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The effect of neural mobilisation on cervico-brachial pain

Cato Annalie Henning née Basson

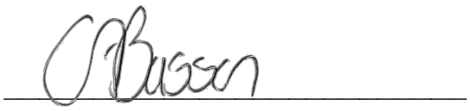
Supervisors Prof A.V. Stewart and Prof W. Mudzi

A thesis submitted to the Faculty of Health Sciences, University of the Witwatersrand, in fulfilment of the requirements for the degree of Doctor of Philosophy

Johannesburg 2017

Declaration

I, Cato Annalie Henning née Basson declare that this thesis is my own work. It is being submitted for the degree of Doctor of Philosophy at the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree examination at this or any other University



Signature

Date 19 May 2017

Dedication

This work is dedicated to my parents Gerhard and Jeanette Basson, my husband and daughter Ockert and Jeanét Henning with gratitude for their love and support.

Publications and presentations arising from this thesis

Presentations

Title: Prevalence of neck and upper limb pain in private practice in Pretoria, South Africa. Oral presentation presented at the South African Society of Physiotherapists First Symposium “Physiotherapy: Exercise experts from prevention to participation” Date: 19-23 March 2014

Title: The effectiveness of neural mobilisation in the treatment of neuro-musculoskeletal conditions: a systematic review and meta-analysis. Oral presentation presented at the World Confederation of Physical Therapists World Congress, Singapore, 1-4 May 2015

Title: The effectiveness of neural mobilisation in the treatment of neuro-musculoskeletal conditions: a systematic review and meta-analysis. Invited keynote lecture, Col·legi de Fisioterapeutes de Catalunya 6th Congress, Barcelona 27 November 2015

Title: The effectiveness of neural mobilisation in the treatment of neuro-musculoskeletal conditions: a systematic review and meta-analysis. Invited keynote lecture, 5th Biennal Phsyiotherapy Conference Dubai May 2016.

Title: Management of nerve-related neck and arm pain. Invited keynote lecture, 5th Biennal Phsyiotherapy Conference Dubai May 2016.

Title: Neuropathic pain is common in acute/sub-acute cervico-brachial pain and can be treated effectively with neural mobilisation. Oral presentation PainSA Congress, 12-14 May, Cape Town, South Africa

Title: The effect of neural mobilisation on cervico-brachial pain. Oral presentation at the World Confederation of Physical Therapists World Congress, 2-4 July 2017, Cape Town, South Africa

Publications

Basson C, Stewart A, Mudzi W. The effect of neural mobilisation on cervico-brachial pain: design of a randomised controlled trial. BMC musculoskeletal disorders. 2014;15(1):419.

Basson A, Olivier B, Ellis R, Coppieters M, Stewart A, Mudzi W. The effectiveness of neural mobilizations in the treatment of musculoskeletal conditions: a systematic review protocol. JBI Database of Systematic Reviews and Implementation Reports. 2015;13(1401):65-75.

Basson CA, Olivier B, Coppieters M, Ellis R, Stewart A, Mudzi W. The effectiveness of neural mobilisation in the treatment of neuro-musculoskeletal conditions: a systematic review and meta-analysis. Physiotherapy. 2015;101, Supplement 1:e127-e8.

Basson CA, Olivier B, Coppieters M, Ellis R, Stewart A, Mudzi W. The effectiveness of neural mobilisation in the treatment of neuro-musculoskeletal conditions: a systematic review and meta-analysis. (updated). Journal of Orthopaedic & Sports Physical Therapy – accepted.

Abstract

Neck pain is one of the most common debilitating musculoskeletal complaints seen in physiotherapy practice. It is often associated with headache, upper back and shoulder/arm pain (cervico-brachial pain) and such patients are more disabled than patients with neck pain only. Cervico-brachial pain syndrome is an upper quarter pain syndrome in which neural tissue sensitivity to mechanical stimulus is thought to play a role.

Neuropathic pain is a problem associated with and prevalent in neck and arm pain. Psychosocial factors, such as fear-avoidance beliefs and catastrophising, have been shown to play an important role in treatment outcomes.

Neural mobilisation (NM) is often used to influence the neural structures in conditions with signs of neural involvement or neural mechano-sensitivity. It seems reasonable to use neural mobilisation in cervico-brachial pain as neural structures play an important role in this condition

The optimal treatment intervention for cervico-brachial pain is yet to be established. The prevalence of cervico-brachial pain in a South African population is also unknown.

Aims of the study

The aims of the study were to:

i. To establish the prevalence of cervico-brachial pain in patients being seen in physiotherapy practices in Pretoria, South Africa.
ii. To establish the effect of neural mobilisation on the pain, function and quality of life of patients with acute and sub-acute cervico-brachial pain.
iii. To establish the influence of high catastrophising scores and neuropathic pain on treatment outcomes.
iv. To establish the effect of demographic factors on the pain, function and quality of life of patients with cervico-brachial pain.

Methods

Research Question 1.

A retrospective survey of physiotherapy patient records dated 1 January 2011 to 31 December 2011 was conducted. The prevalence of patients with neck pain in relation to other musculoskeletal complaints was calculated and expressed as a percentage. Symptoms recorded included the following; headache, dizziness, pins and needles, feeling of weakness, other sensations, more than one symptom and pain in other area/s. Based on body charts, areas of pain were coded as neck pain only, pain in the shoulder, shoulder and upper arm, shoulder to elbow, lower arm, hand, neck and arm up to wrist, neck and arm including hand.

Research Questions 2, 3 and 4

A single blind randomised clinical trial was conducted to establish the effect of neural mobilisation on cervico-brachial pain. The intervention group (IG) received cervical and thoracic mobilisation exercises, advice and NM. The usual care (UC) had the same treatment without NM. Outcomes were assessed at 3 weeks, 6 weeks, 6 months and 12 months.

The Numerical Pain Rating Scale was used to determine the effect of NM on pain. The Patient Specific Functional Scale was used to determine the effect of NM on function and the EuroQual5 instrument was used to establish the effect of NM on the quality of life. At 6 weeks the Global Rating of Change was administered to measure patient's perception of recovery.

The Neuropathic Diagnostic Questionnaire (DN4) was used to classify patients with neuropathic pain and the Pain Catastrophising Scale to identify catastrophisers.

Results and Discussion

Prevalence of neck and radiating arm pain in physiotherapy private practice, Pretoria South Africa

The prevalence of neck pain in private physiotherapy practices in Pretoria, SA is high (46.4% of the total musculoskeletal complaints) with radiating arm pain (52.2% of neck pain population) and pain in other areas (22.6% of neck pain population) being commonly associated with neck pain. Furthermore, other

symptoms such as headache (25.4% of the neck pain population) and paraesthesia (11.2%) are also frequently present. Neck pain is multi-faceted and this has implications for its management. Future studies with a bigger, representative population sample are needed to establish the prevalence of neck pain in SA.

The effect of neural mobilisation on cervico-brachial pain

All patients improved significantly in terms of pain, function and quality of life over the 12-month period. However, the IG had significantly less pain than the UC group at 6 months (p=0.03 95% CI 0.96 - 2.03) and this difference was more pronounced in patients with neuropathic pain (IG 2.91 95%CI 1.74 - 4.08 and CG 5.5 95% CI 3.45 - 7.55 p=0.01). There were no significant differences between groups in terms of function or quality of life.

Patients with neuropathic pain had significantly more pain at 6 months (positive neuropathic pain 3.71 95%CI 2.57 – 4.84; negative neuropathic pain 1.44 95% CI 0.93 – 1.96 p=0.0001) and 12 months (positive neuropathic pain 3.23 95% CI 1.74 – 4.71; negative neuropathic pain 1.38 95% CI 0.88 – 1.91 p=0.01) compared to those without neuropathic pain. At 12 months function was also negatively affected by the presence of neuropathic pain (positive neuropathic pain 23.91 95%CI 20.96 – 26.86; negative neuropathic pain 27.15 95% CI 25.95 – 28.36 p=0.04). It did not have an effect on quality of life.

Catastrophisers had more pain at 6 months (catastrophisers 4.25 95% CI - 1.90 – 10.40; non-catastrophisers 1.70 95% CI 1.22 – 2.17 p=0.02) and 12 months (catastrophisers 3.56 95% CI 1.10 – 6.02) compared to non-catastrophisers (1.47 95% CI 0.96 – 1.99 p=0.02). There was no difference in their function at any time, however at baseline they reported a lower quality of life (Catastrophisers 61.96 95% CI 52.04 – 71.87; non-catastrophisers 75.79 95% CI 71.91 – 79.66 p=0.002).

Conclusion

The addition of NM to cervical and thoracic mobilisation, exercises and advice to stay active, in the management of cervico-brachial pain, resulted in less pain at 6-month follow-up. For patients with neuropathic pain the positive

effect was more pronounced. Adding NM as an adjunct to usual care is effective to improve pain for patients with cervico-brachial pain especially for those with a neuropathic pain component. The presence of neuropathic pain and catastrophising resulted in poor pain-related outcomes.

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Praise to the Lord.

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List of abbreviations

NM – Neural mobilisation

IG – Intervention Group

UC – Usual Care

JBI-MAStARI – Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument

ROM – Range of Motion

CTS – Carpal Tunnel Syndrome

N-LBP – Nerve-related low back pain

N-NAP – Nerve-related neck and arm pain

SLR – Straight Leg Raise

ULNDT1 – Upper limb neurodynamic test 1

DASH – Disability of the Arm Shoulder and Hand

SA – South Africa

CI – Confidence Interval

NPRS – Numerical Pain Rating Scale

VAS – Visual Analogue Scale

PSFS – Patient Specific Functional Scale

EQ5D – EuroQual Instrument

DN4 – Diagnostic neuropathic Pain Questionnaire

PCS – Pain Catastrophising Scale

GROC – Global Rating of Change

1 Chapter One – Introduction to the study

This chapter serves as an introduction and justification for the study.

1.1 Introduction

Neck pain is one of the most common debilitating musculoskeletal complaints seen in physiotherapy practice (Picavet and Schouten, 2003, Binder, 2007, Lindgren, 2008). In a systematic review on the prevalence of neck pain in the adult population, Fejer et al. (2006) found the point prevalence to be 7.6% and the lifetime prevalence to be 48.6%. In the 2015 global burden of disease report, low back pain and neck pain were the leading causes of disability (Vos et al., 2016).

The Bone and Joint decade task force on neck pain, classifies neck pain into four grades (Guzman et al., 2009) namely Grade I - no signs of major pathology and no or little interference with daily activities; Grade II – neck pain with no signs of major pathology, but interference with daily activities; Grade III - neck pain with neurologic signs of nerve compression; Grade IV – neck pain with signs of major pathology. Neck pain is often associated with headache, upper back and shoulder/arm pain (Lindgren, 2008, Salt et al., 2011). A study by Daffner et al. (2003) showed that 65.4% of the neck pain population included in their study had arm pain associated with their neck pain, and that the patients with neck and arm pain were more disabled than

patients with only neck pain. Disability is defined as product of functioning, activity limitations and participation restriction and is influenced by contextual factors such as environmental and personal factors (Jette, 2006, World Health Organization, 2001). It considers the person as a whole, and the influence, for instance functioning, will have on the person.

Different terms are often used to describe patients with upper quadrant pain such as cervico-brachial pain (Allison et al., 2002), nerve-related neck and arm pain (Nee et al., 2012b), complaints of the arm neck and shoulder (van Hulst et al., 2016) and cervical radiculopathy (Young et al., 2009, Salt et al., 2011). Cervico-brachial pain syndrome is an upper quadrant pain syndrome in which neural tissue sensitivity to mechanical stimulus is thought to play a role (Hall and Elvey, 1999, Jull et al., 2008). The diagnosis of cervico-brachial pain is made clinically and there is often no overt neural involvement (Hall and Elvey, 1999). Neural involvement can be assumed if a cluster of clinical findings is present, such as active and passive movement dysfunction, adverse response to neurodynamic testing and evidence of a local cause of neuropathic pain (Hall and Elvey, 1999, Jull et al., 2008).

Neuropathic pain is described as pain initiated or caused by a primary lesion or dysfunction in the nervous system (International Association for the Study of Pain, 2011). The Neuropathic Pain Special Interest Group of the International Association for the Study of Pain, classifies neuropathic pain in three different categories: possible neuropathic pain – anatomical region of symptoms plausible, and history of nerve injury; probable neuropathic pain – negative or positive sensory changes or diagnostic tests positive; definite neuropathic pain – sensory changes and positive diagnostic tests (Haanpää

et al., 2011). Neuropathic pain is a problem associated with and prevalent in many musculoskeletal conditions such as low back pain (Freynhagen and Baron, 2009), chronic radiculopathy (Tampin et al., 2013b) and whiplash associated disorders (Sterling and Pedler, 2009). Neuropathic pain is consistently linked to high levels of pain, disability, poor quality of life and poor response to treatment (Dworkin et al., 2007, Smith et al., 2007, Sterling and Pedler, 2009) and therefore is a difficult condition to treat successfully (Dworkin et al., 2007, Smith et al., 2007).

Psychosocial factors have been shown to play an important role in treatment outcomes (Karels et al., 2010, Pool et al., 2010, Verhagen et al., 2010, Walton et al., 2009). Pool et al. (2010) examined the influence of different psychosocial factors on treatment outcome and found fear of movement to be significantly correlated with poor outcomes in the short and long term. In another study (Karels et al., 2007) catastrophising was significantly linked to persistent symptoms of neck pain over a six-month period. Verhagen et al. (2010) explored the influence of various factors on treatment outcome in neck pain and found pain severity and catastrophising to be the most important determinants of poor recovery. Similar to these findings Thompson et al. (2010) found catastrophising and poor self-efficacy to be associated with higher pain and disability. Catastrophising is a cognitive process that includes elements of magnification, helplessness, rumination and is an important predictor of poor pain-related outcomes (Sullivan et al., 1995). In a study to examine factors influencing return to work in patients with neck/arm/shoulder pain, the authors also concluded that psychosocial factors should be taken into account when interventions are planned (Karels et al., 2010). Other

factors that have been shown to influence treatment outcomes are pain intensity at baseline, high disability at baseline, the presence of low back pain and increasing age (Schellingerhout et al., 2008, Walton et al., 2013a).

Most clinical guidelines do not differentiate between treatment for neck pain and neck and arm pain such as radiculopathy (Childs et al., 2008, Côté et al., 2016). The American Physical Therapy Association recommends mobilisation/ manipulation of the neck and thoracic spine, exercises and education (Childs et al., 2008). The findings of recent Cochrane reviews confirm the above recommendations (Gross et al., 2016, Gross et al., 2015, Miller et al., 2010). The American guidelines (Childs et al., 2008) also recommend that neural mobilisation should be considered for patients with neck and arm pain (level B evidence).

Neural mobilisation (NM) is often used to influence the neural structures in conditions with signs of neural involvement or neural mechano-sensitivity (Allison et al., 2002, Nee et al., 2012b). The axoplasmic flow can be influenced by NM (Shacklock, 2005). Furthermore, NM can have an effect on movement of the nerve and its connective tissue (Coppieters and Alshami, 2007) and the circulation of the nerve by alteration of the pressure in the nervous system and dispersion of intraneural oedema (Brown et al., 2011, Schmid et al., 2012). The excitability of dorsal horn cells can be decreased with NM (Bialosky et al., 2009b). Other effects that have been found are short term hyperalgesia (Beneciuk et al., 2009) and a change in neural tissue mechano-sensitivity (Vicenzino et al., 1996).

NM is defined as an intervention aimed at influencing the neural structures or surrounding tissue (interface) directly or indirectly through manual techniques

or exercise (Coppieters and Alshami, 2007). The interface can be mobilised by mobilising tissue surrounding the nerve along the course of the nerve (Butler, 2000) or using foraminal opening techniques such as the cervical lateral glide (Langevin et al., 2015). Although mobilisation along the course of the nerve is a technique used in clinical practice, the use thereof in the literature could only be identified in one case report of a patient with cervical radiculopathy (Costello, 2009). The treatment was combined with manual therapy and exercises, both of which have been shown to be effective for cervical radiculopathy (Côté et al., 2016). It is therefore difficult to know whether the NM contributed to the treatment effect. The effectiveness of this form of NM has therefore yet to be established. In cervico-brachial pain neural tissue sensitivity to mechanical stimulus is thought to play a role (Hall and Elvey, 1999). It can therefore be reasoned that targeting the neural structures specifically should be an important aim of treatment in patients with cervico-brachial pain.

The efficacy of NM has been studied in various conditions such as low back pain (Cleland et al., 2007a), carpal tunnel syndrome (Baysal et al., 2006), lateral epicondalalgia (Vincenzino et al., 1996) and cervico-brachial pain (Allison et al., 2002, Cowell and Philips, 2002, Nee et al., 2012b). The NM techniques used for cervico-brachial pain are mainly cervical lateral glides and neural gliding exercises (Allison et al., 2002, Coppieters et al., 2003b, Gupta and Sharma, 2012). According to systematic reviews of NM, the evidence for the efficacy of NM is limited (Ellis and Hing, 2008, Medina McKeon and Yancosek, 2008, Su et al., 2016).

1.2 Significance of the study

There is a paucity of studies on acute neck / shoulder / arm pain (cervico-brachial pain) (Bono et al., 2011, Boyles et al., 2011, Thoomes et al., 2013). Neuropathic pain can be a feature in patients with cervico-brachial pain (Salt et al., 2011); these patients have higher levels of pain and disability (Daffner et al., 2003) and have poor treatment outcomes (Nee et al., 2011). There are a limited number of studies with small study populations that have investigated the effect of NM for cervico-brachial pain (Allison et al., 2002, Coppieters et al., 2003b, Gupta and Sharma, 2012, Nee et al., 2012b) and a systematic review on NM concluded that there is limited evidence for the use of NM (Ellis & Hing, 2008). The optimal treatment intervention for cervico-brachial pain has yet to be established (Salt et al., 2011). No literature could be identified on prevalence of neck and radiating arm pain in a South African population. As cervico-brachial pain has a set number of criteria, which cannot be established from patient records, only the prevalence of neck and radiating arm could be investigated.

1.3 Research questions

1.3.1 Research question one

What is the prevalence of neck and radiating arm pain among patients being treated in physiotherapy practices in Pretoria, Gauteng, South Africa?

1.3.2 Research question two

What is the effect of NM on the pain, function and quality of life of patients with acute cervico-brachial pain?

1.3.3 Research question three

Does the presence of high catastrophising scores and neuropathic pain have an influence on treatment outcome?

1.3.4 Research Question four

What is the influence of demographic factors such as age, gender, headache, dizziness, paraesthesia, injury, previous pain, exercise and education on pain, function and quality of life in patients with cervico-brachial pain?

1.4 Hypotheses (H^0 and H^1)

1.4.1 Null Hypothesis 1a

Neural mobilisation does not have an effect on pain in cervico-brachial pain

1.4.2 Alternative Hypothesis 1a

Neural mobilisation has an effect on pain in cervico-brachial pain

1.4.3 Null hypothesis 1b

Neural mobilisation does not have an effect on function in cervico-brachial pain.

1.4.4 Alternative hypothesis 1b

Neural mobilisation has an effect on function in cervico-brachial pain.

1.4.5 Null hypothesis 1c

Neural mobilisation does not have an effect on the quality of life in cervico-brachial pain.

1.4.6 Alternative hypotheses 1c

Neural mobilisation has an effect on the quality of life in cervico-brachial pain.

1.5 Aims of the study

1.4.1 To establish the prevalence of neck and radiating arm pain among patients being treated in physiotherapy practices in Gauteng, South Africa.

1.4.2 To establish the effect of NM on the pain, function and quality of life of patients with acute and sub-acute cervico-brachial pain.

1.4.3 To establish the influence of high catastrophising scores and neuropathic pain on treatment outcomes.

1.4.4 To establish the effect of demographic factors on the pain, function and quality of life of patients with cervico-brachial pain

1.6 Objectives

1.6.1 Research aim one

To establish the prevalence of neck and radiating arm pain, among patients being treated in physiotherapy practices in Pretoria, South Africa.

1.6.1.1 To determine the one year prevalence of patients with neck pain and radiating arm pain in private physiotherapy practices in Pretoria

1.6.1.2 To document the areas of pain and associated symptoms in patients with neck and radiating arm pain

1.6.2 Research aim two

1.6.2.1 To establish the effect of NM on the:

- pain of patients with cervico-brachial pain.
- function of patients with cervico-brachial pain.
- quality of life of patients with cervico-brachial pain.

1.6.2.2 To compare:

- the effect of NM added to usual care (UC) on the above factors with a control group that receives UC only.
- the number of treatment sessions between the NM group (IG) and UC group.
- the effect of NM added to UC on the elbow range of movement of the upper limb neurodynamic test compared to UC only.
- the patient perception of change in pain, function and quality of life between groups

1.6.3 Research aim three

1.6.3.1 To determine:

- the influence of neuropathic pain on treatment outcomes in patients with cervico-brachial pain.

- the effect of high catastrophising scores on treatment outcomes in patients with cervico-brachial pain.

1.6.4 Research aim four

1.6.4.1 To determine:

- The effect of demographic factors such as age, gender, headache, dizziness, paraesthesia, injury, previous pain, exercise and education on the pain, function and quality of life in patients with cervico-brachial pain

1.7 Outline of Chapters

Chapter two – Literature review

Chapter three – Prevalence of neck and radiating arm pain in physiotherapy private practice in Pretoria, South Africa

Chapter four – Outcomes measures

Chapter five – Method of the randomised controlled trial

Chapter six – Results of the randomised controlled trial

Chapter seven – Discussion of the randomised clinical trial

Chapter eight – Concluding comments and recommendations

2 Chapter Two - Literature review

A systematic review of the literature on the effectiveness of neural mobilisation (NM) for neuro-musculoskeletal conditions is presented in this chapter. The effect of different NM techniques on neuro-musculoskeletal conditions was investigated.

2.1 Introduction

The 2010 Global Burden of Disease study revealed that musculoskeletal disorders are the second biggest contributor to disability worldwide (Vos et al., 2012). Low back and neck pain account for 70% of musculoskeletal disability. Low back-related leg pain and nerve-related neck and arm pain might arise as a direct consequence of a lesion or disease affecting the peripheral nervous system (Leaver et al., 2013b, Schafer et al., 2009). The peripheral nervous system is also compromised in common entrapment neuropathies, such as carpal tunnel syndrome (CTS), and may be affected in conditions, such as lateral epicondylalgia (Coombes et al., 2014) and plantar heel pain (Alshami et al., 2008).

Five systematic reviews evaluated the effectiveness of NM. Two reviews (Ballestero-Pérez et al., 2016, Medina McKeon and Yancosek, 2008) focused on CTS (6 studies and 10 studies). It observed a possible trend toward improved outcomes following NM, but concluded that the efficacy of NM in CTS was unclear. Another review (Ellis and Hing, 2008) included various

musculoskeletal conditions (11 studies) and concluded that although there was support for NM, the evidence was limited. A recent review (Su et al., 2016) (20 studies) assed the effect of NM for chronic conditions and concluded that NM is not superior to other interventions. Another review assessed the effect of NM for lower quadrant problems (10 studies) and concluded that there is some evidence for it's effectiveness (Neto et al., 2017). These reviews had different inclusion and exclusion criteria to the current review. A narrative review of NM for spinal radiculopathy concluded that NM might be beneficial for certain subgroups of patients (Efstathiou et al., 2015).

Neural mobilisation (NM) or neurodynamics is an intervention aimed at restoring the homeostasis in and around the nervous system, by mobilisation of the nervous system itself or the structures that surround the nervous system (Coppieters and Butler, 2008). NM facilitates movement between neural structures and its surroundings (interface) through manual techniques or exercise (Nee and Butler, 2006). Human and animal studies reveal that NM reduces intraneural oedema, (Schmid et al., 2012) improves intraneural fluid dispersion (Brown et al., 2011, Gilbert et al., 2015), reduces thermal and mechanical hyperalgesia (Song et al., 2006), and reverses the increased immune responses (Santos et al., 2012, Song et al., 2006) following a nerve injury.

Since the publication of these reviews, additional randomized trials have been published on the effectiveness of NM. The objective of this systematic review was to assess the effectiveness of NM for neuro-musculoskeletal conditions. We hypothesized that an updated systematic review along with meta-

analyses would provide more definite answers regarding the effectiveness of NM for neuro-musculoskeletal conditions.

2.2 Methods

2.2.1 Protocol and registration

The systematic review and meta-analysis protocols were reviewed and published by the Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports (Basson et al., 2015a).

2.2.2 Eligibility criteria

2.2.2.1 Studies

Randomised clinical trials, published in English, which evaluated the effect of NM in participants over the age of 18 with neuro-musculoskeletal conditions indicative of neural tissue dysfunction, were considered for inclusion. Cohort studies and case or case-control studies were excluded. Studies that evaluated the effect of NM in systemic diseases (e.g. fibromyalgia (Torres et al., 2015) and leprosy (Veras et al., 2012b)), central nervous system disorders (e.g., traumatic brain injury (Lorentzen et al., 2012)) and polyneuropathies were excluded. Animal studies or studies on healthy participants were also excluded.

2.2.2.2 Interventions

Studies were included that evaluated NM techniques used for the treatment of disorders of the peripheral nervous system (spinal nerve roots and peripheral nerves) where neurodynamic dysfunction was implicated. NM could be

achieved through active exercises or passive manual therapy techniques. Included techniques could be directed to the nervous system itself e.g., sliding and tensioning techniques (Coppieters and Butler, 2008, Coppieters et al., 2009), or to the structures that surround the nervous system e.g., cervical lateral glide (Elvey, 1986) or techniques clinically described as lumbar foraminal opening techniques (Shacklock, 2005).

2.2.2.3 Outcome measures

Outcome measures of primary interest were pain (numerical pain rating scale, visual analogue scale), disability and or function (Disability of the Arm, Shoulder and Hand Symptom Scale, Neck Disability Index, Oswestry, Patient Specific Functional Scale). Secondary outcomes included quality of life (e.g. WHOQOLF Physical Domain Score), range of motion (ROM) (inclinometer, goniometer), specific diagnostic tests (Tinel's sign, Phalen's manoeuvre), neurodynamic test outcomes Upper Limb Neurodynamic Test 1, 2a, 2b, 3, Straight Leg Raise, Slump), sensation (two point discrimination), muscle force (Dynamometer) and neurophysiological changes.

2.2.3 Search strategy

The databases searched included: MEDLINE (Pubmed), CINAHL Plus, Cochrane Controlled Trials Registered, Physiotherapy Evidence Database (PEDro), ProQuest Central (Family Health, Health and Medical Complete), Nursing and Allied Health Source, EBSCO MasterFile Premier, Science Direct, SCOPUS. The search for unpublished studies included: EBSCO MegaFile Premier. The reference lists of all identified articles were searched for additional studies. The search was conducted to include articles from

January 1980 to April 2016. One previous review (Ellis and Hing, 2008) searched from 1830 and the oldest article included in their review was 1996.

The search terms included: neural, nerve, mobilisation, manipulation, physical therapy, physiotherapy, manual therapy, glide exercises, treatment, intervention, management, modality, stretching, tension, neurodynamics. (Appendix 2.1)

2.2.4 Methodological quality

Two independent reviewers considered records for inclusion and full text were reviewed after identifying relevant titles and abstracts (AB & BO). Articles which fitted the inclusion criteria were assessed by two independent reviewers for methodological quality (AB & BO) using the Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument for critical appraisal (JBI-MAStARI) (Joanna Briggs Institute, 2014) (Appendix 2. 2). The JBI-MAStARI was developed by experts, and reviewed and ratified by the JBI's International Scientific Committee. The JBI-MAStARI was used to establish the quality of studies and for meta-analysis. Disagreements were discussed between the primary and secondary reviewer. Any unresolved issues were resolved through discussion with a third reviewer (RE). Risk of bias was assessed using the GRADE guidelines (Guyatt et al., 2011). This takes into account random sequence generation, concealment of allocation, blinding of outcomes assessment, incomplete outcome data, selective reporting and other bias such as stopping early for benefit or the use of unvalidated outcome measures (Guyatt et al., 2011). Agreement between reviewers was evaluated using Cohen's kappa.

2.2.5 Data collection

Data extracted from studies were grouped together in terms of patient subgroup, patient demographics, interventions, outcome measures, timing of assessments and main results. Authors were contacted where possible for clarification or missing data. Data were subject to double data entry to avoid entry errors.

2.2.6 Data synthesis

Quantitative data, where possible, were pooled in statistical meta-analysis using JBI-MAStARI. Effect sizes expressed as odds ratio (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals (CI) were calculated for analysis. Heterogeneity was assessed statistically using a standard Chi-square test. Meta-analyses were not performed when the Chi-square test had a p-value of less than 0.1 (Joanna Briggs Institute, 2014). The DerSimonian-Laird random effects method was used due to the heterogeneity of studies (Borenstein et al., 2009). Where statistical pooling was not possible the findings are presented in a narrative form.

2.2.7 Levels of Evidence

The JBI grades for level of evidence (The Joanna Briggs Institute Levels of Evidence and Grades of Recommendation Working Party, 2014) were used for making recommendations about treatment efficacy (Appendix 2.3).

2.3 Results

Forty-one articles (21 qualitative and 19 quantitative analysis), including 1759

participants, were included in the review (Figure 2.1). Primary and secondary outcome measures for one study were reported separately in 2 papers, and these 2 papers were therefore treated as one (Coppieters et al., 2003a, Coppieters et al., 2003b). There were 12 studies for carpal tunnel syndrome (CTS), and 11 for nerve-related low back pain (N-LBP), 10 studies for nerve-related neck and arm pain (N-NAP), three for lateral epicondylalgia and one each for cubital and tarsal tunnel syndrome, plantar heel pain and post-operative low back pain. Meta-analysis could be performed for pain and disability in N-LBP; pain in N-NAP; pain, handgrip strength, Phalen's sign, disability, and two-point discrimination in CTS. It was not possible to perform meta-analysis for lateral epicondylalgia, cubital tunnel syndrome, post-lumbar surgery, tarsal tunnel syndrome or plantar heel pain. The excluded studies are listed in Appendix 2.4.

2.3.1 Risk of bias across studies

The overall level of agreement between the primary and secondary reviewers was 0.615 (Cohen's kappa (95% CI 0.412; 0.818)). Outstanding issues were resolved through discussion with a third reviewer. The main areas of disagreement were blinding of participants, whether groups were treated equally and whether appropriate statistical analyses was performed. Seventeen studies had a low risk of bias and 23 studies had an unclear or high risk of bias. The most problematic domains were blinding of assessors and concealed allocation. Incomplete outcome data and high dropout rates were commonly listed as other forms of bias. (Table 2.1) (See study descriptions for risk of bias judgment). Blinding of participants is often difficult in clinical trials although some of the studies used a sham intervention that

successfully blinded participants (Bialosky et al., 2009b, Kavlak and Uygur, 2011).

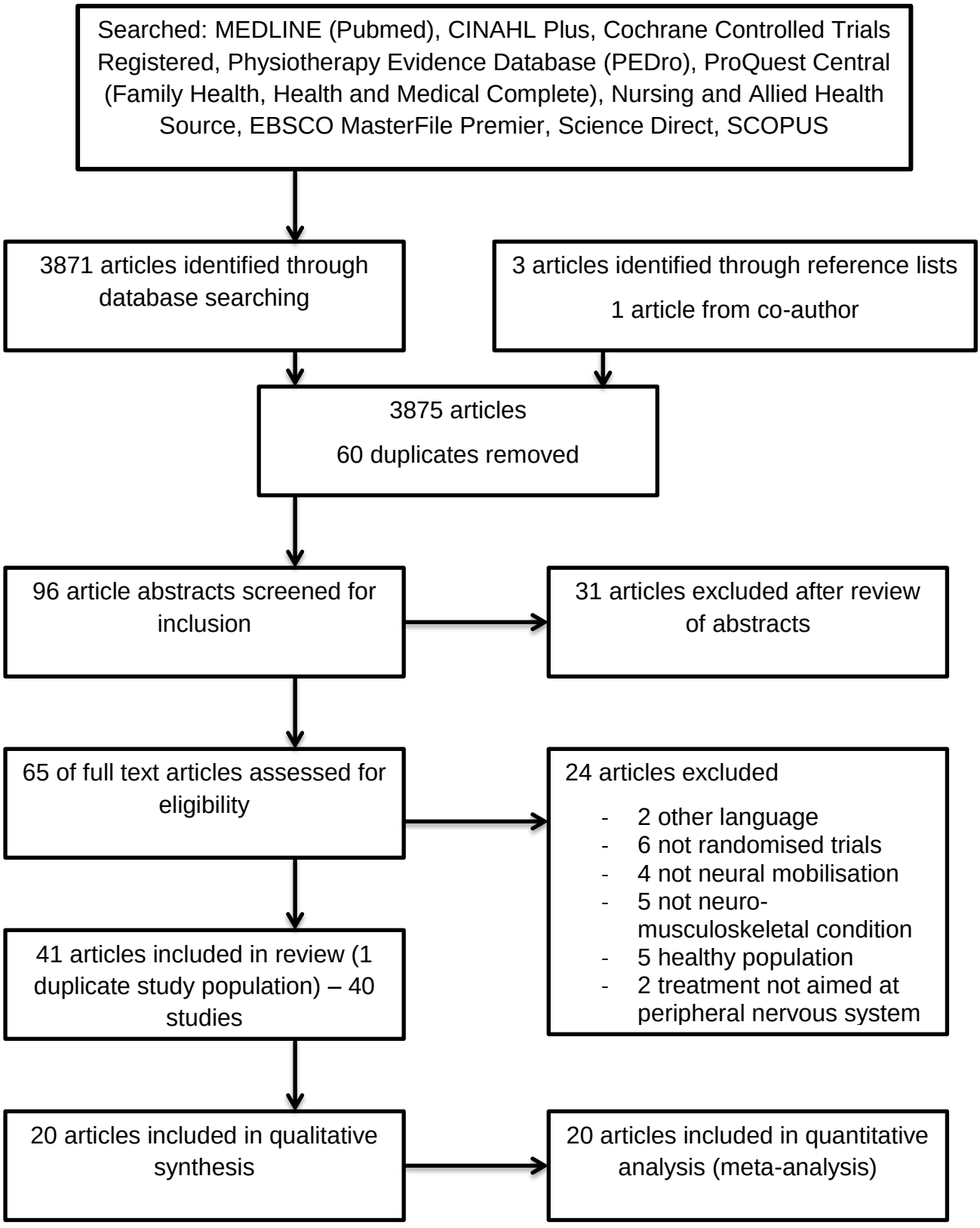


Figure 2.1. Flow diagram of search results and studies included.

Table 2.1. Results of study appraisals

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10
Ahmed et al. (2013)	Y	N	Y	U	N	Y	Y	Y	Y	Y
Akalin et al. (2002)	U	N	U	U	U	Y	Y	Y	Y	Y
Ali et al. (2015)	Y	N	N	U	U	Y	Y	Y	Y	Y
Allison et al. (2002)	Y	U	U	U	Y	Y	Y	Y	Y	Y
Anwar et al. (2015)	Y	N	N	U	N	Y	Y	Y	Y	N
Bardak et al. (2009)	Y	U	Y	U	Y	N	Y	Y	Y	Y
Baysal et al. (2006)	Y	U	Y	U	U	Y	Y	Y	Y	Y
Bialosky et al. (2009b)	Y	Y	Y	N	Y	Y	Y	Y	Y	Y
Brininger et al. (2007)	Y	N	U	N	Y	Y	Y	Y	Y	Y
Cleland et al. (2007a)	Y	U	Y	Y	Y	Y	Y	Y	Y	Y
Coppieters et al. (2003a)	Y	Y	Y	U	Y	Y	N	Y	Y	Y
Coppieters et al. (2003b)	Y	Y	Y	U	Y	Y	N	Y	Y	Y
Dabholkar et al. (2013)	U	N	U	N	N	U	Y	Y	Y	U
Drechsler et al. (1997)	Y	N	U	U	U	U	Y	Y	Y	Y
Dwornik et al. (2009)	Y	N	N	U	U	U	Y	Y	Y	Y
Gupta and Sharma (2012)	Y	N	U	N	N	Y	N	Y	Y	Y
Heebner and Roddey (2008)	Y	U	U	N	U	Y	Y	Y	Y	Y
Horng et al. (2011)	Y	N	Y	N	Y	Y	U	Y	Y	Y
Jain et al. (2012)	Y	U	U	U	U	Y	Y	Y	Y	Y
Kaur and Sharma (2011)	Y	U	U	U	U	Y	Y	Y	Y	Y
Kavlak and Uygur (2011)	N	Y	Y	Y	N	Y	Y	Y	Y	Y
Kumar (2010)	Y	U	U	U	U	U	Y	Y	Y	Y
Langevin et al. (2015)	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
Marks et al. (2011)	Y	U	N	Y	N	N	Y	Y	Y	Y
Mehta et al. (2014)	Y	U	U	Y	U	U	Y	Y	Y	Y
Nagrale et al. (2012)	Y	N	Y	Y	Y	Y	Y	Y	Y	Y
Nar (2014)	Y	U	U	Y	U	Y	Y	Y	Y	N
Nee et al. (2012b)	Y	N	Y	N	Y	U	Y	Y	Y	Y
Oskouei et al. (2014)	Y	Y	Y	U	Y	Y	Y	Y	Y	Y
Patel (2014)	Y	N	U	U	U	Y	Y	Y	Y	Y
Pinar et al. (2005)	Y	N	U	Y	Y	Y	Y	Y	Y	Y
Ragonese (2009)	Y	N	Y	N	Y	N	Y	Y	Y	Y
Rezk-Allah et al. (2011)	Y	N	N	U	U	Y	Y	Y	Y	Y
Saban et al. (2014)	Y	U	Y	Y	Y	Y	Y	Y	Y	Y
Schmid et al. (2012)	Y	N	Y	N	Y	Y	N	Y	Y	Y
Scrimshaw and Maher (2001)	Y	N	N	Y	Y	Y	Y	Y	Y	Y
Svernlov et al. (2009)	Y	U	U	N	Y	U	U	Y	Y	Y
Tal-Akabi and Rushton (2000)	Y	U	U	Y	Y	Y	Y	Y	Y	Y
Vincenzino et al. (1996)	U	Y	Y	Y	Y	U	Y	Y	Y	Y
Waleed Salah El-din (2015)	Y	N	N	Y	N	Y	N	Y	Y	Y
Wolny et al. (2016)	Y	N	Y	N	Y	N	Y	Y	Y	Y
Legend: Y – Yes; N – No; U – Unclear. Q – questions (see Appendix 2.2)										

2.3.2 Meta-analysis

Meta-analyses were conducted for CTS (outcomes: pain intensity, Tinel's test, Phalen's test, grip strength, functional status, two-point discrimination and the Disability of Hand and Shoulder Symptom Scale), N-LBP (outcomes: modified Oswestry Disability Questionnaire and pain intensity) and N-NAP (outcome: pain intensity). Narrative description of the remaining studies is provided, as meta-analysis could not be done on remaining studies. Additional information was requested of nine authors (Allison et al., 2002, Heebner and Roddey, 2008, Horng et al., 2011, Jain et al., 2012, Kumar, 2010, Marks et al., 2011, Scrimshaw and Maher, 2001, Sharma et al., 2011b, Tal-Akabi and Rushton, 2000) of whom one could not be reached (Sharma et al., 2011b).

2.3.3 Techniques used as NM

The NM techniques that were assessed most frequently were nerve gliding exercises for CTS, cervical lateral glides for N-NAP and lateral epicondylalgia, slump mobilisation for N-LBP, and SLR mobilisation for N-LBP, tarsal tunnel syndrome, plantar heel pain and post-operative low back pain. In CTS the terminology used was mostly "nerve gliding exercises"

2.3.4 Carpal Tunnel Syndrome (CTS).

Five studies had a low risk of bias (Bialosky et al., 2009b, Horng et al., 2011, Oskouei et al., 2014, Pinar et al., 2005, Schmid et al., 2012). Four studies had an unclear risk of bias (Baysal et al., 2006, Brininger et al., 2007, Tal-Akabi and Rushton, 2000, Wolny et al., 2016) and the other three had a high risk of bias (Akalin et al., 2002, Bardak et al., 2009, Heebner and Roddey, 2008).

Seven studies (Akalin et al., 2002, Bardak et al., 2009, Baysal et al., 2006, Brininger et al., 2007, Heebner and Roddey, 2008, Horng et al., 2011, Pinar et al., 2005) used nerve gliding exercises as outlined by Totten and Hunter (1991) (which can be considered nerve tensioning exercises), and tendon gliding exercises. The other studies (Bialosky et al., 2009b, Oskouei et al., 2014, Tal-Akabi and Rushton, 2000, Schmid et al., 2012) used a variety of different techniques.

The majority of studies had one intervention where exercises were shown to patients and then instructed to continue for a period of one week, (Schmid et al., 2012) three weeks, (Baysal et al., 2006) four weeks, (Akalin et al., 2002, Brininger et al., 2007, Heebner and Roddey, 2008) eight weeks, (Horng et al., 2011) and ten weeks (Pinar et al., 2005). One study explained the exercises and followed patients up once a week for three weeks (Bardak et al., 2009), another study treated patients passively for three weeks twice a week (Bialosky et al., 2009b) and one study used passive mobilisation three times a week for four weeks (Oskouei et al., 2014). One study did not specify length of treatment and number of interventions (Tal-Akabi and Rushton, 2000).

Most studies used splint wearing as part of the intervention (Akalin et al., 2002, Bardak et al., 2009, Baysal et al., 2006, Brininger et al., 2007, Heebner and Roddey, 2008, Horng et al., 2011, Pinar et al., 2005, Bialosky et al., 2009b, Oskouei et al., 2014). Treatment in comparison groups consisted of splint only (Akalin et al., 2002, Pinar et al., 2005, Schmid et al., 2012, Brininger et al., 2007), splint and ultrasound therapy (Baysal et al., 2006), splint and cortisone injections (Bardak et al., 2009), splint and a sham NM (Bialosky et al., 2009b), splint, advice and tendon gliding exercises (Heebner

and Roddey, 2008), splint and paraffin therapy (Horng et al., 2011), splint, ultrasound and transcutaneous electro-nerve stimulation (Oskouei et al., 2014). One study compared upper limb neurodynamic test (ULNDT) mobilisation to carpal bone mobilisation (Tal-Akabi and Rushton, 2000). Another study compared ULNDT mobilisation to ultrasound and laser therapy (Wolny et al., 2016).

Three studies with a low risk of bias reported improved neurophysiological effects following NM compared to the control groups (improved temporal summation, (Bialosky et al., 2009b) reduced intraneural oedema, (Schmid et al., 2012) and improved median nerve latency (Oskouei et al., 2014). Two studies (Akalin et al., 2002, Baysal et al., 2006) reported improved patient satisfaction and another more rapid improvement in pain in the NM groups (Pinar et al., 2005).

Three studies on CTS measured the Upper Limb Neurodynamic Test 1 (ULNDT1) (Heebner and Roddey, 2008, Oskouei et al., 2014, Tal-Akabi and Rushton, 2000) ROM of which two found no difference between groups (Heebner and Roddey, 2008, Oskouei et al., 2014) and the third reported a decrease in positive ULNDT1 in the NM group.

The clinical outcome measures assessed with meta-analyses were non-significant ($p>0.11$) for CTS (Table 2.2). Although there were a number of studies that reported on Tinel's sign and the Functional Status Score, the heterogeneity was $p<0.1$ for both and therefore meta-analysis was not done on these outcomes (Joanna Briggs Institute, 2014).

Table 2.2 contains the study descriptions and Figure 2.2 and 2.3 are examples of the forest plots for pain and disability (main outcomes). Table 2.3 details the findings for the meta-analyses in CTS.

Table 2.2. Study descriptions CTS

Author **Appraisal** **Risk of bias**	**Patient demographics**	**Intervention Group (IG)**	**Control Group (CG)**	**Outcome**	**Result**
Akalin et al 2002 Appraisal 5 High risk of bias	n = 36 (2 male, 34 female) Age range 38-64 years Mean age 51.93 ±5.1 years Mean group age (years) CG 52.16 (±5.6), IG 51.7 (±5.5) Duration of symptoms (months) CG 47.6 (± 6.8), IG 49.6 (± 5.2)	IG 18 subjects with CTS Same as control plus: Tendon glides in 5 positions. Median nerve exercises in 6 positions. (Each position was maintained for 5seconds 10 reps of each exercise were done 5 times a day) For 4 weeks	CG 18 subjects with CTS Custom made neutral volar wrist splint was instructed to be worn all night and during the day as much as possible for 4 weeks	Undertaken pre treatment and 8 weeks post treatment 1) Phalens sign 2) Tinels sign 3) 2 point discrimination 4) Grip strength 5) Pinch Strength 6) Symptom severity score 7) Functional status score A patient satisfaction investigation undertaken by telephone 8.3 (± 2.5) months post treatment	At the end of treatment a significant improvement was obtained in all parameters in both groups. The nerve and tendon glide group had slightly greater scores but the difference between groups was not significant except for lateral pinch strength. (p=0.026; CG) 30.0±9.3; IG 35.27±9.7) A total of 72% of the control group and 93% nerve and tendon slide group reported good or excellent results in the patient satisfaction investigation, but the difference between the groups was not significant.

Bardak et al 2009 Appraisal 6 High risk of bias	n = 111 Mean age: Group 1 -33 (9.6) Group 2 - 26 (10.3) Group 3 - 22 (9.9)	Group 1 n = 40 with CTS Splint 3 weeks day and night and 3 weeks night only Cortisone injection Nerve & tendon gliding exercises (Totten & Hunter) followed once a week for 3 weeks	Group 2 n = 35 with CTS Splint as for intervention group Cortisone injection (Group 3 not included in analyses Group 3 (n= 36) had only nerve and tendon gliding exercises	Measured pre and post treatment 1) Phalen's test 2) Tinel's test 3) Reverse Phalen's 4) Compression test 5) Two point discrimination 6) Total Symptom Scale 7) Functional Symptom Scale	All groups improved significantly in terms of pain and functionality Group 1 and 2 were better ($p < 0.001$) than group 3 receiving only nerve and tendon gliding exercises ($p = 0.02$) One intervention and follow-up telephonically at 12 months Within group differences reported as percentages and means and standard deviations, but no between group differences values available
Baysal et al 2006 Appraisal 6 Unclear risk of bias	n = 36 (36 female patients – all with clinical and electrophysiological evidence of CTS All with bilateral involvement Mean age – Group 1 47.8 ± 5.5; Group 2 50.1 ± 7.3;	Group 1 CTS (n=12) custom made neutral volar splint (worn for 3 weeks); exercise therapy (nerve and tendon gliding exercises as described by Totten & Hunter, 1991) 5 sessions daily, each exercise	Group 2 CTS (n=12) custom made neutral volar splint (worn for 3 weeks); Ultrasound (15min/session to palmar carpal tunnel, 1mhz, 1.0w/cm2, 1:4, 5cm2 transducer) 1 Rx/day, every 5 days for 3 weeks (total 15 Rx's)	All measures pre-Rx, end of Rx, and 8 weeks Follow Up 1) VAS 2) Tinel's sign 3) Phalen's sign 4) Mean static two-point discrimination – pulp of radial three digits 5) Hand-grip strength – hand-held	No significant differences between groups at the end of treatment and 8 weeks follow up of all measures of Treatment Effect (measures 1, 5, 6, 7, 8, 9, 10) Significant improvement seen in all 3 groups in Tinel's and Phalen's signs at end of treatment and 8 week follow up Significant improvement seen in all 3 groups in grip and pinch strength at 8week follow up. (Group 1: 1.9±2.7

	Group 3 51.4 ± 5.2 Mean duration of symptoms (years) – Group 1 1.5 ± 1.6; Group 2 1.4 ± 0.8; Group 3 1.4 ± 0.8 8 eventual dropouts	repeated 10x/session –for 3 weeks <u>Group 3</u> - (n=12) custom made neutral volar splint (worn for 3 weeks); exercise therapy (nerve and tendon gliding exercises as described by Totten & Hunter, 1991) 5 sessions daily, each exercise repeated 10x/session – continued for 3 weeks; Ultrasound (as for control group)		dynamometer 6) Pinch strength – between thumb and little finger – dynamometer 7) Symptom-severity scale questionnaire (11 item) 8) Functional status scale questionnaire (8 item) 9) Median motor nerve conduction – motor distal latency EMG of abductor pollicis 10) Sensory distal latency – EMG of abductor pollicis 11) Needle EMG of abductor pollicis brevis – looking for denervation 12) Patient satisfaction survey (at 8wks follow-up only)	Group2: 1.6±2.5 Group3: 1.0±1.7) and pinch (Group 1: 0.8±0.9 Group2: 0.6±1.4 Group 3: 0.9±0.7) strength at 8-week follow up ($p<0.05$). No changes seen in two-point discrimination Significant improvement in pain, (Group1: 2.2±3.4 Group 2: 2.5±2.5 and Group 3: 4.5±3.0), symptom (Group 1: 6.3±7.1 Group 2: 5.8±7.2 Group 3: 8.2±5.2) and functional scales (Group 1: 7.8±10.7 Group 2: 10.5±6.8 Group3: 14.4±9.4) of all 3 groups at end-Rx and 8 weeks follow up. Group 3 had the best results at 8 weeks follow-up patient satisfaction questionnaire (Group 2: excellent 3 (25.0%) Group 3: 8 (61.5%)
Bialosky et al 2009	n = 40 CTS Females only	<u>IG</u> with CTS Nerve gliding exercises and	<u>CG</u> with CTS Sham technique to minimise strain on	Measured at pre and post treatment	Significant improvement in both groups immediate post intervention and 3 weeks but not intergroup

Appraisal 9 Low risk of bias	Mean age: NDT 44.3 (6.97) Sham 49.5 (12.35) Follow up immediate and 3 weeks Mean duration of symptoms 156 weeks	splint. Received treatment for 3 weeks Cycle 6 seconds, 5 sets of 10 cycles 1st 3 Rx and 7 sets of 10 in Rx 4-6	nerve and splint. Received treatment for 3 weeks	1) NRS 2) DASH 3) Grip strength 4) Pressure pain sensitivity 5) Temporal summation	differences. Temporal summation only changed in NDT group – positive neurophysiological effect. A mean decrease of self-report of temporal summation pain of –8.8 (SD, 14.7; p=0.02; Cohen's d=0.35) in IG group – positive neurophysiological effect. A mean increase of temporal summation pain of +4.2 (SD, 16.0; p=0.26; Cohen's d=0.13) in participants receiving the sham
Brininger et al 2007 Appraisal 8 Unclear risk of bias	n = 61 – only 51 completed study Mean age: 50 – range 21 – 86 14 male 47 female Follow up 4 weeks and 8 weeks	<u>Group1</u> n = 16 CTS completed n =13 Neutral splint + nerve gliding exercises according to Totten and Hunter 1991 3-5 times/day 10 repetitions <u>Group 3</u> n = 16 completed n = 13 Cock-up splint and nerve gliding exercises as	<u>Group 2</u> n = 17 CTS completed n = 14 Neutral splint <u>Group 4</u> n = 12 completed n = 11 Cock-up splint	Measured at baseline, 4 weeks in clinic and 8 weeks by mail 1) Symptom Specific Scale 2) Functional Status Scale 3) Grip strength 4) Pinch strength	All groups improved over time irrespective of exercise or not – the groups with neutral splints had better outcomes. Symptom specific scale p=0.014; $F_{1.14}$=6.45, Functional status scale p=0.029. $F_{1.14}$=5.10. (mean=2.045) Drop out 10 patients of 61 – influence on results.

		above			
Heebner et al 2008 Appraisal 6 High risk of bias	n = 60 randomised Mean age 52 range 32 – 72 9 male 51 female	IG n = 30 participants with CTS randomised, 25 completed Standard care Nerve gliding exercises according to Sweeney & Harms (based on Totten & Hunter) – tensioner. 3-5x/day 10 repetitions	CG n = 30 participants with CTS randomised, 20 completed Standard care consisting of Advice Splint Tendon gliding exercises	Outcomes measured baseline, 1 month and 6 months 1) DASH 2) Carpal Tunnel Symptom Questionnaire 3) Elbow extension range of ULNDT	Nerve gliding exercise did not improve outcomes – improvement similar in both groups Group one (control) had better outcomes in functional status scale and Carpal Tunnel Symptom Questionnaire. (mean 2.2 for CG and 2.9 for the IG). There were no significant between group differences in ULNDT p=0.366 (values not available)
Horng et al 2011 Appraisal 8 Low risk of bias	n = 60 of which 53 completed Mean age Group 1 = 48.9 (8.9) Group 2 = 51.9 (9.3) Group 3 = 53.6 (9.1) Gender:	Group 2 n = 20 Participants randomised, 19 participants (34 wrists) completed Splint Paraffin Nerve gliding exercise Totten &Hunter	Group 1 n = 20 CTS participants randomised; 18 participants (31 wrists) completed Splint Paraffin Tendon gliding exercise Group 3 n = 20 participants	Measured pre treatment and after 2 months 1) DASH 2) WHO Quality of life 3) Functional Status Scale 4) Phalen's 5) Tinel's 6) Boston CTS	Only Group 1 showed significant improvements in their scores on functional status; the DASH questionnaire; and the physical domain of the WHO Quality of Life Questionnaire Post hoc analyses detected a significant difference (p=0.04) (p=0.04; Group1: -0.4±0.5 Group 2: 0.1±0.5 Group 3: 0.2±0.7) In functional status scores between groups 1 and 2 favouring control.

	male/female Group 1 9/51 Group 2 6/22 Group 3 3/29	Received sheet with exercises – to do 3 times daily. Follow up at 2 months	randomised; 16 participants (24 wrists) completed Splint Paraffin Treatment as for group 2	7) Sensory testing using mono-filament 8) VAS	
Oskouei et al 2014 Appraisal 9 Low risk of bias	n = 20 patients 32 hands Age of 46.7±11 Duration of symptoms 19.6±15.9 months	IG 16 hands Splint as much as possible for 4 weeks TENS Ultrasound NM starting in nerve off tension progressing into tension using elbow Flexion /Extension 3 treatments per week (15 repetitions) for 4 weeks	CG 16 hands Splint as much as possible for 4 weeks TENS Ultrasound 3 treatments per week for 4 weeks	Measured pre and post treatment 1) Boston questionnaire 2) Phalen's test 3) VAS 4) Median nerve tension test	Routine physiotherapy including rest splint, TENS, and therapeutic ultrasound seems to improve the symptom severity scale, visual analogue scale, median nerve tension test, and Phalen's sign in patients with CTS. (IG: 1.53±0.53 CG: 1.7±0.72), VAS (IG: 2.68±1.62 CG:, 3.31±3.05) median nerve tension test (IG: 9.04±9.6 CG: 18.41±11.6) , and Phalen's sign (IG: 19% CG 31%) in patients with CTS ($p<0.05$). The neural mobilisation in combination with routine physiotherapy improved the functional status scale and the median nerve distal motor latency. This combination can be used as an effective non-invasive treatment for patients with CTS.
Pinar et al	n = 26 (female)	IG 14 patients (19 hands)	CG 12 patients (16 hands) patients	Undertaken before and after a 10-week	Pre and post-treatment intra-group analyses of both groups revealed that

2005 Appraisal 7 Low risk of bias	Age range 35-55 years Duration of symptoms (months) CG 47.6 (± 6.8) IG 49.6 (± 5.2)	patients diagnosed with early-middle stages CTS In addition to splint wearing and patient training program treated with nerve gliding exercises (Totten & Hunter) 10 reps 5 sets a day for 10 weeks, combined with a conservative treatment program	diagnosed with early-middle stages CTS Treated in volar splint in neutral worn day & night for 6-weeks then night only from week 6-10, and a patient training program for the modification of functional activities (avoid repetitive activities) with a conservative treatment program.	treatment programme. 1) Tinel Test 2) Phalen Test 3) Pain (VAS) over a day 4) Motor Function manual testing 5) Grip strength (Jamar hand dynamometer) 6) Sensory evaluation (Semmes-Weistein monofilament &2-point discrimination test 7) Electrophysiological Test – Median & Ulnar n. distal latencies	there were no statistically significant differences between the two groups in average muscle strength, functional sensitivity, normal sensory test, or manual muscle tests. Significant progress was detected in both control and experimental groups during the post-treatment phase compared with the initial phase ($p< 0.05$). When the 2 groups were compared the experimental group, in which nerve gliding exercises were added, demonstrated more rapid pain reduction, and greater functional improvement especially in grip strength ($p< 0.05$) (IG: 1±1.6 CG: 1.6±1.8) and greater functional improvement especially in grip strength (IG: 22.0±6.8 CG: 21.7±4.3) ($p< 0.05$).
Tal-Akabi & Rushton 2000 Appraisal 7 Unclear risk of bias	n = 21 Age range 29-85 years Mean age 47.1 (±14.8) Duration of symptoms	<u>Group 1</u> n = 7 with CTS received ULNDT 2a mobilisation based on physiotherapist clinical reasoning	<u>Group 3</u> n = 7 with CTS received no intervention <u>Group 2</u> n = 7 with CTS received Carpal bone mobilisation (anterior-posterior and or posterior-	All taken pre and post treatment 1) Symptoms diary (24hr VAS) 2) Functional box scale 3) Range of motion Wrist flexion/extension 4) ULNDT2a	Only pain relief scale demonstrated a statistically significant difference between the 3 groups ($p<0.01$). VAS: Group 1 mean1.57; Group 2 mean 0.71; Group 3 mean 0.71. No statistically significant difference in effectiveness of treatment was demonstrated between the two intervention groups. The number of patients continuing to surgery was 2 in

	(years) 2.3 (±2.5, range 1-3) All subjects are on the waiting list for surgery	Number of treatments or treatment time not mentioned	anterior) and a flexor retinaculum stretch Treatment time not mentioned	5) Pain relief scale 6) Continuing to have surgery	NDT, 1 in carpal bone mobilisation and 6 in control group. ULTT – Group 1, 5 of 7 negative; Group 2, 4 of 7 negative; Group 3, all still positive
Schmid et al 2012 Appraisal 8 Low risk of bias	n = 21 Age: IG 49.9 (12.5) Splint 57.9 (16.3) Gender (male/female) IG 5/5 CG 7/3 Symptom duration in months (SD) IG 54.6 (47.6) CG 62.8 (56.1) CTS severity Mild IG 4 CG 3 Moderate IG 6	IG 11 with CTS randomised – 1 dropout Received neural gliding aimed at improving nerve excursion - exercises 10 repetitions 10 times per day for one week	CG 10 with CTS randomised Received night splint for one week	Measured before, 10 minutes after and 1 week after intervention 1) Signal intensity at pisiform, radio ulnar and hamate 2) Ligament bowing at hamate 3) Boston questionnaire 4) Pain (VAS) 5) Numbness (VAS) 5) Patient Specific Functional Scale	"The findings of this study suggest that a reduction in intraneural oedema is a therapeutic mechanism of both nerve and tendon gliding exercises and splinting. The chronicity of the symptoms of the patients involved in this study and the short treatment period propose that the reduction in intraneural oedema is associated with the interventions rather than the result of the natural course of CTS.' Boston questionnaire $F_{(1,17)}$=16.70; p . 0.001 Patient Specific Functional Scale $F_{(1,16)}$. 22.10; p < 0.001 Post-hoc comparisons revealed that both groups improved significantly after 1-week intervention (all p < 0.004). No significant interaction or main effects for pain intensity and

	CG 7				numbness were found (all p > 0.16). Signal intensity did not change in patients who were not treated
Wolny et al. (2016) Appraisal 7 Low risk of bias	n=160 initially Analysed (male 18, female 122) Mean age: IG 53.12 CG 51.51 Gender (Male/female) IG 8/62 CG 10/60	IG n=80 with CTS Not analysed n=10 Manual therapy and ULNDT1 sliders and tensioners 2 treatments/ week for 10 weeks	CG n=80 with CTS Not analysed n=10 Ultrasound and laser therapy 2 treatments/ week for 10 weeks	Outcomes measured before and at the end of treatment 1) Two-point discrimination	The outcomes of treatment on two-point discrimination demonstrated that both methods had a significant therapeutic effect (p<0.001). It should be noted, however, that the groups differed significantly before starting the treatment cycle. Larger disturbances of two-point discrimination sensation in symptomatic extremities occurred in the IG group as compared with the CG group. After a course of therapy, there were no statistically significant (p> 0.05) intergroup differences, indicating greater improvement in the NM group (IG: 2.6; 2.25-2.95 CG: 0.5; 0.16-0.84 p<0.001).

Legend: IG – Intervention group; CG – Control group; CTS – Carpal tunnel syndrome; VAS – Visual analogue scale; EMG – Electro-myogram; NRS – Numeric Rating Scale; DASH – Disability of arm, shoulder, hand symptom scale; ULNDT – Upper limb neurodynamic test; WHO – World Health Organization; TENS – Transcutaneous Nerve Stimulation; NM – Neural mobilisation

Table 2.3. Summary of findings of meta-analyses for carpal tunnel syndrome (CTS)

Outcomes (CTS)	**Relative effect (95% CI)**	**No. participants (No. studies)**	**p value**	**Quality of evidence**
Pain (VAS)	-0.22 (-0.74, 0.3) Favours intervention	126 (5) (Bialosky et al., 2009b, Baysal et al., 2006, Pinar et al., 2005, Tal-Akabi and Rushton, 2000, Schmid et al., 2012)	p = 0.52	4 low risk of bias
Hand grip strength	1.18 (-1.29, 3.66) Neutral	139 (4) (Akalin et al., 2002, Baysal et al., 2006, Brininger et al., 2007, Pinar et al., 2005)	p = 0.35	3 low risk of bias
Disability (DASH)	-1.55 (-7.84, 4.75) Favours intervention	153 (3) (Bialosky et al., 2009b, Heebner and Roddey, 2008, Horng et al., 2011)	p = 0.63	2 low risk of bias
Two point discrimination	0.36 (-0.8, 0.08) Favours intervention	173 (3) (Baysal et al., 2006, Bardak et al., 2009, Akalin et al., 2002)	p = 0.11	2 low risk of bias
Phalen's sign	0.81 (0.87, 1.86) Favours intervention	229 (5) (Akalin et al., 2002, Baysal et al., 2006, Bardak et al., 2009, Pinar et al., 2005, Oskouei et al., 2014)	p= 0.42	3 low risk of bias
Legend: CTS – Carpal Tunnel Syndrome; CI – Confidence Interval; VAS – Visual Analogue Scale; DASH - Disability of arm, shoulder, hand symptom scale; No. – number.				

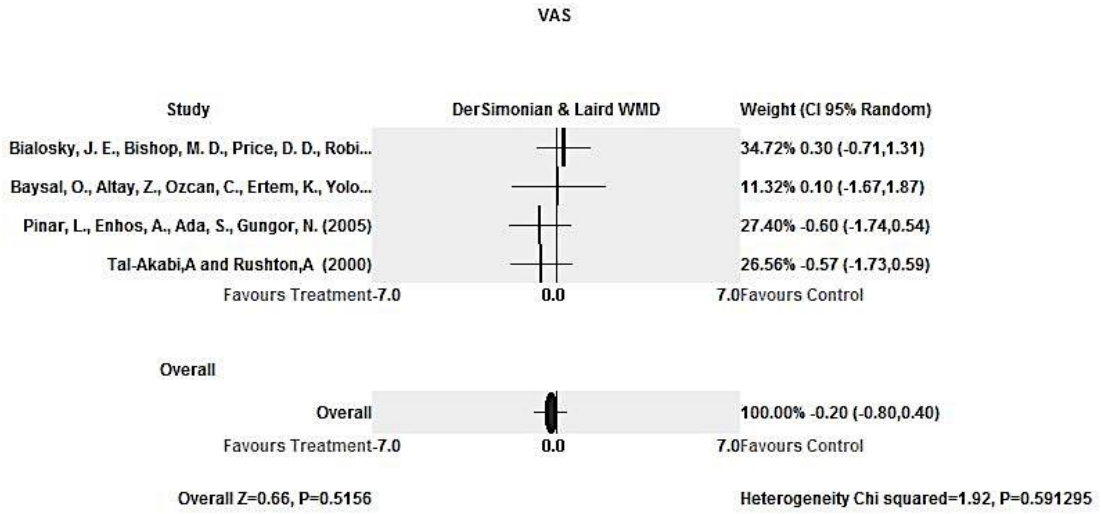


Figure 2.2. Meta-analysis for pain in CTS

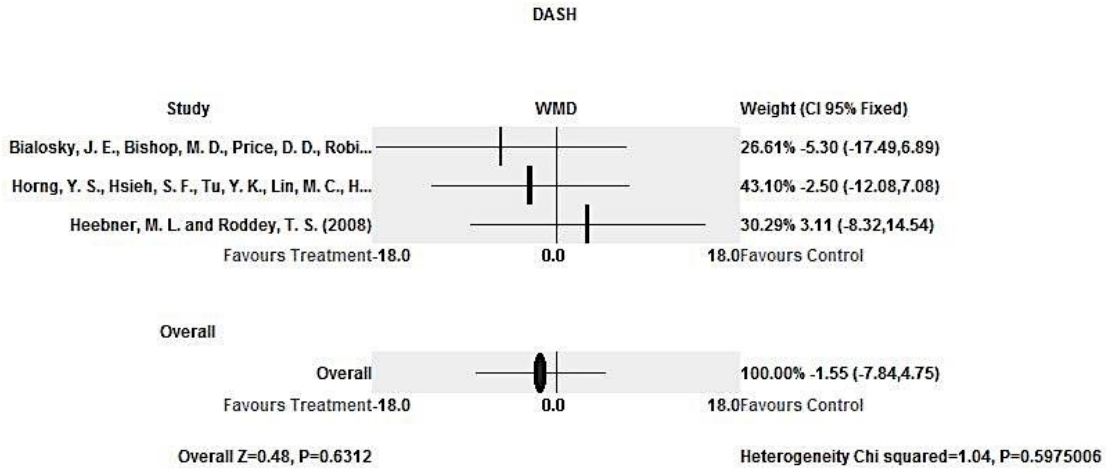


Figure 2.3. Meta-analysis for disability in CTS

2.3.5 Nerve related low back pain (N-LBP)

The majority of studies were high risk of bias (see table 2.1). Five studies used a slump position as the NM (Ali et al., 2015, Cleland et al., 2007a, Jain et al., 2012, Nagrale et al., 2012, Rezk-Allah et al., 2011). All the

studies using slump mobilisation had significant improvements in pain and disability.

The meta-analyses found that NM had a significant effect for both pain (p=0.0001; effect 1.78; 95% CI -2.55 – -1.01) (Cleland et al., 2007a, Dwornik et al., 2009, Jain et al., 2012, Kaur and Sharma, 2011, Nagrale et al., 2012) (p=0.0001) and disability (p=0.0001; effect -9.26; 95% CI -14.5 – -4.01) (Cleland et al., 2007a, Jain et al., 2012, Kaur and Sharma, 2011, Nagrale et al., 2012) (p=0.0006) in participants with N-LBP.

Three studies compared slump with exercises and lumbar mobilisation (Cleland et al., 2007a, Jain et al., 2012, Nagrale et al., 2012) and 1 compared it to stabilisation exercises (Ali et al., 2015). One study could not be included in the meta-analysis as it measured the H-reflex and compared slump with SLR (Rezk-Allah et al., 2011).

The remaining studies used a variety of techniques. SLR mobilisation (Kaur and Sharma, 2011, Rezk-Allah et al., 2011, Ahmed et al., 2013) resulted in a significant improvement in pain and disability ($p<0.05$). SLR was compared to exercises in 2 studies (Ahmed et al., 2013, Kaur and Sharma, 2011). NM techniques which aimed at opening the intervertebral foramina (Mehta et al., 2014) also reported improved pain (p=0.01) in the NM group compared to a group receiving ultrasound, exercises and lumbar mobilisation. Three studies compared two types of NM with each other (Patel, 2014, Rezk-Allah et al., 2011, Waleed Salah El-din, 2015). One compared slump to bent leg raise (Patel, 2014) as described by Hall et al. (2006). Another compared slump to SLR (Rezk-Allah et al., 2011). The third study compared SLR and slump to lumbar mobilisation which included rotation with SLR (Waleed Salah El-din,

2015). All NM groups had an improvement in pain ($p<0.09$) but there were no statistically significant between-group differences ($p>0.5$).

Four studies measured ROM in N-LBP (Dwornik et al., 2009, Kaur and Sharma, 2011, Mehta et al., 2014, Patel, 2014) with two reporting improvement in SLR in the NM group, (Patel, 2014, Kaur and Sharma, 2011) one an improvement in the slump (Mehta et al., 2014) and one non-significant change in Laseque's sign (Dwornik et al., 2009).

Five studies administered treatment over a period of three weeks (Ali et al., 2015, Cleland et al., 2007a, Jain et al., 2012, Mehta et al., 2014, Nagrale et al., 2012) and two studies over a two-week period (Ahmed et al., 2013, Dwornik et al., 2009). One study had a one week intervention,(Patel, 2014) another four weeks (Rezk-Allah et al., 2011) and one study had a treatment period of six weeks (Waleed Salah El-din, 2015).

Figure 2.4 and Figure 2.5 show the results of the meta-analyses and Table 2.4 describes the studies.

Table 2.4. Study descriptions for N-LBP

Author **Appraisal score** **Risk of bias**	**Patient demographics**	**Intervention Group (IG)**	**Control Group (CG)**	**Outcome Measures**	**Result**
Ahmed et al. (2013) Appraisal 7 Low risk of bias	n=30 (14 male, 16 female) Age range (years) 45-67 Mean age (years) IG 53.00 (±1.91) CG 52.60 (±1.60) Duration of symptoms (weeks) IG 4.87 (±1.50) CG 5.26 (±1.75)	IG n=15 participants with sciatica Same treatment as control plus: SLR tibial and peroneal bias 2 sets of 20 mobilisation of each bias. 3 treatments/week for 2 weeks	CG n=15 participants with sciatica Flexion and extension exercises(Elnaggar et al., 1991) 2-3 sets TENS Home exercises 3 treatments/week for 2 weeks	Outcomes measured at baseline and end of treatment 1) NPRS 2) SF12	No Baseline differences. Improvement in both measures in both groups, but significantly more and clinically relevant in the IG group 95% CI; 2.85, 4.09) NRS CG 4.93 ± 1.10 (95% CI (4.34, 5.55) Between groups difference favouring IG 1.46 (14.6%) SF12 IG 65.57 ± 12.00 95% CI (58.97, 72.17) SF12 CG 54.53±7.34 95% CI (50.49, 58.57) Between groups difference favouring IG 11.04 (11.04%)

Ali et al. (2015) Appraisal 6 High risk of bias	n=40 (10 male, 30 female) Age range (years) 20-60 Mean age (years) IG 34.32 (±8.94) CG 33.22 (±7.16)	IG n=22 participants with chronic radicular LBP Same treatment as control plus: Slump slider mobilisation 5 days/week for 3 weeks	CG n=18 participants with chronic radicular LBP Lumbar stabilisation exercises Shortwave diathermy 5 days/week for 3 weeks	Outcomes measured at baseline and end of treatment 1) MODI 2) VAS – 5 point scale	Both groups had a significant improvement in pain (VAS) 95% CI; 2.85, 4.09) NRS CG 4.93 ± 1.10 (95% CI (4.34, 5.55). Between groups difference favouring IG 1.46 (14.6%) SF12 IG 65.57 ± 12.00 95% CI (58.9659, 72.1741) SF12 CG 54.53 ± 7.34 95% CI (50.4905, 58.5695) Between groups difference favouring IG 11.04 (11.04%)Only the IG had a significant improvement in disability (MODI) (IG p=0.003; 2.91±0.69; CG p=0.163; 1.49±0.32).
Cleland et al. (2007a)	n=30 (9 male, 21 female)	IG n=16 participants with LBP	CG n=14 participants with LBP	Outcomes measured at baseline and end	No baseline differences between groups (p>0.05).

Appraisal 9 Low risk of bias	Age range (years) 18-60 Mean age (years) IG 40.0 (±12.2) CG 39.4 (±11.3) Duration of symptoms (weeks) IG 14.5 (±8.0) CG 18.5 (±12.5)	Same treatment as control plus: Slumped stretching exercise (position held 30 seconds, 5 repetitions) Home exercise slump stretches (2 repetitions for 30 seconds) 2 /week for 3 weeks	5 min cycle warm up Lumbar spine mobilisation (PA mobilisations to hypo mobile lumbar segments, grade 3-4) Standardised exercise program (pelvic tilts, bridging, squats, quadruped alternate arm/leg activities; 2 sets 10 repetitions each) 2 /week for 3 weeks	of treatment 1) Body Diagram (for distribution of symptoms) 2) NPRS 3) MODI 4) Fear avoidance beliefs questionnaire	Participants who received slump stretching had significantly greater improvements in disability. Between group difference favouring IG 9.7 95% CI (5.4, 14.0) (9.7 points on the MODI, p<0.001), pain (0.93 points on the NPRS, p=0.001 2.91±0.69; CG p=0.163; 1.49±0.32) and centralisation of symptom distribution (p<0.01).
Dwornik et al. (2009) Appraisal 6 High risk of bias	n=97 (44 male, 53 female) Age range (years) 19-60 Mean age IG and CG (years) 43 (±10) No other data	IG n=42 participants with neurogenic LBP, 5 did not complete treatment 10 treatments over 2 weeks. NM techniques according to Butler(Butler, 1991) of femoral, sciatic, tibial	CG n=45 participants with neurogenic LBP, 2 did not complete treatment 10 treatments over 2 weeks. 10x TENS 10-15 min 10x laser over painful area.	Outcomes measured at baseline and end of treatment 1) Resting muscle tone (quadriceps femoris, biceps femoris, Tibialis anterior, gastrocnemius) measured by EMG	NM had significant effect on resting muscle tone compared to control. Significant improvement in clinical tests (Laseque p=0.0003 between group difference 2.7° (6%) favouring IG) and pain (p=0.00001 difference 1.5 (15%) favouring IG)) and pain (p=0.00001). No

	available	nerves Techniques not described	Movement exercises for intervertebral joints without axial loading	2) ROM of Laseque sign and reverse Laseque sign measured with inclinometer 3) Presence of Bragard sign and reverse Laseque sign 4) VAS	other values available. Drop out of 7 of 87 participants.
Jain et al. (2012) Appraisal 6 High risk of bias	n=30 (11 male, 19 female) Age range (years) 19-60 Mean age (years) IG 34.26 (±5.66) CG 33 (±6.86) Duration of symptoms (weeks) IG 8.067 (±1.10) CG 8.266 (±1.16)	IG n=15 participants with LBP, unilateral limb pain and positive slump All participants were treated for 9 sessions (3 days/ week for 1st week and 2 days/week for next 3 weeks) Same treatment as control plus: slump stretching from 2nd week	CG n=15 participants with LBP unilateral limb pain and positive slump All participants were treated for 9 sessions (3 days/week for 1st week and 2 days/ week for next 3 weeks) PA mobilisation of lumbar spine, exercises	Outcomes measured at baseline, 1, 2, 3, 4 and 5 weeks 1) VAS 2) MODI	For pain (VAS) significant differences were found at the end of 2nd, 3rd, 4th and 5th week (p=0.0185,p=0.000, p=0.000 and p =0.000, respectively) between the 2 groups, in favour of the experimental group. MODI between the groups was non-significant differences at the end of 1st week (p=0.4375), 2nd week (p=0.4515), 3rd week (p=0.078) and 4th week (p=0.0865). No means or SD values

					available
Kaur and Sharma (2011) Appraisal 6 High risk of bias	n=27 Age range (years) 18-45 No other data available	IG n=12 participants with sub-acute Neurogenic LBP: pain in lower lumbar region with or without radiation to lower limb; without any neurological deficits and positive SLR. 10 sessions over 2 weeks Passive SLR	CG n=15 participants with sub-acute Neurogenic LBP: pain in lower lumbar region with or without radiation to lower limb; without any neurological deficits and positive SLR. 10 sessions over 2 weeks Advice Exercise	Outcomes measured at baseline and end of treatment 1) VAS 2) Hip flexion ROM 3) Werneke overlay template 4) MODI	Between groups analysis of all the variables demonstrated a significant post-intervention difference ($p<0.05$) in patient reported VAS scores, (mean change of 3 (30%) favouring IG; IG 2, 95% CI (0.74, 3.26) CG; 4, 95% CI (2.74, 5.26)), hip flexion ROM (74.6° for IG and 60° for the CG) hip flexion ROM and disability scores (MODI- IG -6 and CG -2). A statistically significant reduction in the area of reported symptoms for NM within the IG (50.3%) but not for the CG (25.1%).
Mehta et al. (2014) Appraisal 5	n=50 (22 male, 28 female) Mean age (years) IG 45.58 (±6)	IG n=25 participants with sub-acute LBP and a capsular pattern of restriction	CG n=25 participants with sub-acute LBP and a capsular pattern of restriction	Outcomes measured at baseline and end of treatment	Both treatment techniques improved pain and disability but the NM group improved sooner than

High risk of bias	CG 46 (±6.8) Gender: IG (12 males, 13 females) CG (10 males and 15 females) No other data available	3 weeks treatment on alternate days and follow up on week 4 Ultrasound Exercise NM from static opener progressing to dynamic end range closer 30 mobilisations of 3 sets with 30 sec. rest	3 weeks treatment on alternate days and follow up on week 4 Ultrasound Exercise Maitland joint mobilisation	1) VAS 2) ROM lumbar spine 3) ROM Slump test 4) MODI	the other group. VAS p=0.0133(IG: 4.6 CG: 6.3) p=0.0133 Slump ROM (IG: 2.4 CG 2.7 p=0.0038) At 4 weeks post-treatment
Nagrale et al. (2012) Appraisal 9 Low risk of bias	n=60 (19 male, 39 female) Mean age (years) IG 38.2 (±3.47) CG 37.76 (±4.70) Symptom duration (weeks) IG 15.26 (±2.57) CG 14.76 (±1.79)	IG n=30 participants with non radicular LBP with positive slump and SLR > 45° Same treatment as control plus: Slump stretching 5x 30 second hold	CG n=30 participants with non radicular LBP with positive slump and SLR > 45° 3 weeks treatment PA mobilisation of lumbar spine Stabilisation exercises according to Childs et al(Childs et al., 2004)	Outcomes measured at baseline, 1, 2, 3 and 6 weeks. 1) NPRS 2) MODI 3) Fear Avoidance Beliefs Questionnaire	There were large within-group changes for all outcomes with p<0.01 and large between group (IG: 28±3.93 CG: 39.5±7.25) and 6 (IG: 28.2±4.11 CG; 44.1±6.40) for the MODI and weeks 1 (IG: 5.4±0.93 CG: 6.1±1.09), 2 (IG: 3.6±0.77 CG: 4.7±0.94), 3, (IG: 2.1±0.54 CG: 3.7±0.95) and 6 (IG: 2.4±0.80 4.3±1.12) NPRS and FABQ at

					p<0.01. Significant differences favouring the slump stretching group at p<0.01.
Patel (2014) Appraisal 5 High risk of bias	n=50 Age range (years) 30-60 No other data available	<u>Group A</u> n=25 participants with LBP and a positive SLR of more than 15° BLR(Hall et al., 2006) 30 sec. x 3 4 treatments for a week <u>Group B</u> n=25 participants with LBP and a positive SLR of more than 15° Slump stretching exercise 30 sec. x 3 4 treatments for a week		Outcomes measured at baseline and end of treatment 1) VAS 2) ROM of SLR	Results of the study shows that both the techniques BLR and Slump are effective in reducing pain and alter the ROM (p≤0.05) p=0.003 pre test mean 67.6, post test mean 85), than the Group B (p=0.07 pre test mean 70.4 post test mean 85.68 of passive SLR. However group A showed greater improvement in pain and ROM of passive SLR (p=0.003), than the group B in participants with LBP.
Rezk-Allah et al. (2011) Appraisal 6	n=40 Age range (years) 35-50	<u>Group A</u> n=20 Slump group. Positive findings of electromyography, prolonged latency of H-reflex > 30 msec. Slump to full range –		Outcomes measured at baseline and end of treatment 1) VAS	Significant reduction in pain and H-reflex latency (p<0.01) in comparison to pre-treatment values, no significant difference in pain intensity

High risk of bias	Mean age (years) Group A 43.95 (±4.84) Group B 44.9 (±4.55) No other data available	held for 60 seconds x 5 3 treatment/week for 4 weeks <u>Group B</u> n=20 SLR group. Positive findings of electromyography, prolonged latency of H-reflex > 30 msec. SLR to onset of symptoms or resistance- held for 60 seconds x 5 3 treatments/week for 4 weeks		2) H-reflex latency	(Group A: t=13.85, p=0.0001 Group B: t=14.25, p=0.0001) and H-reflex latency (t=2.92, p=0.0058) between groups post-treatment. NM significantly improved symptoms and decreased nerve root compression.
Waleed Salah El-din(Waleed Salah El-din, 2015) Appraisal 6 High risk of bias	n=60 Age range (years) 30-50 Mean age (years) IG 44.2 (±6.16) CG 42.93 (±5.73) Duration of symptoms (weeks) Pain for longer than	<u>IG</u> n=30 participants with chronic radicular LBP MRI compromise of nerve SLR and Slump mobilisation to onset of symptoms 3 treatments/week for 6 weeks <u>CG</u> n=30	NOTE – used rot SLR (Maitland) in Comparison Group described as mobilisation group	Outcomes measured at baseline and end of treatment 1) VAS 2) Oswestry Disability Index 3) MRI compromise of nerve	Manipulation and NM The lumbar manipulation (with SLR) techniques were more effective than NM techniques on leg pain (P=0.006), Group A: 3.03±1.88 Group B: 1.83±1.31 p=0.006), MODI (Group A: 23.9±4.9 Group B: 18.4±6.87 p=0.001), and degree of nerve root compression

	3 months No other data available	Posterior-anterior mobilisation 3-4 repetitions (Maitland) Lumbar rotation with SLR 3-4 repetitions			(P=0.037).

Legend: IG – Intervention group; CG – Control group; SLR – Straight leg raise; BLR – Bent leg raise; TENS – Transcutaneous Electro-nerve stimulation; NPRS – Numeric pain rating scale; SF – Short form; LBP – Low back pain; MODI – Modified Oswestry Disability Index; EMG – Electro-myogram; VAS – Visual analogue scale; ROM – Range of motion.

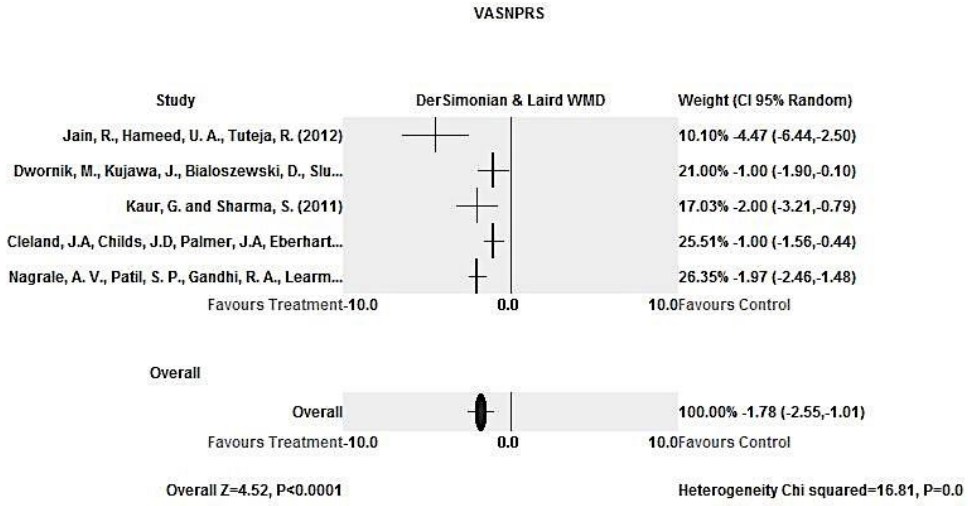


Figure 2.4. Meta-analysis for pain in nerve-related low back pain (N-LBP)

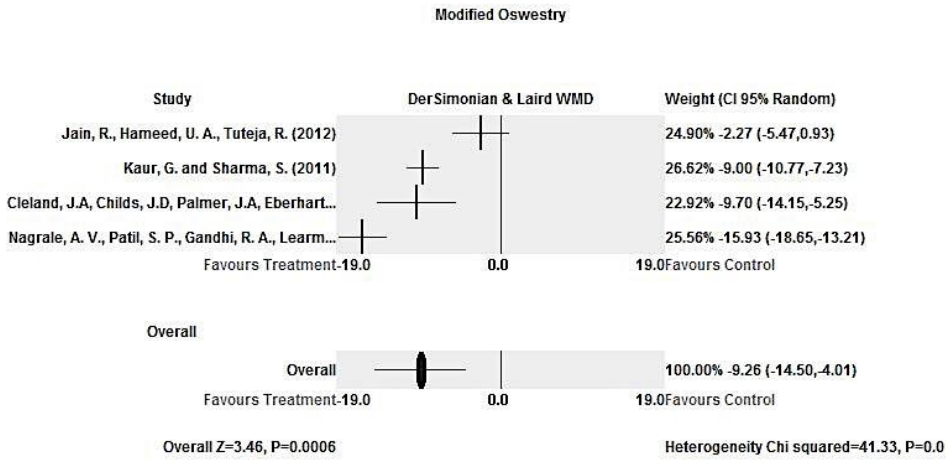


Figure 2.5. Meta-analysis for disability in N-LBP

2.3.6 Nerve-related neck and arm pain (N-NAP)

Five of the 10 studies had a low risk of bias (Table 2.1) (Allison et al., 2002, Coppieters et al., 2003b, Langevin et al., 2015, Nee et al., 2012b, Ragonese, 2009). Outcome measures included pain, McGill Pain Questionnaire, Neck

Disability Index, Global Rating of Change, Patient Specific Functional Scale, Cervico-brachial Pain Questionnaire; DASH and Northwick Park Questionnaire; active ROM; shoulder girdle elevation force and ROM during neurodynamic testing.

Pain (VAS and NPRS) was the only outcome measure on which meta-analysis could be performed. Participants who received cervical lateral glides had a significantly better outcome for pain than the control groups (p=0.0003; effect 1.89; 95%CI -3.14, -0.64) (Figure 2.6).

Two studies used only one intervention,(Coppieters et al., 2003b, Marks et al., 2011) two had 10 sessions of treatment (Kumar, 2010, Nar, 2014) and one had five sessions over a seven day period (Gupta and Sharma, 2012). Three studies mention only the length of treatment (four weeks, (Langevin et al., 2015) eight weeks (Allison et al., 2002) and six months (Anwar et al., 2015)). One study had four treatments over a period of two weeks (Nee et al., 2012b). Another study administered three treatments per week over three weeks (Ragonese, 2009).

Four studies evaluated cervical lateral glide techniques (Allison et al., 2002, Coppieters et al., 2003b, Nee et al., 2012b, Ragonese, 2009) and all reported a significant improvement in pain for the groups receiving NM (meta-analysis: p<0.001) (Figure 2.4). Cervical lateral glide was compared to mobilisation of the gleno-humeral joint and thoracic spine, (Allison et al., 2002) ultrasound, (Coppieters et al., 2003a, Coppieters et al., 2003b) exercise and a combination of NM and exercise (Ragonese, 2009) and advice only (Nee et al., 2012b). These studies all had a low risk of bias. Another study with a low risk of bias (Langevin et al., 2015) used mobilisation techniques aimed at

opening the cervical foramina (including cervical lateral glide) and compared it to cervical spine mobilisation (Langevin et al., 2015). Both groups had significant improvement in disability and pain ($p<0.05$) but there were no between group differences.

Four studies used nerve mobilisation exercises (Gupta and Sharma, 2012, Marks et al., 2011, Nar, 2014, Kumar, 2010). One found cervical spine mobilisation more effective than NM to improve ROM of the cervical spine ($p<0.05$) and the ROM during neurodynamic testing ($p=0.01$) (Marks et al., 2011). The use of a tensioning technique (Nar, 2014) resulted in significant improvements in pain ($p<0.001$) in the NM group compared to interferential therapy, traction and exercises. Median nerve sliders (Gupta and Sharma, 2012) improved pain in the NM group compared to exercise and ergonomic advice ($p<0.05$). When comparing tensioning techniques for the radial nerve to McKenzie exercises (Kumar, 2010) it was found that the McKenzie exercise group had better outcomes in pain ($p<0.001$). The above studies all had a high risk of bias. One study did not specify the kind of NM used in combination with cervical spine mobilisation and exercises and compared it to cervical spine mobilisation and exercises only (Anwar et al., 2015). The addition of NM resulted in improvement in disability ($p<0.05$).

The effect of NM on disability could not be explored by meta-analysis as different outcome measures were used. One low risk of bias study (Nee et al., 2012b) reported better outcomes (number needed to treat) for the Neck Disability Index and the Patient Specific Functional Scale in the NM group compared to advice to stay active. Two high risk of bias studies reported better outcomes ($p<0.05$) on the Neck Disability Index in the groups receiving

NM compared to groups receiving mobilisation and exercise (Anwar et al., 2015, Gupta and Sharma, 2012). One study did not report the outcomes for the Neck Disability Index (Nar, 2014). One other study also measured the Neck Disability Index (Langevin et al., 2015) but found that the NM group improved to the same extent as the comparison group. One low risk of bias study found that NM resulted in no adverse effects (Nee et al., 2012b).

There were 5 studies in N-NAP that assessed ROM (Coppieters et al., 2003a, Gupta and Sharma, 2012, Kumar, 2010, Marks et al., 2011, Ragonese, 2009). Two studies reported an improvement in ULNDT1 elbow extension range in the NM groups (Coppieters et al., 2003a, Gupta and Sharma, 2012). In another study there was no significant difference between groups (Ragonese, 2009) and the last study measured neck ROM and found improved extension and rotation towards the painful side in the group receiving joint mobilisation (Marks et al., 2011). Table 2.5 contains the study descriptions and Figure 2.6 shows the forest plot for the meta-analyses on pain in N-NAP.

Table 2.5. Study descriptions N-NAP

Author **Appraisal score** **Risk of bias**	**Patient demographics**	**Intervention Group (IG)**	**Control Group (CG)**	**Outcome**	**Result**
Allison et al. (2002) Appraisal 9 Low risk of bias	n=30 (20 females, 10 males) Age range 18-75 years Median duration of symptoms (months) IG 12 CG 12 Articular Treatment 72	IG n=17 participants with cervico-brachial pain Cervical lateral glide, shoulder girdle oscillation, muscle re-education, home mobilisation. Duration of treatment 8 weeks.	CG n=10 participants with cervico-brachial pain Received no intervention for the initial 8 weeks (At the end of the study they were given neural treatment as a cross over protocol.) Articular treatment n=9 patients with cervico-brachial pain. Gleno-humeral joint mobilisation, thoracic mobilisation and home exercise. Duration of treatment 8 weeks.	Outcomes measured at baseline, 4 weeks into treatment and post treatment. 1) McGill pain questionnaire. 2) Northwick Park questionnaire 3) Pain (VAS)	Both manual therapies combined with home exercises are effective in improving pain intensity, pain quality scores and functional disability levels. A group difference was observed for the VAS scores at 8 weeks with the NM having a significantly lower score ($p<0.001$ relative % change 66 favouring NM).
Anwar et al. (2015) Appraisal 5 High risk of bias	n=40 Age and duration of symptoms not available	IG n=20 participants with cervical radiculopathy Moist heat Mobilisation and isometric exercises Neural mobilisation	CG n=20 participants with cervical radiculopathy Moist heat Mobilisation and isometric exercises	Outcomes measured at baseline and end of treatment 1) VAS 2) NDI	Addition of neurodynamics to a multimodal program resulted in a significant improvement in disability ($p<0.05$). $p<0.05$; 1.53 +/- 0.52). No other values available

		(technique not mentioned) Treated over a period of 6 months	Treated over a period of 6 months		
(Coppieters et al., 2003a, Coppieters et al., 2003b) Appraisal 8 Low risk of bias	n=20 (16 females, 4 males) Age range 35- 65 years Mean age (years) IG 49.1 (±14.1) CG 46.6 (±12.1) Mean duration of symptoms (months) IG 2.7 CG 3.2	IG n=10 participants with brachial or cervico-brachial neurogenic pain Received NM treatment (contra-lateral glide of cervical segment) One intervention and immediate follow-up	CG n=10 participants with brachial or cervico-brachial neurogenic pain Received Ultrasound dose of 0.5 W/cm², 5mins sonation time, 20% size of head 5cm², frequency 1MHz. One intervention and immediate follow up	Outcomes measured at baseline and end of treatment 1) Elbow extension ROM during NTPT1 2) Pain (NPRS) neck and arm. 3) Symptom distribution.	Significant differences in treatment effects between 2 groups could be observed for all outcome measures (p≤0.306). For the mobilization group the increase in elbow extension from 137.3º to 156.7º, the 43% decrease in area of symptom distribution and decrease in pain from 7.3 to 5.8 were significant (p≤0.0003). For ultrasound group, there were no significant differences.
Gupta and Sharma (2012) Appraisal 5 High risk of bias	n=34 initial 37 (16 females, 18 males) Age range 18 – 40 Median age 29.5	IG n=16 participants with cervico-brachial pain n=2 discontinued Median slider applied 3 x 10 repetitions 5 treatments over 7 days	CG n=18 participants with cervico- brachial pain n=1 discontinued Exercise (isometric), posture, advice to move regularly. Frequency not clear	Outcomes measured at baseline and end of 7 days 1) NDI 2) Cervico-brachial pain questionnaire 3) VAS 4) Pain free elbow	Both groups showed statistically significant improvement in pain intensity, (0.95; Z=4.94, elbow extension ROM (12.50°; Z=5.02), NDI and CBSQ (both decrease of 5 in IG compared to CG decrease of 2 for the NDI and 1 for CBSQ

	No other data available			extension	(p<0.05). However, experimental group receiving NM showed better improvement compared to conventional group.
Kumar (2010) Appraisal 5 High risk of bias	n=30 (20 females, 10 males) Age range (years) 25 to 68 No other data available	Group B n=10 participants with cervical radiculopathy Active or passive through range and end range oscillation in ULNDT 2a position moving distal component Shortwave Traction 10 treatments over 10 days	Group A n=10 participants with cervical radiculopathy McKenzie exercises Shortwave Traction Group C with cervical radiculopathy n = 10 Shortwave Traction 10 treatments over 10 days	Outcomes measured at 1st, 5th and 10th day 1) VAS 2) Pain recovery percentage 3) ROM	Pain reduction in first 5 days was most in patients treated with McKenzie method and best symptom relief achieved (p=0.0001 (Group A: t =10.24, p=0.0001, Group B: t=5.106, p=0.001 and group C:t=14.596, p=0.0001). Conventional method gave more relief between 5th and 10th day of treatment, Range of motion recovery was even in all groups. NM shows poor improvement possibly because of provocation to the nerve roots.
Langevin et al. (2015) Appraisal 9 Low risk of bias	n=36 (male 12, female 24) Mean age (years) IG 42.8 (±10.4) CG 47.8 (±11.3)	IG n=18 participants with cervical radiculopathy Stabilisation and mobility exercises Cervical mobilisation techniques aimed at opening	CG n=18 participants with cervical radiculopathy Cervical and thoracic mobilisations, as well as stabilisation and mobility exercises.	Outcomes measured at baseline, 4 weeks and 8 weeks post treatment 1) NDI	Both groups showed statistically and clinically significant improvement from baseline to week 4 and to week 8 in NDI ($F_{2,68}$=0.84, p=0.44) QuickDASH ($F_{2,62}$=0.36, p= 0.70), and NPRS

	Symptom duration (weeks) IG 5.4 (±3.2) CG 5.7 (±3.7)	the intervertebral foramina e.g. lateral glide and flexion rotation away from pain. Treatment period of 4 weeks	Treatment period of 4 weeks	2) DASH 3) NPRS Cervico-thoracic mobility	($F_{2,68}$=1.87, p=0.16) scores (p<0.05). Manual therapy and exercises are effective in reducing pain and functional limitations related to cervical radiculopathy. NM yielded no significant (p ≥ 0.14) additional benefits.
Marks et al. (2011) Appraisal 6 High risk of bias	n=20 (male 4, female 16) Mean age (years) CG 53.7 (±9) IG 52.6 (±12.5) Symptoms duration (weeks) CG 215 (±214.2) IG 323 (±404.1)	IG n=10 participants with cervico-brachial pain Nerve tensioner depending on most painful test Once for 15 minutes	CG n=10 participants with cervico-brachial pain Cervical spine mobilisation and first rib Once for 15 minute	Outcomes measured at baseline, post treatment and 1 week follow up 1) VAS neck and arm 2) Active ROM F/E/LF/Rot 3) ULNDT	Significant decrease in neck pain in both groups post-test. (CG – 1.18; IG – 1.2). Significant improvement in CG for cervical extension and lateral flexion towards painful side. Significant improvement in range favouring CG (p=0.015) (CG: 5.2±7.2 IG: 1.2±7.7).
Nar (2014) Appraisal 6 High risk of bias	n=30 (males 9, female 21) Mean age (years) IG 43.93(±7.05)	IG n=15 participants with cervical radiculopathy Interferential therapy Traction Exercise	CG n=15 participants with cervical radiculopathy Interferential therapy Traction Exercise	Measured pre and post treatment 1) VAS 2) NDI	NM along with conventional treatment is more effective than conventional treatment alone. VAS (IG: 2.06+1.33 CG: 3.53+1.12) p=0.01.

	CG 45.06 (±7.46) Gender: IG (11 females, 4 males) CG (10 females and 5 males)	Advice NM using ULNDT1 10 treatment 6 days per week	Advice 10 treatments 6 days per week		
Nee et al. (2012b) Appraisal 7 Low risk of bias	n=60 (38 females, 22 males) Mean age = 47 (±9) Mean group age (years) IG 47(±8) CG 48(±9) Mean duration of Symptoms (weeks) 26 (±12- 77) IG 32 CG 18 Gender: IG (14 males, 26 females) CG (8 male, 12 female)	IG n=40 participants with N-NAP pain Advice to stay active Brief education Cervical lateral glide Nerve sliding exercises 4 treatments over 2 weeks	CG n=20 participants with N-NAP pain Advice to stay active	Outcomes measured at baseline and 3-4 weeks after treatment 1) Global Rating of Change 2) Neck Pain (NPRS) 3) Arm Pain (NPRS) 4) Patient Specific Functional Scale 5) NDI	Numbers needed to treat favoured the intervention group for NDI (IG: 8.9±5.4 CG: 11.2±5), neck pain (IG: 2.6±2.4 CG: 4.2±2.2), arm pain (IG: 2.4±2.1 CG: 4±1.9) and PSFS (IG: 2.0±2.1 CG: 0.4±1). NM provides clinically relevant improvement with no evidence of harm. Risk difference for global rating of change between groups -38 (95%CI -16-60) favouring the IG

Ragonese (2009) Appraisal 7 Unclear risk of bias	n=30 No other demographic data available	IG 1 n=10 with cervical radiculopathy Cervical lateral glide grade 3-4 ULNDT sliders progressing to tensioners Thoracic mobilisation 3 times/week for 3 weeks IG 2 n=10 with cervical radiculopathy Treatments as above plus strengthening of deep neck flexors, lower and middle trapezius and serratus anterior. 3 times /week for 3 weeks	CG n=10 with cervical radiculopathy Strengthening of deep neck flexors, lower and middle trapezius and serratus anterior	Outcomes measured at baseline, end week 1, week 2, week 3 and end of treatment NPRS NDI Neck rotation ROM	All groups improved significantly in terms of pain, (IG 1: 2.4 ± 1.1 IG 2: 0.9 ± 1.2 CG: 1.6 ± 1.5)($p<0.01$), disability (IG 1: 17.2 ± 10.3 IG 2: 7.8 ± 5.5 CG: 10.2 ± 7.1) and ROM (IG 1: 74.3 ± 3.58 IG 2: 71.4 ± 3.67 CG: 74.4 ± 4.12) $p<0.05$). For pain and disability the group receiving NM and exercise did significantly better than the other 2 groups ($p<0.01$)

Legend: IG – Intervention group; CG – Control group; VAS – Visual analogue scale; N-NAP – Nerve-related Neck and Arm Pain; NPRS – Numeric pain rating scale; NDI – Neck disability index; ROM – Range of motion; DASH – Disability of the arm, shoulder, hand symptom scale; ULNDT – Upper limb neurodynamic test; NM – Neural mobilisation.

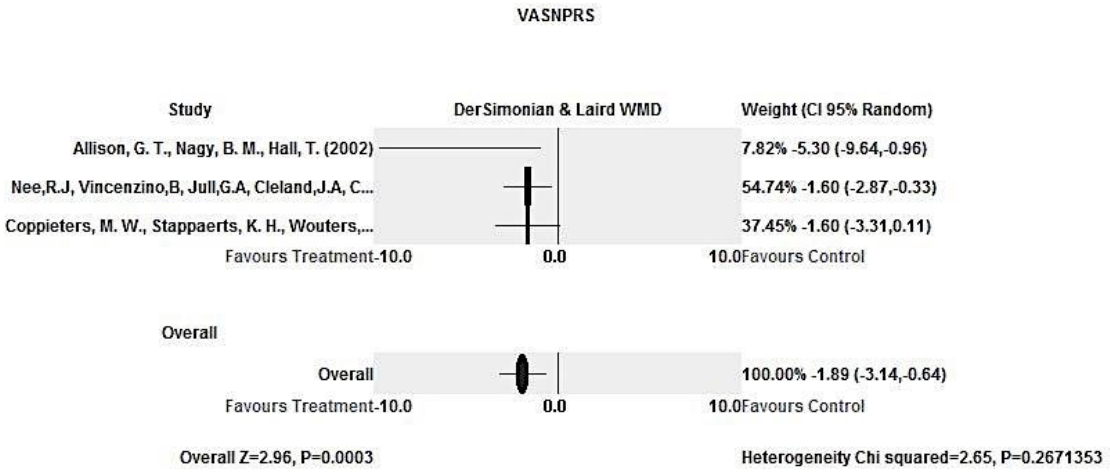


Figure 2.6. Meta-analysis for pain in N-NAP.

2.3.7 Lateral Epicondylalgia

Three studies used NM for the treatment of lateral epicondylalgia (Dabholkar et al., 2013, Drechsler et al., 1997, Vincenzino et al., 1996). One study had a low risk of bias (Vincenzino et al., 1996) and the other two had a high risk of bias (Dabholkar et al., 2013, Drechsler et al., 1997).

One study administered treatment for four days per week over four weeks (Dabholkar et al., 2013) and another did two treatments per week over six weeks (Drechsler et al., 1997). The other study did one intervention over a three day period (Vincenzino et al., 1996).

A low risk of bias study used cervical lateral glides as the intervention (Vincenzino et al., 1996) with significant improvements in pressure pain threshold, pain free grip strength, neurodynamic test ROM and pain scores compared to the placebo and control groups ($p<0.05$). Two studies

(Dabholkar et al., 2013, Drechsler et al., 1997) with a high risk of bias compared NM and radial head mobilisation to exercise (Dabholkar et al., 2013) and friction massage and exercise (Drechsler et al., 1997). One study (Drechsler et al., 1997) concluded that significant improvements ($p<0.05$) in elbow and neurodynamic test ROM were due to radial head mobilisation. The other study (Dabholkar et al., 2013) reported improved grip strength ($p<0.001$), pressure pain threshold ($p=0.031$) and Patient Rated Tennis Elbow Evaluation Questionnaire ($p=0.027$) in the group receiving NM.

Two studies (Drechsler et al., 1997, Vincenzino et al., 1996) on lateral epicondylalgia measured ROM of the ULNDT 2b and both found improved ROM in the groups receiving NM. Due to difference in outcomes measures and techniques used, meta-analysis could not be performed. Table 2.6 describes these studies.

Table 2.6. Study descriptions lateral epicondylalgia

Author **Appraisal Score** **Risk of Bias**	**Patient demographics**	**Intervention Group (IG)**	**Control Group (CG)**	**Outcome**	**Result**
Dabholkar et al. (2013) Appraisal 4 High risk of bias	n=40 No other data available	IG n=20 participants with lateral epicondylalgia Exercise program Radial head mobilisation NM aimed at radial nerve into tension without provoking symptoms Treatment 6 to 7 repetition once a day 4x/week for 4 weeks	CG n=20 participants with lateral epicondylalgia Exercise program Treatment 6 to 7 repetition once a day 4x/week for 4 weeks	Outcomes measured at baseline and post treatment 1) VAS 2) Pain Free Grip Strength 3) Pain Pressure Threshold 4) Patient Rated Tennis Elbow Evaluation Questionnaire	Both groups improved significantly in al outcomes but the Mulligan mobilization with movement of radial head and NM showed more improvement than the exercise group in grip strength (p<0.0001 30.16 +/- 7.33), pressure pain threshold (p=0.031; 4.7 +/- 1.8) and Patient Rated Tennis Elbow Evaluation Questionnaire (p=0.027; 22.75 +/- 5.35).
Drechsler et al. (1997) Appraisal 6 High risk of bias	n=18 (10 females, 8 males) Age range (years) 30-57 Mean age (years) 46 Mean age of groups (years) IG 46.4	IG n=8 participants with lateral epicondylalgia Neural tension group ULTT 2b with 1) Graded flexion and or shoulder abduction 2) Anterior-posterior mobilisations of radial head if radial head mobility was	CG n=10 participants with lateral epicondylalgia Standard treatment group 2 times a week for 6-8 weeks 1) Ultrasound over common extensor tendon 2) Transverse friction to	Outcomes measured at baseline, post treatment and 3 month follow up 1 Self report questionnaire 2 Grip strength 3 Isometric testing	Subjects who received radial head mobilisations improved over time (p<0.05). Results from IG were linked to radial head treatment and isolated effects could not be determined. There were no long-term positive

	CG 45.5	judged hypo mobile Home exercise plan to mimic ULTT2b 10 reps a day increasing but not exceeding 2 sets a day. 2x week for 6-8 weeks	tendon (1 min per session) 3) Stretch and strengthen wrist extensors 5-10 reps 30 seconds. Dumbbells gradually increasing to 3 sets 15 reps 4) Home exercise program stretch and strengthen	extension of 3rd finger 4 ULNDT2b 5 Radial head mobility 6 Elbow extension ROM during ULNDT.	results in the standard treatment group. ($p<0.05$ F_4 71)
Vincenzino et al. (1996) Appraisal 7 Low risk of bias	n=15 with lateral epicondylalgia (8 females, 7 males) Age range 22.5 - 66 years Mean age (years) 44(±2) Duration of symptoms (months) 8(±2) Range of duration (months) 2 - 36	<u>IG</u> Contralateral glide C5/6 grade 3 with affected arm in a predetermined position All treatment were applied in 3 sets of 30 seconds with 60 second rest periods Subjects received 1 of the 3 treatment conditions for 3 days in a random order.	<u>CG</u> Arm rested on abdomen with no manual contact <u>Placebo group</u> Manual contact was applied as in the treatment group with patients arm rested on abdomen but no glide was applied	Outcomes measured at baseline (immediately before) and after treatment 1) ULNDT2b (measuring degrees of abduction) 2) Pain free grip strength (hand held dynamometer) 3) Pressure pain threshold 4) Pain via VAS (over 24 hours) 5) Function VAS (over 24hours)	The treatment group produced significant improvements in pressure pain threshold pain free grip strength, neurodynamics and pain scores relative to the placebo and control groups ($p< 0.05$). (Mean 45 kPa for IG), pain free grip strength (mean 33.2N for IG), neurodynamics (7° for IG) and pain scores (1.7 cm)

Legends: IG – Intervention Group; CG- Control Group; VAS – Visual Analogue Scale; ULNDT – Upper limb neurodynamic test

2.3.8 Other conditions

Four studies were identified that used NM for other conditions including tarsal tunnel syndrome and plantar heel pain (Kavlak and Uygur, 2011, Saban et al., 2014), cubital tunnel syndrome (Svernlov et al., 2009) and post-lumbar surgery (Scrimshaw and Maher, 2001). Three studies were low risk of bias studies (Kavlak and Uygur, 2011, Saban et al., 2014, Scrimshaw and Maher, 2001) and one had a high risk of bias (Svernlov et al., 2009).

Mobilisation using SLR, deep calf massage and exercises compared to ultrasound and exercise resulted in a significant improvement in pain ($p=0.034$) in plantar heel pain (Saban et al., 2014). Using SLR with tibial nerve bias compared to exercises and supportive inserts improved Tinel's sign and two-point discrimination ($p<0.05$) in tarsal tunnel syndrome (Kavlak and Uygur, 2011). Other outcomes such as disability, muscle strength, pressure pain threshold and thermal pain threshold were not significantly different between the NM groups and usual care groups (Kavlak and Uygur, 2011, Saban et al., 2014).

Patients with post-lumbar surgery received SLR and usual care compared to usual care only. However a SLR NM did not have any added benefit to usual care in post lumbar surgery (Scrimshaw and Maher, 2001). Lastly nerve-tensioning exercises (Svernlov et al., 2009) did not result in improved pain and disability ($p>0.05$) when compared to a control group and a group that received an elbow brace for patients with cubital tunnel syndrome. Table 2.7 describes the studies.

Table 2.7 Study descriptions other conditions.

Author	Patient demographics	Intervention Group (IG)	Control Group (CG)	Outcome Measures	Result
Kavlak and Uygur (2011) Appraisal 8 Low risk of bias	n=28 Mean age (years) IG 40.71 (±12.84) CG 43.64 (±14.72) Duration of symptoms (years) IG 3.40 (±-5.06) CG 2.54 (±2.43)	IG n=14 participants with tarsal tunnel syndrome Strengthening and stretching exercise plus NM of the tibial nerve in slump for 6 weeks. Follow up every 10 days to check compliance	CG n=14 participants with tarsal tunnel syndrome Strengthening and stretching exercises for 6 weeks. Follow up every 10 days to check compliance	Outcomes measured at baseline and at 6 weeks 1) VAS 2) ROM of talar and sub-talar joints 3) Strength of muscles innervated by tibial nerve 4) Two-point discrimination 5) Light touch Tinel's	Conservative treatment of tarsal tunnel syndrome is effective in increasing ROM and muscle strength and alleviating pain;(CG 78.6% still positive compared to 100% in the IG) the addition of NM to this treatment did not enhance the treatment effects about these parameters. However, the decrease in Tinel's sign and 2-point discrimination (IG 1.46 ± 0.30 and CG 1.39 ± 0.44) values imply that sensory parameters may benefit from NM.
Saban et al. (2014) Appraisal 9 Low risk of bias	n=69 (male 30, female 39) Mean age (years) IG 54(±12) CG 52 (±13)	IG n=33 participants with plantar heel pain syndrome Deep calf massage Stretching exercises as for SLR	CG n=36 participants with plantar heel pain syndrome Stretching exercises 3 times per day with 5 repetitions for each	Outcomes measured at baseline and 4 to 6 weeks post-treatment 1) Foot and ankle computerized adaptive test of Lower Extremity	The overall group-by-time interaction was statistically significant (p = 0.034) for Functional Scale points, with a change of (mean (CI) 15 (9-21) for IG and 6 (1-11) for the CG

	Duration of pain at admission (weeks) IG 19 (±19) CG 25 (±21)	Ultrasound SLR exercises with belt 3 times per day with 5 repetitions for each stretch, using intermittent stretching of 20 s followed by 10 s of rest	stretch, using intermittent stretching of 20 s followed by 10 s of rest. Ultrasound	2) Functional Scale	respectively. Both treatment protocols resulted in an overall improvement 95%CI for within group changes on functional scale IG 9-21 and CG 1-11). Both treatment protocols resulted in an overall improvement; however, IG treatment was significantly more effective in treating heel pain than CG treatment.
Scrimshaw and Maher (2001) Appraisal 8 Low risk of bias	n=81 (30 females, 51 males) Mean age (years) IG 55 (±17) CG 59 (±16) Duration of symptoms IG <6 weeks 2 >6 weeks 19 >6 months 14 CG <6 weeks 8 >6 weeks 14 >6 months 24	IG n=35 participants undergoing lumbar discectomy (n=9), fusion (n=6) or laminectomy (n=20) Same as control plus neural mobilization (SLR) added. Exercises were encouraged for up to 6 weeks post discharge	CG n=46 participants undergoing lumbar discectomy (n=7), fusion (n=9) or laminectomy (n=30) Standard post operative care (exercises for lower limb and trunk) Exercises were encouraged for up to 6 weeks post discharge	Outcomes measured at baseline, 6 weeks, 6 months and 12 months. 1) Global perceived effect 2) VAS 3) McGill pain questionnaire 4) Quebec disability scale. 5) SLR 6) Time taken to return to work	All patients received the treatment as allocated with 12-month follow up data available for 94% of those randomized. There were no statistically significant or clinically significant benefits provided by the neural mobilizations treatment for any outcome.
Svernlov et al. (2009)	n=70 Mean group age	Group B n=23 participants cubital tunnel syndrome Excluded from analysis n	Group A n=26 participants cubital tunnel syndrome Excluded from analysis	Outcomes measured at baseline and at 6 months	57 patients were followed for 6 months. 51 (89.5%) were improved at the follow-

Appraisal 5 High risk of bias	(years) Group A 43 (range 18–72 / ±13.2) Group B 44 (range 26–67 / ±10.1) Group C 44 (range 17–72 / ±14.8) Duration of symptoms (months) Group A 13.5 (range 3–72 / ±15.7) Group B 10.5 (range 3–42 / ±9.6) Group C 9.5 (range 3–24 / ±5.8) Gender: Group A (9 females, 12 males) Group B (8 females, 7 males) Group C (10 females, 5 males)	= 8 – final n = 15 with Nerve gliding/tensioning exercises(Byron, 1995) 6 exercises maintained for 30seconds x 3 with 1-minute rest twice a day. Increased to 3 x /day if not aggravated. Exercise sheet given to patients.	n=5 – final n=21 Elbow brace that prevents more than 45° flexion for 3 months at night <u>Group C</u> n=21 included excluded from analysis n=6 – final n=15 Information on condition	1) Canadian 2) Occupational Performance Measure 3) Grip strength 4) Adduction strength 5th digit 5) VAS	up. There were no significant differences between the groups in any of the recorded variables. Night splints and nerve gliding exercises did not add favorably to treatment outcomes.

Legend: IG – Intervention group; CG – Control group; VAS– Visual analogue scale; ROM – Range of motion; SLR – Straight leg raise; M – Male; F – Female; SD – Standard Deviation

2.3.9 Outcomes measures

Pain intensity was reported in all but 6 studies (Akalin et al., 2002, Bardak et al., 2009, Brininger et al., 2007, Heebner and Roddey, 2008, Saban et al., 2014, Drechsler et al., 1997). Disability and function was not consistently measured and the outcome measures varied greatly between studies. Only one study reported quality of life measures (Horng et al., 2011) and one study reported that adverse events were investigated (Nee et al., 2012b). Neurophysiological effects were reported in six studies (Bialosky et al., 2009b, Dwornik et al., 2009, Kavlak and Uygur, 2011, Oskouei et al., 2014, Rezk-Allah et al., 2011, Schmid et al., 2012)

2.3.10 Neurophysiological parameters

Secondary outcomes measures reported in a number of studies were neurophysiological parameters. In CTS positive neurophysiological effects such as a decreased intra-neural oedema, decreased temporal summation and median nerve latency were found in the groups that received NM (Bialosky et al., 2009b, Oskouei et al., 2014, Schmid et al., 2012). Two studies on N-LBP also found positive effects. The H-reflex latency was improved from pre-treatment compared to post treatment in a study comparing slump and SLR (Rezk-Allah et al., 2011) and a decrease in nerve compression (measured by magnetic resonance imaging) was reported in another study (Waleed Salah El-din, 2015). Lastly, a decrease was found in sensory parameters in a study on tarsal tunnel syndrome in Tinel's sign, light touch and 2-point discrimination values (Kavlak and Uygur, 2011).

2.4 Discussion

NM is effective in reducing pain and disability in certain neuro-musculoskeletal conditions when compared to usual care. Conditions where NM can be recommended (JBI grades of evidence) are N-LBP, N-NAP, tarsal tunnel syndrome and plantar heel pain. Currently there is no evidence for the use of NM for CTS, post-lumbar surgery and cubital tunnel syndrome.

2.4.1 Carpal Tunnel Syndrome

NM for CTS did not show significant effects for the clinical outcomes assessed. This finding is supported by a recent review on the effect of nerve gliding exercises for CTS (Ballestero-Pérez et al., 2016). The majority of studies had a low risk of bias, which should strengthen the confidence in the findings from a research methodological point of view. However, several studies gave patients home exercises with only one intervention before follow-up. One study had three interventions and a follow-up at 11 months (Bardak et al., 2009). Although these studies can inform clinicians about these types of treatment schemes, some clinicians favour a more progressive exercise regime with closer monitoring and follow-up (Coppieters and Alshami, 2007, Schmid et al., 2012). Perhaps as a consequence, some studies had high patient dropout rates (Brininger et al., 2007, Horng et al., 2011). Furthermore, many studies (Akalin et al., 2002, Bardak et al., 2009, Baysal et al., 2006, Brininger et al., 2007, Heebner and Roddey, 2008, Horng et al., 2011, Pinar et al., 2005) evaluated tensioning techniques. Given the decrease in blood circulation in the median nerve in CTS (Bland, 2005) along with increased neural mechano-sensitivity in response to local inflammation (Dilley et al., 2005, Fernandez-de-las-Penas et al., 2009), increasing the tension in the

nerve may further diminish circulation and aggravate symptoms. More studies are required that evaluate the effects of more modern NM concepts (Coppieters and Alshami, 2007), including 'sliding techniques', before conclusions can be reached regarding the effect of NM for CTS (and other conditions). Sliding techniques resulted in a reduction in intraneural oedema in CTS and improvement in pain and function (Schmid et al., 2012).

2.4.2 Nerve–related low back pain

Evidence for effective management of patients with N-LBP is scarce (Lee et al., 2013, Rubinstein et al., 2011). Furthermore, N-LBP is also a risk factor for chronicity (Grotle et al., 2007) and therefore effective management is important. People with N-LBP distal to the buttocks with a positive slump test and pain for longer than three months had a significant and clinically relevant (Farrar et al., 2001) improvement in pain and disability (Cleland et al., 2007a, Jain et al., 2012, Nagrale et al., 2012). Using other forms of NM such as SLR (Kaur and Sharma, 2011) techniques aimed at opening the foramina (Mehta et al., 2014) bent leg raise (Patel, 2014) and mobilisation of other nerves (Dwornik et al., 2009) also resulted in improved pain and disability. A recent review on lower quadrant NM for healthy and low back pain populations also found that NM improved pain and disability (Neto et al., 2017). The findings of the review support the findings of a previous study (Schafer et al., 2011) that suggest that patient outcomes can be improved when treatment is targeted at subgroups of patients with N-LBP. Therefore, NM exercises, incorporating the slump and SLR tests, can be recommended for N-LBP.

2.4.3 Nerve-related neck and arm pain

As the evidence for non-surgical management of N-NAP is scarce, (Bono et al., 2011, Boyles et al., 2011, Salt et al., 2011) it is recommended that treatment be aimed at specific subgroups (Salt et al., 2011). Using cervical lateral glide techniques for people with N-NAP had a positive effect on pain, with a clinically meaningful effect size (Abbott and Schmitt, 2014, Cleland et al., 2008).

The effect of NM on disability in N-NAP also seems positive (Gupta and Sharma, 2012, Nee et al., 2012b, Anwar et al., 2015, Ragonese, 2009). However, as this was not measured consistently, no firm conclusions can be made. Measuring function in these patients is important, as they are more disabled than patients with non-specific neck pain (Daffner et al., 2003). Future studies should investigate function and disability using common outcomes measures such as the NDI or Patient Specific Functional Scale.

2.4.4 Lateral Epicondylagia

A recent review on physical therapy for lateral epicondylalgia concluded that the intervention groups all improved significantly compared to control groups regardless of type of intervention (Weber et al., 2015). However, the studies on NM were not included in that review. In a study with low risk of bias the use of cervical lateral glides improved pain in epicondylalgia (Vincenzino et al., 1996). Due to the low quality of the other studies (Dabholkar et al., 2013, Drechsler et al., 1997), differences in techniques used and conflicting outcomes it is not possible to make recommendations on the use of NM for lateral epicondylalgia.

2.4.5 Other conditions

Two studies support the use of SLR for patients with plantar heel pain and tarsal tunnel syndrome (Kavlak and Uygur, 2011, Saban et al., 2014). This is in accordance with other studies that illustrated that SLR transmits movement to the tibial nerve (Coppieters et al., 2006) and can have an effect on the pain and movement of a patient with sub-calcaneal heel pain (Meyer et al., 2002). As these studies are low risk of bias the use of NM for these conditions can be recommended.

Two studies (Scrimshaw and Maher, 2001, Svernlov et al., 2009) found no added benefit when using NM in addition to usual care for post-lumbar surgery and cubital tunnel syndrome. There is insufficient evidence for the use of NM in these conditions and more studies are needed before NM can be considered for these conditions.

2.4.6 Outcomes measures

In studies evaluating CTS and N-LBP, similar outcomes measures were used and therefore a meta-analysis could be performed. Unfortunately, this was not the case for most other conditions. Pain was measured in most studies, however the method of assessment was not consistent across studies. Future studies should consider a core set of clinical outcome measures to establish the effectiveness of NM on neuro-musculoskeletal conditions.

2.4.7 Neural mobilisation techniques

Two NM techniques consistently produced good results in conditions considered difficult to treat (Luijsterburg et al., 2007, Salt et al., 2011). Slump

mobilisations improved pain and disability in N-LBP (Cleland et al., 2007a, Jain et al., 2012, Nagrale et al., 2012, Patel, 2014). Cervical lateral glides improved pain in N-NAP and epicondylalgia (Allison et al., 2002, Coppieters et al., 2003b, Nee et al., 2012b, Vincenzino et al., 1996).

Our findings showed that tensioning techniques improved pain and disability in the treatment of chronic nerve-related conditions, such as N-LBP (Cleland et al., 2007a) and plantar heel pain (Saban et al., 2014, Kavlak and Uygur, 2011). More recently, sliding techniques are often advocated as they expose the nervous system to less strain (Coppieters and Alshami, 2007), which might be more advantageous when nerve mechano-sensitivity is still increased (Coppieters and Butler, 2008). Therefore the choice of technique should be based on sound clinical reasoning (Eva, 2005, Nee and Butler, 2006). Unfortunately, the reasoning process behind the choice of techniques is absent or unclear in many studies.

The terminology can also be confusing. Some studies explicitly state whether 'sliding techniques' or 'tensioning techniques' were used (Ali et al., 2015, Gupta and Sharma, 2012, Marks et al., 2011), but other studies use the more generic term 'nerve gliding exercises'. In order not to confuse generic 'gliding' exercises with specific 'sliding' exercises, we recommend abandoning the term 'nerve gliding exercises' and use NM or neurodynamic techniques to refer to techniques that aim to mobilise the nerve or its surrounding structures. The need for consistent use of terminology is evident.

2.4.8 Neurophysiological effects

An improvement in neurophysiological parameters was found in a number of studies such as a decrease in intra-neural oedema (Schmid et al., 2012). A

decrease in intraneural oedema is supported by two studies on unembalmed cadavers, which demonstrated the ability of NM to disperse intraneural fluid (Brown et al., 2011, Gilbert et al., 2015). As ischemia of the median nerve contributes to the symptoms of CTS, (Han et al., 2009) a decrease in intraneural oedema would be important in the management of CTS. Sensory parameters may also benefit from NM (Kavlak and Uygur, 2011). One of the aims of NM is to restore neurophysiological homeostasis of the targeted nerve and the findings of the review support that NM has this effect.

Although not included in this review a study by (Sterling et al., 2010) found that the cervical lateral glide decreased spinal hyper excitability. Furthermore it has been shown that NM has the ability to modulate the expression of endogenous opioids (Santos et al., 2014).

2.4.9 Risk of bias across and within studies

This review was limited to the inclusion of randomised clinical trials. We included all randomised clinical trials regardless of quality in an endeavour to include all conditions treated and all techniques used. High risk of bias was mostly due to lack of blinding of participants, assessors and group allocation. Nineteen studies had a low risk of bias. Only two other language studies were identified and not included (Bahrami et al., 2006, Leonelli et al., 2013). Potential publication bias could not be assessed further using Funnel plots as less than 10 trials were included in the meta-analyses (Anzures-Cabrera and Higgins, 2010).

2.5 Strengths and limitations

This study included an additional 20 articles, which were not included in the most comprehensive review so far (Su et al., 2016). The increase in studies on CTS, N-LBP and N-NAP, and the performance of meta-analyses where possible, provided a better overview of the clinical effectiveness of NM. However, there is still a paucity of information on many relevant conditions, such as cubital tunnel syndrome and post-lumbar surgery.

Analysing results for the various conditions such as CTS and N-LBP separately, made it possible to evaluate the effect of NM on these conditions. Meta-analyses could be performed for a number of outcomes and this gives a clearer picture of the effect of NM in regard to certain outcomes. Two systematic reviews could not make any firm recommendations regarding the effect of NM (Ellis and Hing, 2008, Medina McKeon and Yancosek, 2008), however, a more recent review on nerve-gliding exercises for CTS (Ballestero-Pérez et al., 2016) came to the same conclusion as the current review in that nerve-gliding exercises does not have an effect on most clinical outcomes in CTS. Another review concentrated on the effect of NM on the lower quadrant in patients and healthy individuals (Neto et al., 2017) and similar to the current review found NM to have a positive effect on pain and disability in N-LBP. Su et al. (2016) did not find that NM had a positive effect in chronic musculo-skeletal conditions. It must be borne in mind that their review pooled results of different conditions together and only considered chronic conditions, which is different to the study population of this review.

Although authors were contacted where possible, all the information that was needed was not always available and some authors could not be reached.

The majority of studies had a small number of study participants and therefore results are not necessarily generalizable.

2.6 Recommendations

The JBI grades of evidence (The Joanna Briggs Institute Levels of Evidence and Grades of Recommendation Working Party, 2014) were used for making recommendations (Appendix 3).

- Cervical lateral glide mobilisation improves pain in nerve-related neck and arm pain (Level A).
- Slump and SLR mobilisation improves pain and disability in nerve-related low back pain (Level A).
- NM has positive neurophysiological outcomes in CTS (Upper limb neurodynamic test 1) and N-LBP (Slump and SLR) (Level A).
- NM does not have an effect on most of the clinical outcome measures in CTS (Level A).
- NM improves pain in tarsal tunnel syndrome and plantar heel pain (single low risk of bias study evidence).

2.6.1 Implications

The findings of this review may help inform clinicians with regard to the management of chronic N-LBP, N-NAP and plantar heel pain.

Sound clinical reasoning remains essential when treating nerve-related conditions with NM.

2.6.2 Caution

- Due to the limited evidence and often, small study samples conclusions may change over time.

2.7 Conclusion

The slump and SLR mobilisation and cervical lateral glide have been shown to improve pain and function in patient groups that are often resistant to treatment, such as chronic N-LBP and N-NAP and plantar heel pain. The findings of this review may help inform guidelines on the management of CTS, and low back and neck pain.

There were nine studies on N-NAP of which only four had a low risk of bias. Most of the studies had a low number of study participants (60 participants in the biggest study). Function was not measured consistently and none of the studies on N-NAP evaluated the effect of NM on quality of life. Furthermore, none of the studies used mobilisation along the course of the nerve to treat N-NAP. The review supports the need for more studies with a bigger study population on N-NAP.

3 Chapter Three - Prevalence of neck and radiating arm pain among patients treated in private practices in Pretoria, South Africa

To answer the first research question, a survey of patients attending private physiotherapy practices in Pretoria, South Africa was conducted. This chapter will describe the method, results and discuss the study.

3.1 Introduction

Neck pain is a common musculoskeletal problem with a point prevalence of 4.9% (Hoy et al., 2014) and a lifetime prevalence ranging between 14.2% and 71% (Fejer et al., 2006). However, there is very little information on the prevalence of neck pain in South Africa.

Low back and neck pain are the conditions that contribute most to years lived with disability (Vos et al., 2016). Globally the disability adjusted life years of neck pain was 23.9 million in 1990 and increased to 33.6 million in 2010; an increase of 41% (Hoy et al., 2014). The prevalence of neck pain in the sub-Saharan Southern Africa region is outranked only by Western Europe, North America and East Asia (Vos et al., 2012, Hoy et al., 2014). However, in estimating the burden of disease in 2000 for South Africa (SA), musculoskeletal disorders ranked 20th (Bradshaw et al., 2003). A more recent

fact sheet on health statistics, ranked musculoskeletal diseases as 16th in SA (World Health Organization, 2010). The latest available information (World Health Organization, 2012) ranks musculoskeletal disorders as 12th in terms of burden of disease. There is, therefore, a big discrepancy in ranking of musculoskeletal diseases in SA compared to the global burden of disease studies (Hoy et al., 2014, Vos et al., 2012, Vos et al., 2016). According to Rice et al. (2016) there is little information available for Sub-Saharan Southern Africa in terms of the global burden of pain. A systematic review on low back pain in Africa concluded that the prevalence of low back pain is similar to that of the global burden of disease (Woolf and Pfleger, 2003). It is also becoming a more common problem in SA (Louw et al., 2007). No such information could be found for neck pain and considering the high prevalence and associated levels of disability globally; the importance of more information on neck pain in SA is evident.

In 2015 nearly a quarter of households (23,5%) had at least one member who belonged to a medical aid (Statistics South Africa, 2015). In metropolitan areas such as Pretoria the number is higher where 26.4% of people have access to medical aids (Statistics South Africa, 2015). Studying this group of people in private practice is therefore of interest and given the specific nature of the condition that was being looked at, it was decided that the information would be available in the private sector. A follow up study in the public sector could be done, bearing in mind that patients are not often able to attend for a course of treatment.

Radiating arm pain is commonly associated with neck pain with more than 65% of the neck pain population presenting with neck and radiating arm pain

(Daffner et al., 2003, van Hulst et al., 2016). These patients are more disabled than patients with only neck pain and are more likely to utilise healthcare (Daffner et al., 2003, Huisstede et al., 2008).

There are only a few studies on the prevalence of neck pain in the SA population (Brink et al., 2009, Mafanya and Rhoda, 2011, Smith et al., 2009), and most were done on an adolescent population. In a study of risk factors for neck pain amongst 181 adolescents, the prevalence of neck pain was 53.7% (Mafanya and Rhoda, 2011). Smith et al. (2009) reported a 20% prevalence of neck pain in adolescent computer users (n=1073). Similarly a 26% reported neck pain was documented in a study on the sitting posture of SA adolescents, (Brink et al., 2009). A study on the prevalence of musculoskeletal disorders of office workers in a private hospital in SA (Zungu and Ndaba, 2009) found a prevalence of 76% of musculoskeletal complaints, with low back pain the most common complaint followed by neck pain. No studies could be found on the prevalence of neck pain in private physiotherapy practices in South Africa.

Therefore the aims of this study were to:

- determine the prevalence of patients with neck pain and radiating arm pain in private physiotherapy practices in Pretoria.
- document the areas of pain and associated symptoms in patients with neck pain and radiating arm pain.

3.2 Methods

3.2.1 Materials and setting

Convenience sampling was undertaken by approaching physiotherapists attending North Gauteng Orthopaedic Manipulative Physiotherapy Group meetings (n=70 physiotherapists). The meetings were held between March 2012 and July 2012. This group of physiotherapists was selected as they have a special interest in treatment of musculoskeletal disorders. Six practices (9% of this physiotherapy population) gave consent to have their records surveyed.

3.2.2 Design

A retrospective survey of physiotherapy patient records dated 1 January 2011 to 31 December 2011 was conducted. The prevalence of patients with neck pain in relation to other musculoskeletal complaints was calculated and expressed as a percentage.

3.2.3 Procedure

All records of patients with neck pain were analysed by the researcher to obtain a common set of data. This included: age, gender, area/s of pain, associated symptoms and whether pain was due to injury or of insidious onset. Data were directly entered into an Excel spread sheet using coding. Specific care was taken to ensure that none of the data could be linked back to identify individuals. This was done by selecting patient records in random order, whilst ensuring that all records were surveyed. Participating practice owners identified patient records for the year 2011 and practices were numbered to ensure that information could not be linked to a specific practice.

The age, gender and body chart was the only information accessed, and the researcher was the only person with access to the data.

Symptoms recorded included the following: headache, dizziness, pins and needles, feeling of weakness, other sensations, more than one symptom and pain in other area/s. Based on body charts, areas of pain were coded as neck pain only, pain in the shoulder, shoulder and upper arm, shoulder to elbow, lower arm, hand, neck and arm up to wrist, neck and arm including hand.

3.2.4 Data analysis

Descriptive statistics were used to analyse the data. Age was expressed as a mean and standard deviation. Percentages were calculated for the proportion of neck pain relative to other musculoskeletal complaints, areas of pain and associated symptoms. The researcher was the only person with access to the data (for confidentiality purposes) and did all the analysis using Microsoft Excel (2011).

3.2.5 Ethical approval

Approval for the study was obtained from the Human Research Ethics Committee of the University of the Witwatersrand (Ethical clearance number M111002). As it was a retrospective survey, using patient records only, patient permission was waived. All participating practice owners received information letters describing the study and gave written consent for their records to be surveyed (Appendices 3.1 and 3.2).

3.3 Results

Records in six practices were analysed. Four of the six practices were sole owner practices. One of the practices was in an industrial set-up treating workers from factories. Two practices were general practices and the remaining three concentrated on musculoskeletal problems.

The total number of records reporting on musculoskeletal complaints was n=1337. The non-specific neck pain or neck and arm pain population comprised 46.1% (n=616) of the records and n=720 (53.9%) were other musculoskeletal complaints. The neck/arm pain population consisted of 63.1% (n=389) females and 36.9% (n=227) males. The mean age of the neck/arm pain population was 44.5 (± 15.2) years. Pain was due to injury in 21.4% (n=132) of the records and was of insidious onset in the rest of the sample.

3.3.1 Area of symptoms

Two hundred and ninety five (47.8 %) of the neck/arm pain population had only neck pain; the remaining 52.2% (n=363) had neck and radiating arm pain. The area most commonly associated with neck pain was the shoulder (n=127, 20.6%) followed by symptoms in the arm including the hand (n=80, 13%). Symptoms in the shoulder and upper arm (n= 48, 7%) and symptoms in the arm up to the wrist (n=44, 7.1%) were also common. Only 2 (0.3%) records reported symptoms in the neck and lower arm and n=26 (4.2%) reported symptoms in the neck and hand. Table 3.1 illustrates the occurrence of pain in the different areas and practices.

Table 3.1. Distribution of neck and radiating arm pain according to body area and physiotherapy practices

Area of pain	Practice 1 n = 215 (%)	Practice 2 n = 52 (%)	Practice 3 n = 168 (%)	Practice 4 n = 72 (%)	Practice 5 n = 88 (%)	Practice 6 n = 21 (%)
Neck only	84 (39.1)	39 (75)	97 (57.7)	31 (43.1)	40 (45.4)	5 (23.8)
Neck and shoulder	31 (14.4)	10 (19.2)	19 (11.3)	19 (26.4)	23 (26.1)	4 (19.1)
Neck, shoulder and upper arm	4 (1.9)	2 (3.8)	14 (8.3)	7 (9.7)	4 (4.4)	0
Neck up to elbow	12 (5.6)	0	7 (4.2)	2 (2.9)	7 (7.9)	3 (14.3)
Neck & lower arm	2 (0.9)	0	0	0	0	0
Neck & arm up to wrist	24 (11.2)	1 (1.9)	11 (6.5)	3 (4.2)	3 (3.4)	2 (9.5)
Neck and hand	13 (6.5)	0	3 (1.8)	6 (3.6)	4 (4.4)	0
Neck & arm including hand	38 (17.7)	0	17 (10.1)	4 (23.8)	8 (9.1)	7 (33.3)

The prevalence of areas of symptoms varied among the practices with the arm and hand symptoms being more prevalent in one of the practices than shoulder pain. Another practice did not have any records reporting pain up to the elbow, lower arm, hand and only one with pain in hand and arm. The areas of pain per practice is illustrated in Figure 3.1

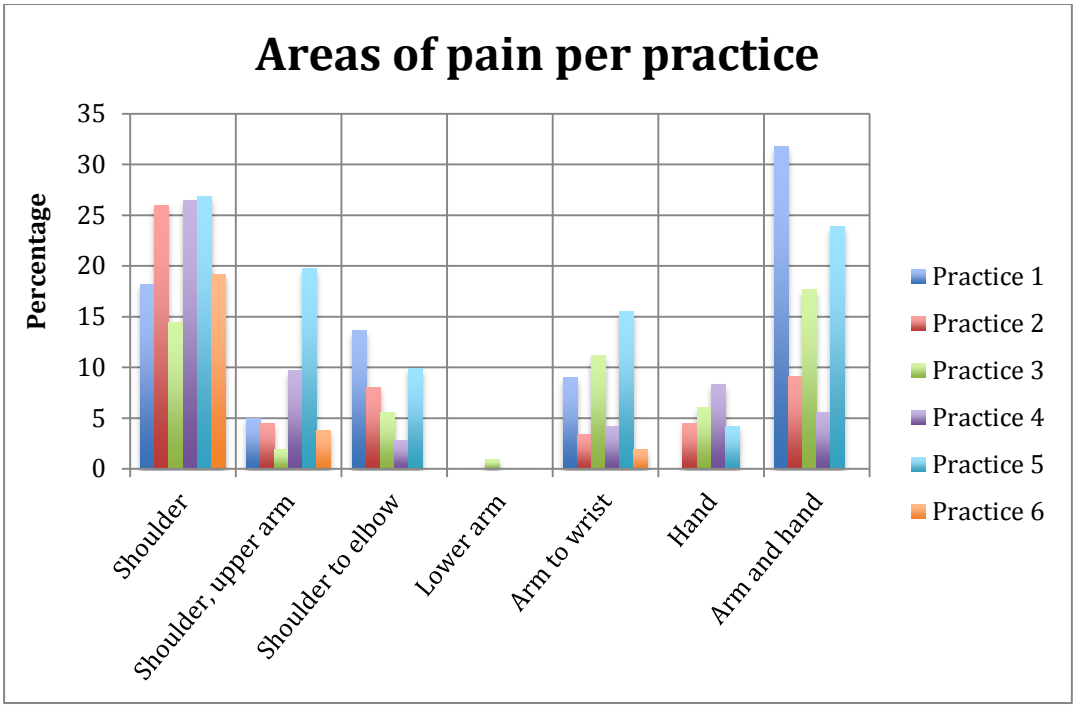


Figure 3.1 Distribution of body areas of radiating arm pain per practice

3.3.2 Symptoms associated with neck and radiating arm pain

The symptom most commonly reported with neck/and radiating arm pain was headache (n=156, 25.4%) followed by pain in another area such as the lower back (n=139, 22.6%), and pins and needles were described in n=69 (11.2%) of the records. There were also some less common sensations (n=67, 10.7%). Of these the most common was numbness (n=26, 4.2%) and burning (n=13, 2.1%). There were five (0.8%) records that reported a “lame feeling” and three (0.5%) each of the following – ache, cold, stiffness and shooting pain. Sensations of swelling, heaviness and pounding were described in two (0.3%) records each. Only one record described tenderness. There were 169 (27.4%) records that did not report any associated symptoms. The areas of pain for the 2011 retrospective survey and the clinical trial (see Chapter 4

onwards) were similar. Figure 3.2 illustrates the areas of pain for the two groups.

Associated lumbar pain was reported in 78 (12.6%) of the neck pain population and thoracic pain in 46 (7.5%) cases. Thoracic and lumbar pain was associated with neck pain by n=21 (3.4%) of the population and leg pain by n=10 (1.6%) of the population. The results for associated symptoms in the 2015 clinical trial group (see Chapter 4 onwards) were similar except for more patients reporting headache (n=40, 29.2%) and dizziness (n=4, 2.9%) than in the 2011 retrospective survey group. Figure 3.3 shows the associated symptoms.

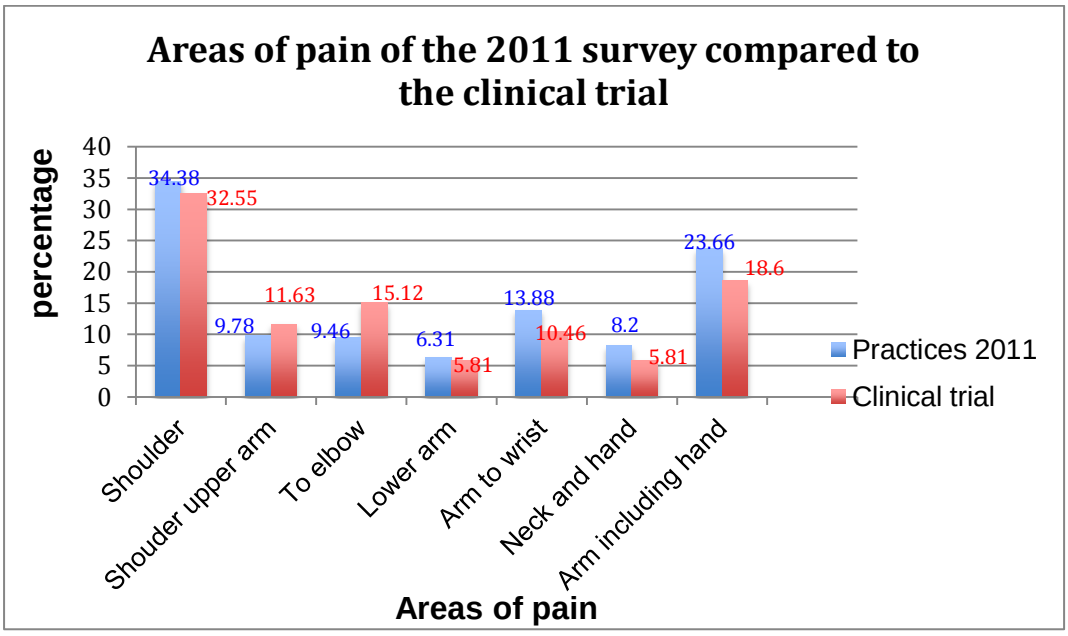


Figure 3.2 Areas of pain for 2011 retrospective survey and the clinical trial

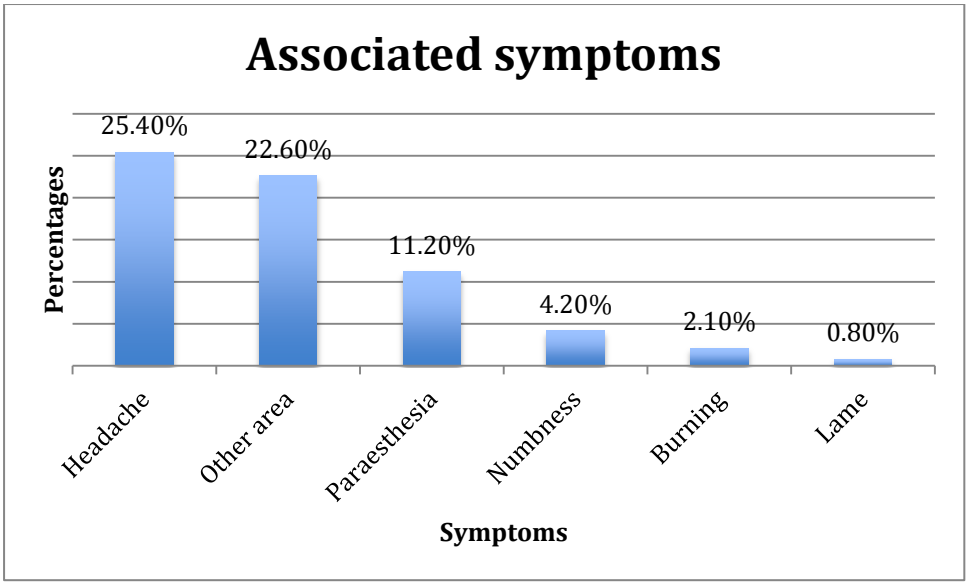


Figure 3.3 Symptoms associated with neck and radiating arm pain

3.4 Discussion

The aim of this study was to establish the prevalence of neck pain in private physiotherapy practices, in Pretoria South Africa. Neck pain or neck and arm pain comprised 46.1% of all musculoskeletal complaints seen in these physiotherapy private practices. This finding is similar to a national survey of general practitioner practices in the Netherlands (Bot et al., 2005), which concluded that neck pain is prevalent and commonly seen. A more recent population- based study in Sweden also found bothersome neck pain to be a common complaint (Skillgate et al., 2012). Huisstede et al. (2008) report that physiotherapists saw 54.5% of persons with complaints of arm neck and shoulder pain who used health-care. In their study, these health-care users had more continuous, severe pain and interference with daily activities than those who did not seek healthcare.

The prevalence of neck pain varies between 20% and 53% in studies on South African adolescents (Brink et al., 2009, Mafanya and Rhoda, 2011, Smith et al., 2009, Zungu and Ndaba, 2009). This wide range is similar to the findings of a systematic review on the prevalence of neck pain in which the lifetime prevalence of neck pain ranged between 14.2% and 71% (Fejer et al., 2006). The prevalence in this study is 46.1% of all musculoskeletal complaints seen in private physiotherapy practices. No studies on the prevalence of neck pain in the physiotherapy private practices in SA could be found in a literature search. However, the results of this study are similar to the SA studies on adolescents. This high prevalence of neck pain seen in private practice has important implications in terms of management, especially in light of the fact that neck pain contributes significantly to disability worldwide (Hoy et al., 2014).

In this study 52.2% of the population had neck and radiating arm pain, which is similar to the findings of other studies (Daffner et al., 2003, Huisstede et al., 2008, van Hulst et al., 2016). Leaver et al. (2013b) also found an extremely high prevalence of upper limb pain (80%) in a population with new onset of non-specific neck pain. The high prevalence of neck pain in physiotherapy practices found in this study is disquieting as health-care users, i.e. patients who seek physiotherapy treatment, tend to have more pain and are more disabled (Huisstede et al., 2008).

One of the factors associated with poor recovery of neck pain is pain in other areas (Croft et al., 2001, Viikari-Juntura et al., 2001). More than 25% of the population in this study had pain in other areas associated with their neck pain. Once pain has become chronic, effective management becomes more

challenging with uncertain outcomes (Valat, 2005). Furthermore, more than 50% of the study population had radiating arm pain and there is limited evidence for the effective management of neck and radiating arm pain (Childs et al., 2008, Gross et al., 2009, Salt et al., 2011). This highlights the importance of accurate information on the prevalence of neck pain in SA. As neck pain comprises more than 46% of the musculoskeletal population seen in the private practices surveyed, physiotherapists should have knowledge of the optimum management strategies for neck/and arm pain.

Considering the global impact of neck pain (Hoy et al., 2014, Vos et al., 2012) and the high incidence of neck pain found in this study there is a clear need for epidemiological studies on the prevalence of musculoskeletal complaints in SA. Identifying prognostic factors assists in predicting outcomes (Carroll et al., 2008) and assists in the planning of effective management strategies to address these problems at an early stage. There is a need for more studies on the prevention of neck pain and effective management strategies. Even though prevention is important, there is limited evidence for effective preventative strategies. There is some support for the use of exercise and education in the prevention of neck pain (Hurwitz et al., 2008, Linton and van Tulder, 2001).

Neck pain is most prevalent in middle age (Bot et al., 2005, Hoy et al., 2014, Huisstede et al., 2008, Skillgate et al., 2012), which is similar to the findings of this study (44+/- 15.2). As people age, the prevalence will most likely increase (Hoy et al., 2014). Management of an ageing population will therefore become increasingly important.

Neck pain is more prevalent in females than males (Bot et al., 2005, Cote et al., 2004, Huisstede et al., 2008, Skillgate et al., 2012) as was the case in this study. Skillgate et al. (2012) found in their study that females were more likely to have neck pain than males and that they were less likely to recover from pain. Being female is one of the non-modifiable risk factors for developing neck pain (Hogg-Johnson et al., 2008). Data from two population based surveys in the Netherlands confirm that women consistently have a higher prevalence of musculoskeletal pain irrespective of anatomic site (Wijnhoven et al., 2006). They cite three possible reasons for this 1) women are more willing to report pain than men 2) biological and physiological differences between the sexes 3) women are more exposed to risk factors than men (Wijnhoven et al., 2006).

As is the case in this study, shoulder pain is commonly associated with neck pain (Bot et al., 2005, McLean et al., 2011). In a study of new onset neck pain (Leaver et al., 2013b), neck pain was also commonly associated with headache (64%), low back pain (39%), dizziness (31%) and nausea (23%). The prevalence of headache (26.1%) and low back pain (12.6%) is considerably lower in this study than the study by Leaver et al. (2013b). Here dizziness is only mentioned once and there is no mention of nausea. The small number of practices surveyed and the fact that I could only report on recorded symptoms may in part explain the differences in findings. Furthermore, pain and areas of pain were recorded meticulously in the practices surveyed, but symptom description was often vague. Therefore the recorded symptoms (such as dizziness and nausea) may not be accurate. The study by Leaver et al. (2013b) reports on patients seeking manual

therapy for a new episode of neck pain and therefore may represent a skewed population which could further explain the difference in findings. Dizziness and nausea are commonly in co-existence with neck pain and headache (Malmström et al., 2007, Reid et al., 2015). The high percentage of patients reporting dizziness and nausea in the study by Leaver et al. (2013b) seems to be more in line with other studies than the findings here. The low reporting of dizziness and nausea in this study should therefore be interpreted with care.

Finding practices willing to participate in this study was very challenging. According to M'kumbuzi et al. (2004) record keeping of physiotherapists in SA is compromised. They collected data from six state hospitals, five private physiotherapy practices and two community physiotherapy services to evaluate record retrieval. Although the retrieval of records was significantly higher in private practice (87.4%) than in public hospitals (34.7%), some records were incomplete (M'kumbuzi et al., 2004). They stated that it seemed that practices were more concerned with rendering physiotherapy services than keeping a record of the service. Other reasons given for poor record-keeping were being too busy and not having considered the consequences of not having good records (M'kumbuzi et al., 2004). Another study retrieved 100 randomly selected records in a hospital and also found that physiotherapy records were incomplete (Philips et al., 2006). There are, however, no recent studies on recordkeeping amongst South African physiotherapists and there is therefore no current evidence to support that record keeping is still compromised in physiotherapy practice. Good record keeping helps to maintain the quality of practice (Martin and Moriarty, 2012) and as first line practitioners in SA we have a responsibility to our profession and patients to

maintain a high quality of care. With the rise in malpractice claims in SA (Malherbe, 2013, Pepper and Slabbert, 2011), record keeping has vital legal implications (Glasper, 2011). The reluctance of physiotherapists to make their records available is therefore of concern.

3.5 Strengths and limitations

No other studies could be identified on the prevalence of neck pain in private practice in SA. Furthermore no studies could be identified which describe sensations associated with neck pain such as paraesthesia, numbness, and burning to mention a few. Only one study was identified that reported on associated symptoms of neck pain and radiating pain (Leaver et al 2013) in an acute neck pain population.

A requirement for establishing prevalence of a condition is to have a randomly selected, representative sample of the population. This was a sample of convenience with a very low number of practices surveyed and a low number of patient records. The findings of this study should therefore be interpreted with caution although most findings are similar to other publications. Some of the records were incomplete with regards to associated symptoms. Furthermore the study could only report on symptoms as recorded by the physiotherapist and this could potentially create a false impression.

3.6 Recommendations

There is a need for bigger population based studies on the prevalence of neck pain in SA. Prevention and effective management of neck pain is important to avoid the consequences of chronic pain and its related disability.

3.7 Conclusion

The prevalence of neck pain in private physiotherapy practices in Pretoria, SA is high with radiating arm pain and pain in other areas being commonly associated with neck pain. Furthermore, other symptoms such as headache and paraesthesia are also frequently present. Neck pain is multi-faceted and this has implications for its management. Future studies with a bigger, representative population sample are needed to establish the prevalence of neck pain in SA.

4 Chapter Four – Outcomes measures

This chapter will discuss the different outcomes measures used in the randomised clinical trial.

4.1 Outcomes measures – research question two

What is the effect of NM on the pain, function and quality of life of patients with acute cervico-brachial pain?

4.1.1 Numerical Pain Rating Scale

The Numeric Pain Rating Scale (NPRS) (Appendix 4.1) is an 11-point scale where patients are asked to rate their pain as 0 representing “no pain” and 10 “worst pain possible”. In a study comparing three pain measures (Bolton and Wilkinson, 1998) the NPRS was the most responsive pain measure with an effect size of 0.86 (Bolton and Wilkinson, 1998). The validity of the NPRS in an acute setting was established by Bijur et al. (2003) and is strongly correlated with the visual analogue scale (r= 0.94, 95% CI 0.93 – 0.95) (Bijur et al., 2003). A reduction of 1.3 points in mechanical neck pain (Cleland et al., 2008), is considered clinically meaningful. Reliability of the NPRS was established as good (*r* = 0.72 to 0.78) (Good et al., 2001). The NPRS is as sensitive to change as the visual analogue scale which is currently considered the “gold standard” (Holdgate et al., 2003).

4.1.2 The Patient Specific Functional Scale

The Patient Specific Functional Scale (PSFS) (Appendix 4.2) is a self-report measure to rate activity limitation and function. Patients are asked to nominate three to five activities that are difficult to perform and rate them on an 11 point scale where 0 equals “unable to perform activity” and 10 represents “able to perform activity as before”. In this study patients were asked to nominate three activities. The scale was initially developed for patients with back pain and validated for patients with neck pain by Westaway et al. (1998). The scale has excellent reliability (r = 0.92) and validity (r=0.73 - 0.83) when compared to the Neck Disability Index and r=0.52 - 0.62 compared with the prognosis rating (Westaway et al., 1998). Cleland et al. (2006) compared the Neck Disability Index and the PSFS in patients with cervical radiculopathy and found that the PSFS was more responsive than the Neck Disability Index in this population (Cleland et al., 2006). In their study the reliability was good with an interclass coefficient (ICC) of 0.82. The minimally clinically important change for the PSFS was 2.0 (Cleland et al., 2006). Hefford et al. (2012) found the PSFS to be a valid, reliable and responsive measure of function for patients with upper extremity problems.

4.1.3 EuroQuol 5 Instrument

The EuroQuol 5 Instrument (EQ5D) (Appendix 4.3) is a quality of life measurement and was used to rate the quality of life of study participants. It has two sections: the first part consists of five domains namely mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each section is rated by three descriptions from “I have no problem” to “I am unable”. The second section of the questionnaire has a 20cm Visual Analogue Scale with

“best imaginable health state” at the one end and “worst imaginable health state” at the other end and marked 0 - 100. The construct validity was established by measuring it against the SF-12 and positive correlations were found (r=0.41). It has excellent reliability (ICC 0.82) (Coons et al., 2000). In another study, the test–retest reliability ranged between 69.8 and 99.7% for the EQ5D dimensions and Kappa coefficients were 0.67. Correlation coefficients with other measures of self-rated health indicated validity (r = 0.56) (Ravens-Sieberer et al., 2010).

In a study of patients receiving knee arthroscopy, the psychometric properties of three quality of life measures were compared and the authors recommend the use of the EQ5D in this acute musculoskeletal population (Goodwin et al., 2011). The quality of life using the EQ5D was measured in patients with cervical radiculopathy and whiplash associated disorder and health related quality of life was worse in these populations compared to a healthy group (Peolsson et al., 2014).

4.1.4 Global Rating of Change Scale

Patients were asked to complete the Global Rating of Change Scale (GROC) (Appendix 4.4) at six weeks after treatment had commenced. This scale measures the patient’s impression of improvement after an intervention. According to a Cochrane review, there are eight different scales to measure change, in use. In this study an 11 point Likert scale was used with -5 representing very much worse, 0 is unchanged and +5 is fully recovered (Kamper et al., 2009). The test-retest reliability has an ICC of 0.9. The scale has significant correlation with importance of change (*r*=0.72) and magnitude of change (*r*=0.91) on the Roland Morris, Oswestry, Pain Rating Scale and

the EQ5D (Kamper et al., 2009). The GROC is often used in studies on neck and arm pain to establish patient's perception of change (Cleland et al., 2007b, Nee et al., 2012b, Walker et al., 2008).

4.1.5 Upper Limb Neurodynamic Test 1

The Upper Limb Neurodynamic Test 1 (ULNDT1) is described as the straight leg raise test of the arm (Butler, 2000). The upper limb nerves are elongated and moved in their nerve bed (Coppieters et al., 2009) as was verified in an "in vivo" study. The test consists of different components of movement: patient supine, neck in neutral, shoulder abduction to ± 110°, extended wrist and fingers, forearm supination, shoulder lateral rotation and the amount of elbow extension is then measured (Butler, 2000). The reliability of measuring onset of pain and sub-maximal pain in a clinical setting in patients with cervico-brachial pain was established as excellent by Coppieters et al. (2002) (ICC ≥ 0.98; SEM ≤ 3.4°). The ULNDT1 is a valid test to identify peripheral neuropathy (Nee et al., 2012a). It is also a test that is used in a cluster of tests to diagnose cervical radiculopathy and has a specificity (negative likelihood ratio) of 0.90 (95% CI 0.82–0.98) (Wainner et al., 2003).

4.2 Outcomes Measures – research question three

Does the presence of high catastrophising scores and neuropathic pain have an influence on treatment outcome? Two questionnaires were used to establish which patients had neuropathic pain and which patients were catastrophisers.

4.2.1 Neuropathic Pain Diagnostic Questionnaire

The Neuropathic Pain Diagnostic Questionnaire (DN4) (Appendix 4.5) (Bouhassira et al., 2005) consists of two sections namely an interview and examination. The interview has two questions, the first about the characteristics of the pain (e.g. burning) and the second about associated symptoms (such as pins and needles) to which the answer is either yes or no. In the examination, tests for hypoesthesia to touch and prick in the painful area as well as whether or not brushing aggravates the pain, are done. Each positive answer scores a point with a total score of 10. A patient with a score of 4/10 or more can be diagnosed with neuropathic pain (Bouhassira et al., 2005). The sensitivity of the test at the cut off of four is 82.9 and the specificity is 89.9. The inter-rater reliability has Kappa values of between 0.70 and 0.96 (Bouhassira et al., 2005). Recently the DN4 was compared to three other neuropathic pain questionnaires (ID Pain, the painDETECT questionnaire and the Leeds Assessment of Neuropathic Signs and Symptoms) (Gudala et al., 2017) to assess the ability of the questionnaires to detect neuropathic pain in patients with chronic low back pain. Receivers Operating Characteristic (ROC) curves were used to assess the diagnostic accuracy of the questionnaires. The DN4 had an area under the curve of (AUC) $>$ 0.8 indicating excellent discrimination in this population (Gudala et al., 2017). This tool is recommended for use to identify patients with neuropathic pain by the “South African Management of Neuropathic Pain Guidelines” (Chetty et al., 2012).

4.2.2 Pain Catastrophising Scale

The Pain Catastrophising Scale (PCS) (Appendix 4.6) is a questionnaire that establishes the levels of catastrophic thinking present in patients. The questionnaire has three components: magnification, rumination and helplessness. Participants are asked to reflect on past painful experiences and to indicate the degree to which they experience each of 13 thoughts or feelings when experiencing pain. It is scored on a 5-point scale from 0 “not at all” to 4 “all the time” with a maximum score of 52. A score above 24 classifies the patient as a catastrophiser (Sullivan et al., 1995). The internal consistency of the three subscales are Cronbach’s α of Rumination α = 0.85, Magnification α = 0.75 and Helplessness α = 0.85 (Osman et al., 2000). The criterion reliability as tested by Osman et al. (2000) could correctly identify 77.1% of the cases. This also confirms the findings of (Sullivan et al., 1995) that the three dimensions represent a single construct. It can be evaluated as an interval level scale (Walton et al., 2013b).

4.3 Demographic information – research question four

What is the influence of demographic factors such as age, gender, headache, dizziness, paraesthesia, injury, previous pain, exercise and education on pain, function and quality of life in patients with cervico-brachial pain?

Participants were asked to complete a demographic questionnaire (Appendix 4.7) that included age, gender, duration of symptoms, previous neck pain,

injury or insidious onset, education, occupation, exercise, presence of headache or dizziness and an indication of the area of pain on a body chart.

The demographic questionnaire was compiled and then distributed to four manual therapists with an interest in neck pain. Feedback was incorporated into the questionnaire and after the third round of feedback consensus was obtained from all therapists.

5 Chapter Five – Method: randomised clinical trial

This chapter will discuss the method employed for the randomised clinical trial. The primary outcomes of interest were pain, function and quality of life. Secondary outcomes assessed were the effect of the presence of neuropathic pain and pain catastrophising on treatment outcomes. The primary outcome point was at six weeks.

5.1 Study design

A randomised clinical trial (RCT) was used to answer the aims of the study. There were no changes to the methods of the clinical trial after the trial design. Trial registration Number: PACTR201303000500157

The RCT comprised of two groups, a control group and an experimental group. The control group received “usual care” (UC) as identified by a review of the literature. The intervention group (IG) received NM in addition to the UC.

5.1.1.1 The aims of the study were to establish the effect of NM on the:

- pain of patients with cervico-brachial pain.
- function of patients with cervico-brachial pain.
- quality of life of patients with cervico-brachial pain.

5.1.1.2 To compare:

- the effect of NM added to UC (IG) on the above factors with a control group that received UC only.
- the number of treatment sessions between the NM group (IG) and UC group.
- the effect of NM added to UC (IG) on the elbow range of movement of the upper limb neurodynamic test compared to UC.

5.1.1.3 To determine:

- the influence of neuropathic pain on treatment outcomes in patients with cervico-brachial pain.
- the between group differences in terms of pain, function and quality of life in patients with neuropathic pain.
- the effect of high catastrophising scores on treatment outcomes in patients with cervico-brachial pain.
- the effect of age, gender, headache, hours sitting, previous neck pain/arm pain, education, exercise, paraesthesia and dizziness on treatment outcomes.

5.2 Participant selection procedure

Patients were screened for inclusion into the study from March 2012 to November 2015. Patients were recruited from private physiotherapy practices, whose owners had agreed to take part in the study. These practices are situated in the Pretoria region, Gauteng, South Africa. Patients were referred to private practices by general practitioners or were self-referred. Patients

presenting with cervico-brachial pain were screened for eligibility and invited to take part in the study (Figure 5.1).

5.2.1 Inclusion criteria

- Patients over the age of 18, with cervico-brachial pain as defined by Hall and Elvey (Hall and Elvey, 1999). To be included patients had to present with at least five of the following characteristics:
    - antalgic posture
    - active movement dysfunction of the cervical spine
    - passive movement dysfunction of the cervical spine which is associated with active movement dysfunction.
    - adverse responses to neurodynamic tests which related specifically and anatomically to the active and passive movement dysfunction.
    - mechanical allodynia in response to palpation of specific nerve trunks.
    - evidence from the physical examination and patient history of a local cause of the neurogenic pain (Hall and Elvey, 1999).
- Patients must have had a positive upper limb neurodynamic test 1 (ULNDT1). The ULNDT1 was considered positive if the patient's pain was reproduced or partially reproduced by the test and changed by structural differentiation (Nee et al., 2012a).
- Patients with pain from recent onset (one day) up to 12 weeks, recurrent or first incident.

- Patients with bilateral arm pain were included if they complied with the other inclusion criteria. These patients received NM for both arms if they were part of the IG.

5.2.2 Exclusion criteria

- Absence of a positive neurodynamic test.
- Previous surgery or recent fractures of the cervical spine.
- Serious neurological signs such as signs of spinal cord pressure or involvement of more than two nerve roots. (These patients were excluded based on neurological examination).
- Conditions with long tract signs. (Long tract signs are neurological signs such as clonus, muscle spasticity, or bladder involvement that usually indicate a lesion in the middle or upper parts of the spinal cord or in the brain (Mosby, 2009).)
- Pathological diseases such as rheumatoid arthritis, neurological diseases, stroke, cerebral palsy, carcinoma or other red flags.

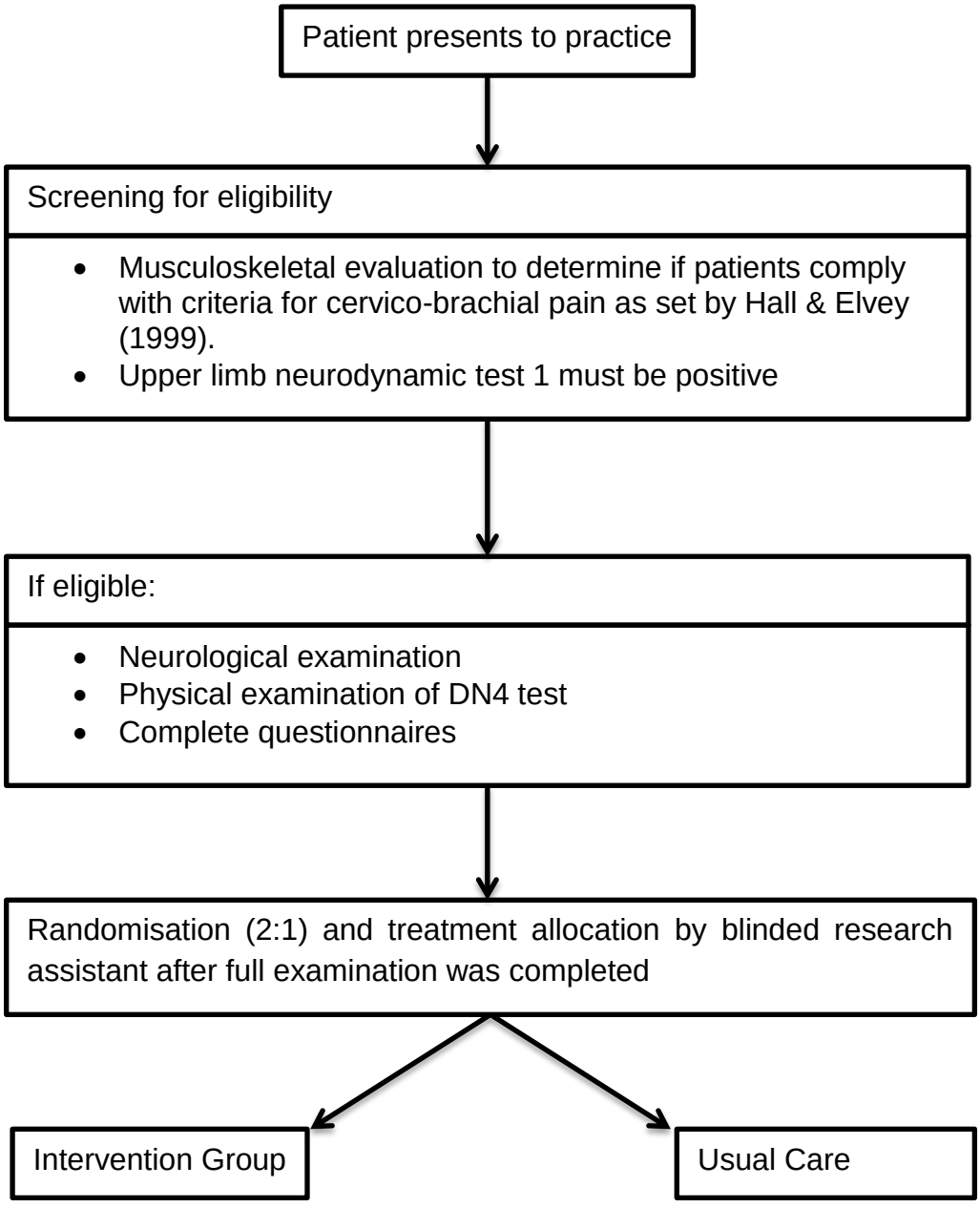


Figure 5.1. Screening and allocation of patients

5.3 Sample size

Primarily this study set out to assess whether, 6 weeks after onset of treatment the Numerical Pain Rating Scale (NPRS) score in the intervention group was reduced compared to the UC group. The sample size calculation is reported for the NPRS, which require the largest sample size. A sample size of 60:26 i.e. a total sample of 86 patients had an 85% power to detect a clinically relevant increase of 2 for the change from baseline at six weeks in the NPRS score. A standard deviation of 2.05 was assumed as derived from the effect size reported by Bolton and Wilkinson (1998). The standard deviation was furthermore inflated by $\sqrt{2}$ since change from baseline was of interest. A dropout rate of 15 – 20% was assumed. One-sided testing was done at a 0.05 level of significance (nQuery advisor 7).

5.4 Interventions

The American Physical Therapy Association Guidelines (Childs et al., 2008) as well as the Australian Guidelines (TRACsa, 2008) both recommend the use of a multimodal intervention comprising of gentle exercise, advice to stay active and cervical mobilisation / manipulation. The UC was done according to these guidelines. No specific mobilisation/ manipulation technique has been shown to be superior to another (Gross et al., 2010, Miller et al., 2010). Therefore, as most physiotherapists in South Africa have been Maitland trained, the patients received Maitland mobilisation (Hengeveldt et al., 2005) of the cervical and thoracic spine. The UC consisted of posterior/anterior and unilateral posterior/anterior mobilisation of the cervical and thoracic spine,

exercises and advice to stay active. Exercises included postural correction, deep neck flexor training according to Falla et al. (2007) and strengthening and mobilising exercises progressing to the use of yellow Theraband ™ as described by Gross et al. (2009). All study patients received advice to stay active (Childs et al., 2008). The number of treatments was determined by the treating physiotherapist and was recorded. Patients in the UC group did not receive any NM.

The IG received NM in addition to UC. The NM used in this study were done as described by Butler (2000), a gentle soft tissue mobilisation of the neural container/ interface “along the tract” (Butler, 2000) pp. 380,) of the nerve – directly where the nerve is palpable and indirectly where it lies deeper. The treatment concentrated on areas where the nerve was mechano-sensitive to palpation and was done from the hand or elbow (depending on patient’s area of pain) and followed up along the arm, first rib, scalene and into the neck. Mobilisation was first done in a position where the nerve is relaxed, not to provoke any of the patient’s symptoms. Palpation was done in such a way as to only provoke minimal symptoms and disappear as soon as it was stopped. The basic principles of neural mobilisations were used to progress treatment; that is to commence treatment in the acute phase with the nerve in a neutral, non-tension position and to progress into a more tensioned position as pain and irritability improved (Butler, 2000, Nee et al., 2011).

5.5 Outcome measures

The primary outcomes were pain (Numeric Pain Rating Scale – NPRS), function (Patient Specific Functional Scale – PSFS) and quality of life (EuroQual Instrument – EQ5D). These self-report outcomes were followed up at three weeks, six weeks, six months and 12 months. The other two measures (Diagnostic Neuropathic pain questionnaire – DN4 and Pain Catastrophising Scale – PCS) were administered at baseline, six months and 12 months. Outcomes measures were discussed in chapter 4. Follow-up of the primary outcomes was done telephonically at three weeks and six weeks. The Global Rating of Change was completed at six weeks. At six months and 12 months patients were asked to return to the practices for measurement of the ULNDT1 and the physical examination of the DN4. All other questionnaires were also completed at six months and 12 months. (See Table 5.1)

Table 5.1. Outcomes measures and timeline of measurements

Measure	Baseline	3 weeks	6 weeks	6 months	12 months
NPRS	✔	✔	✔	✔	✔
PSFS	✔	✔	✔	✔	✔
EQ5D	✔	✔	✔	✔	✔
DN4	✔			✔	✔
PCS	✔			✔	✔
GROC			✔		
ULNDT1	✔			✔	✔
Demographics	✔				
Neural conduction	✔				

Legend: NPRS – Numerical Pain Rating Scale; PSFS – Patient Specific Functional Scale; EQ5D – EuroQual Instrument; DN4 – Diagnostic Neuropathic Questionnaire; PCS – Pain Catastrophising Scale; GROC – Global Rating of Change; ULNDT1 – Upper Limb Neurodynamic Test 1.

5.6 Randomisation and group allocation

Block randomisation with a 2:1 ratio in blocks of 6 was done (Dumville et al., 2006, Shen and Lu, 2006). An unequal randomisation is ideal for smaller randomised controlled trials and multicentre trials (Moher et al., 2009). Randomisation was done using a computer random number generator (Schulz and Grimes, 2002).

Two research assistants were used in the study. Research assistant one was a qualified physiotherapist blinded to patient group allocation. She conducted all the follow-up measurements. Research assistant two was an administrative person, naïve to the study content and at another location than treating practices. She had the list with randomisation and was responsible for informing physiotherapists of patient number and treatment allocation.

The treating physiotherapists screened patients for eligibility and did a full clinical evaluation, which included neurological testing, the physical examination of the DN4 and the ULNDT1. They also administered the baseline set of questionnaires.

Treatment (group) allocation was given to participating physiotherapists after all baseline measurements were done thus ensuring concealed allocation. An independent research assistant (two), naïve to study content, was contacted by telephone by the treating physiotherapists. She gave the treating physiotherapist a sequential patient number as well as the treatment allocation (intervention or usual care).

The physiotherapists involved in the study, then received an envelope with the consent form (Appendix 5.1), patient information leaflet (Appendix 5.2), treatment recording sheet (Appendix 5.3) and all questionnaires. This included the NPRS, PSFS, EQ5D, DN4, PCS and the demographic information. The research assistant (one) doing follow up measurements (qualified physiotherapist) was blinded to group allocation. Treatment recording sheets were only collected at the end of the data collection period. The treatment sheets were used to assess whether treatment allocation was followed and to establish the number of treatment sessions.

5.7 Ethical Considerations

Written consent (Appendix 5.1) to take part in the study was obtained from all study participants and they received an information sheet (Appendix 5.2) explaining the study. Written consent was obtained from treating

physiotherapists. Ethical approval for the study was obtained from the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg, South Africa (Appendix 5.4)

5.8 Procedure

5.8.1 Familiarisation of physiotherapists

Four physiotherapists in private practice (including the researcher) were the treating physiotherapists. All the treating physiotherapists had a post-graduate qualification in orthopaedic manual therapy with knowledge of NM. The average age of treating physiotherapists was 37.5 (range 31- 53) and the time qualified as manual therapists was seven years except for one therapist who had been qualified as a manual therapist for 30 years.

All participating physiotherapists took part in a training workshop run by the researcher. The training workshop consisted of: training of the application of neural mobilisation along the tract of the nerve, protocol for treatment groups, administration of the outcomes measures, baseline measures as well as patient screening; that is inclusion and exclusion criteria. The NM technique was practised on models and the models rated the technique from “feels the same”, “feels similar”, “does not feel at all the same”. After two rounds of practising the technique on different models, all physiotherapists performed the technique in the same way. The range of ULNDT1 was measured using a standard goniometer to measure the range of elbow extension (Sterling et al., 2002). Measurement of the elbow range for the ULNDT1 was demonstrated and all therapists had time to practise before inter-rater reliability on non-

injured participants was established with an ICC of 0.67 and a reliability coefficient of 1.2.

The inter- and intra-rater reliability of the researcher and research assistant was established for the ULNDT1. The inter-class correlation coefficient was good at 0.85, (95%CI 0.66-1.06). The intra-class correlation coefficient for researcher 1: 0.85, (95%CI 0.64 -1.06) and for researcher 2: 0.70 (95%CI 0.31- 1.09), which was acceptable.

5.9 Initial assessment

Patients presenting at participating physiotherapy practices with neck and shoulder/arm pain were screened for inclusion into the study by treating physiotherapists. Suitable candidates received a full musculoskeletal examination to confirm that they complied with the criteria for cervico-brachial pain as described above (Hall and Elvey, 1999). They completed all the questionnaires as discussed after it was established that they complied with the inclusion criteria.

The physical examination included the ULNDT1. The test was done as described above (Butler, 2000). The examination section of the DN4, that is; testing for hypoesthesia to touch, and prick and pain caused by brushing was done at baseline, six months and 12 months. Neural conduction tests of sensation, muscle power and reflexes were done according to Petty and Moore (1998). (See Table 5.1 for timelines of measures)

5.10 Statistical Considerations

Primarily this study set out to assess whether, six weeks after onset of treatment the NPRS score in the intervention group reduced compared to the UC group.

5.10.1 Data Analysis

The data summary employed descriptive statistics, namely for continuous variables means, standard deviations and 95% confidence intervals and is reported by study group (intervention & usual care) for the NPRS, PSFS and EQ-5D. Categorical data such a catastrophising (yes & no) and neuropathic pain (yes & no) were summarised using frequencies, percentages that were displayed in cross tables.

The two treatment groups were compared with respect to the change from baseline at six weeks in the NPRS, PSFS and EQ-5D scores using an analysis of covariance (ANCOVA) with baseline scores, catastrophising (yes & no) and neuropathic pain (yes & no) as covariates. For the total assessment period of 12 months the interaction between visits and treatment were assessed with respect to NPRS, PSFS and EQ-5D scores in a linear mixed model analysis. Effect sizes are expressed as Cohen's *d* for the NPRS. To establish the effect of demographic factors on the outcomes measures (NPRS, PSFS and EQ5D), the individual level based mixed effects models and also population level based Generalized Estimating Equations (GEE) models were utilised. GEE based analysis was used for each variable of gender, pain before, accident, education, sit/day, exercise, headache, dizzy, paraesthesia and area.

For all data description and analyses an intention-to-treat analysis was performed, where data were missing multiple imputation procedures were used. Statistical testing was done at the 0.05 level of significance.

6 Chapter six – Results of the randomised clinical trial

This chapter will describe the results of the study. Results will be presented as per the objectives of the study.

6.1 Demographic and Clinical Profile of Participants

Participants for the study were recruited from February 2012 to October 2014. Data collection was completed in November of 2015. There were 60 patients in the Intervention Group (IG) and the Usual Care (UC) group consisted of 26 patients. Figure 6.1 illustrates the recruitment of patients and their follow up.

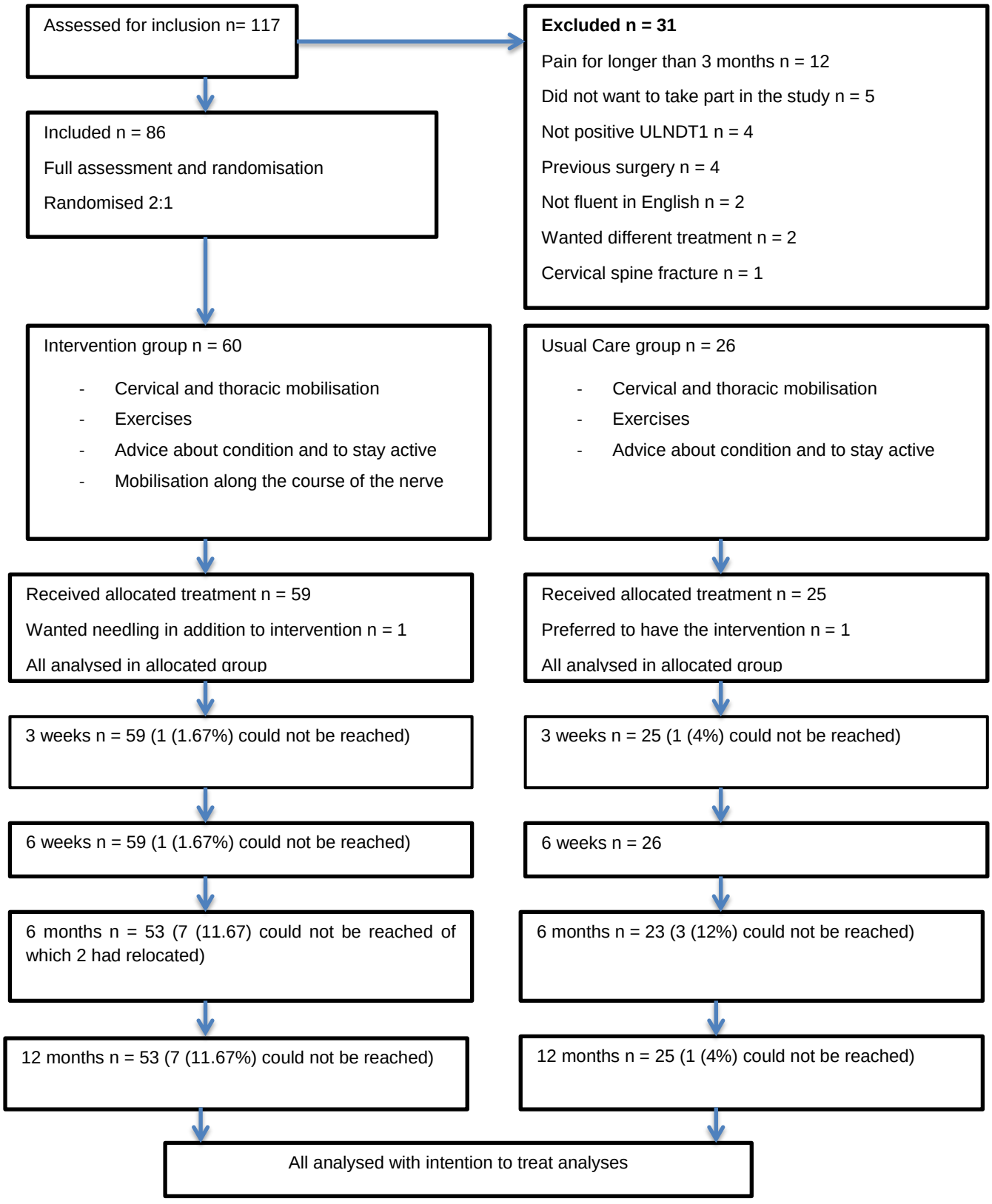


Figure 6.1 Flow diagram of participant recruitment and follow-up.

The demographic and clinical information for the study sample is illustrated in Tables 6.1a and 6.1b below.

Table 6.1a. Demographic information for continuous data

	Intervention Group n = 60	**Usual Care n = 26**	
	Mean (Standard deviation)	Mean (Standard deviation)	p value
Age	46.47 (14.09)	48.61 (13.64)	0.51
Duration of pain (days)	30.19 (27.39)	23.46 (22.90)	0.28
Hours sitting per day	6.72 (2.96)	7.23 (2.97)	0.46

Table 6.1b. Demographic and clinical information for categorical data

Demographic	**Intervention group** n = 60 (%)	**Usual Care** n = 26 (%)	**p value**
Had pain before	49 (81.67)	21 (80.77)	0.92
Pain due to injury/ accident	20 (33.33)	8 (30.77)	0.82
Regular exercise	39 (65)	13 (50)	0.19
Headache	35 (58.53)	15 (57.69)	0.96
Dizziness	17 (28.33)	4 (15.38)	0.20
Paraesthesia	32 (53.33)	14 (53.85)	0.96
Education < 12 years	0	0	
Education 12 years	12 (20)	6 (23.1)	0.75
Education College/ University	48 (80)	20 (76.92)	0.75

The study participants comprised of more females than males (75% to 25%). This distribution was also mirrored in the study groups with 75% females in the IG and 76.9% females in the UC group. There were no significant differences in any of the baseline measures ($p>0.05$). A large proportion of patients had previous neck pain (IG 49 (81.67%) and UC 21 (80.77%) $p = 0.92$). The most

common symptom associated with neck and arm pain was headache (IG 35 (58.53) and UC 15 (57.69%), p = 0.96) followed by pins and needles (IG 32 (53.33) and UC 14 (53.85%), p = 0.97).

Table 6.2 illustrates the distribution of pain for the different upper limb areas

Table 6.2. The distribution of pain for the different upper limb areas

Intervention Group (n=60)	n (%)	Usual Care Group (n=26) n (%)	p = 0.83
Shoulder	19 (31.67)	9 (34.62)	NS
Shoulder and upper arm	7 (11.67)	3 (11.54)	NS
Upper arm and elbow	8 (19.23)	5 (13.33)	NS
Lower arm	4 (6.67)	1 (3.85)	NS
Arm up to wrist	5 (8.33)	4 (15.38)	NS
Hand	4 (6.67)	1 (3.85)	NS
Arm and hand	13 (21.67)	3 (11.54)	NS

The body area most commonly reported to be painful was the shoulder (IG 19 (31.67%) and the UC 9 (34.62%). There were no significant differences between the groups for the distribution of pain (p = 0.831)

The distribution of the study sample by occupation is illustrated in Table 6.3 below.

Table 6.3. The distribution of the study sample by occupation

Occupation	**Intervention Group** n = 60(%)	**Usual Care** n = 26 (%)	**p value**
Sedentary	36 (60)	17 (65.4)	0.64
House wife	7 (11.7)	1 (3.8)	0.25
Allied Health	4 (6.7)	4 (15.4)	0.20
Miscellaneous	13 (21.7)	4 (15.4)	0.50

The occupations of patients were grouped together in common themes. The majority of patients had sedentary occupations (IG 36 (60%) and UC 17

(65.4%)). There were no significant differences between the groups (p>0.05). Table 6.4 illustrates the Upper Limb Neurodynamic Test (ULNDT1) demographics

Table 6.4. Positive Upper Limb Neurodynamic Test Responses: Left, right and bilateral.

Upper limb neurodynamic test	**Intervention Group** n = 60(%)	**Usual Care** n = 26 (%)	**p value**
Left	29 (48.33)	13 (50)	0.89
Right	23 (38.33)	12 (46.15)	0.25
Bilateral	8 (13.33)	1 (3.8)	0.19

In the IG there were more patients with bilateral positive ULNDT1 compared to the UC (IG 13.33% compared to 3.8% in the UC) but the difference was not significant. The distribution of the neurological findings for the study participants is shown in Table 6.5.

Table 6.5. The distribution of the neurological findings.

Neurological Findings	**Intervention Group** n = 60(%)	**Usual Care** n = 26 (%)	**p value**
No changes	12 (21.66)	7 (29.92)	0.57
Myotome	28 (46.66)	11 (42.31)	0.71
Sensation	38 (63.33)	16 (61.54)	0.87
Reflexes	18 (30)	8 (30.77)	0.94
2 changed	22 (36.66)	9 (34.66)	0.86
3 changed	8 (13.33)	4 (15.38)	0.80

Only about a quarter of patients had no neurological changes (IG 21.7%; UC 26.9%). Sensory changes were the most common neurological changes found (IG n=38 (63.3%) and for the UC n= 16 (61.5%)).

6.2 The effect of NM on pain

The Numerical Pain Rating Scale (NPRS) was used to measure pain. Figure 6.2 shows the changes in the NPRS over the study period.

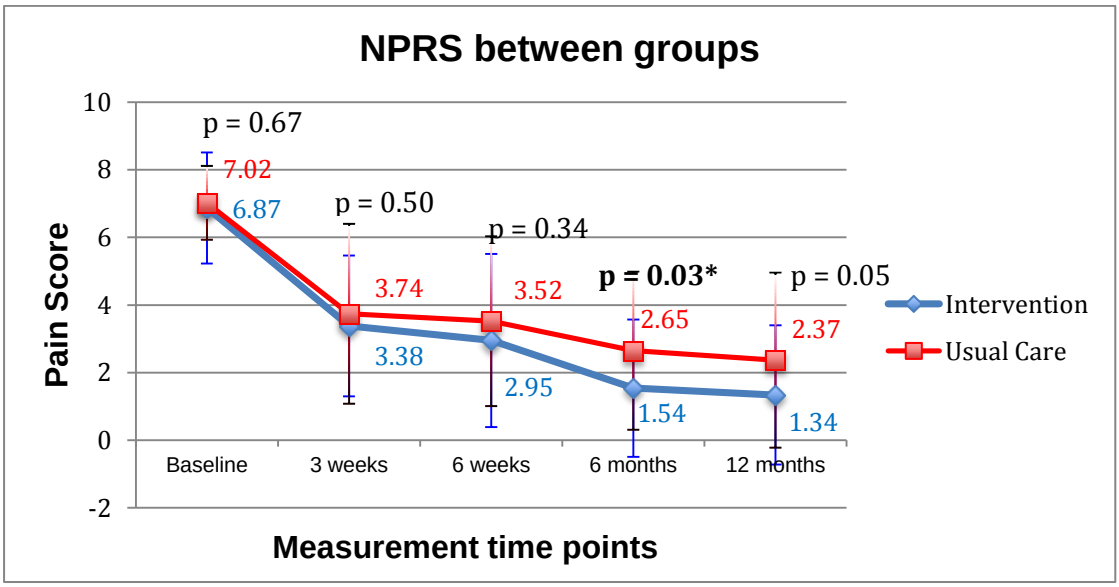


Figure 6.2. Difference in measurements of the NPRS between groups

The IG had significantly less pain at 6 months compared to the UC (p=0.03: IG 95% CI 1.01 – 2.06; UC 95% CI 1.70 – 3.59). At all other time points there was not a significant difference between groups (baseline p=0.67: IG 95% CI 6.45 – 7.29; UC 95% CI 6.57 – 7.23; 3 weeks p=0.50: IG 95% CI 2.84 – 3.91; UC 95% CI 2.67 – 4.82; 6 weeks p=0.34: IG 95% CI 2.29 – 3.61; UC 95% CI 2.51 – 4.54; 12 months p= 0.05: IG 95% CI 0.81 – 1.87; UC 95% CI 1.32 – 3.59). At 6 weeks n=13 (15.1%) of the IG had no pain and n=2 (7.6%) of the

UC had no pain. At 6 months n=23 (26.7%) of the IG had no pain and n=7 (26.9%) of the UC had no pain. At 12 months n=30 (50%) of the IG was pain free (p=0.32) whereas only n=10 (38.46%) of the UC was pain free. There was a significant difference for the whole group in the NPRS at all measurement points compared to baseline (p = 0.0001)

Most of the demographic factors did not have any significant effect (p>0.05) on the NPRS except for paraesthesia, which had a negative effect on pain (p=0.0116; CI 0.16 – 1.26). (See Appendix 6.1)

Table 6.6 illustrates the effect sizes of change of the NPRS for the two groups at different time points.

Table 6.6. Effect sizes at different time points for the NPRS between the two groups

IG	n=26	Cohen's *d*	Effect size *r*	95% C I	PS	UC	n=60	Cohen's *d*	Effect size *r*	95% CI	PS
0 – 1		1.85***	0.68	-2.46 – -1.24	90			1.56***	0.61	-2.46 – -0.68	86
1 – 2		0.2	0.10	-0.62 – -0.47	56			0.13	0.05	-0.9 – -0.64	53
2 – 3		0.63**	0.29	-1.15 – -0.11	66			0.36*	0.15	-1.14 – -0.04	58
3 – 4		0.07	0.05	-0.62 – 0.47	53			0.14	0.05	-0.91 – -0.62	53
0 – 3		2.99***	0.83	-3.73 - -2.26	98			2.39***	0.76	-3.33 – -1.34	94
0 – 4		3.03***	0.83	-3.78 – -2.29	98			2.39***	0.76	-3.40 – -1.39	94

Legend: CI – Confidence Interval; PS – Probability of superiority (PS gives the percentage of occasions when a randomly sampled member of the distribution with the higher mean will have a higher score than a randomly sampled member of the other distribution(Fritz et al., 2012)); 0-1 baseline to 3 weeks; 1-2 3 weeks to 6 weeks; 2-3 6 weeks to 6 months; 3-4 6 months to 12 months; 0-3 baseline to 6 months; 0 – 4 baseline to 12 months Effect sizes using Cohen's *d* *Small (*d* – 0.2) **Medium (*d* – 0.5) ***Large (*d* – 0.8)

From baseline to three weeks both groups showed a large effect (Cohens *d* IG=1.89; UC=1.56) with both groups having around 3 points less pain on an 11-point scale. A large effect size was found in the IG from baseline to six months (Cohen's *d*=2.99) where patients had on average 5.3 points less pain on an 11-point scale. A large effect was also seen in the UC for the same time frame (Cohen's *d*=2.39), with the UC having an average of 4.3 points less pain on an 11-point scale. At six weeks to six months the IG had an intermediate effect and the UC a small effect.

6.3 The effect of NM on function

The Patient Specific Functional Scale (PSFS) was used to measure function. Figure 6.3 shows the outcomes for the two groups.

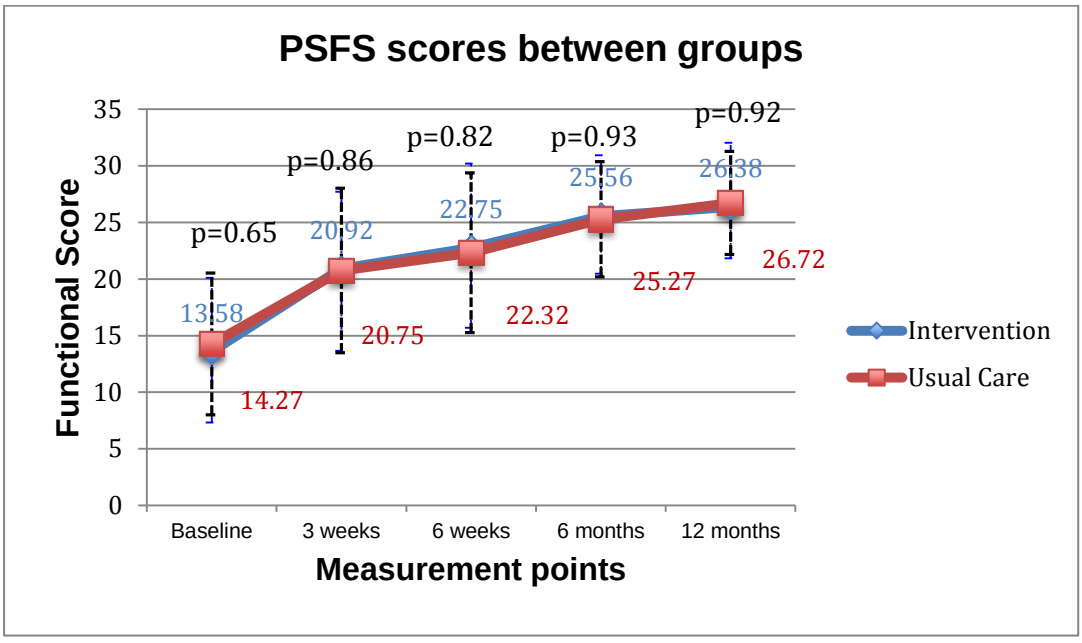


Figure 6.3. Difference in measurements of the PSFS scores between groups

There were no significant differences between groups in their PSFS scores at any time points (baseline p=0.65: IG 95% CI 11.90 – 15.27; UC 95% CI 11.73 – 16.80; 3 weeks p=0.86: IG 95% CI 19.17 – 22.68; UC 95% CI 17.82 – 23.69; 6 weeks p=0.82: IG 95% CI 20.83 – 24.68; UC 95%CI 19.47 – 25.18; 6 months p=93: IG 95% CI 24.18 – 26.95; UC 95% CI 23.21 – 27.32; 12 months p=0.92: IG 95% CI 24.92 – 27.85; UC 95% CI 24.88 – 28.56). At 12 months follow-up only n=17 (28.33%) of the IG and n=3 (30.76%) of the UC had regained full function. Both groups improved significantly over time (p=0.0001). (See Appendix 6.1)

Table 6.7 illustrate the demographics that had an influence on function.

Table 6.7 Demographics that had an influence on function as measured by the PSFS

Demographics	**Fixed effect = p**	**95% Conf. Interval**
Accident	0.02*	-3.59 – -0.36
Gradual onset	0.03*	0.18 – 3.36
Paraesthesia	0.001*	-3.58 – -0 .92

Legend: Conf: confidence; * significant <0.05

The demographics that had an effect on function were, whether symptoms were due to an accident/injury (p=0.02; 95%CI -3.59 – 0.36) and these patients did not do as well as those with a gradual onset (p=0.03; 95%CI 0.18 – 3.36). Paraesthesia also had a significant effect on function as measured by the PSFS (p =0.001; 95%CI -3.58 – -0.92).

6.4 The effect of NM on quality of life

6.4.1 Health state of the EQ5D

The EuroQual 5D instrument (EQ5D) was used to measure quality of life.

Figure 6.4 illustrates the changes over time between groups.

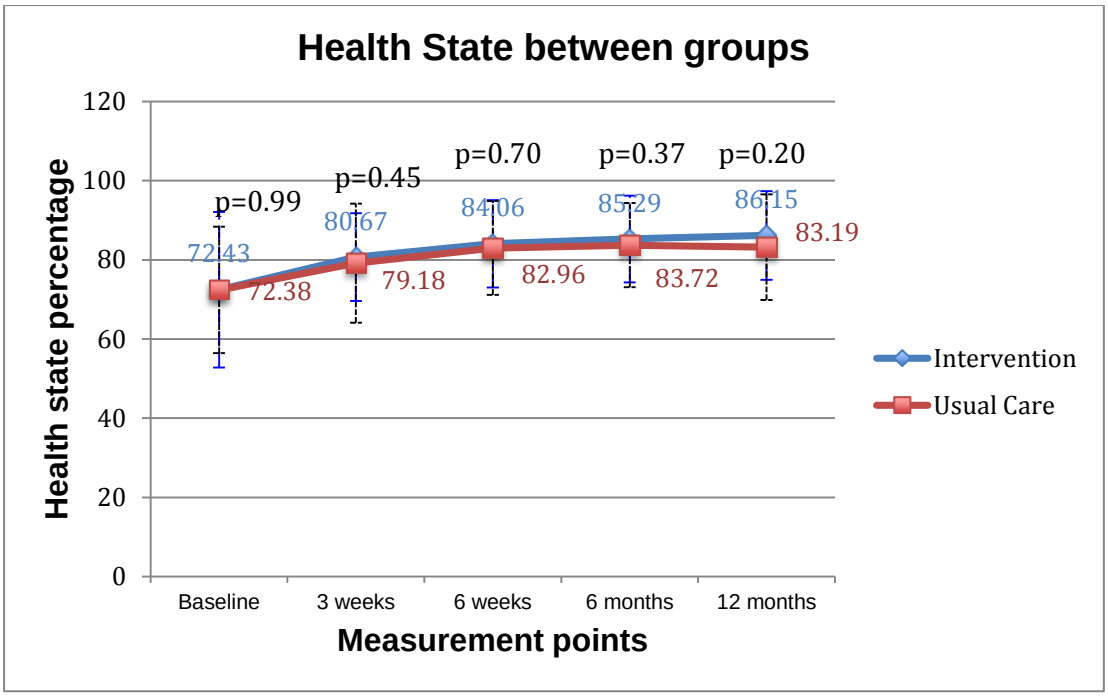


Figure 6.4. Difference in measurements of the health state of the EQ5D between groups.

There were no significant differences in terms of the health state between groups at any time point (Baseline p=0.99: IG 95% CI 67.36 – 77.50; UC 95% CI 65.94 – 78.83; 3 weeks p=0.45: IG 95% CI 77.81 – 83.53; UC 95% CI 73.10 – 85.26; 6 weeks p=0.70: IG 95% CI 81.20 - 86.91; UC 95% CI 78.17 – 87.75; 6 months p=0.37: IG 95% CI 82.45 – 88.12; UC 95% CI 79.41 – 88.03; 12 months p=0.20: IG 95% CI 83.26 – 89.04; UC 95% CI 77.79 – 88.59).

Both groups improved significantly over time (p=0.0001) but there were no between group differences (Baseline p=0.99; 3 weeks p=0.45; 6 weeks p=0.70; 6 months p=0.37; 12 months p=0.20). (Appendix 6.1). The demographics that had a significant effect on the health state are illustrated in Table 6.9.

Table 6.8. Demographics that had a significant effect on the Health State of the EQ5D.

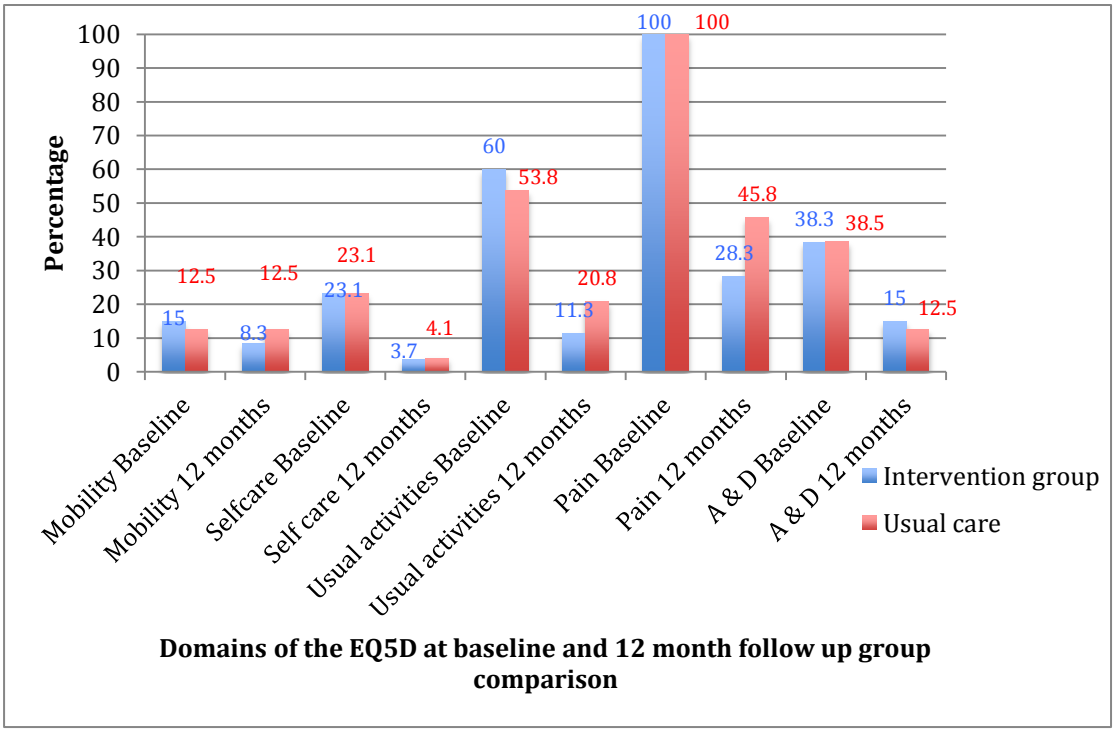
Demographics	**Fixed effect = p**	**95% Conf. Interval**
Area of pain		
Shoulder	0.0001*	-15.53 – -6 .86
Upper arm	0.004*	-9.74 – -1.85
Arm up to hand	0.005*	-10.94 – -1.94
Hand	0.0001*	-15.65 – -4.59
Whole arm including hand	0.01*	-8.70 – -1.20
Hours sitting per day	0.02*	24.95 – 2.28
Headache	0.03*	-5.76 – -0.24
Dizziness	0.0001*	-9.33 – -3.11
Paraesthesia	0.001*	-9.39 – -4.08

Legend: Conf. – confidence; *significance <0.05

A number of demographic variables had an effect on the health state (see Table 6.8). The area of pain and the presence of paraesthesia and dizziness resulted in a significantly poorer quality of life (p=0.0001). Other demographics that had a significantly negative influence on health state were longer hours sitting per day (p=0.02) and the presence of headache (p=0.03).

6.4.2 Domains of the EQ5D

The five domains that the EQ5D measures are mobility, self-care, usual activities, pain and anxiety and depression. Between groups comparison of the percentage of patients presenting with restriction in the different domains of the EQ5D at baseline and 12-month follow-up is illustrated in Figure 6.5.



Legend: A&D – Anxiety and depression

Figure 6.5. Between group comparison of restrictions in the different domains of the EQ5D at baseline and 12 month follow-up.

At baseline there were no significant differences in any of the domains ($p>0.05$). (Appendix 6.1 pp. 29-36)

6.4.2.1 Mobility

At baseline 15% of the IG and 12.5% of the UC had moderate problems with mobility. There was no significant difference between groups at any time points (p>0.05). The percentage of patients who had problems with mobility did not change much over the study period (12 months IG 12.5%; UC 8.3%).

6.4.2.2 Self-care

At baseline 23.12% of the IG and 23.07% of the UC reported moderate difficulty with self-care. At 12 months this had decreased to 3.77% (n=2) in the IG and 4.16% (n=1) in the UC. There were no significant differences between the groups at any time points (p>0.05).

6.4.2.3 Usual activities

There were 60% (n=36) in the IG and 53.85% (n=14) of the UC with some problems with usual activities. At baseline 1.89% (n=1) of the IG and 4.16% (N=1) of the UC stated that they could not perform their usual activities at all. At 12 months 11.32% (n=6) of the IG and 20.8% (n=5) of the UC still had some problems with usual activities. There were no significant differences between the groups at any time points (p>0.05).

6.4.2.4 Pain

At baseline 33.33% (n=20) of the IG and 23.07% (n=6) of the UC reported extreme pain. At 12 months 3.77% (n=2) of the IG and 4.16% (n=1) of the UC still reported extreme pain. At 12 months only 28.33% (n=17) still reported moderate pain in the IG whereas 45.8% (n=11) of the UC still had moderate pain. However, this was a non-significant difference (p=0.13). There were no significant differences between the groups at any of the time points (p>0.05)

6.4.2.5 Anxiety and depression

At baseline 38.33% (n=23) of the IG and 38.46% (n=10) of the UC had moderate anxiety and depression. This had decreased to 15% (n=9) in the IG and 12.5% (n=3) in the UC at 12 months. There were no significant differences between groups at any time points (p>0.05).

6.5 Patient's' perspective of change in their condition

The global rating of change questionnaire was administered at six weeks to measure the patient's' perspective of change in their condition. Figure 6.6 illustrates the findings.

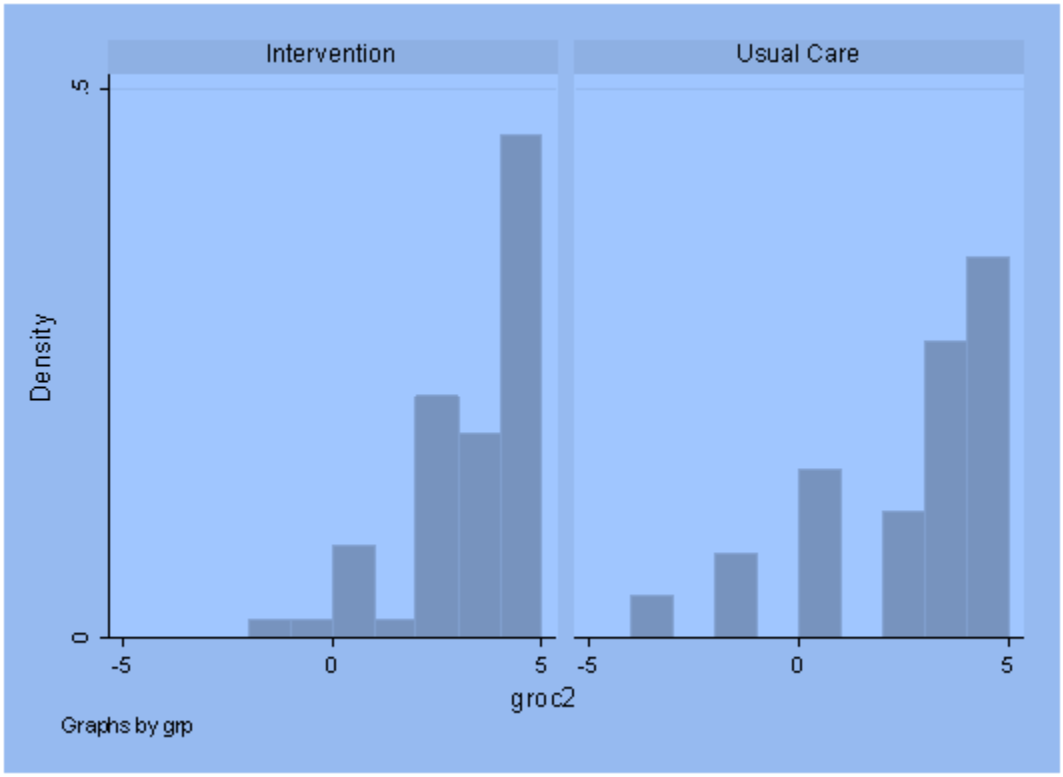


Figure 6.6. Distribution of the Global Rating of Change between groups at 6 weeks.

There were no significant differences between the two groups at 6 weeks in terms of their perception of change in their condition (p=0.36). The majority of responses in the IG and UC were between +3 (better) and +5 (completely recovered). There was one patient that was at -1 and one at -2 (slightly worse) in the IG. Two in the UC were -2 (slightly worse) and one was -4 (worse). (Appendix 6.1)

6.6 Number of treatments

Figure 6.7 illustrates the distribution of treatments between the groups.

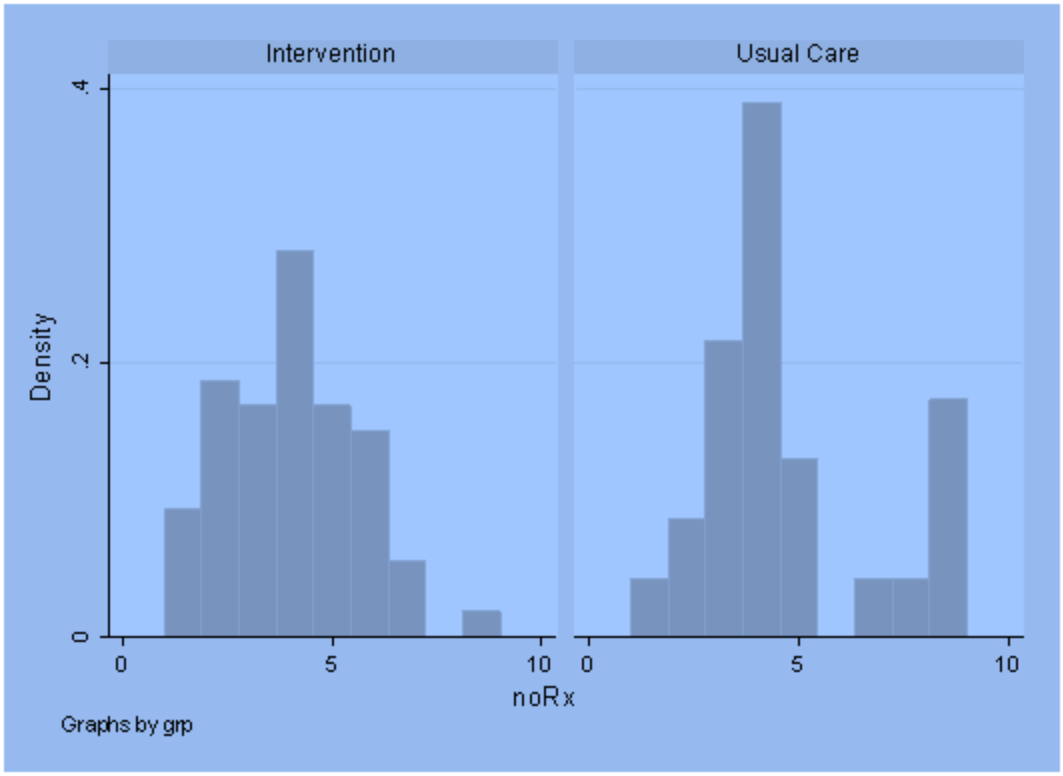


Figure 6.7 Distribution of the number of treatments between groups.

There were no significant differences between groups with regards to the number of treatments they received (p=0.10; IG 3.92± 1.78; UC 4.69± 2.34).

The mean number of treatments was 4.2± 1.98 (Appendix 6.1 pp. 15). However, in the IG there were four patients (6.6%) who needed seven to nine treatments compared to six patients (23.08%) in the UC. This is a significant difference (p=0.03) favouring the IG (Appendix 6.1 pp. 35). All four patients in the IG were classified as having neuropathic pain whereas two of the six patients in the UC were classified as having neuropathic pain. Two of each group were catastrophisers.

6.7 Neuropathic pain

The Neuropathic Pain Diagnostic Questionnaire (DN4) was used to identify patients with neuropathic pain. A total of 45 patients (52.32% of the whole group) i.e. UC (n=13) and IG (n=32) were identified with neuropathic pain at baseline (p=0.78). Eleven patients in the whole group could still be classified as having neuropathic pain at 12 months. There were no differences between the groups at 6 months (IG n=9; UC n=4; p=0.96) or 12 months (IG n= 7; UC n=4; p=0.63) in terms of number of patients identified with neuropathic pain.

6.7.1 Neuropathic pain and pain

Table 6.9 illustrates the findings for patients with neuropathic pain and the NPRS.

Table 6.9. Between group comparison of the number of patients with neuropathic pain and their NPRS scores.

Intervention Group	n	mean	95% Conf. Interval	Usual Care	n	mean	95% Conf. Interval	p
Baseline	32	7.09	6.50 - 7.68		13	7.11	6.62 - 7.61	0.95
6 months	9	2.91	1.74 - 4.08		4	5.5	3.45 - 7.55	**0.01***
12 months	7	2.93	0.85 - 5.00		4	3.75	-0.01 7.51	0.58

Legend: *significant p<0.05; Conf. – confidence.

The patients with neuropathic pain were comparable at baseline with respect to NPRS (p=0.95). There were no significant differences between groups at three weeks and six weeks (p>0.05). At six months patients with neuropathic pain had significantly less pain in the IG (p=0.01) compared to the UC. This was a large effect with the IG having on average 2.59, on an 11-point scale, less pain than the UC group (*d* = -1.77 95% CI -1.77 - -0.41). At 12 months there was no longer a significant difference between groups (0.58).

The between group differences for patients with neuropathic pain compared to those without neuropathic pain in terms of the NPRS is illustrated in Table 6.10

Table 6.10. DN4 positive (neuropathic pain) compared to DN4 negative (not neuropathic pain) with regards to NPRS

Positive	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**Negative**	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**p**
Baseline	45	7.10	1.44	6.66 – 7.53		41	6.72	1.54	6.23 – 7.20	0.24
6 months	13	3.71	1.87	2.57 – 4.84		62	1.44	2.02	0.93 – 1.96	**0.0001***
12 months	11	3.23	2.21	1.74 – 4.71		65	1.38	2.14	0.88 – 1.91	**0.01***

Legend: *significant p<0.05; Conf. – confidence.

Patients with neuropathic pain compared to those not classified with neuropathic pain, were comparable at baseline (p=0.95). However, at 6 months and at 12 months patients with neuropathic pain had significantly more pain than those without (6 months: p=0.0001: mean pain for neuropathic pain was 3.71 compared to 1.54 for the non-neuropathic pain) (12 months: p=0.01: mean pain for neuropathic pain 3.23 compared to 1.38 for the non-neuropathic pain).

6.7.2 Neuropathic pain and function

Table 6.11 illustrates the differences between groups of patients with neuropathic pain in terms of the PSFS

Table 6.11. Between group comparison of the number of patients with neuropathic pain and their PSFS scores

Intervention Group	n	mean	95% Conf. Interval	Usual Care	n	mean	95% Conf. Interval	p
Baseline	32	14.5	12.18 – 16.82		13	13.92	10.08 – 17.76	0.79
6 months	9	24.11	21.30 – 26.92		4	23.25	14.12 – 32.38	0.75
12 months	7	23.86	19.41 – 28.31		4	24	17.25 – 30.75	0.69

Legend: *significant p<0.05; Conf. – confidence.

Groups with neuropathic pain were comparable at baseline with respect to function (0.79). Although both groups improved significantly (p=0.0001) over time there were no significant between group differences at any time points (p>0.05).

Table 6.12 illustrates the findings for patients with neuropathic pain compared to those without neuropathic pain and the PSFS.

Table 6.12. DN4 positive (neuropathic pain) compared to DN4 negative (not neuropathic pain) in terms of the PSFS

Positive	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**Negative**	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**p**
Baseline	45	14.33	6.34	12.43 – 16.24		41	13.20	6.53	11.13 – 15.26	0.41
6 months	13	23.85	4.16	21.33 – 26.36		62	26.21	5.36	24.85 – 27.57	0.14
12 months	11	23.91	4.39	20.96 – 26.86		65	27.15	4.85	25.95 – 28.36	**0.04***

LEGEND: * significance<0.05; Conf. – confidence.

At baseline and 6 months patients with neuropathic pain and patients without neuropathic pain were the same in terms of function (p>0.05). However at 12 months patients with neuropathic pain were more limited in terms of function (PSFS score 23.9) compared to patients without neuropathic pain (PSFS score 27.15) (p= 0.04)

6.7.3 Neuropathic pain and health state of the EQ5D

The differences between groups for patients with neuropathic pain in terms of their health state is shown in Table 6.13

Table 6.13. Between group comparison of patients with neuropathic pain and their health state as measured by the EQ5D

Intervention Group	n	mean	95% Conf. Interval	Usual Care	n	mean	95% Conf. Interval	p
Baseline	32	71	63.57 – 78.43		13	68.92	59.55 - 78.29	0.75
6 months	9	83.11	72.17 – 94.05		4	79.50	54.97 - 104.03	0.69
12 months	7	77.57	65.72 – 89.42		4	83.75	66.11 - 101.39	0.44

LEGEND: * significance<0.05; Conf. – confidence.

There were no significant differences in the health state as measured by the EQ5D in the groups with neuropathic pain at baseline ($p = 0.75$). Although health state improved, there were no significant between group differences at any time points ($p>0.05$).

The differences in terms of the health state for patients with neuropathic pain compared to patients not classified with neuropathic pain are shown in Table 6.14.

Table 6.14 DN4 positive (neuropathic pain) compared to DN4 negative (not neuropathic pain) with regards to health state of the EQ5D

Positive	n	Mean	Std. Dev.	(95% Conf. Interval)	Negative	n	Mean	Std. Dev.	(95% Conf. Interval)	p
Baseline	45	70.4	19.12	64.65 – 76.15		41	74.63	17.78	69.02 – 80.24	0.29
6 months	13	82	14.05	73.51 – 90.49		62	85.61	10.46	82.96 – 88.27	0.29
12 months	11	79.82	12.05	71.72 – 87.91		65	86.11	11.11	83.35 – 88.86	0.09

LEGEND: * significance<0.05; Conf. – confidence.

There were no significant differences between patients with neuropathic pain compared to patients without neuropathic pain at any time point in terms of the health state of the EQ5D (p>0.05)

6.8 Pain Catastrophising

The two groups were comparable with regards to pain catastrophising at baseline (p=0.30). There were n=23 (26.74%) of patients identified as catastrophisers in the whole group. At 12 months only n=7 (8.14%) of the whole group could still be classified as catastrophisers. As treatment was not aimed at changing catastrophising, comparisons between treatment groups are not reported.

6.8.1 Pain Catastrophising and pain

Table 6.15 shows the findings of patients classified as catastrophisers compared to those who were not catastrophisers in terms of pain as measured by the NPRS.

Table 6.15 PCS positive (catastrophisers) compared to PCS negative (non-catastrophisers) in terms of the NPRS

Positive	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**Negative**	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**p**
Baseline	23	7.35	1.05	6.90 – 7.81		61	6.80	1.60	6.39 – 7.21	0.13
6 months	4	4.25	3.86	-1.90 – 10.40		70	1.70	2.00	1.22 – 2.17	**0.02***
12 months	7	3.56	2.67	1.10 – 6.02		68	1.47	2.12	0.96 – 1.99	**0.02***

LEGEND: * significance<0.05; Conf. – confidence.

Patients, who could be classified as catastrophisers, were comparable to those that were not catastrophisers at baseline in terms of pain as measured by the NPRS (p=0.13). However, at 6 months (p=0.02) and 12 months (p=0.02) pain catastrophisers reported significantly more pain than patients who were not classified as catastrophisers. At 6 months there was a 2.56 difference on an 11-point scale and at 12 months still more than a 2 points difference between the catastrophisers and non-catastrophisers.

6.8.2 Pain catastrophising and function

Catastrophisers compared to non-catastrophisers in terms of the PSFS is illustrated in Table 6.16

Table 6.16 PCS positive (catastrophisers) compared to PCS negative (non-catastrophisers) in terms of PSFS

Positive	n	Mean	Std. Dev.	(95% Conf. Interval)	Negative	n	Mean	Std. Dev.	(95% Conf. Interval)	p
Baseline	23	12.35	6.37	9.59 – 15.10		61	14.34	6.40	12.70 – 15.98	0.21
6 months	4	24.25	4.5	17.09 – 31.41		70	25.83	5.30	24.56 – 27.09	0.56
12 months	7	25.14	5.49	20.06 – 30.22		68	26.79	4.87	25.62 – 27.97	0.40

LEGEND: * significance<0.05; Conf. – confidence.

There were no significant differences at any time points between catastrophisers and non- catastrophisers in terms of function as measured by the PSFS (P>0.05).

6.8.3 Pain catastrophising and health state of the EQ5D

Catastrophisers compared to non-catastrophisers in terms of the health state of the EQ5D is illustrated in table 6.17.

Table 6.17. PCS positive (catastrophisers) compared to PCS negative (non-catastrophisers) in terms of health state of the EQ5D

Positive	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**Negative**	**n**	**Mean**	**Std. Dev.**	**(95% Conf. Interval)**	**p**
Baseline	23	61.96	22.94	52.04 – 71.87		61	75.79	15.12	71.91 – 79.66	**0.002***
6 months	4	87	8.72	73.13 – 100.87		70	85.01	11.32	82.31 – 87.71	0.73
12 months	7	84.86	8.86	76.66 – 93.05		68	85.09	11.69	82.25 – 87.92	0.96

LEGEND: * significance<0.05; Conf. – confidence.

At baseline the pain catastrophisers had a significantly lower health state than the non-catastrophisers (p=0.002). At 6 months (p=0.73) and 12 months (p=0.96) there were no significant differences between the groups. The demographics that had a significantly negative effect on catastrophising were longer duration of pain (p=0.04; 95% CI 0.01 – 0.11) and the presence of paraesthesia (p=0.01; 95% CI 0.74 – 5.96). (Appendix 6.1)

6.9 Outcomes of the ULNDT1

The measurement of the ULNDT1 at the elbow is shown in Table 6.18

Table 6.18 ULNDT1 measurements at the elbow at different time points

Intervention Group	**n = 60**			**Usual Care**	**n = 26**		
ULNDT left	**n**	**Mean**	**SD**	**n**	**Mean**	**SD**	**p value**
Baseline	36	110°	29.81	12	96°	46.63	0.23
6 months	32	134°	28.81	12	80°	31.43	**0.0001***
12 months	24	145°	26.81	11	120°	34.85	**0.03***
ULNDT right							
Baseline	32	98°	26.20	13	80°	31.63	0.06
6 months	25	136°	28.14	10	135°	29.46	0.93
12 months	20	136°	24.14	8	90.5°	44.85	**0.0001***

Legend: SD – standard deviation; * - significance <0.05

At baseline the ROM for the ULNDT1 was similar for both groups (p>0.2308). At the six-month follow-up there was a significant difference in the ROM on the left side favouring the IG (p=0.0001). At the 12-month follow-up the ROM improved significantly on the left and right side of the IG (p<0.05) compared to the UC. As a number of patients were not prepared to come in to the practice for measurements and were only followed up telephonically, the dropout for the ULNDT1 was therefore higher than for the self-report questionnaires. On the left side, at 12 months n=12 (33.3%) in the IG were lost to follow-up and n=1 (8.3%) lost in the UC. At 12 months on the right side the loss to follow-up was n=7 (37%) in the IG and n=5 (38%) in the UC (Appendix 6.1 illustrates the measurements pp. 10-11).

6.10 Summary

All patients improved significantly in terms of primary outcomes namely pain, function and quality of life over the 12-month period. However, the IG had significantly less pain than the UC at six months (p=0.03 95% CI 0.9606 - 2.0281) and this difference was more pronounced in patients with neuropathic pain (p=0.01). Therefore the null hypotheses 1a can be rejected and the alternative hypothesis accepted. There were no significant differences between groups in terms of function or quality of life. The findings support the null hypotheses 1b and 1c and the alternative hypotheses can be rejected.

At six weeks there was no significant differences between groups with respect to perceived change although the majority felt better or were completely recovered. Both groups received four treatments on average.

Secondary outcomes were the effect of neuropathic pain and pain catastrophising on cervico-brachial pain. Patients with neuropathic pain had significantly more pain at six (p=0.0001) and 12 months (p=0.01) compared to those without neuropathic pain. At 12 months, function was also negatively affected by neuropathic pain (p=0.04). Catastrophisers had significantly more pain at six (p=0.02) and 12 months (p=0.02) compared to non-catastrophisers. There was no difference in their function, however at baseline they reported lower quality of life (p=0.002).

7 Chapter seven – Discussion of the randomised clinical trial

In this chapter the results of the randomised clinical trial (RCT) will be discussed. This study examined the effect of neural mobilisation (NM) on pain, function and quality of life of patients with cervico-brachial pain. The primary outcomes were pain as measured by the Numerical Pain Rating Scale (NPRS), function as measured by the Patient Specific Functional Scale (PSFS) and quality of life as measured by the EuroQual Instrument (EQ5D). There were two groups of patients: the intervention group (IG) received cervical and thoracic spine mobilisation, exercise and advice to stay active with the addition of NM. The usual care group (UC) received the same treatment without NM. Furthermore, the influence of the presence of neuropathic pain and catastrophising on treatment outcomes was explored. Outcomes were assessed at three weeks, six weeks, six months and 12 months with the primary outcome point at six weeks.

7.1 A brief overview of results

At six weeks there were no significant differences between groups in any of the outcome measures. However at six months the IG had significantly less pain (p=0.03) than the UC group. The improvement in pain was maintained at 12 months follow-up, but the between group difference failed to reach significance (p=0.05). At 6 months follow up the patients with neuropathic pain in the IG also had significantly less pain (p=0.01) than the UC and

improvement was maintained at 12 months. This supports the alternative hypothesis 1a. There were no between group differences in terms of function and quality of life at any of the measurement time points and therefore the null hypotheses 1b and 1c can be accepted and the alternative hypotheses rejected. However, both groups improved significantly in terms of pain, function and quality of life from baseline to the 12 months follow-up.

More than half of the study population had neuropathic pain (IG n=32; UC n=13) at baseline but this number had decreased to around 13% (UC 15% n=4; IG 11.7% n=7) at 12 months follow-up. Patients with neuropathic pain reported more pain and lower function than patients without neuropathic pain.

Only about 28% of the total sample could be classified as catastrophisers and after 12 months follow-up this had decreased to 8%. This group reported a worse quality of life at baseline, and significantly more pain at follow-up than non-catastrophisers.

7.2 Study population

According to the Bone and Joint decade task force on neck pain (Guzman et al., 2009), the majority of the study sample could be classified with Grade III neck pain as they presented with neurological changes. The remainder of the population had Grade II neck pain as all the patients had functional limitations. Considering the poor prognosis of acute idiopathic neck pain (level I evidence) and the associated disability (Hush et al., 2011), as well as limited evidence for the effective management of acute/sub-acute Grade II and III neck pain (Salt et al., 2011, Thoomes et al., 2013), favourable treatment outcomes, as was found in this study, can have important implications in

terms of preventing the transition of acute pain to chronic pain.

More than half of the sample could be classified as having 'probable neuropathic pain' according to the updated classification of the International Association for the Study of Pain special interest group on neuropathic pain (Finnerup et al., 2016, Haanpää et al., 2011). They describe this as a history of a neurological lesion and a neuro-anatomically plausible area of symptoms and sensory changes. In an overview of 55,686 insurance claims for painful neuropathic disorders, back and neck pain with neuropathic involvement were the most common problems (Berger et al., 2004). Similarly Baron et al. (2016) found that a neuropathic pain component is common and under-recognised in patients with low back pain. The findings of this study would therefore support this in an acute/sub-acute neck pain population. However, the findings should be confirmed in a larger study population. The high prevalence of neuropathic pain in the study population has important implications on treatment outcomes as these patients are often resistant to treatment, have poorer health and a higher utilisation of heath care (Baron et al., 2016, Berger et al., 2004, Smart et al., 2012b). Therefore, the significant improvement in the IG of patients with neuropathic pain, at six months and of both groups in function and quality of life is very encouraging.

The baseline pain scores of patients in this study are higher than in most of the studies on NM for cervico-brachial pain (Allison et al., 2002, Gupta and Sharma, 2012, Kumar, 2010, Langevin et al., 2015, Marks et al., Nee et al., 2012b) where the studies had a pain score of four to five. Only three studies reported a high pain score similar to this study (Coppieters et al., 2003b, Nar, 2014, Kumar, 2010). High pain scores at baseline have been shown to be a

predictor of poor outcomes (Miedema et al., 2016, Walton et al., 2013a). Healthcare users e.g. seeking physiotherapy treatment, report higher pain and disability (Huisstede et al., 2008) than those who do not use healthcare. The patients in this study all sought health care and that could possibly be part of the reason for the high levels of reported pain. Therefore, the overall improvement of both groups in this study is better than expected. This study population, which presented with many features that should result in poor treatment outcomes, improved significantly in terms of pain, function and quality of life and treatment effect was maintained at 12 months follow-up.

7.3 Demographics

At baseline, all patients were asked to complete an information sheet to gather information on demographics. Groups were similar at baseline.

7.3.1 Age

Neck pain is most prevalent in middle age (Bot et al., 2005, Hoy et al., 2014, Huisstede et al., 2008, Skillgate et al., 2012), which is similar to the findings of this study. The median age of patients was 46.5 years in the IG and 48.1 years in the UC. This is also similar to the “Global burden of disease 2015” study that found the peak age to be around 44 years of age (Vos et al., 2016). Most of the other studies on cervico-brachial pain have a similar age range except for two studies, one where the median age was 29.5 years (Gupta and Sharma, 2012) and the other where the median age was 52 (±9) years (Marks et al., 2011).

7.3.2 Gender

Neck pain is more prevalent in females (Hoy et al., 2014, Huisstede et al., 2008, Wijnhoven et al., 2006). Women have also been shown to be more likely to develop neck pain and less likely to recover according to a study by Skillgate et al. (2012).

The majority of patients were female with 75% in the IG and 76.9% in the UC. In the other studies on NM for cervico-brachial pain the distribution of females to males were similar ranging between 66% and 75%. One study had more males than females (Gupta and Sharma, 2012). The gender distribution of this study is therefore similar to the literature.

7.3.3 Duration of symptoms

A number of the studies on NM for cervico-brachial pain or cervical radiculopathy were done on a more chronic population (Allison et al., 2002, Marks et al., 2011, Nee et al., 2012b). Unfortunately, the majority of studies had no information on the duration of symptoms (Anwar et al., 2015, Gupta and Sharma, 2012, Kumar, 2010, Nar, 2014, Ragonese, 2009). Two studies included patients with a symptom duration of between five and a half weeks to just over three months (Coppieters et al., 2003b, Langevin et al., 2015). The mean duration of pain in the IG was 30.1 days and for the UC it was 23.5 days. One of the exclusion criteria of this study was pain for longer than three months as the intention was to include only acute and sub-acute patients with cervico-brachial pain. There are fewer studies on acute neck pain compared to studies on chronic neck pain (Hush et al., 2011) & (PubMed search 29 October 2016). There are even fewer studies on acute cervico-brachial pain (Salt et al., 2011). The management of patients in the acute phase is

extremely important in order to prevent the transition to chronic pain especially in light of the poor prognosis of neck pain (Hush et al., 2011).

7.3.4 The presence of previous episodes of neck pain

One of the risk factors for chronicity is a history of neck pain (Bruls et al., 2015, Walton et al., 2013a). In the IG 81.7% of patients had previous episodes of neck pain and in the UC 80.8%. This high incidence of previous pain means that these patients have a poor prognosis compared to first onset neck pain (Bruls et al., 2015, Walton et al., 2013a). This could in part explain why a high percentage of patients still reported some measure of pain at 12 months follow-up.

7.3.5 Pain due to accident or injury compared to gradual onset

There is very weak evidence that the mechanism of injury plays a role in symptom presentation (Walton et al., 2009). However, whiplash associated disorders often have associated factors that impact on treatment outcomes (Anstey et al., 2016, Smith et al., 2016, Sterling and Pedler, 2009). In the IG 33.3% of the population had pain they ascribed to injury or accident and 30.8% in the UC had pain ascribed to injury or accident. In this study, function was negatively affected in those reporting an accident or injury as the cause of their pain compared to those with a gradual onset of symptoms. This is in line with studies that have shown that high disability in whiplash-associated disorder is associated with poor treatment outcomes (Peolsson et al., 2014, Smith et al., 2016).

7.3.6 Regular exercise

Sixty-five per cent of the IG exercised regularly and 50% of the UC exercised regularly. This did not influence any of the treatment outcomes. This is similar to studies reported in the literature that found no association between exercise, pain and function in patients with neck pain (Hogg-Johnson et al., 2008, Walton et al., 2009). In contrast, Palmlöf et al. (2016) found that leisure time physical activity has a protective effect in the development of neck pain.

7.3.7 Education

Some studies have shown lower education levels to be associated with poor prognosis (Hendriks et al., 2005, Walton et al., 2013a). In this study, all participants had a minimum of 12 years of education, and the majority of the study population (IG 80%; UC 76.9%) had college or university education. In this study none of the study population had an education of less than 12 years. The majority of the study population (IG 80%; UC 76.9%) had college or university education. The remainder had 12 years' education. This may account for the fact that education had no effect on any of the treatment outcomes.

7.3.8 Occupation

Patient occupation can have an influence on the development of neck pain (Cho et al., 2012, Hanvold et al., 2014, Viikari-Juntura et al., 2001). Sixty per cent of the IG and 65.4% of the UC had sedentary occupations. This has been associated with neck and shoulder complaints (Cho et al., 2012, Larsson et al., 2007). Ergonomic advice (van Vledder and Louw, 2015) as well as postural correction (Brink et al., 2015, Lluch et al., 2014) could assist patients with sedentary occupations to manage symptoms.

7.3.9 Hours sitting per day

Longer hours spent sitting per day has been associated with poorer quality of life in older people (Meneguci et al., 2015). Furthermore, hours of computer exposure are associated with upper quadrant musculoskeletal complaints (Gerr et al., 2004, Smith et al., 2009). The average sitting time of the study population was around seven hours per day, which is an extremely long period and this could possibly have contributed to the onset of symptoms. Jensen (2003) recommended three to four hours of sitting to prevent onset of symptoms. In this study, longer hours seated was associated with poor quality of life and this is consistent with findings in the literature (Meneguci et al., 2015, Rebar et al., 2014).

7.3.10 The presence of headache and dizziness

Headache is commonly associated with neck pain (Ashina et al., 2015, Leaver et al., 2013b) and is associated with poor treatment outcomes (De Pauw et al., 2015, Walton et al., 2013a). In the IG 58.5% and in the UG 57.8% of the study population had headaches associated with their cervico-brachial pain. Dizziness was less frequently present (IG 28.3%; UC 15.4%). Both headache and dizziness had negative effects on the quality of life in this study. Headache is consistently linked to poor quality of life (Diener, 2001, Lantéri-Minet et al., 2010, Zimmer et al., 2014) as was the case in this study. Dizziness has also been found to have an impact on quality of life (Reid et al., 2015). As headache and dizziness is frequently associated with cervico-brachial pain it is important to assess for these symptoms. Mobilisation and exercise has been shown to be effective in treating these symptoms (Jull et al., 2002, Reid et al., 2015). The presence of these symptoms was not re-

assessed and therefore it is not known whether this had an influence on the improvement in quality of life.

7.3.11 Paraesthesia

Paraesthesia is commonly associated with cervico-brachial pain (Hall and Elvey, 1999, Nee et al., 2012b). Paraesthesia reflects hyper-excitability or reduced inhibition of the nervous system (Schmid et al., 2013) and is thought to be due to neuro-inflammation or partial nerve injury (Djouhri et al., 2012, Schmid et al., 2013). Fifty three per cent of the study population presented with paraesthesia and this is the same percentage as in a study by Nee et al. (2012b). The presence of paraesthesia was the only demographic factor that had a negative effect on pain, function and quality of life. No studies could be found that evaluated the effect of paraesthesia on pain, function and quality of life. Considering the high prevalence of paraesthesia in this population and the impact it has, there is a need for further investigation into the effect of paraesthesia on different treatment outcomes as well as effective management strategies to improve paraesthesia.

7.4 The effect of NM on pain

The pain in both groups improved significantly from baseline to three weeks follow-up, and this improvement was also clinically important (more than three points on an 11 point scale) (Cleland et al., 2008, Farrar et al., 2001, Pool et al., 2007). This improvement can be expected taking natural recovery into consideration (Leaver et al., 2013a, Vasseljen et al., 2013). In their population-based study, Vasseljen et al. (2013) found the mean improvement

in new-onset neck pain was 0.9 on an 11-point scale, whereas the improvement in the IG was 3.5 and 3.3 in the UC at three weeks follow-up. This difference, which is higher than the expected rate of recovery, can probably be ascribed to treatment effect especially in light of the higher baseline pain than in the general population (Vasseljen et al., 2013). Both groups showed improvement at the six weeks follow-up although the improvement from three weeks to sig weeks was no longer clinically important. This is similar to the findings of previous studies that found a significant improvement in the first four weeks after onset of pain (Leaver et al., 2013a, Trott et al., 2014) in patients receiving manual therapy. At 6 months there was a significant difference (p=0.03) between the groups and this can only be ascribed to the addition of NM to the treatment of the IG. The difference was more marked in patients with neuropathic pain (p=0.01). The IG had a mean improvement of 2.5 more than the UC on an 11-point scale. This is a very meaningful clinical difference as a change of 1.3 is considered meaningful in a neck pain population (Cleland et al., 2008). An increased rate of recovery can therefore be important and may prevent the transition to chronic pain. Chronic pain is described as pain lasting beyond normal healing time (Merskey and Bogduk, 2011) and is often associated with central sensitisation in musculoskeletal conditions (Nijs et al., 2010).

Three trajectories of recovery have been identified (van Hulst et al., 2016, Walton et al., 2014) and around 60-65% of patients will have a modest rate of recovery. According to a systematic review, the prognosis of patients with acute neck pain is not as favourable as previously believed (Hush et al., 2011). Improvement is expected within the first six and a half weeks; however,

neck pain severity remains high at 12-month follow-up. In line with this finding, studies have found that improvement takes place in the first two months after which levels of pain and disability will remain the same up to twelve months (Hush et al., 2011, Maher, 2013, Vasseljen et al., 2013, Walton et al., 2014). In contrast to these findings the IG kept on improving from six weeks to six months at a moderate level (Cohen's *d*=1.4) and the UC had a small improvement (Cohen's *d*=0.87) from six weeks to six months. This is therefore, different from the natural course of neck pain (Hush et al., 2011, Vasseljen et al., 2013, Walton et al., 2014) at the 6-month follow-up. None of the studies on cervico-brachial pain (Basson et al., 2015b) or a review on the effectiveness of non-invasive treatment of cervico-brachial pain (Salt et al., 2011) had follow-up measurements at six months, therefore they could not be compared to this study.

At 12 months both groups had significant improvement in pain ($p< 0.0001$) compared to baseline, but the difference between groups failed to reach significance ($p=0.05$). The IG was compared to an effective management protocol and therefore the natural history is not known. However, literature would suggest a less favourable outcome (Hush et al., 2011, Maher, 2013, Vasseljen et al., 2013, Walton et al., 2014). At 12 months follow-up 50% of the IG (95% CI 0.81 – 1.87) had no pain, whereas more than 60% (95% CI 1.32 – 3.41) of the UC still had pain. The use of a multi-dimensional pain measure such as the McGill Pain Questionnaire could possibly have shed more light on differences at the 12-month time point. A follow-up measurement of the Global Rating of Change (GROC) – which was only measured at the primary end point of six weeks – could also have added more information if it had

been measured at six months and 12 months. Although both groups improved significantly (effect size from baseline to 12 months, Cohen's *d* IG 3.03 and UC 2.36), the presence of pain at six and 12 months is much higher than previously suggested (Côté et al., 2016, Leaver et al., 2013a, Walton et al., 2014). A clinical practice guideline on management for neck pain (Côté et al., 2016) recommends "Clinicians should educate and reassure patients about the benign and self-limiting nature of the typical course of NAD grades I–III" (pp. 2001). In light of the findings of this study the outcome of grade II and III neck pain may not be as benign as it is believed to be and would agree with the findings of Hush et al. (2011) that the prognosis of acute neck pain is poor. Therefore adding neuroscience education instead of using only advice to stay active may be beneficial for patients with cervico-brachial pain. There is evidence that neuroscience education improves pain and disability in chronic musculo-skeletal conditions (Louw et al., 2011).

Both treatment groups received cervical and thoracic joint mobilisation in combination with exercises and advice to stay active. This multimodal treatment approach is widely accepted as effective for the management of non-specific neck pain (Gross et al., 2009, Côté et al., 2016, Childs et al., 2008, Hurwitz et al., 2008). There is, however, limited evidence for the management of cervico-brachial pain (Salt et al., 2011) and cervical radiculopathy (Boyles et al., 2011, Thoomes et al., 2013) and therefore most guidelines suggest a similar approach for cervico-brachial pain. The findings of this study support the recommendation that this is an effective treatment approach for patients with cervico-brachial pain as both groups improved significantly in terms of pain. In two systematic reviews both exercises (Gross

et al., 2016) and mobilisation (Gross et al., 2015) have been shown to have an effect on pain. The use of these two modalities as part of the treatment could explain the similar improvement in the two treatment groups.

All patients were given the same exercises. At 12 months there was a tendency for the IG to have better pain outcomes but it failed to reach significance. The addition of nerve-sliding exercises to the IG group may have added to the treatment effect.

7.4.1 Neural mobilisation

The NM used in this study was “mobilisation along the tract of the nerve” (Butler, 2000) and the technique has been described as follows “a gentle soft tissue mobilisation of the neural container/interface “ along the tract” of the nerve (Butler (2000) pp. 380) – directly where the nerve is palpable and indirectly where it lies deeper. Butler (2000) proposes that this technique be used in acute and sub-acute pain. Only one case report could be identified that used a similar technique (Costello, 2009) which resulted in a decrease in pain and improved function. This technique is commonly used in clinical practice, but no other studies exist to support the use thereof.

The aim of neural mobilisation is to restore the homeostasis in and around the nerves (Coppieters and Butler, 2008) by reducing inflammation, improving circulation and the ability of the nerve to adapt to the strain and excursions needed for movement (Topp and Boyd, 2006). A positive neurodynamic test was one of the inclusion criteria for this study. The upper limb neurodynamic test (median nerve bias) (ULNDT1) tests the mechano-sensitivity of the nerve (Coppieters et al., 2005, Schmid et al., 2013). Mechano-sensitivity has been shown to be due to disruption of axoplasmic flow of the nerve (Dilley and

Bove, 2008) and local inflammation of the nerve trunk (Dilley et al., 2005, Schmid et al., 2009). Neural mobilisation has been shown to reduce intra-neural oedema in unembalmed cadavers (Brown et al., 2011, Gilbert et al., 2015). Using NM for carpal tunnel syndrome also resulted in a decrease in intraneural oedema (Schmid et al., 2012). Furthermore, NM decreases temporal summation (Bialosky et al., 2009b), central hyper excitability (Sterling et al., 2010), H-reflex latency (Rezk-Allah et al., 2011), nerve compression (Waleed Salah El-din, 2015) and improves median nerve latency (Oskouei et al., 2014). These studies used different types of NM techniques for instance nerve-gliding exercises, straight leg raise, slump mobilisation and ULNDT mobilisation. Therefore the findings cannot necessarily be extrapolated. It does seem, however, as if neurophysiological changes occur when the nervous system is targeted regardless of the technique used. Neurophysiological parameters were not measured in this study and it is therefore not possible to say if such changes are responsible for the treatment effect. Based on the existing evidence it is plausible that some of the effects can be ascribed to positive neurophysiological changes.

Using the cervical lateral glide in patients with chronic whiplash associated disorder resulted in a decrease in spinal hyper-excitability (Sterling et al., 2010). However, the effect of manual therapy techniques on central pain modulating systems is still unclear (Voogt et al., 2014), but it seems as if it may have a desensitising effect (Santos et al., 2014, Bialosky et al., 2009a).

Greening et al. (2005) established a change in the transverse movement of the median nerve at the wrist in patients with non-specific arm pain. There are however, no changes in longitudinal sliding of the median nerve at the elbow

in patients with non-specific arm pain (Dilley et al., 2008). The mobilisation along the tract of the nerve used in this study could possibly have had a biomechanical effect on the nerve, surrounding tissue and the movement of the nerve (Topp and Boyd, 2006).

Using NM in patients with nerve-related neck and arm pain, poorer treatment outcomes were associated with the presence of neuropathic pain (measured with the Leed's Assessment of Neuropathic Signs and Symptoms), younger age and a decrease in elbow joint range with the ULNDT (Nee et al., 2013). The NM used in their study was cervical lateral glides and neural sliding exercises. Nee et al. (2013) reasoned that the patients with neuropathic pain and decreased elbow range with the ULNDT1 represented a group with a more sensitised nervous system and therefore the techniques were not as effective in this group of patients. Follow-up in this study was at five to six weeks. At this point in this study there were no significant differences between the groups. It is thus possible that Nee et al. (2012b) may have seen a difference at six months in patients with neuropathic pain as was the case in this study. The patients with neuropathic pain were significantly better ($p=0.01$) in the IG compared to the UC at six months and although the difference at 12 months was not significant there was still almost a point difference between the two groups favouring the IG.

Santos et al. (2015) found that NM relieves pain by modulating endogenous analgesia in rats with neuropathic pain. The rats also showed improvements in mobility and strength following NM. In another study they also found that NM resulted in a reduction of hyperalgesia and allodynia (Santos et al., 2012). The effect of NM on the group of patients with neuropathic pain in this study

could possibly be due to similar changes. The fact that a significant difference between the groups was only visible at six months was unexpected. The length of time for these changes to be observed lends credibility to the argument of neurophysiological changes being responsible for the improvement in pain.

Joint mobilisation / manipulation has also been shown to have a hypoalgesic treatment effect (Bialosky et al., 2009a, Bialosky et al., 2014, Voogt et al., 2014). The combination of exercise and mobilisation has a medium and long-term (one year follow-up) effect on pain in chronic non-specific/ mechanical neck pain (Miller et al., 2010, Walker et al., 2008). More recently a systematic review found moderate improvement at long-term follow-up with mobilisation in acute neck pain (Gross et al., 2015). Similarly exercise improves pain and function in short and long term follow-up (Gross et al., 2016). This could possibly explain the fact that there was no longer a significant difference between the groups at the 12-month follow-up.

7.4.2 The influence of demographics

The only demographic factor that had a significantly negative effect on pain was the presence of paraesthesia ($p=0.01$). The presence of paraesthesia was reported in 53.5% of the study population. The high prevalence of paraesthesia can be expected in this study sample with a high prevalence of neurological changes (75%). It has also been described as a symptom frequently present in nerve-related conditions such as cervico-brachial pain (Hall and Elvey, 1999, Moloney et al., 2011). Sensory profiles of patients with non-specific arm pain and cervical radiculopathy differ (Moloney et al., 2013). In non-specific arm pain there is widespread sensitivity to thermal and

pressure pain whilst in cervical radiculopathy thermal and vibratory hypoaesthesia together with localized cold and pressure pain sensitivity is present (Moloney et al., 2013). In this study population there has been no attempt to differentiate between the two groups, therefore both sensory profiles were probably present. In a study on the sensory profiles of patients with neuropathic pain, Freeman et al. (2014) found that there was a strong correlation between pain intensity and presence of paraesthesia in patients with HIV neuropathic pain and diabetic peripheral neuropathy. This could possibly explain the impact of paraesthesia on pain. The presence of paraesthesia was only established at baseline and no follow-up was done to establish whether paraesthesia was still present at 12 months. Considering the impact of the presence of paraesthesia on pain, it is important to take note of this during evaluation of a patient, and to reassess its presence after intervention.

7.4.3 Summary

In patients with cervico-brachial pain, NM added to usual care, consisting of cervical and thoracic mobilisation, exercise and advice to stay active, improved pain significantly more than the treatment without the addition of NM, at six-month follow-up; however, at 12 months follow-up the difference was no longer significant. This difference was more marked in patients with a neuropathic pain component. In light of the fact that neuropathic pain can contribute to central sensitisation and chronic pain states (Berger et al., 2011), early treatment for these patients is important. As stated before, neuropathic pain leads to higher pain, disability (Baron et al., 2016, Jensen et al., 2001, Smart et al., 2012a), poor treatment outcomes and higher cost (Schmidt et al.,

2009).

7.5 The effect of NM on function

The impact that a condition has on an individual's function is important to the patient, society and employers (Turner et al., 2004, Üstün et al., 2010). Functional limitation and disability contributes to the burden of disease (Hoy et al., 2014) and the impact of neck pain on an individual. There was no significant difference between groups at any of the follow-up measurements although both groups improved significantly over time in terms of function as measured by the PSFS. The improvement was maintained at the 12-month follow-up. The improvement was also clinically meaningful for this patient population (IG mean at baseline 4.46 and UC 4.75 compared to IG mean at 12 months 8.79 and UC 8.9 i.e. a change of more than 4). Young et al. (2010) found the minimal clinically important difference of the PSFS to be 2.2. As is the case with pain, studies found that function would improve over the first six and a half weeks after onset of neck pain with no further improvement up to 12 months (Hush et al., 2011). Contrary to this finding the patients in both groups kept on improving up to 12 months. However, at 12 months follow-up just over 30% (IG n=17; UC n=8) of patients had regained full function. The findings of this study therefore support the use of cervical and thoracic joint mobilisation in combination with exercises (Côté et al., 2016, Gross et al., 2009) to improve function in patients with cervico-brachial pain. The addition of NM does not add anything to treatment outcome in terms of function. As has been discussed for pain, the study population prognosis in terms of full functional recovery is poor. Given this finding for pain and function,

recommendations about the benign nature of especially cervico-brachial pain, should be reconsidered. It may be important to inform patients that it is not unusual to still have some pain and functional limitations at 12 months after onset of pain.

Similar to the findings of this study, Langevin et al. (2015) reported a significant improvement in disability using the Neck Disability Index (NDI) and the Disability of Arm, Shoulder and Hand (DASH) questionnaires in both groups receiving mobilisation, traction and exercise for patients with cervical radiculopathy, but there were no between group differences. They compared foraminal opening techniques to other mobilisation techniques of the neck.

Four other studies, however, found significant improvement in the NDI in the groups receiving NM compared to mobilisation and exercise (Anwar et al., 2015), interferential therapy, traction and exercise (Nar, 2014), exercise and advice to stay active (Gupta and Sharma, 2012) and NM and exercise compared to exercise only (Ragonese, 2009). Another study found that the “number needed to treat” favoured the group receiving NM compared to advice to stay active (Nee et al., 2012b).

With the exception of a high risk of bias study by Anwar et al. (2015), the other studies did not have mobilisation as part of the treatment for the comparison group. Although NM did not contribute to improvement in function in this study, comparing the results from the other studies (Anwar et al., 2015, Gupta and Sharma, 2012, Nar, 2014, Nee et al., 2012b, Ragonese, 2009), it seems as if exercise alone is not enough to improve disability. In a systematic review with meta-analysis, Bertozzi et al. (2013) concluded that exercise improves pain in chronic non-specific neck pain, but does not have a

significant effect on disability. It seems as if the combination of mobilisation and exercise has a better effect on function than either alone. This is in line with guideline recommendation (Childs et al., 2008, Côté et al., 2016) and systematic reviews (Gross et al., 2016, Gross et al., 2015, Miller et al., 2010). Function and/or disability were evaluated in only six of the ten studies on NM for cervico-brachial pain and cervical radiculopathy (Anwar et al., 2015, Gupta and Sharma, 2012, Langevin et al., 2015, Nar, 2014, Nee et al., 2012b, Ragonese, 2009). As functional limitations play an important role in the presentation of this patient group, measurement of function should be an important aspect to assess in cervico-brachial pain.

A review on exercise for neuropathic pain (Dobson et al., 2014) concluded that exercise improves nerve function, neuropathic pain, sensory dysfunction and functional mobility. Another review also recommends exercise as safe and beneficial for neuropathic pain (Cooper et al., 2016). These findings may in part explain the fact that there were no differences between the IG and UC for patients with neuropathic pain as both groups received exercises as part of the treatment regime.

Turner et al. (2004) found that in patients with low back pain, there were distinct groups, and that for the group with pain of seven to ten out of ten; a decrease of two points was necessary for improvement in disability compared to a decrease of one out of ten in the group with less pain. In Carpal Tunnel Syndrome the relationship was not as linear. It seems clear that a decrease in pain will lead to an improvement in function. It is therefore plausible that the significant decrease of pain from baseline to 12 months in both groups contributed to the improvement in function. Initially pain decreased more than

2 points which is necessary for improvement in function (Turner et al., 2004). At six months when there was a significant difference in pain between groups the median pain was below four and therefore a decrease of one point would be enough to lead to an improvement in function, further explaining the non-significant between group difference at six months.

Psychosocial factors have also been shown to have an effect on disability and function (Feleus et al., 2007, Lee et al., 2016, Peters et al., 2005, Vranceanu et al., 2009). In this study the only psychosocial aspect measured was pain catastrophising. The presence of catastrophising had no effect on function in this study population. This is similar to a systematic review by Lee et al. (2015) who found self-efficacy and psychological distress mediated the role between pain and disability, but not catastrophising.

7.6 The effect of NM on quality of life

Both groups improved significantly over time in terms of the health state of the EQ5D, but there were no between group differences at any time-points. The addition of NM to the treatment regime of the IG did not add to improved health related quality of life. Only one study on NM for carpal tunnel syndrome measured quality of life and the group receiving NM did not improve as much as the group receiving tendon gliding exercises, splinting and paraffin baths (Horng et al., 2011). None of the other studies on NM identified in the systematic review (Basson et al., 2015b) evaluated quality of life.

Considering the high burden of disease of neck pain (Hoy et al., 2014), measuring the quality of life of patients with neck pain is important. Spinal

pain is associated with lower function and quality of life equal to that of other chronic diseases such as chronic obstructive pulmonary disease and rheumatoid arthritis (Fanuele et al., 2000). Furthermore, patients with neck and radiating arm pain have more pain and disability than those with only neck pain (Daffner et al., 2003). More than half of the study population had neuropathic pain and this is also associated with higher pain and disability and poor quality of life (Smart et al., 2012a, Smith et al., 2007, Sterling and Pedler, 2009).

The EQ5D domains of pain, followed by usual activities and then anxiety and depression were most affected. This is similar to the findings of a population based sample of patients with musculoskeletal diseases (Picavet and Hoeymans, 2004). They concluded that people with musculoskeletal diseases have a significantly lower quality of life compared to the general population. In this study all domains improved over the 12-month period except for mobility, which remained about the same. This is not unexpected, as problems with mobility would probably not be directly related to the presence of cervico-brachial pain.

A number of demographic factors had an impact on the health state of the EQ5D. The area of pain was associated with a worse quality of life with the exception of pain in the lower arm. This could be due to less than 6% of patients having pain in this area. The finding that radiating pain is associated with poorer quality of life is similar to other studies that found neck and radiating pain to be associated with more pain, disability and poor quality of life (Daffner et al., 2003, Huisstede et al., 2008).

Dizziness is commonly associated with neck pain (Leaver et al., 2013b, Reid et al., 2015). The presence of dizziness in persons with neck pain may be due to a number of factors such as disturbed postural control, neck movement control, head and neck awareness and oculomotor disturbances (Kristjansson and Treleaven, 2009). In this study sample 24.4% reported dizziness associated with their cervico-brachial pain and it had a significantly negative effect on quality of life (p=0.0001). Reid et al. (2015) also found dizziness to have a substantial effect on the functional, emotional and physical wellbeing of patients. Complaints of dizziness should therefore be taken seriously as this has such a significant impact on quality of life.

The presence of paraesthesia also had a significantly negative effect (p=0.001) on patient's quality of life. Whilst this can be observed in clinical practice with anecdotal reports of interference with sleep and concentration, literature to support this could not be found. Future studies should assess for the presence of paraesthesia before and after treatment.

Other factors that had a significant effect on quality of life were the number of hours sitting per day (p=0.02) and the presence of headache (p=0.03). Sixty per cent of the study population had sedentary occupations. However, occupation did not have a significant effect on pain, function or quality of life. Some studies have shown a relationship between hours of computer use and neck/shoulder/arm pain (Jensen, 2003, Smith et al., 2009, Waersted et al., 2010) and found that longer hours sitting in front of a computer was associated with an increase in pain and especially hand and wrist symptoms. In a study on the effect of hours sitting in an older population, it was found that especially the physical domain (using the World Health Organisation Quality

of Life instrument) and social participation were affected adversely in those that sat for longer (Meneguci et al., 2015). Physical activity, on the other hand enhances all dimensions of quality of life (Gill et al., 2013). However, here regular exercise did not have a significant effect on quality of life. Therefore it seems as if sustained positions and posture have more of an impact on quality of life in cervico-brachial pain. This is supported by a study that found sitting posture, especially sitting with the neck flexed to be a risk factor for developing neck pain (Ariëns et al., 2001).

The last factor that had a significant impact on quality of life was the presence of headache. Headache is commonly associated with neck pain (Ashina et al., 2015, Leaver et al., 2013b, Smith et al., 2009) and 58% of this study sample complained of headache. The presence of headache has been shown to have a negative effect on function, emotions, concentration, close relationships and quality of life (Diener, 2001, Lantéri-Minet et al., 2010, Zimmer et al., 2014). The presence of headache in neck pain is also associated with poor treatment outcomes (Leaver et al., 2013b). The co-existence of musculoskeletal conditions is common and the presence of multiple musculoskeletal conditions results in a group whose quality of life is most adversely affected (Picavet and Hoeymans, 2004).

There are multiple factors that should be taken into account in terms of quality of life when assessing patients. Although certain aspects cannot be modified by treatment interventions, others, such as dizziness and headache can often be successfully treated with the management strategy used in this study (Childs et al., 2008, Côté et al., 2016, Reid et al., 2015). However, the addition of NM did not contribute to improved quality of life when compared to

the UC.

7.7 Patient's perspective of change in their condition

The perception of treatment effect was measured using the Global Rating of Change questionnaire at six weeks, as this was the primary treatment endpoint. It was expected that there would be a between group difference at this point. However, there were no significant differences between groups. This supports the findings that pain, function and quality of life had all improved significantly but that there were no between group differences at six weeks. The majority of participants reported an improvement of "better" to "completely recovered" (3-5 on a scale of -5 to 5). This is probably a reflection of the significant improvement observed in pain, function and quality of life in both groups.

Only one study on NM for nerve-related neck and arm pain has measured the Global Rating of Change (Nee et al., 2012b). In their study the "number needed to treat" (NNT) favoured the NM group in comparison to advice to continue activities. Although there was not a significant difference between groups in this study, the IG was compared to an effective UC treatment. In a study on patient satisfaction with musculoskeletal care in Australia, patients specifically valued interpersonal aspects, advice on their condition and self-management (Hush et al., 2012). Both groups had advice and received personal attention and treatment. This could have added to the perceived improvement in the condition of both groups. Both management strategies (IG

and UC) of patients with acute /sub-acute cervico-brachial pain resulted a perceived improvement at six weeks follow-up.

7.8 Number of treatments

The mean number of treatments given in both groups was four. In other studies on cervico-brachial pain and cervical radiculopathy the number of treatments varied greatly from only one treatment (Coppieters et al., 2003b, Marks et al., 2011) to treatment administered over a six-month period (Anwar et al., 2015). More commonly five to ten treatments were documented (Gupta and Sharma, 2012, Kumar, 2010, Langevin et al., 2015, Nar, 2014, Ragonese, 2009). Only one other study used four treatments (Nee et al., 2012b) and the NNT favoured the NM group in terms of pain and disability when compared to advice to stay active.

There were, however, significantly more patients in the UC group ($p=0.03$) that needed between seven and nine treatments compared to the IG. All the patients that needed more treatment in the IG had neuropathic pain at baseline. This can be expected as studies frequently report that these patients are poor responders to treatment (Berger et al., 2004, Smith et al., 2007, Sterling and Pedler, 2009) and cost of care is substantially higher than patients with nociceptive pain (Schmidt et al., 2009).

Other factors also related to treatment outcomes are social class, catastrophising, anxiety and depression, severity of baseline neck pain and disability, presence of comorbid back pain, and older age (Hill et al., 2007). Patients in this study had a high level of pain and low functional capacity but

despite this, the majority of patients only needed four treatments. Of the patients that needed more treatments, two patients in each group were catastrophisers. It is therefore not possible to assess if catastrophising could account for the need for more treatment. Anxiety and depression were not evaluated in this study except for the anxiety/depression domain of the EQ5D. In the IG only one patient had extreme anxiety/depression and one had moderate anxiety/depression. In the UC only one patient had moderate anxiety/depression. It is therefore difficult to know whether anxiety/depression had an influence on the number of treatments needed.

Patient expectations have been shown to influence treatment outcomes (Bishop et al., 2013, Hill et al., 2007). It is possible that patients in the UC did not expect as much benefit from treatment as those in the IG. However, it was explained to them that they were receiving evidence informed treatment. Using a sham treatment in the usual care group may have made the two groups more comparable as the IG had an extra intervention (NM) in comparison to the UC. Treatment expectations may not have been similar even though both groups had an active intervention. The fact that both groups improved significantly could account for the mean number of treatments to be equal in both groups.

7.9 The influence of neuropathic pain on pain, function and quality of life in patients with cervico-brachial pain

Neuropathic pain is defined as "pain caused by a lesion or disease of the somatosensory nervous system" (International Association for the Study of Pain, 2011) (web page). Neuronal damage causes maladaptive changes in the nociceptive pathways such as altered gene expression and changes in ion channels (Zhou and Luo, 2015), neuro-immune interactions (Thacker et al., 2007) and aberrant synaptic connectivity (Costigan et al., 2009). Neuropathic pain is associated with cervico-brachial pain and cervical radiculopathy, especially in the presence of negative neurological symptoms such as loss of sensation, reflexes and muscle weakness (Hall and Elvey, 1999, Nee and Butler, 2006).

Fifty two per cent of the study population presented with neuropathic pain at baseline as defined by the DN4 (Bouhassira et al., 2005). Other studies have found that the incidence of neuropathic pain in musculoskeletal conditions is under recognised (Freynhagen and Baron, 2009, Tampin et al., 2013a). The high percentage of patients with a predominantly neuropathic pain component could possibly be ascribed to the presence of referred pain of neural origin (Tampin et al., 2013a) and the high incidence of negative neurological changes found in the study population (78.3%). At 12 months the percentage of patients who still presented with neuropathic pain was 12.8%. This is higher than the prevalence of neuropathic pain in a nationwide survey (23712 respondents), which reported a prevalence of 6.9% (Bouhassira et al., 2008). The high prevalence of neuropathic pain in this study population might in part

explain the findings of other studies that patients with nerve-related neck and arm pain are more disabled and have more pain than patients with only neck pain (Daffner et al., 2003, Sarquis et al., 2016).

The number of patients that could be classified with neuropathic pain at 12 months follow-up (n=11; 12.8%) was significantly less than at baseline (n=45; 52.3%) ($p<0.0001$). It seems as if the IG treatment as well as the UC treatment was effective in reducing the number of patients with neuropathic pain. However, it is also possible that a neuropathic pain presentation in the acute/sub-acute population may resolve over time. As the presence of neuropathic pain is often the driver behind the development of chronic pain (Baron et al., 2016, Freynhagen and Baron, 2009, Moalem and Tracey, 2006), the fact that the number of patients with neuropathic pain decreased significantly can have an important impact on long-term treatment outcomes.

A study on neuropathic pain in acute whiplash-associated disorder (Sterling and Pedler, 2009) found 34% of their study population presented with pain of predominantly neuropathic origin. As has been discussed before, these patients presented with a more complex pain presentation and higher disability. In a study on the incidence of neuropathic pain in an acute pain service (Hayes et al., 2002), the incidence was between 1-3%, however, 55% of these patients had on-going pain at 12 months follow-up despite aggressive multimodal treatment. Therefore identifying patients with neuropathic pain in the acute phase and treating them effectively is very important. The incidence of neuropathic pain in a group of patients with chronic cervical radiculopathy and non-specific neck and arm pain was 25.8% (Tampin et al., 2013b). At follow-up, the percentage patients in this study, who could still be classified as

having neuropathic pain was about half the number in the study by Tampin et al. (2013b). It therefore seems as if the treatment intervention in the acute phase (for both IG and UC), improves outcomes even for patients with neuropathic pain. As neuropathic pain is a risk factor for the development of chronic pain (Doth et al., 2010), and early spontaneous afferent input has been shown to be a trigger for neuropathic pain (Xie et al., 2005), early and effective treatment is very important.

At 12 months follow-up in this study, only two (both in the IG) of the seven patients with neuropathic pain were pain free and only three had regained full function. The presence of neuropathic pain therefore has negative implications in terms of pain-related treatment outcomes. These findings are similar to findings in chronic pain conditions with a predominantly neuropathic pain component (Baron et al., 2016, Berger et al., 2004, Lopez-de-Uralde-Villanueva et al., 2015, Smart et al., 2012a).

Surprisingly, there was not a significant difference between patients with neuropathic pain compared to those without neuropathic pain in terms of their health related quality of life. This is in contrast to other studies that have shown the presence of neuropathic pain to have a negative impact on quality of life (Doth et al., 2010, Smart et al., 2012a, Smith et al., 2007). It is possible that the impact of neuropathic pain in an acute and sub-acute population, on quality of life, is not as substantial as in a more chronic population. The significant decrease in pain in both groups from baseline to 12 months may have had a positive impact on the quality of life in patients (Cuesta-Vargas et al., 2013). Neuropathic pain is prevalent in patients with cervico-brachial pain.

As this is associated with higher levels of pain and disability, assessment for the presence of neuropathic pain is important.

7.10 The influence of pain catastrophising on pain, function and quality of life in patients with cervico-brachial pain

Pain catastrophising has emerged as one of the most powerful psychological predictors of pain-related outcomes (Park et al., 2016, Sullivan et al., 2001). The Pain Catastrophising Scale (PCS) was developed as an instrument to identify pain-related catastrophic thinking in clinical and non-clinical populations (Edwards et al., 2006, Sullivan et al., 1995). Catastrophising has been described as an excessively negative orientation towards any painful stimuli or health condition (Sullivan et al., 1995). It has been suggested as a multi-dimensional construct with three dimensions namely magnification, rumination and helplessness. Catastrophisers have been characterised as chronic worriers who experience higher levels of anxiety in a wide range of health related situations (Vasey and Borkovec, 1992). Pain catastrophising has been linked to high pain reports, disability, poor quality of life (Geelen et al., 2016, Sullivan et al., 1998) and poor treatment outcomes (Verhagen et al., 2010).

In this study 27% (n=23) patients could be classified as catastrophisers at baseline. At six months only 6% (n=5) were still catastrophisers and at 12 months seven patients (8%) could still be classified as catastrophisers. Wirth et al. (2016) have shown that there is a significant improvement in

psychological parameters within the first month of acute/ sub-acute neck pain. They also found that those patients who did not show an improvement in the psychological parameters were more likely to report poor treatment outcomes (Wirth et al., 2016). Their findings are similar to this study. It seems to be natural for some patients to catastrophise when confronted by pain, however, as pain decreases the majority of patients will have a decrease in their pain catastrophising scores (Racine et al., 2016). It is therefore important not only to assess patients at the first consultation for the presence of pain catastrophising, but also to reassess at one-month follow-up. If pain catastrophising is still present once pain has decreased, other treatment options should be considered.

Catastrophising has consistently been linked to poor pain related outcomes and high reports of pain (Karels et al., 2007, Rivest et al., 2010, Vranceanu et al., 2014). In this study, catastrophisers reported significantly more pain at six months ($p=0.02$) and 12 months ($p=0.02$) follow-up. The difference was more than two points on an 11-point scale which is also a clinically meaningful difference (Cleland et al., 2008). Furthermore, at 12 months follow-up only one of these patients was pain-free. Therefore the presence of catastrophising had a negative influence on pain related treatment outcomes (Catastrophisers: mean 3.56; 95% CI 1.10 – 6.02 compared to non-catastrophisers: mean 1.47; 95% CI 0.96 – 1.99). This finding is supported by studies in the literature (Leung, 2012, Quartana et al., 2009).

Racine et al. (2016) found a temporal relationship between pain and catastrophising, where a decrease in pain was related to a decrease in catastrophising scores. Therefore either targeting catastrophising could lead

to a decrease in pain report, or treating pain could lead to a decrease in catastrophising. In this study, treatment was not aimed at changing catastrophising, but rather at improving pain. Only eight per cent of the study population were still catastrophisers at 12 months follow-up and this seems to support the findings by Racine et al. (2016). The relationship between pain and catastrophising in a chronic population is multifaceted (Quartana et al., 2009, Sullivan et al., 2001) and therefore targeting pain in a chronic population will probably not have the same outcomes. It therefore underlines the importance of treating pain effectively in the acute and sub-acute stage. There was no significant difference between catastrophisers and non-catastrophisers in terms of function ($p>0.05$). This finding is contrary to other studies, which found that catastrophising negatively impacted on function (Arnow et al., 2011, Dimitriadis et al., 2015, Sullivan et al., 1998). It must be borne in mind that these observations were in a chronic population. However, Lee et al. (2015) found self-efficacy and psychological distress mediated the role between pain and disability, but not catastrophising. Only two of the seven patients who could still be classified as catastrophisers at 12 months, had regained full function. This seems to indicate that catastrophising had some influence on function. The small number of patients at six months (n=5) and 12 months (n=7) could have had an influence on the statistical analyses as a larger study is needed to identify differences (Hackshaw, 2008). Therefore the findings should be interpreted with caution; Catastrophisers: mean 25.14; 95% CI 20.06 – 30.22 compared to non-catastrophisers: mean 26.75: 25.62 – 27.97. Catastrophising has also been associated with bed rest and immobility, which may interfere with healing mechanisms (O'Sullivan,

2005, Verbunt et al., 2008). Whilst it may not be able to transform a catastrophiser to a non-catastrophiser, the frequency of catastrophising thoughts experienced may be reduced by strategies such as engagement in physical activity (Smeets et al., 2006), emotional disclosure (Keefe et al., 2008) and activity encouragement (Smeets et al., 2006). The advice to stay active may have assisted some of the catastrophisers in this study.

Pain catastrophising has been shown to have a negative impact on quality of life and pain related suffering (Geelen et al., 2016, Wade et al., 2011). Similarly this study population classified as catastrophisers reported significantly (p=0.002) poorer quality of life at baseline compared to non-catastrophisers. However, at six months and 12 months follow-up there were no significant differences between catastrophisers and non-catastrophisers. Again, the small number of patients that could still be classified as catastrophisers at six months (n=5) and 12 months (n=7) could have influenced the statistical analysis. The wide 95% confidence interval in the group of catastrophisers (mean 84.86; 95% CI 76.66 – 93.05) compared to the non-catastrophisers (mean 85.2; 95% CI 82.25 – 87.92) illustrates the point. A larger study is therefore required to investigate findings on the effect of catastrophising on function and quality of life of patients with cervico-brachial pain.

Depression has also been shown to be associated with high pain catastrophising (Park et al., 2016). Five of the seven patients who could still be classified as catastrophisers at 12 months, had moderate to extreme anxiety and depression on the dimensions of the EQ5D at baseline, however, only three still reported moderate anxiety and depression at 12 months follow-

up. Although the influence of depression and anxiety does not seem to have played such an important role in catastrophising in this study population, no firm conclusion can be made due to the low number of patients who could still be classified as catastrophisers. Information on the influence of depression on catastrophising in an acute cervico-brachial pain population is not known. However, Wirth et al. (2016) found depression at baseline and continued anxiety to be predictors of poor treatment outcomes in acute neck pain.

The demographic factors that had a negative influence on catastrophising were longer duration of pain ($p=0.04$) and the presence of paraesthesia ($p=0.01$). No studies could be identified that evaluated the effect of the duration of pain and paraesthesia in patients with high pain catastrophising. The components of catastrophising such as magnification and helplessness could contribute to duration of pain playing a role and result in higher catastrophising. Therefore, the longer pain is present the more catastrophisers would worry about the pain, the seriousness of the problem and their ability to manage it. It is possible that the presence of paraesthesia is seen as a threatening symptom and therefore it could have a negative impact on catastrophising.

Catastrophising should be evaluated in patients with cervico-brachial pain. Other treatment options should be considered for those patients still presenting with high catastrophising scores at one-month follow-up as they tend to have poor treatment outcomes (Wirth et al., 2016). Even though only a small percentage of patients continue to catastrophise at 12 months follow-up, they have significantly more pain ($p=0.02$) at follow-up than non-catastrophisers.

7.11 The upper limb neurodynamic test outcomes

The upper limb neurodynamic test 1 (ULNDT1) (Butler, 1991) evaluates the mechano-sensitivity of the median nerve (Greening et al., 2005). It is a valid way of identifying patients with peripheral neuropathic pain (Nee et al., 2012a) and a positive test was an inclusion criterion for this study. The elbow range of motion (ROM) was measured as described before (Basson et al., 2014). Groups were similar at baseline however, at 12 months follow-up the ROM of the left arm ($p=0.03$) and the right arm ($p=0.0001$) of the IG were significantly improved compared to the UC. A number of studies on NM for cervico-brachial pain measured the elbow ROM of the ULNDT (Coppieters et al., 2003b, Gupta and Sharma, 2012, Marks et al., 2011) and two of the three studies found a significant improvement in the group receiving NM (Coppieters et al., 2003b, Gupta and Sharma, 2012), whereas the other study reported a significant improvement in the group that received joint mobilisation (Marks et al., 2011). As the condition improves, it can be expected that mechano-sensitivity would also decrease. It seems however that a technique targeting the nerve improves neural mechano-sensitivity more than mobilisation and exercise only. Neural mechano-sensitivity can limit normal movement (Dilley et al., 2005) and therefore improvement in the ROM of the ULNDT is important for return to full function.

7.12 Significance of the study

This study had a bigger study population than any of the studies identified in the systematic review. The systematic review identified 10 studies on nerve-related neck and arm pain (cervico-brachial pain and cervical radiculopathy). Of these studies only four were low risk of bias studies. Studies had low numbers of study participants ranging from 20 to 40 participants with the exception of one study (Nee et al., 2012b) that had a study population of 60. The meta-analysis of the systematic review concluded that cervical lateral glides improve pain in cervico-brachial pain. The findings of this study support the meta-analysis. A meta-analysis could not be done for function or disability in the systematic review and in this study NM did not have an effect on function. The bigger study population in my study made it possible to investigate the impact of some of the demographic factors on pain, function and quality of life in this patient population.

No studies could be identified that evaluated the effect of mobilisation along the course of the nerve. This technique is commonly used in clinical practice and has the advantage of being very gentle and therefore ideal for an acute population where there is often increased mechano-sensitivity of the nerves.

There is a paucity of studies on cervico-brachial pain and especially in the acute / sub-acute population. The presence of neuropathic pain in an acute/sub-acute population with cervico-brachial pain has not been established. The presence of neuropathic pain has been studied in an acute whiplash associated disorder population (Sterling and Pedler, 2009). As mobilisation along the tract of the nerve is a gentle technique it had a good

treatment effect even in this very sensitised population. The NM used in this study had a very positive outcome in patients with neuropathic pain.

There was one study that treated patients over a six-month period and evaluated treatment at baseline and end of treatment. None of the other studies had a follow-up period of more than eight weeks. Therefore, this study could establish that treatment effect was maintained at one-year follow-up. It also highlighted the fact that despite a significant improvement in all treatment outcomes at least half of the study population still had pain and disability after a year. If patients had not been followed up at 6 months, the significant effect of NM would not have been visible.

There are only a few studies that have assessed the impact of pain catastrophising on neck pain. Unfortunately at 6 months and 12 months the few patients who were still catastrophisers made it difficult to make any firm conclusions about the impact of catastrophising on cervico-brachial pain.

Disability or function is not often measured in patients with cervico-brachial pain and none of the studies identified with the systematic review measured the quality of life of patients with cervico-brachial pain. No other studies could be identified that established the effect of paraesthesia on the pain, function and quality of life of patients with cervico-brachial pain.

7.13 Summary

The addition of NM to the treatment had a significantly positive effect on pain when compared to the UC at six months follow-up especially in the group of patients with neuropathic pain. However, at 12 months there were no

significant between group differences in terms of pain, function and quality of life although both groups had a significant improvement in all primary outcomes. Despite the significant improvement in both groups in terms of all outcome measures, 50% - 60% of the population still had on-going pain and only around 30% had regained full function. The presence of neuropathic pain and pain catastrophising were associated with poor pain related treatment outcomes across the whole study population.

8 Chapter Eight – Conclusion

This chapter contains the concluding statements of the different objectives of the study as well as recommendations for future research and clinical practice. The study limitations will also be discussed.

8.1 Prevalence of neck pain and radiating arm pain in private physiotherapy practice in Pretoria, Gauteng, South Africa

The retrospective survey of physiotherapy records revealed a high prevalence of neck pain and radiating arm pain seen in private physiotherapy practice in Pretoria. More than 50% of the survey population had radiating arm pain associated with their neck pain. This is similar to other studies in this field. As is the case in most musculoskeletal conditions, the majority of the population were women (63%). The median age (44) was also similar to population-based studies (Vos et al., 2012).

In my study shoulder pain was most commonly associated with neck pain. Radiating pain into the arm and hand was the second most common reported area of pain. Very few of the survey records reported pain in the lower arm associated with neck pain. Headache and pain in other areas such as the lower back or thoracic area were symptoms often reported with neck pain. Other symptoms that were often present were paraesthesia, burning and numbness.

8.2 The effect of neural mobilisation on the pain, function and quality of life of patients with cervico-brachial pain

The patient population presented with a number of factors associated with poor treatment outcomes, such as high pain and functional limitation at baseline, presence of neuropathic pain, neurological changes, headaches and pain in other areas. The addition of neural mobilisation (NM) to the usual care resulted in improved pain at six months especially in the group of patients with a predominantly neuropathic pain component. Both groups improved significantly over the first six months and the improvement was still evident and maintained at 12 months follow-up. However, in the IG 50% of patients still had some pain at 12 months and more than 60% of the UC still had pain at 12 months follow-up. It is therefore evident that even though patients with cervico-brachial pain improve, their prognosis of being pain free is poor.

Both groups improved significantly in terms of function and quality of life over the 12 month follow-up period, but there were no between group differences. However, a disquieting observation was the fact that only around 30% of the population had recovered full function at 12 months follow-up despite having improved significantly over the time period. The measurement of disability is not routinely done in trials on cervico-brachial pain. Furthermore, quality of life is very rarely assessed.

8.3 Neuropathic pain

More than 50% of the patient population could be classified with neuropathic pain. Using NM improved pain significantly for patients with neuropathic pain. Patients with neuropathic pain had more pain at six and 12 months follow-up compared to patients without neuropathic pain. They also had poorer function at 12 months follow-up.

8.4 Pain catastrophising

The number of patients who could be classified as catastrophisers was just over a quarter of the study population and this had decreased to less than 10% at 12 months follow-up. They reported a poorer quality of life at baseline than non-catastrophisers. At 6 months and 12 months follow-up they also had significantly more pain than non-catastrophisers. Being a catastrophiser did not impact on function. Quality of life was also not affected, as is normally the case in chronic populations.

8.5 Number of treatments and patient's perception of change

The mean number of treatments was four. In light of the patient population with high pain and disability at baseline, the number of treatments seems reasonable. In the UC more patients needed seven to nine treatments compared to the IG. The majority of patients reported being "better" to "completely recovered" at six weeks follow-up.

8.6 The upper limb neurodynamic test

The range of motion of the elbow during the upper limb neurodynamic test 1 (ULNDT1) had improved significantly more in the IG at 12 months follow-up compared to the UC.

8.7 Study limitations

The retrospective survey to establish the prevalence in physiotherapy private practice was a sample of convenience and included just over 1300 records. Therefore the findings, while useful, are not representative of a broader private practice population.

The presence of neuropathic pain and pain catastrophising was only measured at baseline, six months and 12 months. If these were also measured at three weeks and six weeks like the other outcomes, it might have given a clearer picture of the changes in these parameters. The Global Rating of Change was only measured at six weeks, as this was the primary end-point. If this was measured at six months and 12 months as well, it may have made it possible to see differences that could not otherwise be identified.

As not all the patients who were followed up were prepared to come in to the practices for the re-assessments, the dropout rate for re-measurements of the upper limb neurodynamic test was high. Therefore, these results should be interpreted with care.

8.8 Research recommendations

From the retrospective survey it is clear that there is a need for a more representative survey to establish the prevalence of neck and radiating arm pain in the general population of South Africa. This is important in light of the impact neck pain has globally with no information on local prevalence and the impact thereof.

Although there is an increase of studies on NM as is evidenced by the systematic review, of the 20 additional studies identified in our review, only eight were low risk of bias studies. There is a need for high quality studies with bigger study populations to investigate the effect of NM on neuro-musculoskeletal conditions. As a number of studies have found positive neurophysiological changes when using NM as a treatment technique, future studies should endeavour to establish what changes are responsible for positive treatment outcomes.

There is a need for more studies to establish the optimal treatment approach for cervico-brachial pain especially in an acute/sub-acute population. Furthermore, there is very little information on the presence of neuropathic pain in this population and the best management strategies to employ in this population.

In light of the findings of this study, that paraesthesia had a significant impact on pain, function and quality of life; future studies should investigate this further and attempt to find treatments that will effectively address the presence of paraesthesia.

There is a need for a core set of outcomes measures that can be used in neck pain studies. These should include outcomes that not only assess pain, but disability or function and also quality of life.

8.9 Clinical Recommendations

As neuropathic pain is so prevalent in patients with cervico-brachial pain, clinicians should routinely screen for the presence of neuropathic pain. In the presence of neuropathic pain, mobilisation along the course of the nerve should be added to the management of these patients. Complaints of paraesthesia should be taken seriously and re-assessed if present.

Given the fact that at least 50% of the population still reported some pain after 12 months and only 30% had recovered full function, clinicians should consider including pain neuroscience education as part of the treatment approach for patients with cervico-brachial pain.

In the presence of pain catastrophising in the acute/sub-acute population, re-assessment should be done at one-month follow-up. If pain catastrophising is still present, alternative treatment strategies such as a cognitive-behavioural therapy should be considered.

8.10 Concluding paragraph

Cervico-brachial pain is prevalent and these patients have a complex pain presentation with associated factors such as neurological deficit and neuropathic pain. These are prognostic factors associated with poor treatment

outcomes. However, both groups improved significantly in terms of pain, function and quality of life. The addition of mobilisation along the course of the nerve to usual care resulted in a significant improvement in pain at six-month follow up and this was more pronounced in patients with neuropathic pain. The presence of neuropathic pain and pain catastrophising had a negative influence on pain-related outcomes.

9 Appendices

Appendix 2.1: Example search strategy (PubMed/ MEDLINE)

Treatment technique	Management type	Condition	Type of study
Nerve tissue/therapy[mh]	Conservative intervention[tw]	Radiculopathy[mh]	Randomized controlled trial[mh]
Nerve treatment[tw]	Conservative approach[tw]	Musculoskeletal pain[mh]	Clinical trial[mh]
Neural treatment[tw]	Conservative management[tw]	Referred pain[mh]	Randomised control*[tw]
Neurodynamic*[tw]	Conservative therap*[tw]	Nerve tissue/injuries [mh]	Randomized control*[tw]
Nerve stretch*[tw]	Physical approach[tw]	Radicular pain[tw]	Randomised control trial[tw]
Nerve tension[tw]	Physical intervention[tw]	Nerve pain[tw]	Randomized control trial[tw]
Neural tension[tw]	Physical management[tw]	Neuropathy[tw]	Controlled clinical trial[tw]
Nerve mobili*[tw]	Physical therapy[tw]		Randomi*[tw]
Neural mobili*[tw]	Physiotherapy[tw]		RCT[tw]
Nerve modalit*[tw]	Manual therapy[tw]		Trial[tw]
Neural modalit*[tw]			Placebo[tw]
Nerve glid*[tw]			Group*[tw]
Neural glid*[tw]			

Search strategy in the PubMed Advanced Search Builder:

#1 Nerve tissue/therapy[mh] OR Nerve treatment[tw] OR Neural treatment[tw] OR Neurodynamic*[tw] OR Nerve stretch*[tw] OR Nerve tension[tw] OR Neural tension[tw] OR Nerve mobili*[tw] OR Neural mobili*[tw] OR Nerve

modalit*[tw] OR Neural modalit*[tw] OR Nerve glid*[tw] OR Neural glid*[tw]

Number of articles found 9022

#2 Conservative intervention[tw] OR Conservative approach[tw] OR Conservative management[tw] OR Conservative therap*[tw] OR Physical approach[tw] OR Physical intervention[tw] OR Physical management[tw] OR Physical therapy[tw] OR Physiotherapy[tw] OR Manual therapy[tw]

Number of articles found 61848

#3 Radiculopathy[mh] OR Musculoskeletal pain[mh] OR Referred pain[mh] OR Nerve tissue/injuries [mh] OR Radicular pain[tw] OR Nerve pain[tw] OR Neuropathy[tw]

Number of articles found 57929

#4 Randomized controlled trial[mh] OR Clinical trial[mh] OR Randomised control*[tw] OR Randomized control*[tw] OR Randomised control trial[tw] OR Randomized control trial[tw] OR Controlled clinical trial[tw] OR Randomi*[tw] OR RCT[tw] OR Trial[tw] OR Placebo[tw] OR Group*[tw])

Number of articles 3446845

#1 AND #2 AND #3 AND #4 **Number of articles 26**

Appendix 2.1 Search Strategy

Appendix 2.2 Joanna Briggs Institute Meta Analysis of Statistics Assessment and Review Instrument for critical appraisal (JBI-MAStARI)

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer _____ Date _____

Author _____ Year _____ Record Number _____

	Yes	No	Unclear	Not Applicable
1. Was the assignment to treatment groups truly random?	☐	☐	☐	☐
2. Were participants blinded to treatment allocation?	☐	☐	☐	☐
3. Was allocation to treatment groups concealed from the allocator?	☐	☐	☐	☐
4. Were the outcomes of people who withdrew described and included in the analysis?	☐	☐	☐	☐
5. Were those assessing outcomes blind to the treatment allocation?	☐	☐	☐	☐
6. Were the control and treatment groups comparable at entry?	☐	☐	☐	☐
7. Were groups treated identically other than for the named interventions	☐	☐	☐	☐
8. Were outcomes measured in the same way for all groups?	☐	☐	☐	☐
9. Were outcomes measured in a reliable way?	☐	☐	☐	☐
10. Was appropriate statistical analysis used?	☐	☐	☐	☐
	☐	☐	☐	☐

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

Appendix 2.3 JBI Grades of level of evidence



New JBI Grades of Recommendation

Developed by the Joanna Briggs Institute Levels of Evidence and Grades of Recommendation Working Party October 2013

JBI Grades of Recommendation	
Grade A	A 'strong' recommendation for a certain health management strategy where (1) it is clear that desirable effects outweigh undesirable effects of the strategy; (2) where there is evidence of adequate quality supporting its use; (3) there is a benefit or no impact on resource use, and (4) values, preferences and the patient experience have been taken into account.
Grade B	A 'weak' recommendation for a certain health management strategy where (1) desirable effects appear to outweigh undesirable effects of the strategy, although this is not as clear; (2) where there is evidence supporting its use, although this may not be of high quality; (3) there is a benefit, no impact or minimal impact on resource use, and (4) values, preferences and the patient experience may or may not have been taken into account.

The FAME (Feasibility, Appropriateness, Meaningfulness and Effectiveness) scale may help inform the wording and strength of a recommendation.

F – Feasibility; specifically:

- What is the cost effectiveness of the practice?
- Is the resource/practice available?
- Is there sufficient experience/levels of competency available?

A – Appropriateness; specifically:

- Is it culturally acceptable?
- Is it transferable/applicable to the majority of the population?
- Is it easily adaptable to a variety of circumstances?

M – Meaningfulness; specifically:

- Is it associated with positive experiences?
- Is it not associated with negative experiences?

E – Effectiveness; specifically:

- Was there a beneficial effect?
- Is it safe? (i.e is there a lack of harm associated with the practice?

Appendix 2.4 Excluded studies

1. Bahrami et al. (2006) Reason for exclusion – article in Arabic, could only locate abstract in English
2. Beneciuk et al. (2010) Reason for exclusion – healthy population
3. Coppieters et al. (2004) Reason for exclusion – case report
4. Castellote-Caballero et al. (2013) – healthy population
5. Day et al. (2014) – not a randomised controlled trial
6. De-la-Llave-Rincon et al. (2012) Reason for exclusion – not a randomised controlled trial
7. Ferreira et al. (2016) Reason for exclusion – design of a trial.
8. Leonelli et al. (2013) Reason for exclusion – other language (Italian)
9. Lorentzen et al. (2012) Reason for exclusion – not neuro-musculoskeletal condition
10. Madenci et al. (2012) Reason for exclusion – massage techniques used not aimed at neural tissue
11. Rodriguez Torres et al. (2015) Reason for exclusion – rheumatologic condition and treatment not aimed at peripheral nervous system
12. Rozmaryn et al. (1998) Reason for exclusion – not a randomised clinical trial
13. Sansare et al. (2013) Reason for exclusion – healthy population, not neural mobilisation
14. Saranga et al. (2003) Reason for exclusion– healthy population
15. Savva and Giakas (2013) Reason for exclusion – case report
16. Schafer et al. (2011) Reason for exclusion – not a randomised clinical trial
17. Sharma et al. (2011a) Reason for exclusion – not a randomised clinical trial
18. Sharma et al. (2016) Reason for exclusion – healthy population, not testing treatment effect
19. Sterling et al. (2010) Reason for exclusion – treatment not aimed at peripheral nervous system

20. Szlezak et al. (2011) Reason for exclusion – not neural mobilisation, healthy population
21. Veras et al. (2012a) Reason for exclusion – not a neuro-musculoskeletal condition
22. Villafane et al. (2013) Reason for exclusion – not neuro-musculoskeletal condition
23. Villafane et al. (2012) Reason for exclusion – not a neuro-musculoskeletal condition
24. Young et al. (2009) Reason for exclusion – manual technique used not neural mobilisation

Appendix 3.1 Consent Form Prevalence

Consent – Prevalence

By signing below, I ……..……. agree to take part in a research study entitled “The prevalence of cervico-brachial pain in physiotherapy practice in Gauteng, South Africa”

I declare that:

- I have read the information sheet and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is voluntary and I have not been pressurised to take part.

Signed at (place) .....…..…….. on (date) ……...…….. 2012.

Signature of participant

Declaration by Researcher

I …… declare that:

- I explained the information in this document to ……..
- I encouraged him/her to ask questions and took adequate time to answer them.

• I am satisfied that he/she adequately understands all aspects of the research, as discussed

Signed at (place) .....…….…….. on (date) ……...…….. 2012.

Signature of Researcher

Appendix 3.2 Information of Prevalence study

INFORMATION FOR PARTICIPATING PHYSIOTHERAPISTS

Study title: Prevalence of neck and radiating arm pain in physiotherapy practice in Gauteng.

Hello, I am Annalie Basson, a physiotherapist doing my PhD at the University of the Witwatersrand

Introduction:

I am doing research on the prevalence of neck/shoulder/arm pain (also referred to as cervico-brachial pain) in physiotherapy practices in Gauteng. In this study we want to find out how many of the neck pain patients that we see in physiotherapy practice will have cervico-brachial pain. Currently the prevalence of neck/ shoulder/ arm pain in Gauteng is unknown.

Participation: I am requesting permission for access to your patient records from January 2011 to December 2011.

What is involved in the study – This study is a retrospective study. The main aim of this study is to establish how many of the neck pain patients treated in physiotherapy practice in 2010 have shoulder/arm/hand (cervico-brachial) pain. If you agree to participate in the study you will be required to make your patient records of the year 2010 available to us for analyses. Firstly files of all patients treated for neck pain will be retrieved. The data needed on each patient is; age, gender, area of pain and whether pain was due to injury or of insidious onset. We will collect the data in the practice of participating physiotherapists. We would like to involve as many practices as possible in the Gauteng area.

The participant will be given pertinent information on the study while involved in the project and after the results are available.

Confidentiality: Confidentiality of files will be maintained. Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Research Ethics Committee.

Contact details of researcher – Please contact me at telephone number 0832289934 for any further information.

Contact details of REC administrator and chair – for reporting of complaints / problems. **Prof Cleaton Jones** 0117171234

Appendix 4.1 Numerical Pain Rating Scale (NPRS) and physical measures

Numerical Pain rating Scale **PT no**

Please indicate on the line the intensity of your pain today



No Pain Moderate Pain Worst Possible Pain

Reflexes:

Sensation:

Muscle Power:

ULNDT1: L

ULNDT1: R

Appendix 4.2 Patient Specific Functional Scale (PSFS)

Patient Specific Functional Scale **Patient number**

Initial Assessment

I am going to ask you to identify three important activities that you are unable to do or are having difficulty with as a result of your neck/shoulder/arm pain problem. Today, are there any activities that you are unable to do or having difficulty with because of your neck/shoulder/arm pain problem? (Clinician: show scale to patient and have the patient rate each activity).

Follow-up Assessments:

When I assessed you on (state previous assessment date), you told me that you had difficulty with (read all activities from list at a time). Today, do you still have difficulty with: (read and have patient score each item in the list)?

Patient-specific activity scoring scheme (Point to one number):

0 1 2 3 4 5 6 7 8 9 10

Unable to perform activity

Able to perform activity to same level as before

Activity (Date) **Initial**				
1				
2				
3				

Total score

Appendix 4.3 EuroQual 5D Instrument



Health Questionnaire

English version for South Africa

Patient Number _____

By placing a tick in one box in each group below, please indicate which statements best describe your own state of health TODAY.

Mobility

I have no problems in walking about ❑

I have some problems in walking about ❑

I am confined to bed ❑

Self-Care

I have no problems with self-care ❑

I have some problems washing or dressing myself ❑

I am unable to wash or dress myself ❑

Usual Activities (*e.g. work, study, housework, family or leisure activities)*

I have no problems with performing my usual activities ❑

I have some problems with performing my usual activities ❑

I am unable to perform my usual activities ❑

Pain/Discomfort

I have no pain or discomfort ❑

I have moderate pain or discomfort ❑

I have extreme pain or discomfort ❑

Anxiety/Depression

I am not anxious or depressed ❑

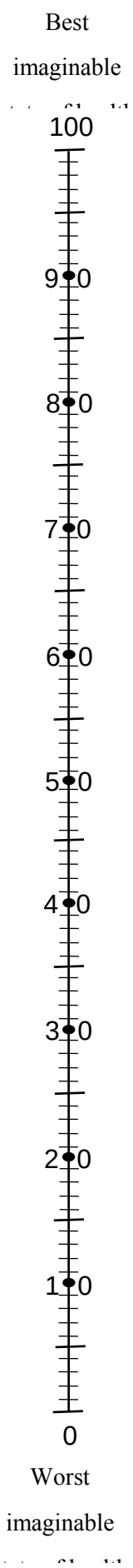
I am moderately anxious or depressed ❑

I am extremely anxious or depressed ❑

To help people say how good or bad their state of health is, we have drawn a scale (rather like a thermometer) on which the best state you can imagine is marked 100 and the worst state you can imagine is marked 0.

We would like you to indicate on this scale, in your opinion, how good or bad your own health is today. Please do this by drawing a line from the box below to whichever point on the scale indicates how good or bad your state of health is today.

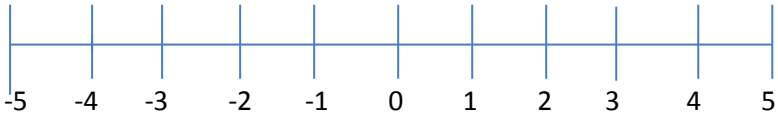
Your own state of health today



Appendix 4.4 Global Rating of Change Scale

Global Rating of Change **PT no** **Appendix 8**

With respect to your neck and shoulder/arm pain, how would you describe yourself now compared to when you started with treatment?



Very much worse Unchanged Completely recovered

Appendix 4.5 Neuropathic Pain Diagnostic Questionnaire (DN4)

DN4 Questionnaire **Patient number**

Please complete the questionnaire by ticking one answer for each item in the 4 questions below:

INTERVIEW OF THE PATIENT

Question 1: Does the pain have one or more of the following characteristics?

	Yes	No
1 – Burning		
2 – Painful cold		
3 – Electric Shocks		

Question2: Is the pain associated with one or more of the following symptoms in the same area?

	Yes	No
4 – Tingling		
5 – Pins and Needles		
6 – Numbness		
7 - Itching		

EXAMINATION OF THE PATIENT

Question 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

	Yes	No
8 – Hypoesthesia to touch		
9 – Hypoesthesia to prick		

Question 4: In the painful area, can pain be caused or increased by

	Yes	No
10- Brushing		

Appendix 4.6 Pain Catastrophising Scale (PCS)

Copyright © 1995
Michael JL Sullivan

PCS

Client No.: _____ Age: _____ Sex: M(__) F(__) Date: _____

Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feelings that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the following scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

0 – not at all **1** – to a slight degree **2** – to a moderate degree **3** – to a great degree **4** – all the time

When I'm in pain …

1. ☐ I worry all the time about whether the pain will end.
2. ☐ I feel I can't go on.
3. ☐ It's terrible and I think it's never going to get any better.
4. ☐ It's awful and I feel that it overwhelms me.
5. ☐ I feel I can't stand it anymore.
6. ☐ I become afraid that the pain will get worse.
7. ☐ I keep thinking of other painful events.
8. ☐ I anxiously want the pain to go away.
9. ☐ I can't seem to keep it out of my mind.
10. ☐ I keep thinking about how much it hurts.
11. ☐ I keep thinking about how badly I want the pain to stop.
12. ☐ There's nothing I can do to reduce the intensity of the pain.
13. ☐ I wonder whether something serious may happen.

…Total

Appendix 4.7 RCT Demographic Questionnaire

Patient Information Patient Number_____

Please answer and tick where applicable

Age:

Male / female

For how long have you had the pain and/ or symptoms? _____

Have you had neck and / or arm pain before? Yes / No

Is the pain due to an injury or accident? Yes / No

Or, did the pain start without any specific incident Yes/ No

Schooling and Education: - Less than 12 years

- 12 Years

- College / University

What is your occupation? _____

How many hours a day do you sit? _____

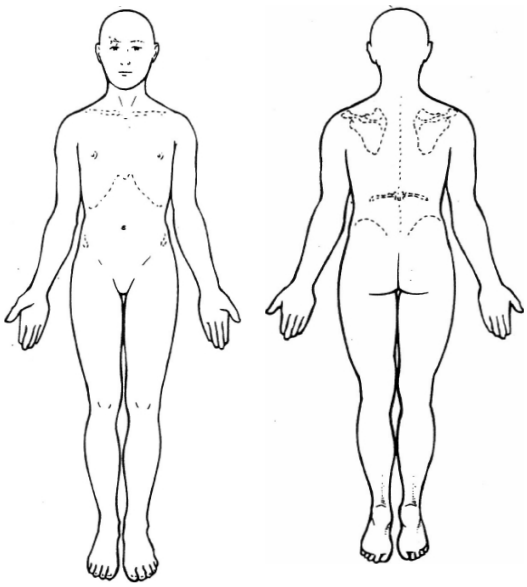
Do you participate in sport or do exercises? Yes / No

Do you have headaches? Yes / No

Do you have any dizziness? Yes / No

Do you have any pins and needles? Yes / No

Please indicate the area of your pain on the pictures below



Appendix 5.1 Consent Form Patient RCT

Consent – Patients

By signing below, I ……..…… agree to take part in a research study entitled "The effect of neural mobilisation on cervico-brachial pain

I declare that:

- I have read the information sheet and consent form and it is written in a language with which I am fluent and comfortable.
- I have had a chance to ask questions and all my questions have been adequately answered.
- I understand that taking part in this study is **voluntary** and I have not been pressurised to take part.
- I may choose to leave the study at any time and will not be penalised or prejudiced in any way.

Signed at (*place*) ..... on (*date*) ……..…….. 2014.

.....

Signature of participant

Declaration by physiotherapist

I …… declare that:

- I explained the information in this document to ……..
- I encouraged him/her to ask questions and took adequate time to answer them.
- I am satisfied that he/she adequately understands all aspects of the research, as discussed above

Signed at (*place*) ..... on (*date*) ……..…….. 2014.

.....

Signature of physiotherapist

Appendix 5.2 Patient Information leaflet RCT

INFORMATION FOR PATIENTS

Study title: Neural mobilisation for cervico-brachial pain

Hello, I am Annalie Basson, a registered physiotherapist studying at the University of the Witwatersrand

Introduction:

I am doing research on the influence of neural mobilisation on neck and shoulder/arm pain (also referred to as cervico-brachial pain). Neural mobilisation is a gentle technique that is applied along the nerves in the arm. Research is just the process to learn the answer to a question. In this study we want to learn if adding neural mobilization to usual physiotherapy for neck pain will have an effect on the pain, function and quality of life of patients with cervico-brachial pain. Currently neck/ shoulder/ arm pain is treated in the same way as neck pain alone and there is not a lot of research on the treatment of neck/ shoulder/ arm pain. I would like to see if we can improve the treatment outcomes by adding neural mobilizations.

Invitation to participate: I am inviting you to take part in this research study

What is involved in the study – This study is a randomized clinical trial Patients will be randomly assigned to a group that receive usual physiotherapy for neck pain and a second group that will receive usual physiotherapy as well as neural mobilization. The usual physiotherapy will consist of mobilization of the neck, exercises and advice. This is according to research the best way to treat a neck. The treating physiotherapists will evaluate your problem and ask you to complete certain questionnaires. The questionnaires that you will be asked to complete will ask questions about the pain that you have, how the pain affects your daily activities and your quality of life such as dressing yourself. There is another questionnaire on how the pain makes you feel. The questionnaires will take about 10 to 15 minutes to complete. The first treatment will take about an hour and thereafter between half an hour and three quarters of an hour. The questionnaires and certain measurements will be done again at three weeks, six weeks, 6 months and 12 months. The initial re-assessments will be arranged at times when you are receiving treatment. The follow-up assessments will be arranged at a time suitable to you. The follow up assessments will take 15 to 20 minutes. I need

102 patients for this study. We will be treating patients in four different private practices in Johannesburg and Pretoria.

Benefits: Physiotherapy (as described above) has been shown to be effective in relieving pain and function in patients with neck pain when compared to patients that receive only normal care from their doctor. In clinical practice we have found neural mobilisations to be effective in treating arm pain. However, there is no research to support this finding.

The participant will be given pertinent information on the study while involved in the project and after the results are available.

Participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which you would otherwise be entitled, and you may discontinue participation at any time without penalty or loss of benefits to which you are otherwise entitled.

Confidentiality: Efforts will be made to keep personal information confidential. Absolute confidentiality cannot be guaranteed. Personal information may be disclosed if required by law.

Organizations that may inspect and/or copy your research records for quality assurance and data analysis include groups such as the Research Ethics Committee.

If results are published it may lead to cohort identification.

Contact details of researcher/s – Please contact me at telephone number 0832289934 for any further information or to report any study related adverse events.

Contact details of REC administrator and chair – for reporting of complaints / problems.

Prof Cleaton Jones 0117171234

Appendix 5.3 Treatment recording sheet

Treatment Recording Sheet **Appendix 11**

Patient Number: _____

Date	Treatment	Outcome

Appendix 5.4 Ethical Consent form

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG
Division of the Deputy Registrar (Research)

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)
R14/49 Ms Cato A Henning

CLEARANCE CERTIFICATE	M111002
PROJECT	The Effect of Neural Mobilisation on Cervico-Brachial Pain
INVESTIGATORS	Ms Cato A Henning.
DEPARTMENT	Department of Physiotherapy
DATE CONSIDERED	28/10/2011
M1110020DECISION OF THE COMMITTEE*	Approved unconditionally

Unless otherwise specified this ethical clearance is valid for 5 years and may be renewed upon application.

DATE 28/10/2011 **CHAIRPERSON** .....
(Professor PE Cleaton-Jones)

*Guidelines for written 'informed consent' attached where applicable
cc: Supervisor : Prof A Stewart

DECLARATION OF INVESTIGATOR(S)

To be completed in duplicate and **ONE COPY** returned to the Secretary at Room 10004, 10th Floor, Senate House, University.
I/We fully understand the conditions under which I am/we are authorized to carry out the abovementioned research and I/we guarantee to ensure compliance with these conditions. Should any departure to be contemplated from the research procedure as approved I/we undertake to resubmit the protocol to the Committee. **I agree to a completion of a yearly progress report.**
PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES...

R14/49 Ms Cato Annalie Henning nee Basson

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M16111160

NAME: (Principal Investigator)	Ms Cato Annalie Henning nee Basson
DEPARTMENT:	Physiotherapy Four Private Practices in the Pretoria and Johannesburg Area
PROJECT TITLE:	The Effect of Neural Mobilisation on Cervico-brachial Pain
DATE CONSIDERED:	Adhoc
DECISION:	Approved unconditionally
CONDITIONS:	Renewal for 5 Years Valid for the Period 01 December 2016 - 31 December 2021 Previously M111002
SUPERVISOR:	
APPROVED BY:	Professor P Cleaton-Jones, Chairperson, HREC (Medical)
DATE OF APPROVAL:	20/01/2017

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary in Room 301, Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in November and will therefore be due in the month of November each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature

Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

Appendix 6.1

Demographics NPRS	Mixed Effect = p	95% Conf Interval		Fixed effect = p	95% Conf Interval	
Age	0.9007	-.0153609	.0174488	0.9331	-.0191382	.0208461
Gender	0.4215	-.7504157	.3139368	0.5105	-.8626698	.429669
Duration of pain (days)	0.2373	-.0040245	.0135823	0.3625	-.0057502	.0156966
Had neck pain before	0.4000	-.3385814	.8478083	0.4843	-.4623806	.9736396
Accident/injury	0.3855	-.279396	.7228287	0.4662	-.3795446	.8270399
Gradual onset	0.4715	-.6708521	.3105682	0.5489	-.7719431	.4110825
Education	0.7143	-.4503818	.6573109	0.7565	-.5691604	.7824948
Hours sitting/day	0.1450			0.5080		
Exercise	0.3463	-.7060903	.24789	0.4557	-.798625	.3590481
Area of pain	0.1105			0.3269		
Dizziness	0.0504	-.0009765	1.065003	0.0985	-.1025388	1.197857
Headache	0.0249*	.0681796	1.01083	0.0629	-.0292057	1.109123
Pins and Needles	0.0020*	.2594739	1.157325	**0.0116***	.1593464	1.256762

Neuropathic pain and NPRS

Group	N	mean	Std Dev	95% Conf Interval	
Baseline					
Intervention	32	7.0875	1.6358	6.4977	7.6772
Usual Care	13	7.1154	0.8193	6.6202	7.6105
p = 0.9538					
6 months					
Intervention	9	2.9111	1.5235	1.7400	4.0821
Usual Care	4	5.5	1.2909	3.4457	7.5542
p = **0.0134**					
12 months					
Intervention	7	2.9285	2.2440	0.8531	5.0039
Usual Care	4	3.75	2.3629	-0.0099	7.5099
P = 0.5802					

Table 7. Neuropathic pain and PSFS

Group	N	mean	Std Dev	95% Conf Interval	
Baseline					
Intervention	32	14.5	6.4257	12.1832	16.8167

Usual Care	13	13.9230	6.3569	10.0816	17.7645
P = 0.7856					
6 months					
Intervention	9	24.1111	3.6552	21.3014	26.9208
Usual Care	4	23.25	5.7373	14.1206	32.3793
P = 0.7466					
12 months					
Intervention	7	23.8571	4.8107	19.4079	28.3063
Usual Care	4	24	4.2426	17.2490	30.7509
P = 0.9618					

Neuropathic pain and health state

Group	**N**	**mean**	**Std Dev**	**95% Conf Interval**	
Baseline					
Intervention	32	71	20.6100	63.5692	78.4307
Usual Care	13	68.9230	15.50517	59.5534	78.2927
P = 0.7454					
6 months					
Intervention	9	83.1111	14.2341	72.1697	94.0524
Usual Care	4	79.5	15.4164	54.969	104.031

P = 0.6879

12 months

Intervention	7	77.5714	12.8174	65.7173	89.4255
Usual Care	4	83.75	11.08678	66.1084	101.3915

P = 0.4424

Patients with no pain at 6 weeks between groups

Results						
	Category 1	Category 2				***Row Totals***
Group 1 UC	2 (4.53) [1.42]	24 (21.47) [0.30]				26
Group 2 IG	13 (10.47) (Doth et al.)	47 (49.53) (Bossuyt et al.)				60
Column Totals	15	71				**86 (Grand Total)**

The chi-square statistic is 2.46. The *p*-value is .116778. The result is *not* significant at $p < .05$.

Patients with no pain at 6 months between groups

	Category 1	Category 2				***Row Totals***
Group 1 UC	7 (9.07) [0.47]	19 (16.93) [0.25]				26
Group 2 IG	23 (20.93) [0.20]	37 (39.07) [0.11]				60
Column Totals	30	56				**86 (Grand Total)**

The chi-square statistic is 1.0397. The *p*-value is .307893. The result is *not* significant at $p < .05$.

Patients with no pain at 12 months between groups

	Category 1	Category 2				***Row Totals***
Group 1 UC	10 (12.09) [0.36]	16 (13.91) [0.32]				26
Group 2 IG	30 (27.91) [0.16]	30 (32.09) [0.14]				60
Column Totals	40	46				**86 (Grand Total)**

The chi-square statistic is 0.9707. The *p*-value is .324497. The result is *not* significant at $p < .05$.

Demographics DN4

Demographics	**DN4**	**Mixed Effect = p**	**95% Conf. Interval**		**Fixed effect = p**	**95% Conf. Interval**	
Gender	0.2005		-.9450815	.202576	0.2199	-.9683493	.2276116
Age							
Had pain before	0.3027		-.2819883	.8979934	0.3240	-.3098382	.9269332
Duration of pain	0.6109		-.0071231	.0120145	0.6104	-.0074142	.0125112
Accident / injury	1.0000		-.4825505	.4825275	0.9968	-.5058978	.5079756
Gradual onset	0.9546		-.4734617	.5014993	0.9570	-.4968905	.5246238
Education	0.4994		-.354606	.7243536	0.5170	-.3819343	.7551827
Hours sitting per day		0.4148					
2		0.266	-2.718309	.7532119			
3		0.935	-1.206745	1.311967			
4		0.427	-1.874362	.7952548			
5		0.397	-.8372212	2.096713			

6	0.351	-1.95241	.698947		
7	0.751	-1.612858	1.166986		
8	0.565	-1.60407	.8791441		
9	0.835	-1.933369	1.565596		
10	0.585	-.9815596	1.732		
11	0.829	-1.381388	1.718733		
12	0.777	-1.575004	2.096156		
16	0.670	-2.857188	1.843833		
Exercise	0.5499	-.6093008	.3262543	0.5798	-.6252658 .3517578
Headache	0.0684	-.0308445	.8386445	0.0838	-.0546712 .8629553
Dizziness	0.0650	-.0357109	1.144102	0.0720	-.0523239 1.181063
Paraesthesia	**0.0001**	.6690612	1.651187	**0.0001**	.6475926 1.672298
Area	0.1749				
2	0.028	.094278	1.65092		
3	0.520	-.4622191	.9097483		
4	0.699	-1.244469	.8383358		
5	0.756	-.9204903	.670617		
6	0.183	-.3331343	1.723449		
7	0.164	-.2050672	1.187303		

Demographics PCS

Demographics	**PCS**	**Mixed Effect = p**	**95% Conf. Interval**		**Fixed effect = p**	**95% Conf. Interval**	
Gender	0.7401		-3.340092	2.380107	0.7465	-3.496789	2.514983
Age	0.3212		-.0425546	.1290025	0.3340	-.0462948	.1352423
Duration of pain		**0.0319**	.0052353	.1110784	0.0435	.0017341	.1130548
Had pain before		0.8058	-2.47826	3.187703	0.8197	-2.660718	3.357858
Accident / injury		0.4997	-4.002524	1.97935	0.5107	-4.134126	2.086218
Gradual onset		0.6601	-2.385884	3.726237	0.6705	-2.498583	3.842464
Education		0.6244	-3.974884	2.401497	0.6305	-4.136277	2.523526
Hours sitting per day		0.9560					
2		0.898	-10.47692	9.192835			
3		0.747	-5.969375	8.309006			
4		0.832	-8.332626	6.7162			
5		0.676	-6.424773	9.87189			
6		0.946	-7.386854	6.894682			
7		0.796	-6.499044	8.448644			
8		0.898	-6.194899	7.054556			
9		0.913	-9.036602	8.085306			
10		0.401	-4.085475	10.15823			
11		0.635	-6.577116	10.71067			
12		0.409	-13.37063	5.493782			

16	0.878	-13.25761 11.34195		
Exercise	0.2278	-3.84352 .9204699	0.2333	-4.07819 1.001843
Headache	0.1118	-.4904247 4.625459	0.1293	-.6168581 4.74647
Dizziness	0.2133	-.988009 4.402726	0.2610	-1.235717 4.524488
Paraesthesia	0.0089	.8591798 5.835271	0.0126	.737457 5.96132
Area	0.0602			
2	0.001	2.299533 9.662523		
3	0.114	-.8316131 7.528752		
4	0.572	-6.163534 3.40927		
5	0.610	-3.11505 5.286796		
6	0.903	-5.309298 4.689384		
7	0.168	-1.106892 6.23223		

Demographics and PSFS

Demographics	**Fixed effect = p**	**95% Conf. Interval**
Had pain before	0.8412	-2.16 - 1.76
Accident	0.0167*	-3.59 - 0.36
Gradual onset	0.0292*	0.18 - 3.36
Education	0.3650	-2.29 - 0.84
Hours sitting per day	0.2268	

2	0.835	-6.02 - 4.86
3	0.632	-5.02 - 3.05
4	0.556	-5.58 - 3.01
5	0.509	-5.90 - 2.93
6	0.399	-2.37 - 5.93
7	0.344	-5.95 - 2.08
8	0.813	-3.45 - 4.39
9	0.458	-3.12 - 6.93
10	0.721	-3.40 - 4.91
11	0.916	-4.67 - 4.19
12	0.975	-4.98 - 4.83
16	0.237	-2.70 - 10.94
Exercise	0.9711	-1.60 - 1.54
Headache	0.5788	-1.99 - 1.11
Dizziness	0.7029	-1.44 - 2.13
Paraesthesia	0.0010*	-3.58 - 0.92
Area of pain	0.1098	
2	0.073	-4.29 - 0.19
3	0.665	-2.43 - 1.55
4	0.042	0.11 - 5.91
5	0.494	-1.49 - 3.08

6	0.675	-2.23 - 3.44
7	0.959	-2.07 - 1.96

Demographics and Health State

Demographics	**Fixed effect = p**	**95% Conf. Interval**
Gender	0.936	-3.03 - 3.29
Age	0.058	-0.19 - 0.003
Duration of episode	0.225	-.084 - 0.02
Had pain before	0.249	-1.44 - 5.54
Accident/ injury	0.792	-2.52 - 3.30
Gradual onset	0.654	-2.11 - 3.36
Education	0.621	-4.15 - 2.48
Hours sitting per day	0.0196*	
2	0.019	-24.95 - 2.28
3	0.986	-8.47 - 8.32
4	0.207	-14.35 - 3.12
5	0.068	-17.64 - 0.64
6	0.928	-8.10 - 8.88
7	0.176	-14.04 - 2.58
8	0.081	-14.75 - 0.85

9	0.432	-14.65 - 6.28
10	0.082	-15.95 - 0.96
11	0.340	-13.60 - 4.71
12	0.858	-11.11 - 9.25
16	0.811	-16.02 - 12.54
Exercise	0.510	-1.86 - 3.75
Headache	0.033*	-5.76 - 0.24
Dizziness	0.000*	-9.33 - -3.11
Paraesthesia	0.000*	-9.39 - -4.08
Area of pain p=0.0000		
2	0.000	-15.53 - -6.86
3	0.004	-9.74 - -1.85
4	0.514	-7.37 - 3.69
5	0.005	-10.94 - -1.94
6	0.000	-15.65 - -4.59
7	0.010	-8.70 - -1.20

Occupation desk job	**Category 1**	**Category 2**	***Marginal Row Totals***
Usual Care	17 (16.02) [0.06]	9 (9.98) [0.1]	26
Intervention Group	36 (36.98) [0.03]	24 (23.02) [0.04]	60

Marginal Column Totals	53	33	86 (Grand Total)

Chi^2 = 0.2224 p = 0.637214

Occupation House wife

	Category 1	**Category 2**	***Marginal Row Totals***
UC Group 1	1 (2.42) [0.83]	25 (23.58) [0.09]	26
IG Group 2	7 (5.58) [0.36]	53 (54.42) [0.04]	60
Marginal Column Totals	8	78	86 (Grand Total)

Chi^2 = 1.3149. The *p*-value is .251501

Occupation Allied Health

	Category 1	**Category 2**	***Marginal Row Totals***
UC Group 1	4 (2.42) [1.03]	22 (23.58) [0.11]	26
IG Group 2	4 (5.58) [0.45]	56 (54.42) [0.05]	60
Marginal Column Totals	8	78	86 (Grand Total)

Chi^2 = 1.6341. The *p*-value is .201143

Occupation Miscellaneous	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	4 (5.14) [0.25]	22 (20.86) [0.06]	26
IG Group 2	13 (11.86) [0.11]	47 (48.14) [0.03]	60
Marginal Column Totals	17	69	86 (Grand Total)

Chi^2 = 0.4514. The *p*-value is .501687

Upper limb neurodynamic test elbow range of movement Usual Care

	UC LEFT B	UC RIGHT B	UC L 6M	UC R 6M	UC L 12M	UC R 12M
	145	70	140	83	173	80
	80	75	70	72	70	80
	100	80	140	148	110	80
	80	80	90	156	120	90
	130	110	110	90	153	180
	120	152	125	160	80	91
	92	68	170	135	145	180
	65	88	145	110	91	143
	80	115	90	160	110	
	30	155	70		182	
	153	135	173		153	
	180	80	125			
		80				
Mean	96	80	125	135	120	90,5
SD	46,63421491	31,43073192	35,96526102	29,46466811	34,85377618	44,89352483

Upper limb neurodynamic test elbow range of movement Intervention group

IG L EFT B	IG RIGHT B	IG L 6M	IG R 6M	IG L 12M	IG R 12M
152	90	160	90	120	156
120	85	120	90	120	100
80	128	165	85	153	140
110	70	150	160	143	153
85	80	100	150	187	150
110	137	160	170	142	120
155	128	110	135	145	170
145	105	135	90	172	130
80	110	142	90	96	123
135	90	120	160	130	165
137	60	137	136	145	180
80	90	125	140	120	172
143	160	140	90	150	180
60	128	130	136	180	158
123	98	90	135	155	135
130	131	90	140	172	132
80	80	150	141	120	160
90	85	180	130	172	135
155	134	155	140	165	150
128	123	140	110	170	90

60	90	152	180	90	
138	80	90	100	128	
60	130	103	120	112	
145	115	165	155	170	
70	125	170	143		
118	95	87			
90	145	134			
137	90	102			
80	110	100			
126	55	102			
100	90	170			
100	90	90			
80					
135					
85					
128					
Mean 110	98	134	136	145	150
SD 29,81032209	26,20781856	28,6289753	28,14823855	26,81252006	24,72049012

ULNDT Left	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	13 (12.7) [0.01]	13 (13.3) [0.01]	26
IG Group 2	29 (29.3) [0]	31 (30.7) [0]	60
Marginal Column Totals	42	44	86 (Grand Total)

Chi^2 0.0202. The *p*-value is .887075.

ULNDT Right	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	12 (10.58) [0.19]	14 (15.42) [0.13]	26
IG Group 2	23 (24.42) [0.08]	37 (35.58) [0.06]	60
Marginal Column Totals	35	51	86 (Grand Total)

Chi^2 =0.4597. The *p*-value is .497774.

ULNDT Bilateral	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	1 (2.72) [1.09]	25 (23.28) [0.13]	26
IG Group 2	8 (6.28) [0.47]	52 (53.72) [0.06]	60
Marginal Column Totals	9	77	86 (Grand Total)

Chi^2 = 1.7425. The *p*-value is .186827

Neurological no changes	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	7 (6.05) [0.15]	19 (19.95) [0.05]	26

IG Group 2	13 (13.95) [0.07]	47 (46.05) [0.02]	60
Marginal Column Totals	20	66	86 (Grand Total)

Chi^2 = 0.2808. The *p*-value is .596164.

Neurological Myotome	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	11 (11.79) [0.05]	15 (14.21) [0.04]	26
IG Group 2	28 (27.21) [0.02]	32 (32.79) [0.02]	60
Marginal Column Totals	39	47	86 (Grand Total)

Chi^2 = 0.1391. The *p*-value is .709209.

Neurological sensation	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	16 (16.33) [0.01]	10 (9.67) [0.01]	26
IG Group 2	38 (37.67) [0]	22 (22.33) [0]	60
Marginal Column Totals	54	32	86 (Grand Total)

Chi^2 = 0.025. The *p*-value is .874337

Neurological reflexes	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	8 (7.86)	18 (18.14) [0]	26
IG Group 2	18 (18.14) [0]	42 (41.86) [0]	60
Marginal Column Totals	26	60	86 (Grand Total)

Chi^2= 0.0051. The *p*-value is .943131

Neurological 2 changed	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	9 (9.37) [0.01]	17 (16.63) [0.01]	26
IG Group 2	22 (21.63) [0.01]	38 (38.37) [0]	60
Marginal Column Totals	31	55	86 (Grand Total)

Chi^2 = 0.0331. The *p*-value is .855615

Neurological 3 changed	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	4 (3.63) [0.04]	22 (22.37) [0.01]	26
IG Group 2	8 (8.37) [0.02]	52 (51.63) [0]	60
Marginal Column Totals	12	74	86 (Grand Total)

Chi^2 = 0.0636. The *p*-value is .800938

Pain free at 12 months	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	10 (12.09) [0.36]	16 (13.91) [0.32]	26
IG Group 2	30 (27.91) [0.16]	30 (32.09) [0.14]	60
Marginal Column Totals	40	46	86 (Grand Total)

Chi^2 = 0.9707. The *p*-value is .324497

Global rating of change measured at 6 weeks – between groups

ranksum groc,by(group)

Two-sample Wilcoxon rank-sum (Mann-Whitney) test

group	obs	rank sum	expected
Intervention	59	2633	2537
Protocol	26	1022	1118
combined	85	3655	3655

unadjusted variance 10993.67

adjustment for ties -188.53

---

adjusted variance 10805.14

Ho: groc2(group==Intervention) = groc2(group==Protocol)

z = 0.924

Prob > |z| = 0.3557

Number of treatments –between groups

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
Interven	60	3.916667	.2295804	1.778322	3.457277	4.376056
Protocol	26	4.692308	.4599974	2.345536	3.744925	5.63969

```
combined |      86    4.151163    .214085    1.985343    3.725504    4.576821
---------+--------------------------------------------------------------------
    diff |           -.775641    .4612129               -1.692813    .1415313
------------------------------------------------------------------------------
    diff = mean(Interven) - mean(Protocol)                        t =  -1.6817
Ho: diff = 0                                     degrees of freedom =       84
    Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0
 Pr(T < t) = 0.0482         Pr(|T| > |t|) = 0.0963          Pr(T > t) = 0.9518
```

Number of treatments per group

```
Two-sample Wilcoxon rank-sum (Mann-Whitney) test
       group     |      obs    rank sum    expected
-------------    +---------------------------------
Intervention  |       60      2501.5        2610
    Protocol    |       26      1239.5        1131
-------------+---------------------------------
    combined |       86        3741        3741
unadjusted variance    11310.00
adjustment for ties     -370.90
                     ----------
adjusted variance      10939.10
Ho: norx(group==Intervention) = norx(group==Protocol)
            z =  -1.037
    Prob > |z| =   0.2996
```

Number of DN4 + at Baseline	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	13 (13.6) [0.03]	13 (12.4) [0.03]	26
IG Group 2	32 (31.4) [0.01]	28 (28.6) [0.01]	60
Marginal Column Totals	45	41	86 (Grand Total)

Chi^2 = 0.0808. The *p*-value is .776223

Number of +DN4 at 6 months	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	4 (3.93) [0]	22 (22.07) [0]	26
UC Group 2	9 (9.07) [0]	51 (50.93) [0]	60
Marginal Column Totals	13	73	86 (Grand Total)

Chi^2 = 0.0021. The *p*-value is .963525

Number of DN4+ at 12 months	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	4 (3.33) [0.14]	22 (22.67) [0.02]	26
IG Group 2	7 (7.67) [0.06]	53 (52.33) [0.01]	60
Marginal Column Totals	11	75	86 (Grand Total)

Chi^2 = 0.2248. The *p*-value is .635415

PCS+ at Baseline	**Category 1**	**Category 2**	***Marginal Row Totals***

UC Group 1	5 (6.95) [0.55]	21 (19.05) [0.2]	26
IG Group 2	18 (16.05) [0.24]	42 (43.95) [0.09]	60
Marginal Column Totals	23	63	86 (Grand Total)

cHI^2 = 1.0738. The *p*-value is .300088

PCS + at 6 months	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	1 (1.51) [0.17]	25 (24.49) [0.01]	26
IG Group 2	4 (3.49) [0.08]	56 (56.51) [0]	60
Marginal Column Totals	5	81	86 (Grand Total)

Chi^2 = 0.2635. The *p*-value is .607708.

PCS + at 12 months	**Category 1**	**Category 2**	***Marginal Row Totals***
UC Group 1	2 (2.12) [0.01]	24 (23.88) [0]	26
IG Group 2	5 (4.88) [0]	55 (55.12) [0]	60
Marginal Column Totals	7	79	86 (Grand Total)

Chi^2 = 0.01. The *p*-value is .920468

NPRS Baseline

Group | Obs Mean Std. Err. Std. Dev. [95% Conf. Interval]

---------+---

Interven | 60 6.87 .2118029 1.640618 6.446183 7.293817

Protocol | 26 7.019231 .2138309 1.090328 6.578838 7.459624

---------+---

combined | 86 6.915116 .1607652 1.490876 6.595472 7.234761

---------+---

diff | -.1492308 .3517494 -.848723 .5502615

---

diff = mean(Interven) - mean(Protocol) t = -0.4243

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.3362 Pr(|T| > |t|) = 0.6725 Pr(T > t) = 0.6638

NPRS 3 weeks

Two-sample t test with equal variances

Group | Obs Mean Std. Err. Std. Dev. [95% Conf. Interval]

---------+---

Interven | 60 3.37948 .2688833 2.082761 2.841446 3.917514

Protocol | 26 3.741842 .521669 2.660001 2.667444 4.816239

---------+---

combined | 86 3.489031 .2439998 2.262761 3.003894 3.974168

---------+---

diff | -.3623615 .5329713 -1.422233 .6975105

---

diff = mean(Interven) - mean(Protocol) t = -0.6799

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.2492 Pr(|T| > |t|) = 0.4984 Pr(T > t) = 0.7508

NPRS 6 weeks

Two-sample t test with equal variances

Group | Obs Mean Std. Err. Std. Dev. [95% Conf. Interval]

---------+---

Interven | 60 2.950316 .3309773 2.56374 2.288032 3.6126

Protocol | 26 3.523077 .4920071 2.508754 2.509769 4.536385

---------+---

combined | 86 3.123476 .2745696 2.546254 2.577558 3.669394

---------+--

diff | -.5727612 .5981373 -1.762223 .6167005

---

diff = mean(Interven) - mean(Protocol) t = -0.9576

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.1705 Pr(|T| > |t|) = 0.3410 Pr(T > t) = 0.8295

NPRS 6 months

Two-sample t test with equal variances

Group | Obs Mean Std. Err. Std. Dev. [95% Conf. Interval]

---------+--

Interven | 60 1.540377 .2626107 2.034174 1.014894 2.06586

Protocol | 26 2.647692 .4584332 2.33756 1.703531 3.591853

---------+--

combined | 86 1.875147 .234792 2.177371 1.408317 2.341976

---------+--

diff | -1.107315 .4998742 -2.10137 -.1132607

---

diff = mean(Interven) - mean(Protocol) t = -2.2152

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.0147 Pr(|T| > |t|) = 0.0295 Pr(T > t) = 0.9853

NPRS 12 months

Two-sample t test with equal variances

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
Interven	60	1.33954	.2653804	2.055628	.8085146	1.870565
Protocol	26	2.370043	.5072743	2.586602	1.325292	3.414794
combined	86	1.651087	.2441761	2.264396	1.1656	2.136575
diff		-1.030503	.5228692		-2.070286	.0092793

diff = mean(Interven) - mean(Protocol) t = -1.9709

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.0260 Pr(|T| > |t|) = 0.0520 Pr(T > t) = 0.9740

PSFS Baseline

Two-sample t test with equal variances

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf. Interval]
Interven	60	13.58333	.8424781	6.525807	11.89754 15.26913
Protocol	26	14.26923	1.22858	6.264552	11.73892 16.79954
combined	86	13.7907	.6921716	6.418936	12.41448 15.16692
diff		-.6858974	1.514224		-3.697097 2.325302

---

diff = mean(Interven) - mean(Protocol) t = -0.4530

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.3259 Pr(|T| > |t|) = 0.6517 Pr(T > t) = 0.6741

PSFS 3 weeks

Two-sample t test with equal variances

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
Interven	60	20.92939	.8771085	6.794053	19.1743	22.68448
Protocol	26	20.75341	1.426372	7.273097	17.81574	23.69107
combined	86	20.87619	.7440048	6.899617	19.3969	22.35547
diff		.1759826	1.62949		-3.064436	3.416401

---

diff = mean(Interven) - mean(Protocol) t = 0.1080

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.5429 Pr(|T| > |t|) = 0.9143 Pr(T > t) = 0.4571

PSFS 6 weeks

Two-sample t test with equal variances

```
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
Interven |      60    22.75731    .9608929    7.443044    20.83457    24.68005
Protocol |      26    22.32593    1.385342    7.063888    19.47276     25.1791
---------+--------------------------------------------------------------------
combined |      86    22.62689    .7862858    7.291715    21.06355    24.19024
---------+--------------------------------------------------------------------
    diff |            .431378    1.721568               -2.992149    3.854905
------------------------------------------------------------------------------
    diff = mean(Interven) - mean(Protocol)                        t =   0.2506
Ho: diff = 0                                     degrees of freedom =       84
Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0

 Pr(T < t) = 0.5986         Pr(|T| > |t|) = 0.8028          Pr(T > t) = 0.4014
```

PSFS 6 months

```
Two-sample t test with equal variances
------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
Interven |      60    25.55664    .6944617    5.379278    24.16703    26.94626
```

Protocol | 26 25.2716 .9985225 5.091486 23.21511 27.3281

---------+---

combined | 86 25.47047 .5678114 5.265666 24.3415 26.59943

---------+---

diff | .2850388 1.243295 -2.18739 2.757468

---

diff = mean(Interven) - mean(Protocol) t = 0.2293

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.5904 Pr(|T| > |t|) = 0.8192 Pr(T > t) = 0.4096

PSFS 12 months

Two-sample t test with equal variances

Group | Obs Mean Std. Err. Std. Dev. [95% Conf. Interval]

---------+---

Interven | 60 26.38526 .7309055 5.661569 24.92272 27.84779

Protocol | 26 26.72498 .8927453 4.552126 24.88634 28.56362

---------+---

combined | 86 26.48796 .5743358 5.326171 25.34603 27.6299

---------+--

diff | -.3397254 1.257428 -2.84026 2.160809

---

diff = mean(Interven) - mean(Protocol) t = -0.2702

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.3938 Pr(|T| > |t|) = 0.7877 Pr(T > t) = 0.6062

EQ5D Health state Baseline

Two-sample t test with equal variances

Group | Obs Mean Std. Err. Std. Dev. [95% Conf. Interval]

---------+--

Interven | 60 72.43333 2.534883 19.63512 67.36104 77.50562

Protocol | 26 72.38462 3.131024 15.96515 65.93615 78.83308

---------+--

combined | 86 72.4186 1.995855 18.5088 68.45031 76.3869

---------+--

diff | .0487179 4.371542 -8.644573 8.742009

---

diff = mean(Interven) - mean(Protocol) t = 0.0111

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.5044 Pr(|T| > |t|) = 0.9911 Pr(T > t) = 0.4956

EQ5D Health state 3 weeks

Two-sample t test with equal variances

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
Interven	60	80.66938	1.427559	11.05782	77.81285	83.52592
Protocol	26	79.17925	2.950915	15.04677	73.10173	85.25678
combined	86	80.21888	1.329177	12.32628	77.57612	82.86164
diff		1.490129	2.906769		-4.2903	7.270558

diff = mean(Interven) - mean(Protocol) t = 0.5126

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.6952 Pr(|T| > |t|) = 0.6095 Pr(T > t) = 0.3048

EQ5D Health state 6 weeks

Two-sample t test with equal variances

Group	Obs	Mean	Std. Err.	Std. Dev.	[95% Conf.	Interval]
Interven	60	84.05784	1.427413	11.0567	81.20159	86.91408
Protocol	26	82.96154	2.324108	11.85067	78.17495	87.74813
combined	86	83.7264	1.212427	11.24358	81.31577	86.13703
diff		1.096297	2.652898		-4.179281	6.371874

---

diff = mean(Interven) - mean(Protocol) t = 0.4132

Ho: diff = 0 degrees of freedom = 84

Ha: diff < 0 Ha: diff != 0 Ha: diff > 0

Pr(T < t) = 0.6598 Pr(|T| > |t|) = 0.6805 Pr(T > t) = 0.3402

EQ5D Health state 6 months

Two-sample t test with equal variances

```
------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
Interven |      60    85.28644    1.415494    10.96437    82.45404    88.11883
Protocol |      26    83.72292    2.091442     10.6643    79.41551    88.03032
---------+--------------------------------------------------------------------
combined |      86    84.81375    1.168461    10.83586    82.49053    87.13696
---------+--------------------------------------------------------------------
    diff |            1.563518    2.553602               -3.5146    6.641636
------------------------------------------------------------------------------
    diff = mean(Interven) - mean(Protocol)                        t =   0.6123
Ho: diff = 0                     degrees of freedom =       84

Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0

 Pr(T < t) = 0.7290         Pr(|T| > |t|) = 0.5420          Pr(T > t) = 0.2710
```

EQ5D Health State 12 months

Two-sample t test with equal variances

```
------------------------------------------------------------------------------
```

```
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Interval]
---------+--------------------------------------------------------------------
Interven |      60    86.14834    1.444462    11.18876    83.25798     89.0387
Protocol |      26    83.19382    2.621993     13.3696    77.79372    88.59391
---------+--------------------------------------------------------------------
combined |      86    85.25511    1.281944    11.88826    82.70626    87.80396
---------+--------------------------------------------------------------------
    diff |           2.954525     2.78929               -2.592284    8.501335
------------------------------------------------------------------------------
    diff = mean(Interven) - mean(Protocol)                        t =   1.0592
Ho: diff = 0                     degrees of freedom =       84

Ha: diff < 0                 Ha: diff != 0                 Ha: diff > 0

 Pr(T < t) = 0.8537         Pr(|T| > |t|) = 0.2925          Pr(T > t) = 0.1463
```

Domains of the EQ5D (Chi-square test)

Mobility Baseline

	Category 1	Category 2	***Row Totals***
Group 1 UC	3 (3.63) [0.11]	23 (22.37) [0.02]	26
Group 2 IG	9 (8.37) [0.05]	51 (51.63) [0.01]	60
Column Totals	12	74	**86 (Grand Total)**

The chi-square statistic is 0.181. The *p*-value is .67049. The result is *not* significant at $p < .05$.

Mobility 3 weeks

	Category 1	Category 2	***Row Totals***
Group 1 UC	1 (2.12) [0.59]	25 (23.88) [0.05]	26
Group 2 IG	6 (4.88) [0.26]	54 (55.12) [0.02]	60
Column Totals	7	79	**86 (Grand Total)**

The chi-square statistic is 0.9187. The *p*-value is .337807. The result is *not* significant at $p < .05$.

Mobility 6 weeks

	Category 1	Category 2	***Row Totals***
Group 1 UC	1 (1.81) [0.37]	25 (24.19) [0.03]	26
Group 2 IG	5 (4.19) [0.16]	55 (55.81) [0.01]	60
Column Totals	6	80	**86 (Grand Total)**

The chi-square statistic is 0.5628. The *p*-value is .453147. The result is *not* significant at $p < .05$.

Mobility 6 months

	Category 1	Category 2	***Row Totals***
Group 1 UC	4 (3.29) [0.16]	19 (19.71) [0.03]	23
Group 2 IG	7 (7.71) [0.07]	47 (46.29) [0.01]	54
Column Totals	11	66	**77 (Grand Total)**

The chi-square statistic is 0.2583. The *p*-value is .611277. The result is *not* significant at $p < .05$.

Mobility 12 months

	Category 1	Category 2	***Row Totals***
Group 1 UC	2 (3.34) [0.54]	22 (20.66) [0.09]	24
Group 2 IG	9 (7.66) [0.24]	46 (47.34) [0.04]	55
Column Totals	11	68	**79 (Grand Total)**

The chi-square statistic is 0.899. The *p*-value is .343048. The result is *not* significant at $p < .05$.

Self care baseline

	Category 1	Category 2	***Row Totals***
Group 1 UC	7 (6.35) [0.07]	19 (19.65) [0.02]	26
Group 2 IG	14 (14.65) [0.03]	46 (45.35) [0.01]	60
Column Totals	21	65	**86 (Grand Total)**

The chi-square statistic is 0.1267. The *p*-value is .721927. The result is *not* significant at $p < .05$.

Self care 3 weeks

	Category 1	Category 2	***Row Totals***
Group 1 UC	4 (4.34) [0.03]	20 (19.66) [0.01]	24
Group 2 IG	11 (10.66) [0.01]	48 (48.34) [0.00]	59
Column Totals	15	68	**83 (Grand Total)**

The chi-square statistic is 0.0451. The *p*-value is .831905. The result is *not* significant at $p < .05$.

Self care 6 weeks

	Category 1	Category 2	***Row Totals***

Group 1 UC	4 (4.27) [0.02]	21 (20.73) [0.00]	25
Group 2 IG	10 (9.73) [0.01]	47 (47.27) [0.00]	57
Column Totals	14	68	**82 (Grand Total)**

The chi-square statistic is 0.0293. The *p*-value is .86419. The result is *not* significant at $p < .05$.

Self care 6 months

	Category 1	Category 2	***Row Totals***
Group 1 UC	2 (1.76) [0.03]	20 (20.24) [0.00]	22
Group 2 IG	4 (4.24) [0.01]	49 (48.76) [0.00]	53
Column Totals	6	69	**75 (Grand Total)**

The chi-square statistic is 0.0503. The *p*-value is .822474. The result is *not* significant at $p < .05$.

Self Care 12 months

Category 1	Category 2		***Row Totals***
Group 1 UC	1 (0.94) [0.00]	23 (23.06) [0.00]	24
Group 2 IG	2 (2.06) [0.00]	51 (50.94) [0.00]	53
Column Totals	3	74	**77 (Grand Total)**

The chi-square statistic is 0.0068. The *p*-value is .934198. The result is *not* significant at $p < .05$.

Usual activities baseline

	Category 1	Category 2	***Row Totals***
Group 1 UC	14 (15.12) [0.08]	12 (10.88) [0.11]	26

Group 2 IG	36 (34.88) [0.04]	24 (25.12) [0.05]	60
Column Totals	50	36	**86 (Grand Total)**

The chi-square statistic is 0.2823. The *p*-value is .595226. The result is *not* significant at $p < .05$.

Usual activities 3 weeks

	Category 1	Category 2	***Row Totals***
Group 1 UC	13 (11.45) [0.21]	12 (13.55) [0.18]	25
Group 2 IG	25 (26.55) [0.09]	33 (31.45) [0.08]	58
Column Totals	38	45	**83 (Grand Total)**

The chi-square statistic is 0.557. The *p*-value is .455452. The result is *not* significant at $p < .05$.

Usual activities 6 weeks

Category 1	Category 2		***Row Totals***
Group 1 UC	10 (7.07) [1.22]	15 (17.93) [0.48]	25
Group 2 IG	16 (18.93) [0.45]	51 (48.07) [0.18]	67
Column Totals	26	66	**92 (Grand Total)**

The chi-square statistic is 2.3334. The *p*-value is .126628. The result is *not* significant at $p < .05$.

Usual activities 6 months

	Category 1	Category 2	***Row Totals***
Group 1 UC	8 (6.84) [0.20]	14 (15.16) [0.09]	22
Group 2 IG	15 (16.16) [0.08]	37 (35.84) [0.04]	52
Column Totals	23	51	**74 (Grand Total)**

The chi-square statistic is 0.4079. The *p*-value is .523061. The result is *not* significant at $p < .05$.

Usual activities 12 months

	Category 1	Category 2	***Row Totals***
Group 1 UC	5 (3.43) [0.72]	19 (20.57) [0.12]	24
Group 2 IG	6 (7.57) [0.33]	47 (45.43) [0.05]	53
Column Totals	11	66	**77 (Grand Total)**

The chi-square statistic is 1.2208. The *p*-value is .269207. The result is *not* significant at $p < .05$.

Pain Baseline

Moderate

	Category 1	Category 2	***Row Totals***
Group 1 UC	20 (18.14) [0.19]	6 (7.86) [0.44]	26
Group 2 IG	40 (41.86) [0.08]	20 (18.14) [0.19]	60
Column Totals	60	26	**86 (Grand Total)**

The chi-square statistic is 0.9047. The *p*-value is .341533. The result is *not* significant at $p < .05$.

Extreme

	Category 1	Category 2	***Row Totals***
Group 1 UC	11 (7.86) [1.25]	15 (18.14) [0.54]	26
Group 2 IG	15 (18.14) [0.54]	45 (41.86) [0.24]	60
Column Totals	26	60	**86 (Grand Total)**

The chi-square statistic is 2.5762. The *p*-value is .108483. The result is *not* significant at $p < .05$.

Pain 3 weeks

Moderate

	Category 1	Category 2	***Row Totals***
Group 1 UC	18 (18.37) [0.01]	7 (6.63) [0.02]	25
Group 2 IG	43 (42.63) [0.00]	15 (15.37) [0.01]	58
Column Totals	61	22	**83 (Grand Total)**

The chi-square statistic is 0.041. The *p*-value is .839557. The result is *not* significant at $p < .05$.

Extreme

	Category 1	Category 2	***Row Totals***
Group 1 UC	3 (2.11) [0.38]	22 (22.89) [0.03]	25
Group 2 IG	4 (4.89) [0.16]	54 (53.11) [0.01]	58
Column Totals	7	76	**83 (Grand Total)**

The chi-square statistic is 0.5892. The *p*-value is .442729. The result is *not* significant at $p < .05$.

Pain 6 weeks

Moderate

	Category 1	Category 2	***Row Totals***
Group 1 UC	11 (13.01) [0.31]	12 (9.99) [0.41]	23
Group 2 IG	32 (29.99) [0.14]	21 (23.01) [0.18]	53
Column Totals	43	33	**76 (Grand Total)**

The chi-square statistic is 1.0285. The *p*-value is .310508. The result is *not* significant at $p < .05$.

Extreme

Category 1	Category 2		***Row Totals***

Group 1 UC	1 (0.30) [1.61]	22 (22.70) [0.02]	23
Group 2 IG	0 (0.70) [0.70]	53 (52.30) [0.01]	53
Column Totals	1	75	**76 (Grand Total)**

The chi-square statistic is 2.3351. The *p*-value is .126489. The result is *not* significant at $p < .05$.

Pain 12 months

Moderate

Category 1	Category 2		***Row Totals***
Group 1 UC	11 (8.10) [1.03]	13 (15.90) [0.53]	24
Group 2 IG	15 (17.90) [0.47]	38 (35.10) [0.24]	53
Column Totals	26	51	**77 (Grand Total)**

The chi-square statistic is 2.2702. The *p*-value is .13188. The result is *not* significant at $p < .05$.

Extreme

	Category 1	Category 2	***Row Totals***
Group 1 UC	1 (0.62) [0.23]	23 (23.38) [0.01]	24
Group 2 IG	1 (1.38) [0.10]	52 (51.62) [0.00]	53
Column Totals	2	75	**77 (Grand Total)**

The chi-square statistic is 0.3394. The *p*-value is .560177. The result is *not* significant at $p < .05$.

Anxiety depression baseline

Moderate

	Category 1	Category 2	***Row Totals***

Group 1 UC	10 (9.98) [0.00]	16 (16.02) [0.00]	26
Group 2 IG	23 (23.02) [0.00]	37 (36.98) [0.00]	60
Column Totals	33	53	**86 (Grand Total)**

The chi-square statistic is 0.0001. The *p*-value is .991041. The result is *not* significant at $p < .05$.

Extreme

	Category 1	Category 2	***Row Totals***
Group 1 UC	1 (0.91) [0.01]	25 (25.09) [0.00]	26
Group 2 IG	2 (2.09) [0.00]	58 (57.91) [0.00]	60
Column Totals	3	83	**86 (Grand Total)**

The chi-square statistic is 0.0142. The *p*-value is .905247. The result is *not* significant at $p < .05$.

Anxiety depression 3 weeks

Category 1	Category 2		***Row Totals***
Group 1 UC	7 (7.32) [0.01]	18 (17.68) [0.01]	25
Group 2 IG	17 (16.68) [0.01]	40 (40.32) [0.00]	57
Column Totals	24	58	**82 (Grand Total)**

The chi-square statistic is 0.0279. The *p*-value is .867238. The result is *not* significant at $p < .05$.

Anxiety depression 6 weeks

	Category 1	Category 2	***Row Totals***
Group 1 UC	10 (7.92) [0.55]	12 (14.08) [0.31]	22
Group 2 IG	17 (19.08) [0.23]	36 (33.92) [0.13]	53
Column Totals	27	48	**75 (Grand Total)**

The chi-square statistic is 1.2078. The *p*-value is .271762. The result is *not* significant at $p < .05$.

Anxiety depression 6 months

Category 1	Category 2		***Row Totals***
Group 1 UC	7 (5.87) [0.22]	15 (16.13) [0.08]	22
Group 2 IG	13 (14.13) [0.09]	40 (38.87) [0.03]	53
Column Totals	20	55	**75 (Grand Total)**

The chi-square statistic is 0.4225. The *p*-value is .515701. The result is *not* significant at $p < .05$.

Anxiety and depression 12 months

	Category 1	Category 2	***Row Totals***
Group 1 UC	3 (3.84) [0.18]	21 (20.16) [0.03]	24
Group 2 IG	9 (8.16) [0.09]	42 (42.84) [0.02]	51
Column Totals	12	63	**75 (Grand Total)**

The chi-square statistic is 0.3217. The *p*-value is .570593. The result is *not* significant at $p < .05$.

GROC Two-sample Wilcoxon rank-sum (Mann-Whitney) test

Group	obs	rank sum	expected
Intervention	59	2633	2537
Usual Care	26	1022	1118
combined	85	3655	3655

z = 0.924

Prob > |z| = 0.3557

Patients that needed 7-9 treatments

Category 1	Category 2		***Row Totals***
Group 1 UC	6 (3.02) [2.93]	20 (22.98) [0.39]	26
Group 2 IG	4 (6.98) [1.27]	56 (53.02) [0.17]	60
Column Totals	10	76	**86 (Grand Total)**

The chi-square statistic is 4.7538. The *p*-value is .029234. The result is significant at $p < .05$.

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