer the review questions. Also, this review has used a validated critical appraisal tool (PEDro scale) for assessing the quality of trials. The inclusion and exclusion criteria used in this review were clearly defined at the outset. The results from the trials in this review are clearly displayed and combined with relevant comparisons of the various studies. The PRISMA guidelines for systematic reviews were used to help when conducting this review [96].

5. RECOMMENDATIONS AND SUGGESTIONS FOR FUTURE RESEARCH

Future studies should include subjects and assessor blinding in order to limit the possibility

of a larger treatment effect [59]. Exercise therapy studies should consider and document the assessment of the use of applied exercises in order to determine treatment effects accurately and be able to reproduce this study [97]. In addition, more studies with specific types of exercise rather than general exercises are also needed to determine the most effective types of exercises for NS-NP patients. Additional RCTs of MT and exercise with control group comparisons and adequate sample sizes are needed to establish the primary effect of an intervention. After that, head-to-head comparisons are suggested so as to determine the superiority of one intervention over another. In order to reduce the clinical diversity in exercise and MT trials and determine the patient population that is more likely to benefit from treatment, a specific subgroup of patients with a specific age range is suggested [98].

6. CONCLUSION

This systematic review has examined the effectiveness of MT and exercise therapy for NS-NP patients. Twenty-five trials of MT and exercise were included and assessed for their methodological quality. Overall, the results of this review support the use of exercise therapy for reducing pain and disability and using MT to reduce pain in NS-NP patients. The qualitative analysis of the included trials showed strong evidence supporting the use of strengthening exercises for the neck muscles in order to reduce pain and disability in the long term, strong evidence for the efficacy of HVLA thoracic thrust manipulation in reducing pain in the short term, and strong evidence for the efficacy of using cervical mobilisation to reduce pain in the short term. However, the qualitative analysis also revealed conflicting evidence regarding the efficacy of HVLA thoracic thrust manipulation compared to a placebo treatment. The effect of MT on disability in the long term is still questionable. There is a need for high quality RCTs with control group comparisons to show the basic effect of MT and exercise for NS-NP patients.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIX I

Table 2.1. Summary of the search terms used with the electronic databases (MEDLINE, CINAHL, CENTRAL and Science direct)

Conditional key terms	Intervention key terms
“Neck pain” or “cervical pain” or “cervicalgia” or “mechanical neck pain” or “nonspecific neck pain” or “cervicodynia” or “neckache”	“manual therapy” or “manipulation” or “spinal manipulations” or “manipulative therapy” or “exerci*” or “exercise therapy” or “rehabilitation” or “strength*” or “train*” or “flexibil*” or “stretch*” or “length*” or “physical activity” or “stabili*” or “postur* correction”

Table 2.2. Terms used in the PEDro database search

Therapy	Body part	Method
(Stretching, mobilisation, manipulation, massage) or (strength training) or (skill training)	(head or neck) or (thoracic spine)	Clinical trial

Table 3.1. Levels of evidence

Strong evidence	consistent findings among multiple high quality RCTs
Moderate evidence	consistent findings among multiple low quality RCTs and/or CCTs and/or one high quality RCT
Limited evidence	one low quality RCT and/or CCT
Conflicting evidence	inconsistent findings among multiple trials (RCTs and/or CCTs)
No evidence	no RCTs or CCTs

*Consistency and quality should be clearly defined a priori
Source: (Van Tulder et al., 2003)*

Table 3.2. Quality of evidence

High	Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Source: (Guyatt et al., 2008)

Table 4.1. Assessment of risk of bias based upon the PEDro criteria

Trials list	*1/ Eligibility criteria	2/ Random allocation	3/ Concealed allocation	4/ Similarity of baseline features	5/ Subject blinding	6/ Therapist blinding	7/ Assessor blinding	8/ Adequate follow up	9/ Intention to treat analysis	10/ Between group statistical measure	11/ Point measure	Total score
McLean et al. 2013	1	1	1	1	0	0	0	0	1	1	1	6
Kjellman and Oberg 2002	1	1	1	1	0	0	0	1	0	1	1	6
Bronfort et al. 2001	1	1	1	1	0	0	1	1	1	1	1	8
Chiu et al. 2004	1	1	1	1	0	0	1	0	1	1	1	7
Ylinen et al. 2003	1	1	0	1	0	0	1	1	1	1	1	7
Viljanen et al. 2003	1	1	1	1	0	0	1	1	1	1	1	8
Dusunceli et al. 2009	1	1	0	1	0	0	1	1	0	1	1	6
Von Trott et al. 2009	1	1	0	1	0	0	0	0	1	1	1	5
Lansinger et al. 2007	1	1	1	1	0	0	0	1	1	1	1	7
Rendant et al. 2011	1	1	1	1	0	0	0	1	1	1	1	7
Hakkinen et al. 2008	1	1	0	1	0	0	1	1	1	1	1	7
Evans et al. 2012	1	1	1	1	0	0	1	1	1	1	1	8
Sillevis et al. 2010	1	1	1	1	0	0	0	1	0	1	1	6
Cleland et al. 2005	1	1	1	1	1	0	1	1	0	1	1	8
GonzalezIglesias et al. 2008	1	1	1	1	1	0	1	1	1	1	1	9
Hoving et al. 2002	1	1	1	1	0	0	1	1	1	1	1	8
Hoving et al. 2006	1	1	1	1	0	0	1	1	1	1	1	8
Masracchio et al. 2013	1	1	1	1	0	0	0	1	1	1	1	7
Saavedra-Hernandez et al. 2012	1	1	1	1	1	1	0	1	1	1	1	9
Saavedra-Hernandez et al. 2013	1	1	1	1	0	1	0	1	1	1	1	8
Bronfort et al. 2012	1	1	1	1	0	0	0	1	1	1	1	7
Cheung Lau et al. 2011	1	1	1	1	0	0	1	1	1	1	1	8
Puentedura et al. 2011	1	1	1	1	0	0	1	0	1	1	1	7
Evans et al. 2002	1	1	1	1	0	0	1	0	1	1	1	7
Dunning et al. 2012	1	1	1	1	0	0	1	1	1	1	1	8

*: not included in overall score, 0=did not satisfy the criterion, 1= satisfied the criterion

APPENDIX II

Studies eligibility

Study	Included\excluded	Reason
McLean et al 2013	in	
Kjellman and Oberg 2002	in	
Bronfort et al 2001	in	
Chiu et al 2004	in	
Ylinen et al 2003	in	
Taimela et al 2000	Ex	different outcomes
Chao Ma et al 2011	ex	(shoulder referred pain)
Salo et al 2010	ex	(different outcome)
Andersen et al 2010	ex	(musculoskeletal pain not specific to neck)
Viljanen et al 2003	In	
Salo et al 2012	ex	(different outcome HRQoL)
YLINEN et al 2006a	ex	(different aim, to evaluate rate of change in neck strength due to neck ms training)
YLINEN et al. 2006b	ex	(different aim to confirm the earlier findings of rate of change in neck strength)
Dusunceli et al 2009	In	
Zebis et al 2011	Ex	Did not clearly state the age of participants
Andersen et al 2012	Ex	Did not clearly state the age of participants
Trott et al 2009	In	
Lansinger et al 2007	In	
Rendant et al 2011	In	
Hakkinen et al 2008	In	
Evans et al 2012	In	
van Schalkwyk and Parkin-Smith 2000	ex	Chiropractic
Wood et al 2001	ex	Chiropractic
Martel et al 2011	ex	Chiropractic
Allison et al 2002	Ex	cervico-brachial pain syndrome (neurological symptoms)
Leaver et al 2010	Ex	different outcomes
Hurwitz et al 2002	ex	Chiropractic
Aquino et al 2009	Ex	Different aim
Pool et al 2006	Ex	different outcomes
Korthals-de Bos et al 2003	Ex	different outcomes

Study	Included\excluded	Reason
Häkkinen et al 2007	Ex	different outcomes (ms. Strength and mobility)
DZIEDZIC et al 2005	Ex	different outcomes
Leaver et al 2007	Ex	different outcomes
MARTÍNEZ-SEGURA et al 2012	Ex	different outcomes (PPT and cervical mobility)
Sillevis et al 2010	In	
Sillevis and Cleland 2011	ex	Secondary Analysis
Cleland et al 2005	In	
Maduro de Camargo et al 2011	Ex	different outcomes (PPT and EMG activity)
Martinez-Segura et al 2006	Ex	different outcome (active CROM)
Gonza´lez-Iglesias et al 2008	In	
McReynolds and Sheridan 2005	ex	Osteopathic
Pool et al 2010	Ex	accompanied with neurological symptoms
Hoving et al 2002	In	
Hoving et al 2006	In	
Skillgate et al 2007	Ex	mixed sample of back and neck patients
Escortell-Mayor et al 2011	Ex	did not state what type of MT used
Gemmell and Peter Miller 2010	Ex	study not completed
MASARACCHIO et al 2013	In	
SAAVEDRA-HERNÁNDEZ et al 2012	In	
SAAVEDRA-HERNÁNDEZ et al 2013	In	
Bronfort et al 2012	In	
Ylinen et al 2007	ex	(osteopathic)
Boyles et al 2010	Ex	Secondary Analysis
Murphy et al 2010	Ex	Chiropractic
Lau et al. 2011	In	
Walker et al 2008	Ex	investigated MT in general including MET and stretching tec.
Skillgate et al 2010	Ex	mixed sample of back and neck patients
PUENTEDURA et al 2011	In	
Evans et al 2002	In	
DUNNING et al 2012	In	

APPENDIX III

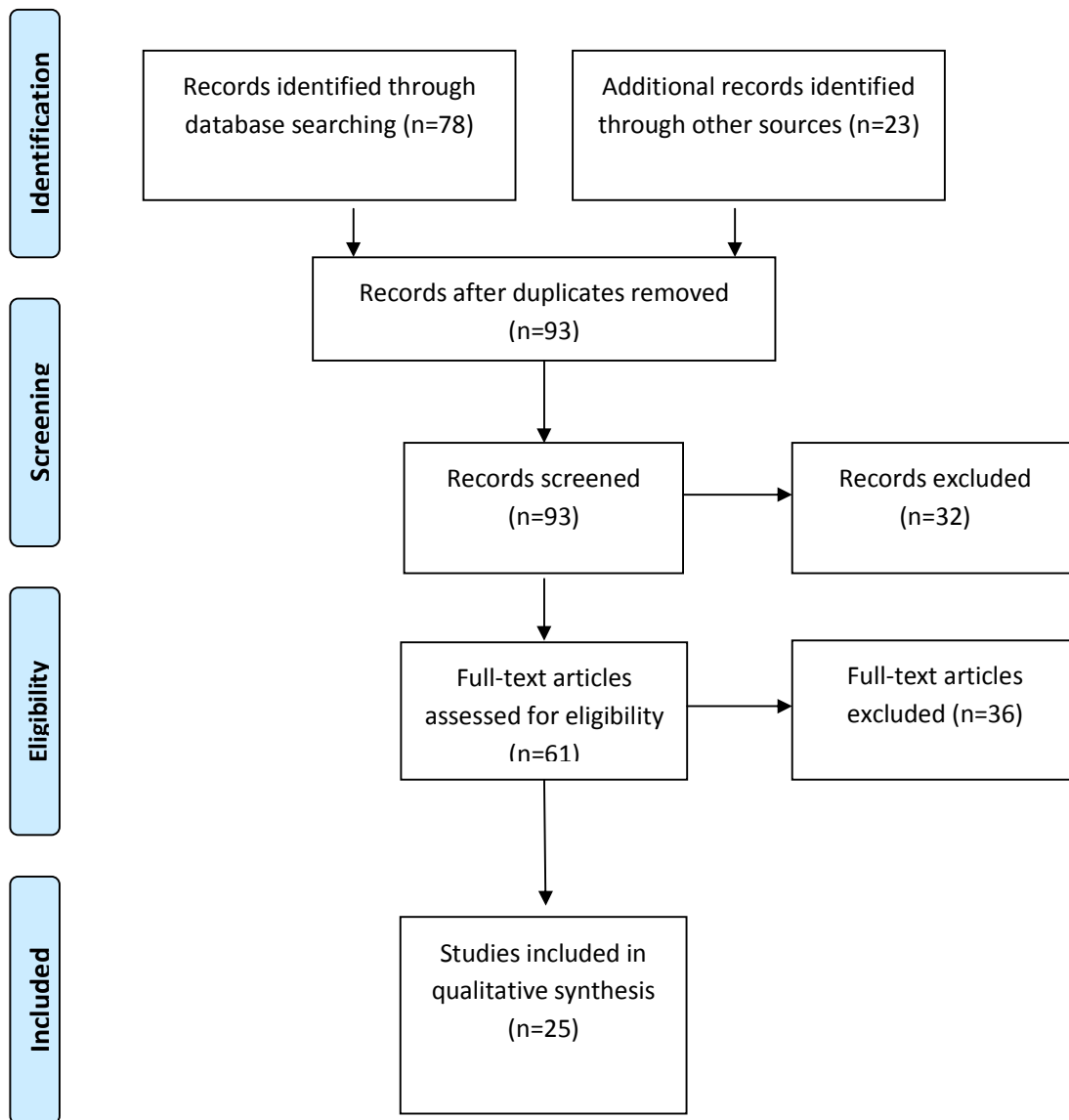


Fig. 1. PRISMA Statement Diagram

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

APPENDIX IV

List of the abbreviations

NS-NP	: Non-specific neck pain
NP	: Neck pain
CNP	: Chronic neck pain
MNP	: Mechanical neck pain
WAD	: Whiplash associated disorders
IASP	: International Association for the Study of Pain
NDI	: Neck disability index
VAS	: Visual analogue scale
NPRS	: Numerical pain rating scale
NPQ	: Northwick Park Questionnaire
MT	: Manual therapy
SMT	: Spinal manipulation therapy
ROM	: Range of motion
CROM	: Cervical range of motion
PEDro scale	: Physiotherapy Evidence Database scale
MMT	: Manual muscle test
TENS	: Transcutaneous electrical nerve stimulation
IRR	: Infra-red radiation
RCT	: Randomised controlled trial
HVLA	: High velocity low amplitude
MRI	: Magnetic resonance imaging
NPAD	: Neck Pain and Disability Scale

APPENDIX V

Summary of the studies characteristics and results

Study	Population	Intervention	Outcome	Results	conclusion
McLean et al. 2013	(n=151) NS-NP patients (90 female) either sub-acute or chronic, 18 years old and over	graded neck and upper limb exercise (GET) Vs usual PT (MT, neural and muscle treatments, modalities, individualised exercise, advice and education)	neck pain and disability (NPQ) (6 weeks, 6 months, and 12 months follow up)	at 12 month follow-up the improvement on NPQ scores was 9.1% and 9.4% respectively for the GET and UP group but treatment main effects were found to be non-significant	Both GET and UP are appropriate clinical interventions for patients with non-specific neck pain
Kjellman & Oberg 2002	(n=77) patients (53 female) with neck complaints aged 18 and over	general ex strength Vs mckenzy Vs control: ultrasound (lowest intensity)	Pain (VAS) and disability (NDI) (after treatment, 6 months, 12 months)	All three groups showed significant improvement regarding the main outcomes but there was no significant difference between the groups	this study could not provide definite evidence of treatment efficacy in patients with neck pain
Chiu et al. 2004	(n=145)patients (100 female) 20 to 65 years old with neck pain complaints lasted over three months	Exercise (deep neck muscles activation +deep neck ms. dynamic Strengthening) Vs IR (control)	Pain (NPRS), disability (NPQ) and ms. Strength (baseline, 6 weeks, 6 months)	Both groups had significant improvement in disability scores after 6 weeks of treatment and the exercise group was significantly better ,also significant group differences was found in pain at 6 month follow up	The effect of exercise was less favourable at 6 months
Ylinen et al. 2003	(n=180)female office workers patients with NS-NP of 6 months duration	Strengthening ex Vs endurance ex Vs control	pain (VAS) and disability (NDI) (baseline and 12 months)	on the one year follow up, there was significant decrease in pain levels among the two ex. groups	both exercises are effective in reducing pain and disability
Viljanen et al. 2003	(n=393) female office workers aged 30 to 60 Y/O with CNP	dynamic ms training Vs relaxation ex Vs control (ordinary activity)	Pain (NPRS) is the primary outcome and disability (8 questions designed	No significant differences between treatment groups and control group in pain intensity and disability	Dynamic muscle training and relaxation training do not lead to better improvements in neck pain compared the control group

Study	Population	Intervention	Outcome	Results	conclusion
			to measure disability), CROM, ms strength and sick leave are secondary outcomes (3, 6, 12 months)	scores	
Dusunceli et al. 2009	(n=60) patients (39 female) aged from 18 to 55 with neck pain lasted for at least 6 weeks	stabilization ex + PT Vs isometric and stretching + PT ex. Vs PT modalities	neck pain (VAS, paracetamol intake) and disability (NDI) (baseline, 1, 3, 6, 9 and 12 months)	all groups showed a significant decrease in VAS scores in first 6 months follow up, marked improvement in disability in the group of stabilisation ex + PT	neck stabilisation ex is superior to the isometric ex in combination with PT for treating neck pain
Hakkinen et al. 2008	(n=101) patients (91 female) aged 20-65 complaining of non-specific chronic neck pain	Strengthening + stretching Vs stretching ex.	Pain (VAS), disability (NDI), ms. Strength, and cervical mobility (baseline, 2, and 12 months)	No significant differences in treatment groups in neck pain and disability	No statistically significant differences in neck pain and disability were observed
Von Trott et al. 2009	(n=121) patients (115 female) aged 55 years or older with CNP	Qigong ex. Vs standard ex. (strength and flexibility ex.) Vs no treatment	Pain (VAS) and disability (NPAD) (baseline, 3, and 6 months)	there was no significant difference for the average neck pain between the qigong and the waiting list group, also no significant difference between the qigong and the exercise therapy group was observed	„,“After 3 and 6 months, they found no significant differences for neck pain, disability, and quality of life among the 3 groups
Lansinger et al. 2007	(n=122) patients (86 female) aged 18 Y/O and over with non-specific chronic neck pain	Qigong ex. Vs standard ex. (strength and stretching ex.)	Pain (VAS) and disability (NDI) (after treatment, 6 months, 12 months)	Both groups significantly improved immediately but no significant differences between groups	both treatments can be recommended for NP patients
Rendant et al. 2011	(n=123) patients (108 female) aged 20-65	Qigong ex Vs cervical rotations and	pain (VAS) and disability (NPAD)	Neck pain and disability results yielded superiority	Qigong was more effective than no treatment in treating NP

Study	Population	Intervention	Outcome	Results	conclusion
	suffering from CNP	strengthening and flexibility exercises Vs no treatment	(baseline, 3 ,and 6 months)	of qigong over no treatment and similar results in the qigong and exercise therapy groups	
Evans et al. 2012	(n=270)patients (194 female) aged 18 Y/O and over with non-specific mechanical chronic neck pain	Exercise therapy alone (low tech) Vs ET + SMT Vs home ex. + advice	pain (NPRS) and disability (NDI, SF-36) (follow ups at: week 4, 12, 26, and 52)	At 12 weeks, significant between group difference in pain and disability were found in favour of ET with and without SMT but at 52 weeks there was no significant between group differences observed	ET with and without SMT are recommended for the short term effects
Evans et al. 2002	(n=191) patients (113 female) between 20 and 65 years of age with a primary complaint of mechanical neck pain that had lasted for 12 weeks or more	SMT + low tech ex Vs high tech ex (neck and upper Body stretching, strengthening, and aerobic ex.) Vs SMT	pain (NPRS) and disability (NDI) (assessed at 3, 6, 12, and 24 months after treatment)	significant reduction of pain within the two groups of exercise	rehabilitative exercise with and without SMT is more effective over two years follow up
Bronfort et al. 2001	(n=191)Patients(113 female) 20 to 65 years of age with primary complaint of CMNP	SMT + low tech ex Vs high tech ex (neck and upper Body stretching, strengthening, and aerobic ex.) Vs SMT	Pain (NPRS) and disability (NDI, SF-36) (after treatment, 5 weeks, 11 weeks, 3 months, 6 months, 12 months)	in terms of pain intensity, there was group differences in favour of the tow exercise groups. No significant group differences for neck disability.	strengthening ex whether alone or in combination of SMT is beneficial for patients with CNP
Sillevis et al. 2010	(n=101)patients (77 female) between 18 and 65 years of age with chronic non-specific neck pain for at least 3 months	HVLA upper thoracic spine thrust man.(pistol grip) Vs placebo	pain intensity (VAS) and activity of autonomic nervous system (assessed before and immediately after treatment)	no statistical significant difference in VAS change score between both groups following the intervention	the thoracic manipulation may not be effective in immediate pain reduction in CNP patients
Cleland et al. 2005	(n=36) patients (27 female) between 18	HVLA thoracic spine thrust man.(pistol	pain (VAS) and disability (NDI)	The mean of VAS change score in pain in the group	thoracic spine manipulation results in immediate reduction of pain in patients

Study	Population	Intervention	Outcome	Results	conclusion
	and 65 years of age with a primary complaint of mechanical neck pain	grip) Vs placebo	(assessed immediately after treatment)	receiving thoracic spine manipulation was 15.5mm compared to a change in the group receiving placebo manipulation of 4.2mm"	with mechanical neck pain
Gonza' lez-Iglesias et al. 2008	(n=45)patients (25 female) between 23 and 44 years of age with acute MNP	Thoracic thrust man. (seated distraction)+ electrotherapy (TENS) +thermal (IRR) Vs electrotherapy (TENS) + thermal (IRR)	Pain (NPRS), disability (NPQ) and CROM (assessed at baseline and one week after last session)	Subjects receiving thoracic spine manipulation experienced greater reductions in both neck pain and disability	Thoracic thrust man. Was effective in reducing pain and disability
Hoving et al. 2002	(n=183)Patients (109 female) between 18 and 65 years of age with nonspecific neck pain	MT (multiple levels cervical mobilisation) Vs PT (exercise) Vs advice	perceived recovery, intensity of pain (NPRS), functional disability (NDI) (assessed after 3 and 7 weeks)	statistically significant differences were found between treatment groups in terms of pain intensity in favour of MT, but not significant with disability"	MT is recommended treatment for NP patients
Hoving et al. 2006	(n=183)Patients (109 female) between 18 and 65 years of age with nonspecific neck pain for at least 2 weeks	MT (mobilisation) Vs PT (exercise) Vs advice	global perceived recovery, intensity of pain (NPRS), functional disability (NDI) (assessed at week 13, 26, and 52)	significant higher improvement scores were observed for MT in all outcomes, but not disability, assessed immediately after treatment	MT is better than the other treatments for short term effect
Masaracchio et al. 2013	(n=64) (50 female) patients between 18 and 65 years with primary complaint of MNP of less than 3 months in duration	upper and middle thoracic spine thrust (pistol grip) +cervical (C2-C7) spine non thrust (grade 3)+ ROM Ex (experimental) Vs cervical spine non thrust + ROM Ex	Pain (NPRS) and disability (NDI) (one week follow up)	significant greater improvement among the experimental group in pain and disability at 1 week follow up	thoracic spine thrust manipulation and cervical spine nonthrust manipulation plus exercise is recommended as short term treatment

Study	Population	Intervention (control)	Outcome	Results	conclusion
Saavedra-Hernandez et al. 2012	(n=80)patients (36 female) with age between 18-65 years and with primary complaint of mechanical idiopathic neck pain	Kinesio taping Vs cervical thrust man. (cradle hold)	pain (NPRS), disability (NDI) and CROM(secondary) (assessed at baseline and 7 days after the treatment)	there was a decrease in pain and disability at 1 week follow up but not statistically significant	reductions in pain and disability were not clinically meaningful
Saavedra-Hernandez et al. 2013	(n=82)Patients (41 female) with with age between 18-65 years and with primary complaint of bilateral chronic mechanical neck pain	cervical spine thrust manipulation vs. cervical (cradle hold), cervico-thoracic junction and thoracic thrust manipulation (seated distraction)	pain (NPRS), disability (NDI) and CROM(secondary) (assessed at baseline and 7 days after the treatment)	similar decreases in Neck Pain in both groups and significant reduction in disability among the full spinal man. Group	manipulation of the cervical and thoracic spine leads to a greater reduction in disability at one week than manipulation of the cervical spine alone
Bronfort et al. 2012	(n=272)patients (177 female) aged 18 to 65 years who had nonspecific neck pain for 2 to 12 weeks	SMT (thrust and nonthrust) (treated level is based on palpation - hypomoblie joints) Vs medications Vs home exercise + advice	pain (NPRS) and disability (NDI), global improvement, medication use, satisfaction, general health status and adverse events (assessed at week 2, 4, 8, 12, 26, and 52")	SMT had statistically significant reductions in pain and disability compared to that of medications but not to home ex	SMT was more effective than medications and had similar effect to home ex.
Cheung Lau et al. 2011	(n=120)patients (60 female) between 18 and 65 years with a diagnosis of chronic mechanical neck pain	Thoracic man. + IRR+ advice Vs IRR+ advice (control)	pain (NPRS), disability (NPQ) and health-related quality of life (SF-36) (assessed immediately after treatment, at 3 months, and 6 months)	significant improvements in pain and disability among the experimental group	TM is effective treatment for MNP
Puentedura et	(n=24)patients (16	thoracic thrust	pain (NPRS) and	significant improvements	a combination of Cervical TJM and

Study	Population	Intervention	Outcome	Results	conclusion
al. 2011	female) between 18 and 65 years of age, with a primary complaint of acute neck pain	(seated and pistol grip positions)+ Ex. Vs cervical thrust+ Ex.	disability (NDI) assessed at week 1, 4, and 6 months	in pain and disability among the Cervical TJM group in all the follow up times compared to the Thoracic group	exercise is more effective than thoracic TJM in treating MNP
Dunning et al. 2012	(n=107)patients (73 female) between 18 and 65 years of age with mechanical neck pain of any duration	Upper cervical + upper thoracic thrust man. (pistol grip) Vs Upper cervical + upper thoracic non thrust mob.	Disability (NDI), pain (NPRS) (assessed at baseline and 48 hours after treatment")	significant reductions of pain and disability among the experimental group compared to that of the comparison group	a combination of upper cervical and upper thoracic TJM is more effective than mobilisation for short term

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