The Effect of Upper Limb Neurodynamic Mobilizations on Pain and Functionality in Patients with Cervicobrachial Pain Syndrome or Cervical Radiculopathy: A Systematic Review and Meta-Analysis

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Abstract:

Cervicobrachial pain syndrome (CBPS) and Cervical Radiculopathy (CR) can be caused by a multitude of various diagnoses and dysfunctional tissue structures. CBPS and CR signs and symptoms include but not limited to radiating pain into the upper extremities, muscular imbalances, tender or painful trigger points, numbness in the upper extremities, and inflamed neural tissue structures. However, the effects of upper extremity neurodynamic mobilizations (NM) use on relieving CBPS and CR symptoms has not been critically evaluated for effectiveness. The purpose of this systematic review and meta-analysis is to assess the level of evidence between multiple studies utilizing NM on upper extremity pain utilizing Visual Analog Scales (VAS), Numeric Pain Rating Scales (NPRS) or Numeric Rating Scale of Pain (NRSP), and Functionality using the Neck Disability Index (NDI) in participants with CBPS or CR, and whether NM provides a clinically beneficial effect. An extensive electronic search was performed utilizing the following databases: Medline (PubMed), Cinahl Plus, EBSCO Host, SPORTDiscus, Science Direct, Scopus, and Google Scholar. A statistically significant difference was seen for Pre vs. Post Intervention/Control VAS Scores (95% CI = 3.76 [2.57 to 4.94], Z = 6.20 (P = 0.00001)). A statistically significant difference was seen for Pre vs. Post Intervention/Control NPRS/NRSP Scores (95% CI = 2.90 [1.35, 4.46], Z = 3.66 (P = 0.0003)). A statistically significant difference was seen with Pre vs. Post intervention/control NDI Scores (95% CI = 2.19 [0.84, 3.54], Z = 3.17 (P = 0.002)). Results from this systematic review and meta-analysis provide plausible data supporting the use of neurodynamic mobilizations as a therapeutic intervention for patients with CBPS and CR. However, with limited current research, more studies are needed to further enhance the quality and understanding of neurodynamic mobilizations as a therapeutic intervention.

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Chapter I

Introduction

Upper extremity injuries are prevalent among various populations including both active and sedentary individuals (Starkey, 2015). Common injuries of the upper extremities, shoulder, and cervical spine that can be debilitating include rotator cuff tears, shoulder labrum disruptions, shoulder dislocations, upper biceps tendon injuries, cervical spine dysfunctions, disc herniation and neural tissue dysfunctions. Cervicobrachial Pain Syndrome (CBPS) is a cervical condition in which the neural tissue is sensitive to mechanical stresses or becomes inflamed and or damaged and is accompanied by neural deficits, altered reflexes, motor and muscle weakness, paresthesia, and may include headache symptoms (Chandan, Sen, & Arfath, 2015) (Mohammed, Elsayed, Elbalawy, & Ghally, 2019) (Nelakurthy, Saharan, Kushmal, & Saharan, 2020) (Sambyal & Kumar, 2013). CBPS is a condition in which there is an increase in the mechanosensitivity of a nerve without confounding neurological deficit (Elvey & Hall, 1997).

CBPS and associated cervical radiculopathy (CR) symptoms is one of the most frequent upper extremity and neck related complaint. It is documented that nearly 50% of the general population will experience some sort of neck and arm pain in their lifetime, with incidence rates being low at 83 per 1000 persons in younger populations and increasing to 203 per 1000 persons in populations within the fifth decade of life (Sambyal & Kumar, 2013)

(Savva, Giakas, Efstathiou, & Karagiannis, 2016). Since CBPS is under the classification of neck pain and arm pain, numbers reported are relatively high in prevalence to global disability. According to recent studies, neck pain is classified as the fourth largest contributor to global disability (Fernandez-Carnero, Sierra-Silvestre, Beltran-Alacreu, Gil-Martinez, & Touche, 2019). Neck Pain (NP) has been found in younger populations with higher prevalence in females 26.4% to males 12.3% (Fernandez-Carnero, Sierra-Silvestre, Beltran-Alacreu, Gil-Martinez, & Touche, 2019). Due to high incidence rates, it is critical that healthcare professionals develop a rehabilitation tool to assist them in treating CBPS or CR patients.

It is also noted that certain sections of the cervical spine have different levels of prevalence. The most affected nerve roots are the cervical (C6) and cervical (C7) nerve roots (Radhakrishnan, Litchy, O'Fallon, & Kurland, 1994). C6 and C7 symptoms can be caused by a disc herniation of the segmental sections of C5-6 and C6-7 cervical discs. It has also been reported that cervical spondylosis can cause symptoms related to CBPS (Radhakrishnan, Litchy, O'Fallon, & Kurland, 1994) (Sambyal & Kumar, 2013). Thus, it is important to consider different diagnoses as causes of CBPS or CR respectively. However as mentioned previously, many of the signs and symptoms remain the same throughout.

With the high prevalence of CR and CBPS among all populations, therapeutic treatments and physical therapy programs utilized to relieve and or reduce symptoms related to CBPS is of high importance. Therapeutic techniques utilized to relieve symptoms of CBPS can include cervical traction, neurodynamic mobilizations (NM), medications, joint manipulations, electrical stimulation, steroid injections, with surgery being the last clinical option (Savva, Giakas, Efstathiou, & Karagiannis, 2016) (Sambyal & Kumar, 2013) (Gupta & Sharma, 2012) (Nelakurthy, Saharan, Kushmal, & Saharan, 2020) (Chandan, Sen, & Arfath, 2015) (Sanz, et al.,

2018) (Fernandez-Carnero, Sierra-Silvestre, Beltran-Alacreu, Gil-Martinez, & Touche, 2019). Fernandez-Carnero et al. (2019) reported that €2,799,000 was allocated for rehabilitation services for NP while only 50.82% of the treatments utilized for managing NP were effective or provided inconclusive evidence of effectiveness of the treatment respectively. The financial burden placed on organizations to effectively treat NP and CBPS or CR is increasing, with little knowledge and evidence on best available treatments. Time can also be a factor for further investigating treatment options. Reducing time invested on non-effective treatments where more beneficial options could be utilized could help reduce costs and expenses incurred as well as reduce the rate of reoccurrence of CBPS or CR. Further investigation and comparison into treatment options, methods, and outcomes is needed to better understand how to increase the effectiveness of treatments for patients with CBPS or CR.

A rehabilitation tool utilized by many clinicians with NP, CBPS, or CR is NM. NM includes the passive or active movement of neural tissue and closely associated soft tissue structures to improve the mechanical and physiological functionality of the nervous system (Basson, et al., 2015) (Basson, 2017) (Ellis & Hing, 2008). It is proposed that physiological changes within the neural tissue itself has been thought to occur with use of two specific mobilization techniques: (1) neurodynamic slider mobilization and (2) neurodynamic tensioner mobilization technique. Neurodynamic slider mobilizations attempt to mobilize the neural tissue, whereas neurodynamic tensioner mobilizations attempt to place tension along the neural structures. However, potential benefits from utilization of both NM techniques include reduced neural tension, improved functionality, and improved biomechanics of neural structures (Basson, et al., 2015) (Basson 2017), (Ellis & Hing, 2008). In a recent study, NM has been shown to have hypoalgesic effects versus a placebo treatment group (Beltran-Alacreu, Jimenez-Sanz, Carnero,

& Touche, 2015). The overall goal of NM is to restore the mechanical and physiological relationship of the nerve with its connective tissue structures (Coppieters & Butler, 2008).

Purpose

The purpose of this systematic review and meta-analysis is to critically assess the level of evidence in the literature and to investigate the efficacy of NM in patients with CBPS or CR across various studies. NM has been used by clinicians in clinical practice with limited viable research evidence discussing the therapeutic efficacy of performing NM on CBPS and CR patients and other associated NP injuries. We anticipated that this systematic review would provide clinicians with evidence-based insights that could be used to integrate NM for CBPS or CR as a therapeutic intervention. Subjective measurements are related to what the patient or participant describes as an issue to them, such as pain, discomfort, and reduced functionality. These can be measured by utilizing either VAS, NDI, or NPRS/NRSP scales. Currently there is a lack of homogenous studies investigating the effects of NM in regard to techniques, measures, protocols, and patient populations. Thus, it is the goal of this study to compare the effect of multiple studies utilizing NM across a variety of patient populations as a treatment method in relieving the signs and symptoms related to CBPS or CR and improving long-term overall health.

Research Questions

1. Will NM improve subjective functionality measured by the Neck Disability Index (NDI) as reported by patients with CPBS or CR?
2. Will NM improve subjective patient reported symptoms of pain as reported with Visual Analog Scale (VAS), Numeric Pain Rating Scale (NPRS), and Numeric Rating Scale of Pain (NRSP) with CPBS or CR?

Hypotheses

- Null Hypotheses:
    - NM will not have an effect on improving pain levels in patients with CBPS or CR.
    - NM will not have an effect on improving functionality in patients with CBPS or CR.
- Alternative Hypotheses:
    - NM will have an effect on improving pain levels in patients with CBPS or CR.
    - NM will have an effect on improving functionality in patients with CBPS or CR.

Study Significance

The studies evaluated within this systematic review and meta-analysis, and the information gathered has the potential to benefit various patient populations in relieving symptoms of CBPS or CR. Data collected and interpreted from these studies can provide practicing clinicians and other health care professionals a formative evaluation of the effectiveness of NM with CBPS or CR. It may also provide a core foundation and understanding of the techniques and rehabilitation programs utilized to treat CBPS or CR. This may lead to better immediate outcomes while simultaneously providing tools and techniques that can be utilized to improve long-term patient health regarding CBPS or CR.

Definition of Terminology

Neurodynamic Mobilizations "… technique involves movement and/or tension of the nervous system, which results in reduced intrinsic pressure of the neural tissue and can reestablish the neural biomechanics" (Mohammed et al., 2019, P. 4207).

Range of Motion "… assessment of all available motions at the involved joint and the joint proximal and distal to the affected area […] Joint movement occurs through physiological and accessory motions" (Starkey & Brown, 2015, p. 17)

Cervicobrachial Pain Syndrome "…cervicobrachial pain syndrome is a condition with increased mechanosensitivity of nerve as predominant feature without any neurological deficit" (Gupta, 2012, p. 127)

Cervical Radiculopathy "Cervical radiculopathy (CR) is a peripheral nervous system disorder affecting the normal functions of cervical nerve roots (CNRs) and is often with chronic pain and functional limitations in daily life" (Savva et al., 2016 p. 20)

Neural Sliders "… involves combination of movement that result in elongation of nerve bed at one joint while reducing the length of nerve bed at adjacent joint" (Chandan et al., 2015, p. 38).

Neural Tensioners "involve increasing distance between each end of nerve bed by elongation" (Chandan et al., 2015, p. 38).

Nucleus Pulposus "jelly-like central region of the intervertebral disc" (3D4Medical, 2017).

Annulus Fibrosus " fibrous layer of the intervertebral disc… composed of more densely packed fibers that act as a ligament to secure the adjoining vertebrae" (3D4Medical, 2017).

Chapter II

Literature Review

Introduction

The aim of this systematic review and meta-analysis is to assess the clinical efficacy of NM when utilized as a treatment protocol in patients with CBPS or CR compared to traditional methods of treatment for pain and functionality. Items to be discussed include anatomy of the cervical spine, shoulder, and arm; the rationale behind utilizing NM as a treatment protocol and describe the NM techniques used within the reported studies.

When attempting to diagnose a patient with CBPS or CR, a clinician must be knowledgeable in the scope of anatomy. CBPS and CR encompasses many different anatomical features within its concept alone, and differing between CBPS, CR, and other potential conditions must be met. CBPS and CR generally originates at the cervical spine with pain and associated symptoms dispersed through the shoulder complex and into the upper arm, elbow, and hand. Thus, it is important to understand the neurovascular and muscular structures and their functions for the cervical spine, shoulder, arm, and hand.

Cervical Spine Anatomy

The cervical spine is comprised of 7 vertebrae held together by intertwining ligaments, membranes, and fascial tissue. C1 (the atlas) and C2 (the axis) vary slightly compared to that of vertebrae C3-7 but are important in the overall motions of the head and cervical spine. The

typical cervical vertebrae C3-7 are comprised of five notable features: The body, vertebral foramen, transverse processes, articular processes, and spinous processes (Agur & Dalley, 2013). Between each vertebral body is a vertebral disc comprised of a nucleus pulposus and the annulus fibrosus. The vertebral discs provide a cushion between vertebral bodies to act as a shock absorber while also limiting motion of the vertebral bodies with each other creating structural stability. C1-2 do not have intervertebral discs as this allows for optimal and proper head movements (3D4Medical, 2017).

Movement of the head and neck is achieved by various musculature that works together to provide optimal, efficient, and correct movement patterns to achieve the desired motion. This region is highly complex in the number of muscles. Three layers of dorsal muscles of the back have been established for better understanding. Within the cervical region, the dorsal superficial layer of muscles includes the occipitalis, levator scapulae, and the trapezius which is divided up into three different sections (Agur & Dalley 2013) (3D4Medical, 2017). The descending (superior), middle and ascending (inferior) portions (Agur & Dalley 2013) (3D4Medical, 2017).

The middle or intermediate layer of musculature comprising that of the cervical region includes the levator scapulae, rhomboid minor, and serratus posterior superior (Agur, 2013). The deep muscles of the cervical spine region include the splenius capitus, sternocleidomastoid, iliocostalis cervicis, semispinalis capitis, semispinalis cervicis, semispinalis thoracis, longissimus capitis, rotatores brevis and longus, external intercostal, and levator costarum longus (Agur & Dalley 2013) (3D4Medical, 2017). Even smaller and more numerous musculature within the suboccipital region is noted and has an effect on causing symptoms related to that of CBPS and CR. Key muscles of this region include the sternocleidomastoid, longus capitus, and scalene muscles (Agur & Dalley 2013) (3D4Medical, 2017) (Starkey, 2015).

This cervical region is important when discussing vascular, venous, and nervous system components. Upper extremity blood supply, both arterial and venous supplies, run nearly parallel to the nervous system through the shoulder and distal arm. The important structure within this region is the brachial plexus when discussing CBPS and CR. Most signs and symptoms related to CBPS or CR may be caused by compression, or irritation of the brachial plexus and the nerves that make up the brachial plexus distally. It is comprised of the C5-T1 nerve roots of the anterior rami and exit through the occipital triangle of the lateral neck (Agur & Dalley 2013). Further structures within this region include the common carotid artery, the subclavian artery, the vertebral artery, internal and external carotid arteries, subclavian vein, internal jugular vein, brachiocephalic vein, and vertebral vein (3D4Medical, 2017) (Agur & Dalley 2013) (Starkey, 2015). All these structures are compressed within a small region of the cervical spine where CBPS and CR can develop.

Shoulder Anatomy

For this study, basic anatomy of the shoulder will be presented. In depth analysis of the shoulder complex and its components and functions will not be evaluated or presented here due to CBPS or CR originating at the cervical spine. The shoulder complex is related to CBPS and CR as most structures and nerves affected by CBPS or CR travel through the shoulder. Symptoms related to CBPS or CR can be radiating and extend into the distal upper extremities from the shoulder to the hand. The shoulder is the connection between the upper appendages and the axial skeleton. Bony structure of the shoulder is "formed by the sternum, clavicle, scapula, and humerus" (Starkey & Brown, 2015, p. 601).

The glenohumeral (GH) joint or shoulder joint is an inherently unstable ball and socket joint with structural stability provided by the muscles of the rotator cuff and the GH ligaments.

The muscles that make up the rotator cuff include the supraspinatus, infraspinatus, teres minor, teres major, and subscapularis (Starkey, 2015). The muscle of the rotator cuff work intricately together to provide structural stability and rigidity to the GH joint. The GH joint has been thought of similar to that of a golf ball sitting on a tee. The socket of the glenoid fossa is further deepened by the glenoid labrum and is surrounded by a capsule, reinforced by the glenohumeral (GH) and coracohumeral (CH) ligaments (Starkey, 2015).

The glenohumeral ligaments include the superior GH ligament, middle GH ligament, anterior band of inferior GH ligament, posterior band of inferior GH ligament, and inferior GH ligament (Starkey, 2015) (Agur, 2013) (3D4Medical, 2017). Each ligament provides different amounts of stability and rigidity dependent on the angle of the humeral head within the glenoid fossa.

Table 1.

GH Ligaments and Limitations on Humeral Head Motion

Rotational position of humeral head	Structure limiting humeral head motion
External rotation at 0 deg.	Superior GH ligament Coracohumeral ligament
External rotation at 45 deg. abduction.	Middle GH ligament Anterior band of infrerior GH ligament
External rotation at 90 deg. abduction.	Inferior GH ligament
Internal rotation at 90 deg. abduction.	Posterior band of inferior GH ligament
Inferior displacement at 0 deg. abduction.	Superior GH ligament Coracohumeral ligament
Inferior displacement at 90 deg. abduction.	Inferior GH ligament

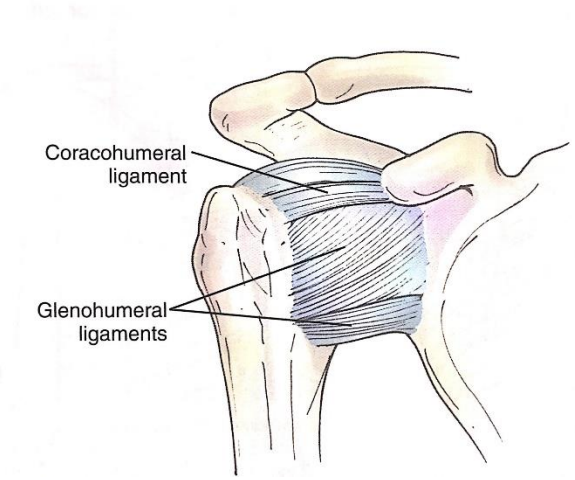


Figure 1. Glenohumeral Capsule and Ligaments (Starkey & Brown, 2015).

The Nervous System and Brachial Plexus

The nervous system is the body's way of communicating between the periphery and the brain. It allows for quick communication of information from sensory input to be integrated by the brain, and then sent back via an action output to the muscles to create a desired movement pattern. Sensory information such as pain, pressure, heat, cold and touch travels through the nervous system to its respective dorsal (afferent) nerve root (3D4Medical, 2017). It is then sent through the spinal cord to the brain for integration. Once an appropriate action is determined by the brain, the motor action is sent back through the spinal cord to the ventral (efferent) nerve root of the same spinal level (3D4Medical, 2017). The motor action is then sent through the nerves to the muscle or muscles to perform the desired motion or action the brain has determined as appropriate.

The brachial plexus is the communication highway between the upper extremities and parts of the shoulder to the brain. As previously mentioned, it consists of 5 nerve roots that branch down and innervate various muscles of the hand, wrist, arm, shoulder, and some back

musculature. The nerve roots for the brachial plexus (Fig. 2) consists of C5-T1 (Agur, 2013) (3D4Medical, 2017). Moving distally from the nerve roots, the brachial plexus turns into the medial and lateral cords which passes anteriorly through the shoulder complex and extends down distally into the arm. (Agur, 2013) (3D4Medical, 2017). From here, further division into four main nerves is seen. The musculocutaneous nerve, median nerve, ulnar nerve, and radial nerve provide the main pathways of the smaller nerves to reach the spinal cord. Table 2 describes the main innervations of the four nerves mentioned here.

Table 2.

Overview of Peripheral Nerves and Their Primary Innervations	
Musculocutaneous Nerve	Innervates all the muscles of the anterior arm.
Median Nerve	Innervates the majority of muscles of the anterior forearm (some forearm musculature is innervated by the ulnar nerve), the lumbricals to digits 2-3, and the intrinsic muscles of the thumb (some intrinsics innervated by the ulnar nerve).
Ulnar Nerve	Innervates the carpi ulnaris and ulnar half of flexor digitorum profundus, the hypothenar and interosseous muscles of the hand, the lumbricals digits 3-4, adductor pollicis, and flexor pollicis brevis.
Radial Nerve	Innervates all the muscles of the posterior compartment of the arm and the forearm.

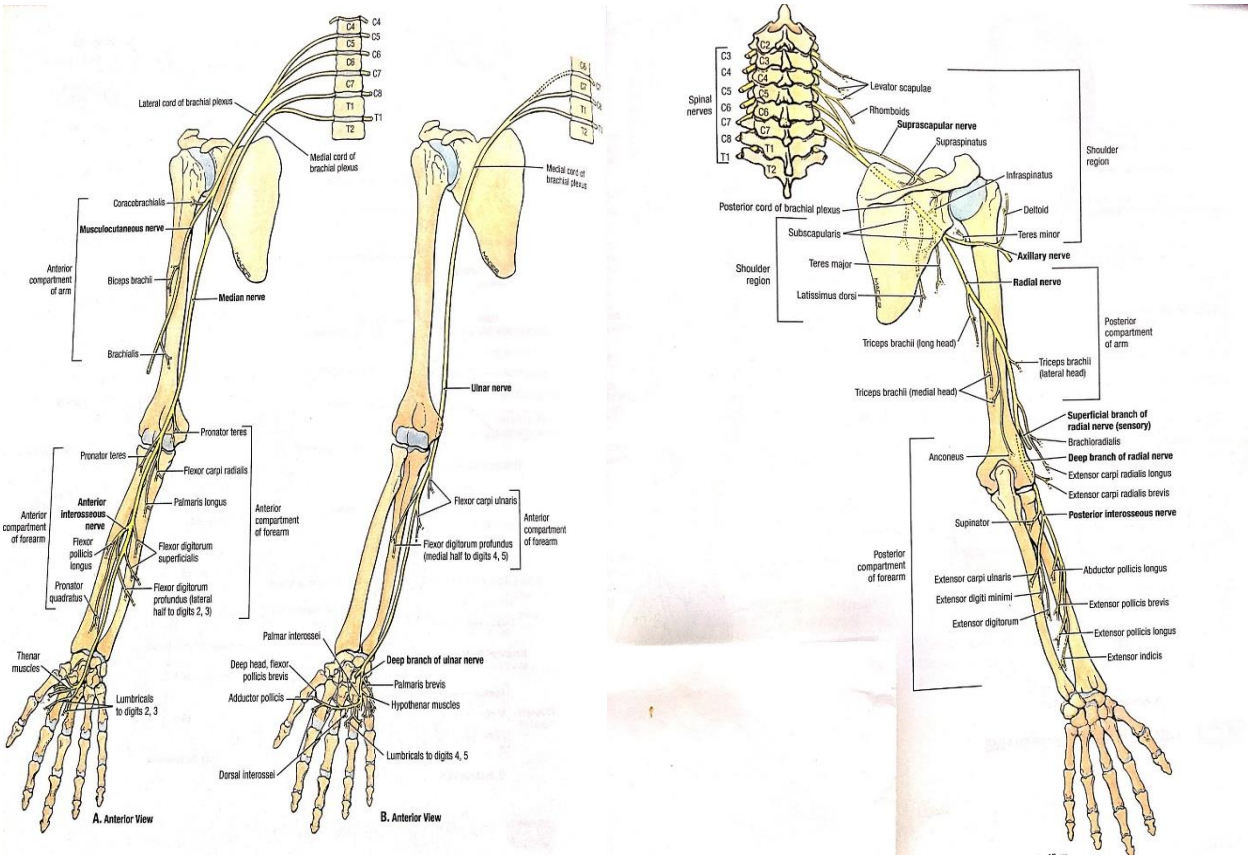


Figure 2. Brachial Plexus and Associated Distal Nerves (Agur & Dalley, 2013).

Some regions of the nervous system and their functions may be affected more than other nerves. Along with knowledge of the anatomy of the nervous system, clinicians can point out the nerve or nerves that are potentially involved via secondary methods. Other useful tools such as dermatome and myotome testing may be prevalent in helping diagnose and determine the proper intervention methods to be used. Dermatomes are the body's segmented sections of the nerves that innervate specific regions (Agur, 2013). As defined by Starkey & Brown, 2015, "each spinal nerve root innervates a discrete area of skin… known as dermatomes, have central autogenous zones that are supplied by only one nerve root, with the peripheral areas being supplied by other nerve roots". Even with merging of the fibers at the brachial plexus, clinicians are still able to

determine the affected nerves based upon any sensory deficits that may be present via dermatome testing (Agur, 2013) (Starkey, 2015). Individuals that may have a compressed, irritated, or inhibited nerve root may present with an area on the skin in the autogenous zone of decreased sensory function while the remaining portion may have an altered function (Starkey, 2015).

Myotomes are the somatic efferent nerve fibers that transport efferent signals from the spinal cord to the skeletal muscles (Agur, 2013). As defined by Agur & Dalley, 2013, “the unilateral muscle mass receiving information from the somatic motor fibers conveyed by a single spinal nerve is a myotome”. Myotome testing can be utilized to determine if a spinal lesion or inhibition is present. If certain muscle actions or motions are not achieved or are unable to be performed by an individual, understanding the myotomes can help clinicians determine which level the nerve is affected. This allows clinicians to provide the proper treatment similar to that of dermatomes.

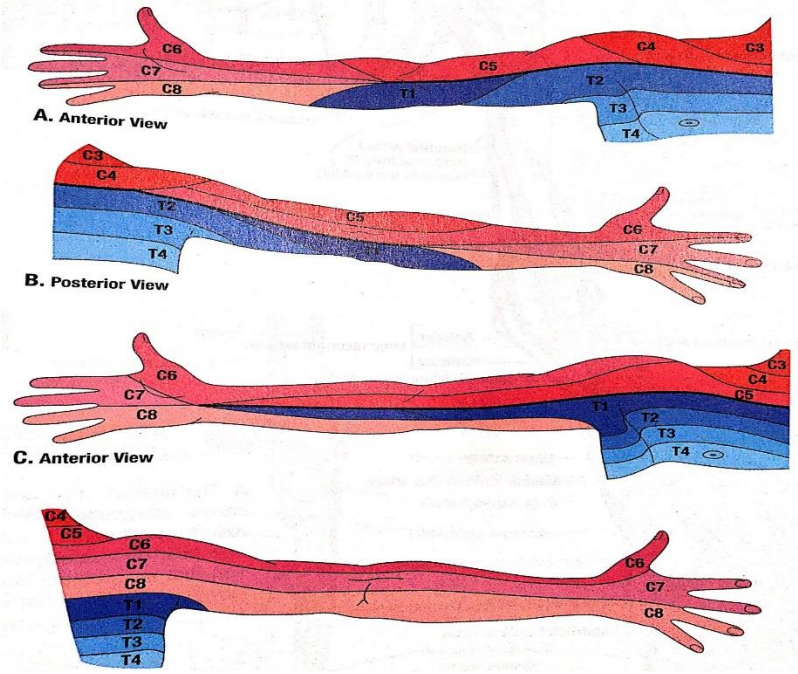


Figure 3. Overview of Dermatomes of the Upper Extremity (Agur & Dalley, 2013).

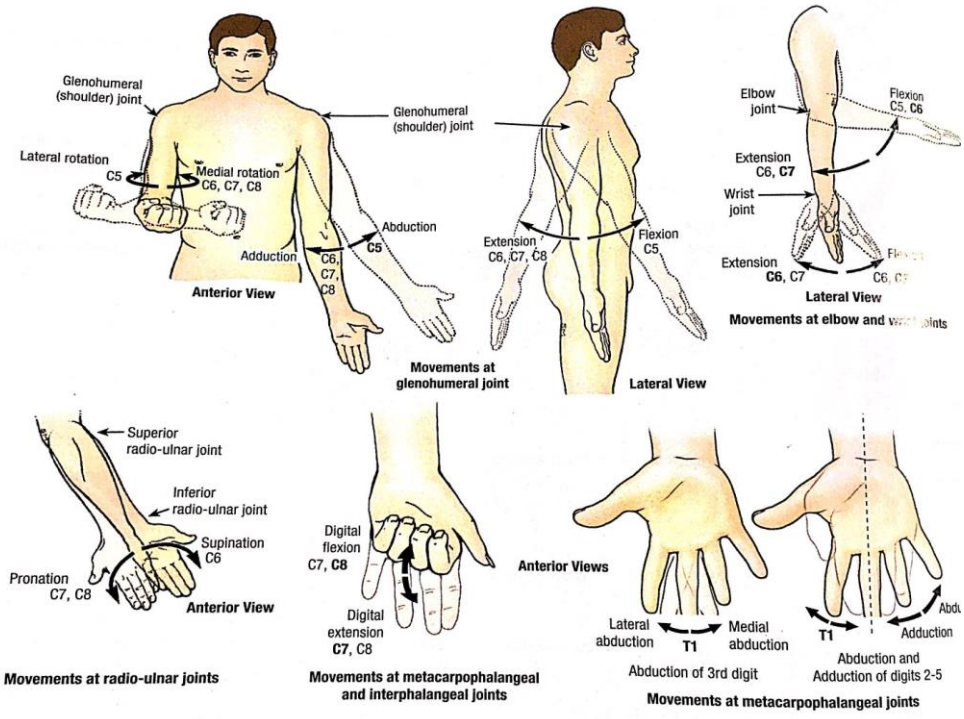


Figure 4. Overview of Upper Limb Myotomes and Motions (Agur & Dalley, 2013).

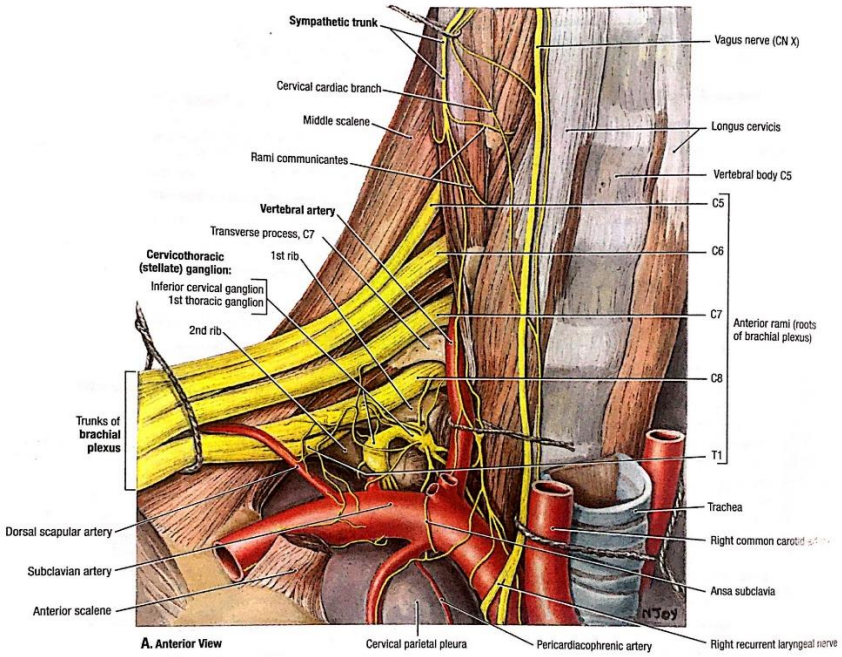


Figure 5. Anterior View Cervical Anatomy (Agur & Dalley, 2013).

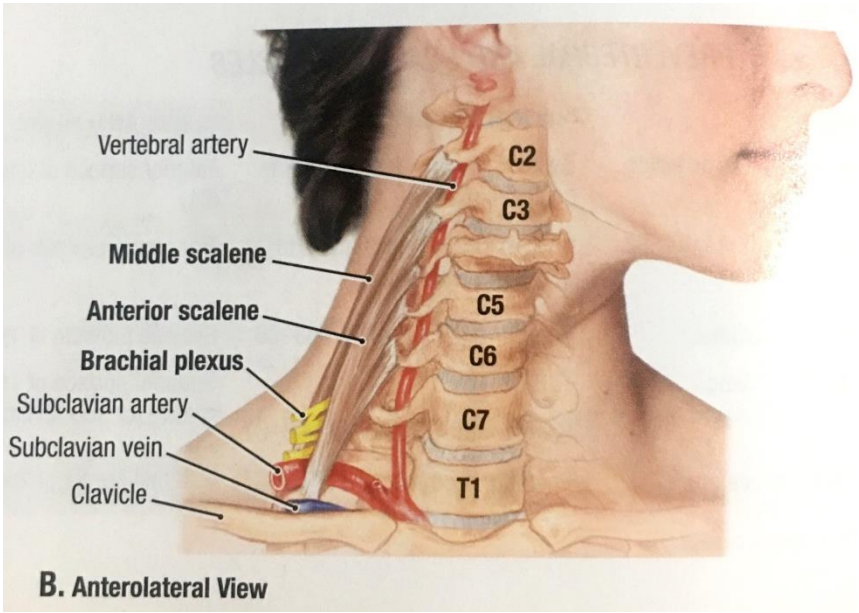


Figure 6. Anterolateral View Cervical Anatomy (Agur, 2013).

Cervicobrachial Pain Syndrome (CBPS) and Cervical Radiculopathy (CR)

CBPS and CR are conditions that are similar in that both affect the neurological structures of the neck, shoulder, and upper limbs (Gupta & Sharma, 2012; Savva et al. 2016). CR has been classified under the umbrella term under CBPS and vice-versa in some cases (Gupta & Sharma, 2012) (Nelakurthy, Saharan, Kushmal, & Saharan, 2020). As defined in the study by Savva et al. 2016, "Cervical Radiculopathy (CR) is a peripheral nervous system disorder affecting the normal function of cervical nerve roots (CNRs) and is often associated with chronic pain and functional limitations in daily life" (p. 20). CBPS on the other hand has "… been coined to describe this upper quarter pain in which neural tissue sensitivity to mechanical stimuli is a primary feature" (Chandan et al. 2015, p.38). As we can see, there is a correlation amongst the definitions of the terms and thus why utilization of both terms is necessary when discussing CBPS and CR. Since CBPS and CR originates within the cervical nerve roots, the most affected nerve root is the C6 nerve, which has been found to occur in 36.1% of all CBPS and CR cases (Gupta & Sharma, 2012, p. 127).

CBPS and CR is diagnosed using special tests and certain signs and symptoms. These specific CBPS or CR related features according to Sanz et al. 2018 include pain in the neck that radiates to the arm, neuropathic irritation, and pain. Other signs and symptoms related to CBPS and CR include numbness, tingling, discomfort in the arm or upper back and chest with or without associated headache (Nelakurthy et al. 2020). Potential sources for CBPS and CR include dysfunctional nervous tissue structures such as "visceral organs, cervical discs, facet joints, upper quarter muscular imbalances with associated trigger or tender points and inflamed neural tissue" (Nelakurthy et al. 2020). Diagnosis according to Elvy & Hall, 1997 can be done through clinical examination and be separated from other conditions by examining for "active

movement dysfunction, passive movement dysfunction, adverse responses to neural tissue provocation tests, hyperalgesic responses to palpation of nerve trunks, hyperalgesic responses to palpation of cutaneous tissue, and evidence of related local area of pathology". It is important to recognize that diagnosis is done through various techniques utilizing various measures and criteria. Thus, proper examination and evaluation will help clinicians in diagnosing CBPS or CR and ultimately provide proper treatment methods to their patients.

Literature Review

Studies investigating CBPS and CR and potential clinically significant treatment methods has been done. However, no known study has compared these studies to determine if NM is an effective treatment method for CBPS or CR. As defined by Chandan et al. (2015), "The term cervicobrachial pain syndrome (CBPS) has been coined to describe this upper quarter pain in which neural tissue sensitivity to mechanical stimuli is a primary feature" (p. 37). Their study investigated the effects of lateral nerve glides over neural tissue mobilizations for the median nerve in patients with CBPS on pain and disability. Twenty subjects divided up into two groups. Group A was provided the cervical lateral glide intervention while group B was provided the neural tissue mobilization intervention. Each group performed 14 days of the intervention. No true control group was utilized during this study.

Increased neural mechanosensitivity can be restored back to normal using different treatment methods. It is unknown how effective these treatments are in comparison to each other when attempting to treat CBPS. Chandan et al. (2015) state that "it has been suggested that enhanced mechanosensitivity of upper limb peripheral nerve trunks may contribute to pathology of CBPS" (p. 38). Methods of treatment targeting increased neural mechanosensitivity include cervical glides, neural sliders or neural tensioners, and neural stretches. Over the past decade,

treatment methods that have been advocated is that of cervical lateral glides, neural stretches, and NM (Chandan et al. 2013). Though each technique utilizes different methods, the same goal is prevalent; to restore the dynamic balance between neural tissue movement and surrounding mechanical interfaces (Chandan et al. 2013).

The techniques utilized by Chandan et al. for their study include cervical lateral glides and neural mobilizations on pain and disability. The author describes cervical lateral glides as "a technique to improve neural mobility. It involves the passive technique where the anatomic tissues or structures surrounding the affected neural tissue are gently mobilized with controlled and gentle oscillatory movements" (Chandan et al. 2013, p. 38). The NM technique used for this study is neural sliders. It involves a combination of movements that results in elongation of the nerve bed at one end while simultaneously reducing the length of the nerve bed at the other end (Chandan et al. 2013). This technique allows for the neural tissue to be mobilized through its surrounding interface.

Outcomes measures used in this study include the Visual Analog Scale (VAS), Disability of Arm, Shoulder, and Hand scale (DASH), and pain pressure threshold. The VAS is a 10cm horizontal line where patients are asked to mark a spot anywhere along the line according to the severity of their pain. According to Gupta & Sharma, decreased pain scores are considered clinically significant with a change score of 10-28mm on a 10cm VAS scale (Gupta & Sharma, 2012). Measurement is then used to quantify if pain levels improve over time with treatment. The DASH is a 30-question questionnaire focused on the shoulder, arm, and hand. Patients respond to each question based on their perceived disability on a scale from no difficulty to unable. Scores are used to determine the overall level of disability. Scores were then compared between day zero, seven, and fourteen. According to data collected from Chandan et al., results

between groups A & B showed significant differences ($P < 0.05$) for the DASH and VAS measures from day zero to day fourteen. The cervical lateral glide group showed a significant change in VAS and DASH measures however, neural slider mobilizations showed a greater change across the three time points as an effective treatment method (Chandan et al. 2013).

A similar study performed by Gupta & Sharma, 2012 investigated the effects of median nerve sliders on pain and disability in CBPS. The author's primary aim was to "… see the effectiveness of neural slider mobilizations as compared to conventional treatment for managing pain and disability in CBPS" (Gupta & Sharma, 2012). Thirty-four participants were included in this study, age range 18-40 years, and were divided up into two groups. The experimental group performed neural sliding techniques assisted by a clinician. The conventional therapy group performed active range of motion exercises for the neck and shoulder. Both groups performed their respective protocols for five sessions total over a 7 day period (Gupta & Sharma, 2012).

Prior to starting the treatment protocol, each participant was instructed to fill out a VAS, Neck Disability Index (NDI), and Cervicobrachial Symptom Questionnaire (CBSQ) (Gupta & Sharma, 2012). Range of motion (ROM) was calculated during pre-testing using an inclinometer to help determine the moment of first pain noticed by the participants. Improvements in degrees ROM would determine if successful treatment application was provided. Gupta & Sharma report statistically significant differences ($P < 0.05$) in VAS, range of motion, NDI, and CBSQ scores between groups comparison from day 1 to day 5. Their results show that the "Mann Whitney U-Test showed statistically significant differences between both groups" (Gupta & Sharma, 2012, p. 129). Their within groups comparison of variables "showed statistically significant improvement after completion of the respective treatment interventions in pain intensity (VAS), pain free elbow extension ROM […], and disability scores as per CBSQ and NDI" (Gupta &

Sharma, 2012, p. 129). In the experimental group, VAS scores improvement after treatment was 0.95, whereas the conventional group was 0.30 (Z-value = 4.94) (Gupta & Sharma, 2012). From their findings, pain-free elbow extension ROM in the experimental group was 12.50 degrees compared to 0.50 degrees (Z-value = 5.01) within the conventional group. The authors also report that NDI and CBSQ disability scores were both 5, compared to 2 and 1 (Z-value = 5.02; P = 0.05 and Z-value = 5.01; P = 0.05) in the conventional group respectively.

These findings reported by Gupta & Sharma represent that NM is a more effective treatment method compared to conventional techniques. However, both treatment methods represented statistically significant improvement within five treatment sessions over a 7 day period in all measures. The authors infer that "… 8-10 sessions will be sufficient for symptoms to resolve completely" (p. 131) when utilizing NM. Improvement within the conventional treatment group was not consistent or constant enough to generalize the effects long term (Gupta & Sharma, 2012).

In another study done by Mohammed et al. 2019, the researchers investigated the effects of NM on pain and hand grip strength in cervical radiculopathy patients. Since grip strength is not evaluated in this study, only pain will be assessed from this article. Thirty patients were split up into three separate groups. Group one received NM for ulnar, radial, and median nerves and a selected physical therapy program. Group two received NM for the radial, and median nerves while also performing the selected physical therapy program. Group three only performed the selected physical therapy program. Each group performed the protocols for four weeks for a total of twelve sessions. Assessment of pain intensity was done utilizing the VAS scale before and after treatment. Results from Mohammed et al. 2019 reveal statistically significant ($p < 0.001$) findings for a decrease of pain scores within each group when comparing before treatment to

after treatment. However, no statistically significant before treatment ($p = 0.71$), and after treatment ($p = 0.32$) between groups findings were present (Mohammed et al. 2019). Even though we can clearly infer that not one group within the three was a far superior treatment method, it can be implied that each treatment alone is still effective at improving pain intensity levels. Clinically this provides better insight into further treatment protocols and parameters for clinicians working with CBPS patients.

Another study done by Sambyal & Kumar, 2013 investigated the effects of NM and conventional therapy in cervical radiculopathy patients. The outcomes measure utilized for this study included VAS. The VAS was provided pre-treatment and once again post-treatment. Twenty patients aged 25-40 years old of either sex and were experiencing neural symptoms related to CR for more than four weeks were included in this study (Sambyal & Kumar, 2013). Patients were split up into two groups randomly. Group A received NM for the radial, medial, and ulnar nerves along with undergoing cervical traction. Group B received a conventional therapy treatment of cervical traction, hot pack, and isometric strengthening exercises for the cervical musculature. Results from Sambyal & Kumar, 2013 show that both treatment methods are effective at relieving pain intensity levels when assessed via the VAS. However, Group A showed to be a more effective treatment method for relieving pain in CR patients. Mean values for the pre-VAS for each group was 6.80 ($SD = 1.54$) and 6.25 ($SD = 1.25$) respectively. Post-VAS measures were 3.35 ($SD = 1.49$) and 4.45 ($SD = 1.63$) respectively (Sambyal & Kumar, 2013). Comparison of the differences of the mean values for Pre and Post VAS between group A and B was ($t = 5.89$) ($p < 0.05$) (Sambyal & Kumar, 2013).

Further evidence of NM and their effectiveness was investigated by Sanz et al. 2017. This study investigated the effectiveness of median nerve NM versus over-the-counter medicine

(OTC), specifically ibuprofen, in subjects who had been diagnosed with cervicobrachial pain. It is mentioned by the authors that the first line of treatment for cervicobrachial pain is oral ibuprofen and NM (Sanz et al. 2017). Sixty-two patients were included in this study and were randomly assigned to one of two groups. Only fifty participants completed the trial. Both groups were demographically homogenous at the start of the study. Group one consisted of a 1200 mg/day oral ibuprofen treatment for six weeks (Sanz et al. 2017). Group two consisted of a median nerve NM technique for six weeks (Sanz et al. 2017). Outcomes measures for this study included the NPRS, cervical range of motion (CROM), and upper limb function test or the Quick DASH. Results from their study inferred that oral ibuprofen treatment ($\eta^2 = 0.612$ - 0.755) was more effective than the NM ($\eta^2 = 0.816 – 0.821$) for all assessments ($p < 0.05$) when assessing mean value scores (Sanz et al. 2017). Both treatments were effective however, with the potential that NM may provide long term lasting effects compared to a short-term fix with oral ibuprofen. NM also offers a non-pharmacological treatment option for patients that may not, or are unable take medications due to underlying conditions.

In a study done by Savva et al. 2016, they investigated the effectiveness of NM with intermittent cervical traction in the management of CR. The primary goal of this study was to observe the effects of NM with intermittent cervical traction (ICT) on pain, disability, function, grip strength and cervical range of motion (Savva et al. 2016). Forty-two participants diagnosed with unilateral CR were included in this study and were randomly allocated to either the control or intervention groups. The intervention consisted of twelve sessions with 6 sets of 60s grade II-IV ICT while simultaneously applying NM (Savva et al. 2016). Participants in the control group did not perform any type of treatment and were advised to refrain from OTC and prescription medication for four weeks. According to Savva et al. 2016, the intervention group had shown

significant improvements in NDI scores (mean difference = -16.95; 95% CI = -22.47 to -11.43, ES = 0.42), NPRS scores (mean difference = -3.74; CI = -4.92 to -2.96, ES = 0.37) compared to that of the control group NDI scores (mean differences = 1.52; CI = -3.03 to 6.07), and NPRS scores (mean differences = -0.05; CI = -1.11 to 1.02). There was a moderate effect size difference (ES = 0.37) for between group comparison for NPRS scores and a large effect size difference (ES = 0.42) for between group comparison for NDI scores (Savva et al. 2016). It can be inferred from this study that use of NM with intermittent cervical traction can be an effective treatment method for relieving pain and increasing function in patients with CR.

A recent study performed by Kim, Chung, & Jung (2017) evaluated the effects of NM on patients with cervical radiculopathy. Primary and secondary outcomes investigated included pain, disability, ROM, and deep flexor endurance. Scales and or questionnaires utilized for this study include the Numeric Pain Rating Scale (NPRS), the Neck Disability Index (NDI), Cervical range of motion (CROM), and deep flexor muscle endurance (Kim, Chung, & Jung, 2017). Their study examined NM with manual cervical traction (NMMCT) compared with manual cervical traction (MCT) alone in thirty patients reporting cervical radiculopathy symptoms (Kim, Chung, & Jung, 2017). Both interventions were applied to either group respectively three times per week over an 8-week period (Kim, Chung, & Jung, 2017).

Findings from their study shows a significant decrease in all outcome's measures for the NMCT group compared to that of the MCT alone group for pain, functionality, and ROM. For pain, the NMCT group had a significantly larger decrease than that of the MCT group; NMCT change: -4.87 ± 0.92 and MCT change: -3.87 ± 0.99; F = 8.70; P = 0.006 (Kim, Chung, & Jung, 2017). Findings on functionality were similar, with a larger decrease for that of the NMCT group (pre: 21.67 ± 4.12 points, four weeks: 14.67 ± 3.09 points, and eight weeks: 10.60 ± 2.82 points;

F = 83.67; P = 0.000) compared to the MCT group (pre: 22.07 ± 2.99 points, four weeks: 18.13 ± 3.18 points, and eight weeks: 14.27 ± 3.83 points; F = 105.85; P = 0.000) respectively (Kim, Chung, & Jung, 2017). ROM for the NMCT group was significantly better than the MCT group for all motions measured. NMCT flexion change: 15.33 ± 3.96° and extension change: 14.67 ± 3.33°; MCT flexion change: 11.87 ± 2.62° and extension change: 10.73 ± 2.81°; flexion – F = 12.02; P = 0.002; extension – F = 64.04; P = 0.000; NMCT left side change: 10.33 ± 4.35° and right side change: 10.80 ± 2.81°; MCT left side change: 7.00 ± 2.73° and right side change: 7.93 ± 2.40°; left side – F = 9.05; P = 0.006; right side – F = 11.81; P = 0.002; NMCT left side rotation change: 10.13 ± 2.23° and right side rotation change: 11.73 ± 2.91°; MCT left side rotation change: 7.47 ± 2.29° and right side rotation change: 8.73 ± 2.19°; left side – F = 20.78; P = 0.000; right side – F = 11.41 and P = 0.002 (Kim, Chung, & Jung, 2017).

It is noted within the study by Kin, Chung, & Jung (2017) of some limitations of their study. These being the use of ultrasound to verify nerve excursion during NM, the age range of the participants which was narrow for this study, if the treatment utilized within this study can be applied to acute patients and patient with bilateral symptoms, and that the objective measurements of the weakened upper-limb muscle strength, dysesthesia, and radiation pain could not be obtained (Kim, Chung, & Jung, 2017). This study however provides data that supports the use of NM as a treatment method in patients with cervical radiculopathy pain.

Calvo-Lobo, et al., (2018) investigated the effects of median nerve NM (MNNM) vs. cervical lateral glides (CLG) vs. oral ibuprofen (OI) on pain intensity, physical functioning, and ipsilateral cervical rotation in patients with cervicobrachial pain. The CLG group was subject to a continuous mobilization style treatment for two minutes with a one-minute break five times a day, five days a week, for six weeks (Calvo-Lobo, et al., 2018). Patients were placed supine with

their shoulder abducted and elbow bent to 90°with both their hands resting on the abdomen or chest as the starting position (Calvo-Lobo, et al., 2018). The applying physiotherapist then stabilized the shoulder with one hand while the other hand performed a contra-lateral gliding technique with the head and neck to the affected side to the point just before pain and symptom reproduction or to the tissue barrier (Calvo-Lobo, et al., 2018).

The second intervention group in the study by Calvo-Lobo, et al., (2018) received a pharmacological treatment of oral ibuprofen (OI) in tablets. This was monitored by a physician with experience in providing OI to patients experiencing cervicobrachial pain. The physician oversaw modulating the doses provided to the patients to help achieve the best hypoalgesic effect for each patient (Calvo-Lobo, et al., 2018). Doses started at 400 mg/day and increased in a linear fashion until a 1200 mg/day dosage wat obtained with dosing being three times per day every eight hours (Calvo-Lobo, et al., 2018).

The last group in the study by Calvo-Lobo, et al., (2018) received a non-pharmacological and non-invasive treatment of median nerve NM (MNNM). A Physiotherapist applied the MNNM to each patient continuously for two minutes with a one-minute break in between five times during each session (Calvo-Lobo, et al., 2018). Patients were subject to five sessions per week for six weeks. Patients started supine on a stretcher with their affected side arm abducted to 90° with external rotation of the arm while simultaneously maintaining a starting position of elbow flexion and wrist and finger flexion (Calvo-Lobo, et al., 2018). From this position, patients were taken through elbow extension while performing wrist and finger flexion until the end point and then taken back to the initial starting position without pausing (Calvo-Lobo, et al., 2018).

Finding from Calvo-Lobo, et al., (2018) study shows that OI may be a better tool for management of pain intensity. However, secondary outcomes measures such as ROM show that MNNM and CLG may be better suited to help improve both secondary to pain reduction (Calvo-Lobo, et al., 2018). Pain intensity as reported by Calvo-Lobo, et al., (2018) shows a large effect size ($F = 22.343$; $P < .001$; $Eta^2 = 0.383$) with a bonferroni's correction showing a statistically significant difference ($P < .01$; 95% CI = 0.22 – 3.26) in favor of the OI treatment at all points of measurement, ROM was shown to have no statistically significant intergroup differences ($F = 1.434$; $P = .245$; $Eta^2 = 0.038$) compared to physical function which showed statistically significant intergroup differences for the Quick DASH ($F = 15.338$; $P < .001$; $Eta^2 = 0.299$) with bonferonni's correction ($P < .01$; 95% CI = 2.86 – 24.67) in favor of the OI treatment (Calvo-Lobo, et al., 2018).

The minimum clinical significane is reported within their study comparing OI vs. MNNM vs. CLG. For OI vs. both MNNM and CLG regarding NRSP only reached a minimum clinical significance of 1.39-points one-hour post-treatment session (Calvo-Lobo, et al., 2018). No minimum clinical significance was seen for the other primary outcomes. CLG vs OI regarding the Quick DASH showed a MCID of 17.1, but no MCID was seen between OI vs MNNM (Calvo-Lobo, et al., 2018). OI was shown to have a better effect at reducing pain, increasing functionality, and improving ROM compared to that of MNNM or CLG treatments in the short-term. However, the utilization for MNNM and CLG secondary to OI or for patients that are unable to take OI medication may help reduce or eliminate any side-effects from OI and provide an effective treatment method for these individuals for the long-term.

It must be noted that there is still a lack of homogenous studies using NM on CR and CBPS patients. Further studies must homogenize the study protocols to better compare results to

determine the overall efficacy of NM as a treatment option. Further studies must homogenize outcomes measures as well to help clinicians better justify treatments for a wide patient population. Thus, the aim of this systematic review and meta-analysis is to assess the level of evidence in the present literature and to determine if NM as a treatment method in CBPS or CR is efficacious for pain and functional improvement.

Chapter III

Methodology

Materials and Methods

To investigate the proposed hypothesis, a systematic review and meta-analysis was performed to assess if NM is an effective treatment method for individuals with CBPS or CR. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were utilized when conducting and reporting the following study methods (Moher, Liberati, Tetzlaff, Altman, & The PRISMA Group, 2010). A comprehensive electronic database search was performed by the primary investigator (B.M.) and a secondary third-party investigator (M.M.) using the following databases: Medline, PubMed Central, Science Direct, EBSCO, SPORTDiscus, and Proquest. The following specific vocabulary and key terms were used in the search: ("neural mobilization" AND/OR "neural mobilisation" AND/OR "nerve mobilization" AND/OR "nerve mobilization") AND ("neural glide" AND/OR "nerve glide") AND ("nerve treatment" AND/OR neural treatment AND/OR "nerve physiotherapy" AND/OR "neural physiotherapy") OR ("neurodynamics" AND/OR "neurodynamic treatment") AND ("cervical radiculopathy" AND/OR "cevicobrachial pain syndrome") AND ("pain" AND/OR "functional ability"). No starting date was set for the search for relevant articles as this was a large limiting factor. All relevant studies that were published up to June 2020 were included in the systematic review and meta-analysis. Studies were not limited to 10 years due to this being an overwhelming restrictive factor in obtaining relevant articles. Reference sections of selected

publications were evaluated by the author (B.M.) for further relevant articles that could be included in this analysis.

Descriptive Criteria of the Studies

Studies were included if (1) were written in English language or were translated into English language, (2) utilized neural mobilizations as a treatment method, (3) full text articles on cervicobrachial pain syndrome (CBPS) or cervical radiculopathy (CR), (4) were randomized controlled trials (RCTs) or case studies with four or more patients, (5) performed NM for either the median, ulnar, or radial nerves or a combination of all three, (6) presented statistical analysis data examining the effects of NM on pain and functionality, Studies were excluded from review if, (1) were not written in English or translated to English, (2) did not investigate NM of the median, ulnar or radial nerves, editorials, or case studies with less than four participants (3) studies that did not investigate NM on pain and or functionality, (4) studies using non-human subjects, (5) corresponding authors did not respond to requests for further data. References in screened and included articles, abstracts, and available conference proceedings (including abstracts, posters, and publications) were also hand searched by 1 author (B.M.).

Study Selection

We identified articles to determine if they met the following inclusion and exclusion criteria. Two reviewers (B.M., M.M.) assessed the titles and abstracts for adherence to the inclusion and exclusion criteria. Articles deemed relevant to the study were full text reviewed by the primary investigator (B.M.) to determine full text inclusion based on the following criteria. Any article discrepancy about inclusion or exclusion criteria was reviewed by the secondary reviewer (M.M.) and further discussion was had to determine eligibility of articles.

Participants: Patients diagnosed with either CBPS or CR with symptoms of pain and decreased functionality unilaterally. No restrictions for age, sex, or activity level were made.

Interventions: Studies utilizing NM as a treatment method in patients with CBPS or CR on pain and functionality.

Outcomes measures: Subjective outcomes measures are pain (VAS, NPRS, NRSP) and functionality (QuickDASH, DASH, or NDI) in patients with CBPS or CR.

Full-text documents identified by the primary reviewer (B.M.) were maintained for examination. (Refer to the PRISMA Flow Diagram (Fig. 25)

Quality Assessment

One reviewer (B.M.) performed quality assessment using a modified Downs and Black scale (Downs & Black 1998). This scale is intended to evaluate the quality of randomized and non-randomized studies and has been established as a reliable tool (test-retest R^2 0.88; interrater R^2 .75) for case-control and cohort studies (Downs & Black, 1998). All categorical questions of the Modified Downs & Black scale were answered to establish that all relevant and required fields of a study were evaluated and that nothing was overlooked or left out due to bias selection (Table. 6).

Each study was then evaluated and assessed for this review using the Oxford Centre for Evidence – Based Medicine levels of Evidence (Howick, et al., 2011) (Oxford Centre for Evidence – Based Medicine, 2011) by the primary investigator (B.M.). Evaluated scores are represented along with the Modified Downs & Black scores in Table. 6.

Data extraction and risk of bias assessment

Data were extracted by 1 reviewer (B.M.) from the articles selected and input into a database including age, sex, number of participants, CBPS or CR diagnosis, pain (VAS, NRSP, or NPRS) scales, and functionality measurements (NDI scales). In case of any questionable data selections, a secondary reviewer (M.M.) reviewed the data and was asked to determine the discrepancy. Data elements extracted include means, standard deviations, and sample sizes. Studies were assessed by the primary investigator (B.M) for clinically relevant data using the PEDro scale. The purpose of the scale is to determine if a randomized controlled trial has provided sufficient statistical information within the results to be interpreted. The scale is not intended to be used as a validation tool or measure to provide evidence that a treatment is clinically useful.

Statistical Analyses

Outcomes measures were calculated utilizing Review Manager 5.4 (RevMan 5.4) of standard mean deviations (SMDs) and 95% CIs to compare pain reduction and functionality differences for those performing NM versus a control treatment or placebo protocol. The SMD, a measure of the effect size, is the mean divided by the standard deviation of the difference between the values of two groups. The Cohen interpretation of the SMD statistic is that a value of 0.2 indicates a *small effect*; 0.5, *medium effect*; and ≥0.8, a *large effect* (Cohen 1998). Calculations performed were configured so that negative values indicated decrements in pain and an increase in functional ability for participants being treated with NM compared to a placebo or control treatment. Where authors did not report standard deviations, we converted 95% CIs and standard errors to standard deviations. The Cochran Q or I^2 test were performed to examine the heterogeneity (homogeneity) of the selected studies. When Q is larger than its expected

value *E*[Q] under the null hypothesis of no heterogeneity, the difference Q – *E*[Q] can be used to obtain the best estimate of heterogeneity. I^2 ranges from 0% to 100%; the higher the percentage, the greater the heterogeneity. It is interpreted as follows; 20% to 50%, *low*; 50% to 75%, *moderate*; and >75%, *high heterogeneity* (Loannidis, Patsopoulos, & Evangelou, 2007) (Deeks , Higgins , & Altman, 2021). We set an a priori α level of .05 for between-groups differences, regardless of variable follow-up times. The MCID used for comparison analysis was 1.4 cm for VAS on a 10 cm scale, 1.3 – 2.17 points for the NPRS/NRSP, and 7.5 – 8.5 points for the NDI (Tashjian, Deloach, Porucznik, & Powell, 2009) (Young, et al., 2009) (Young, Cleland, Michener, & Brown, 2010) (Michener, Snyder, & Leggin) (Cleland , Childs, & Whitman, 2008).

Methodologic Quality Assessment

Studies were evaluated for methodological quality utilizing the PEDro scale database (Physiotherapy Evidence Database, 2021). If a study was not included in the database, the primary investigator (B.M.) evaluated the research article and referred to a second individual (M.M.) if a PEDro question was not understood. Discrepancies were discussed and resolved between the two investigators for each study and scoring was performed. The PEDro scale is intended to be used as a tool in helping users identify studies for internal validity as well as identify if there is sufficient statistical information within the study to make the results interpretable (Physiotherapy Evidence Database, 2021). It is not intended to be used as a measure validating a study's conclusions (Physiotherapy Evidence Database, 2021). The PEDro scale is comprised of 11 questions covering different aspects of a study's validity internally and externally.

It has been demonstrated to have 'fair' to 'excellent' inter-rater reliability (Intraclass Correlation Coefficient 0.53-0.91) for randomized controlled trials of physiotherapy

interventions (Cashin & McAuley, 2020). The inter-rater reliability for the individual PEDro scale items ranges from ‘fair’ to ‘almost perfect’ (Kappa 0.36-1.00) for physiotherapy trials (Cashin & McAuley, 2020). The authors present evidence to support construct validity has been reported for the PEDro scale and the total PEDro score. There is associated findings of data supporting the total PEDro score to discriminate between high-quality and low-quality trials (Cashin & McAuley, 2020). Criterion 2-9 covers help identify RCTs within the PEDro database that are likely to have internal validity (Physiotherapy Evidence Database, 2021). Criterion 10-11 helps establish if a study has provided sufficient statistical information to make their results interpretable (Physiotherapy Evidence Database, 2021). Criterion 1 is utilized to help interpret if the study has external validity, generalizability, or adaptability (Physiotherapy Evidence Database, 2021).

PEDro scale scores range from 0-3 (poor), 4-5 (fair), 6-8 (good), 9-10 (excellent) (Cashin & McAuley, 2020). The methodological assessment performed resulted in one study receiving a poor-methodological quality PEDro score rating (≤ 3; Table. 5), two studies receiving a fair-methodological quality PEDro score rating (≥ 4 ≤ 5; Table. 5), nine studies receiving a good-methodological quality PEDro score rating (≥ 6 ≤ 8; Table. 5), and no studies receiving an excellent-methodological quality rating. The methodological limitations and scores are referenced in Table. 5.

Meta-Analysis

The meta-analysis run for the effect of the NM on pain reduction in CBPS or CR patients is presented in the forest plot in Fig.7, Fig.9, Fig.11. and Fig.13, Fig.15, Fig.17, and for functionality in Fig.19, Fig.21, Fig.22. Heterogeneity was assessed using the Cochrane Q and I^2; high heterogeneity was determined by a Q P value < .10 and I^2 > 50% (Deeks , Higgins , &

Altman, 2021). This test for heterogeneity was utilized to explain variance between studies. The magnitude of heterogeneity was established as: $I^2 = 0 – 40\%$ might not be important heterogeneity; 30 – 60% may represent moderate heterogeneity; 50 – 90% may represent substantial heterogeneity; 75 – 100% may represent considerable heterogeneity (Deeks , Higgins , & Altman, 2021). The observed value of I^2 depends on the magnitude and direction of effects and the strength of evidence for heterogeneity (Deeks , Higgins , & Altman, 2021). A random-effects method was chosen for all data sets as heterogeneity was accounted for between studies (Deeks , Higgins , & Altman, 2021). The random-effects model views each study as random observation from a group of studies and accounts for possible variance due to population differences, study design differences, and protocol application differences. Thus, the random-effects model was adopted for all statistical analyses.

No statistically significant differences were seen for pre-experimental VAS scores (95% CI = -0.02 [-0.32, 0.27], Z = 0.15 (P = 0.88)) Fig. 7 & Fig. 8, and post-experimental VAS scores (95% CI = -0.18 [-0.91, 0.56], Z = 0.47 (P = 0.64)) Fig. 9 & Fig. 10. A statistically significant difference was seen for Pre vs. Post Intervention/Control VAS Scores (95% CI = 3.76 [2.57, 4.94], Z = 6.20 (P = 0.00001)) Fig. 11 & Fig. 12. No statistically significant differences were seen for pre-experimental and post-experimental NPRS/NRSP scores (95% CI = 0.28 (-0.12, 0.68), Z = 1.38 (P = 0.17)) and (95% CI = -0.26 (-2.23, 1.70), Z = 0.26 (P = 0.79)) respectively (Fig. 13, 14, 15, 16). A statistically significant difference was seen for Pre vs. Post Intervention/Control NPRS/NRSP Scores (95% CI = 2.90 [1.35, 4.46], Z = 3.66 (P = 0.0003)) Fig. 17 & Fig. 18. No statistically significant differences were seen for pre-experimental and post-experimental NDI scores (95% CI = 0.04 [-0.35, 0.43], Z = 0.21 (P = 0.83)), (95% CI = 0.30 [-2.03, 2.62], Z = 0.25 (P = 0.80)) respectively (Fig. 19, 20, 21, 22). A statistically significant

difference was seen with Pre vs. Post intervention/control NDI Scores (95% CI = 2.19 [0.84, 3.54], Z = 3.17 (P = 0.002)) Fig. 23 & Fig. 24.

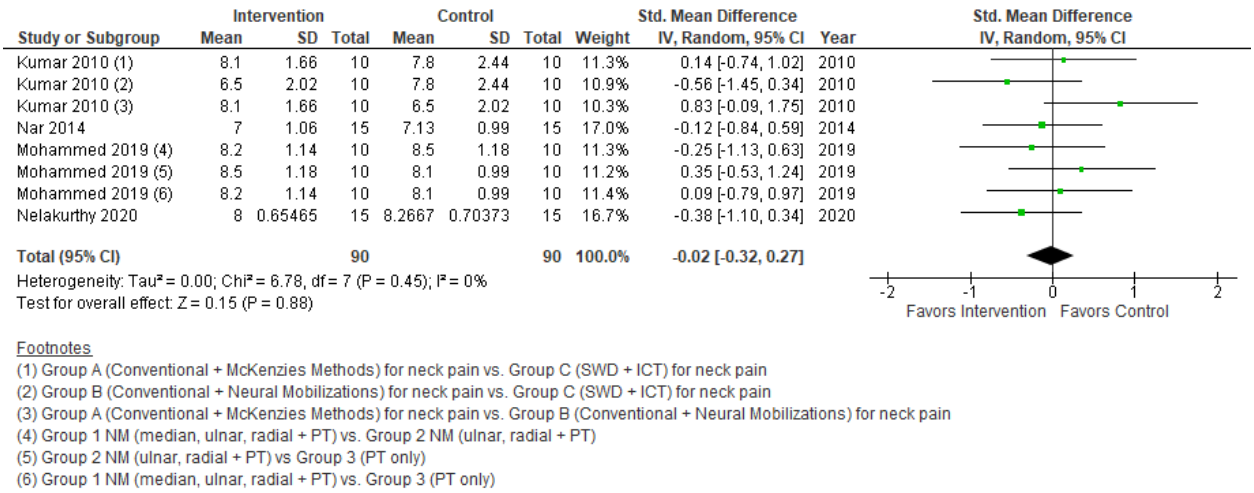


Figure 7. Forest plot for Pre-experimental trial VAS Scores.

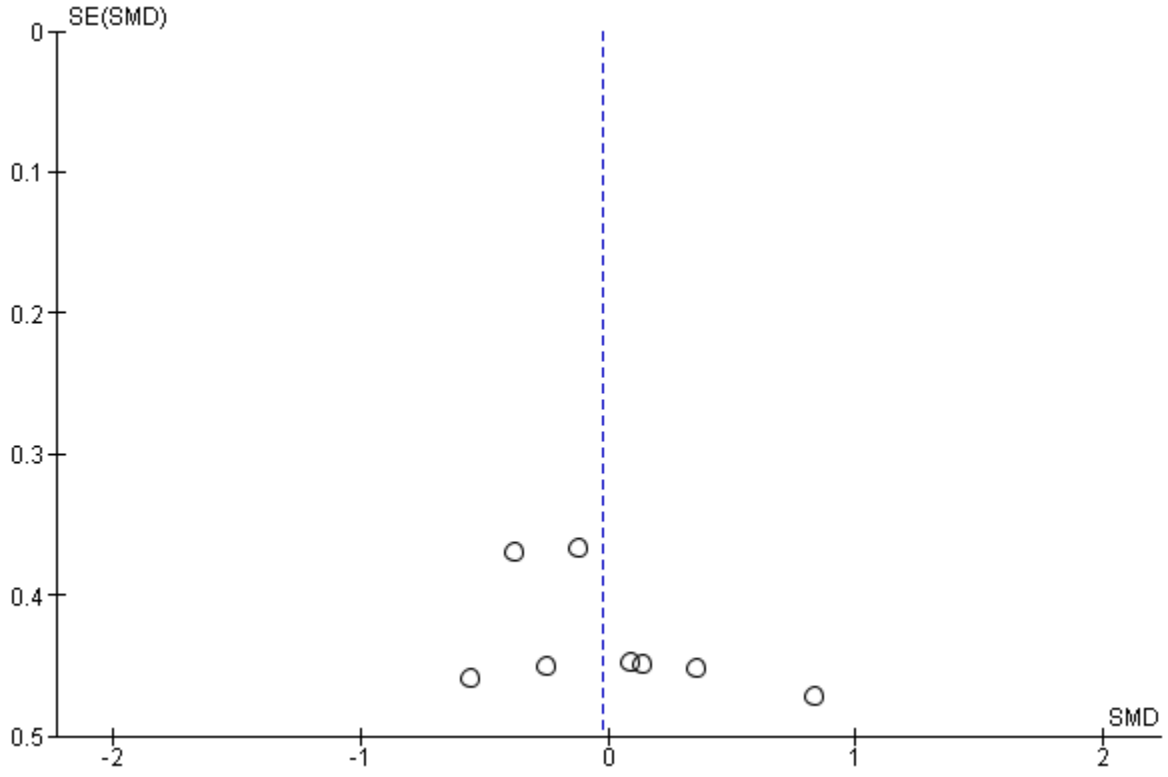


Figure 8. Funnel plot for Pre-experimental trial VAS.

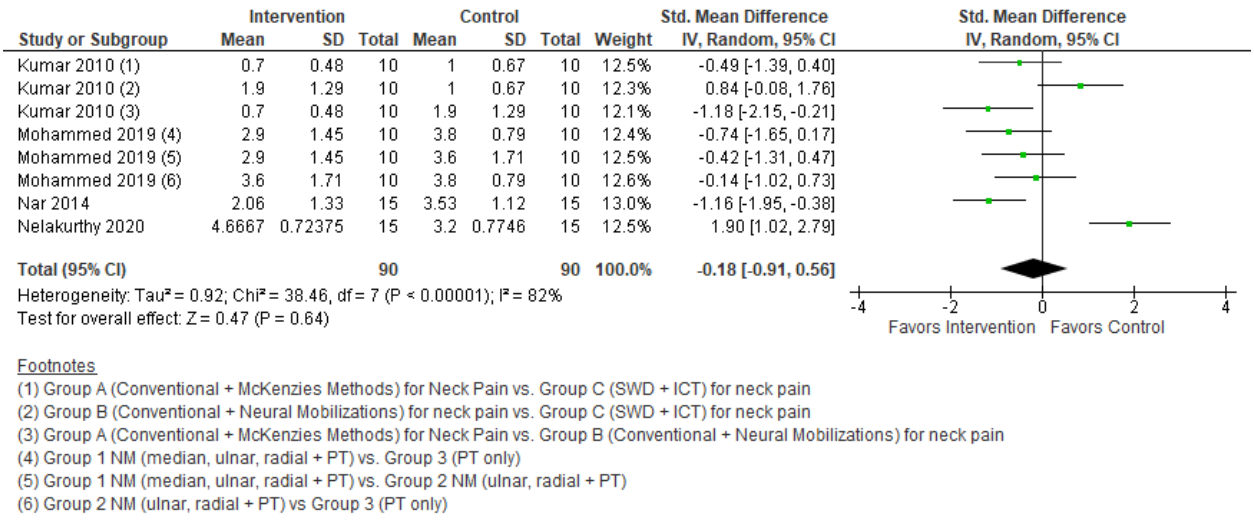


Figure 9. Forest plot for Post-experimental trial VAS Scores.

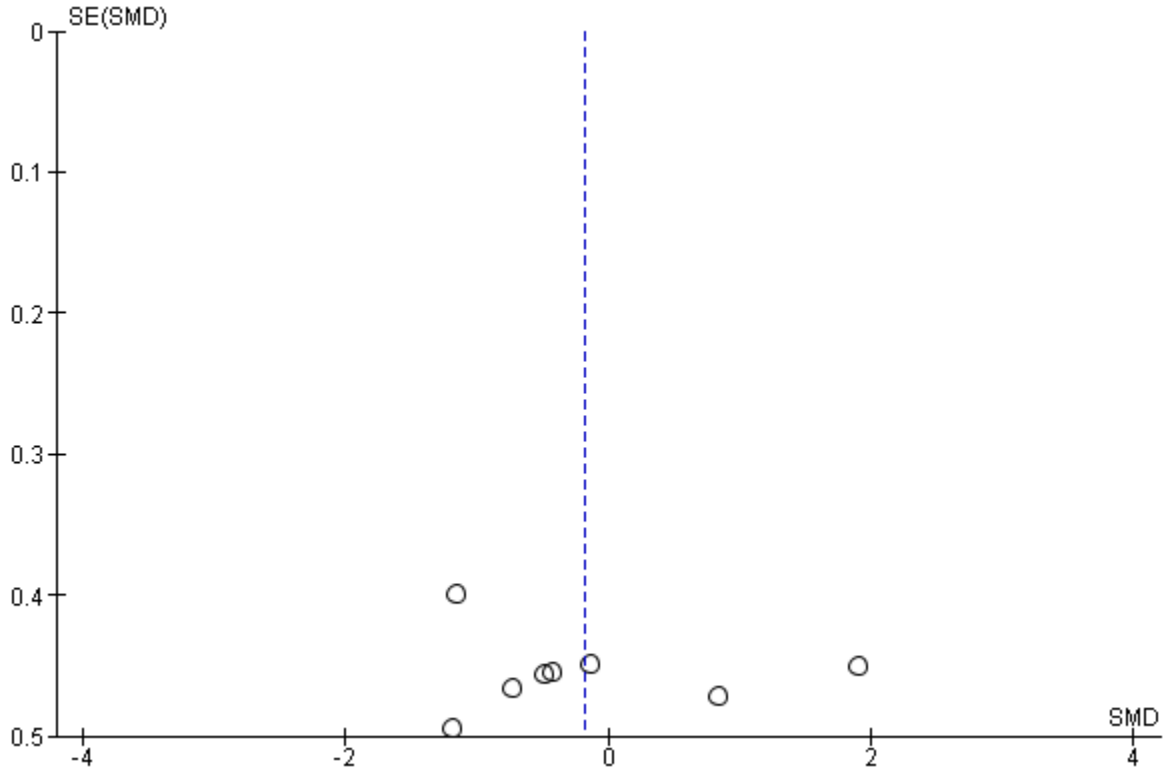
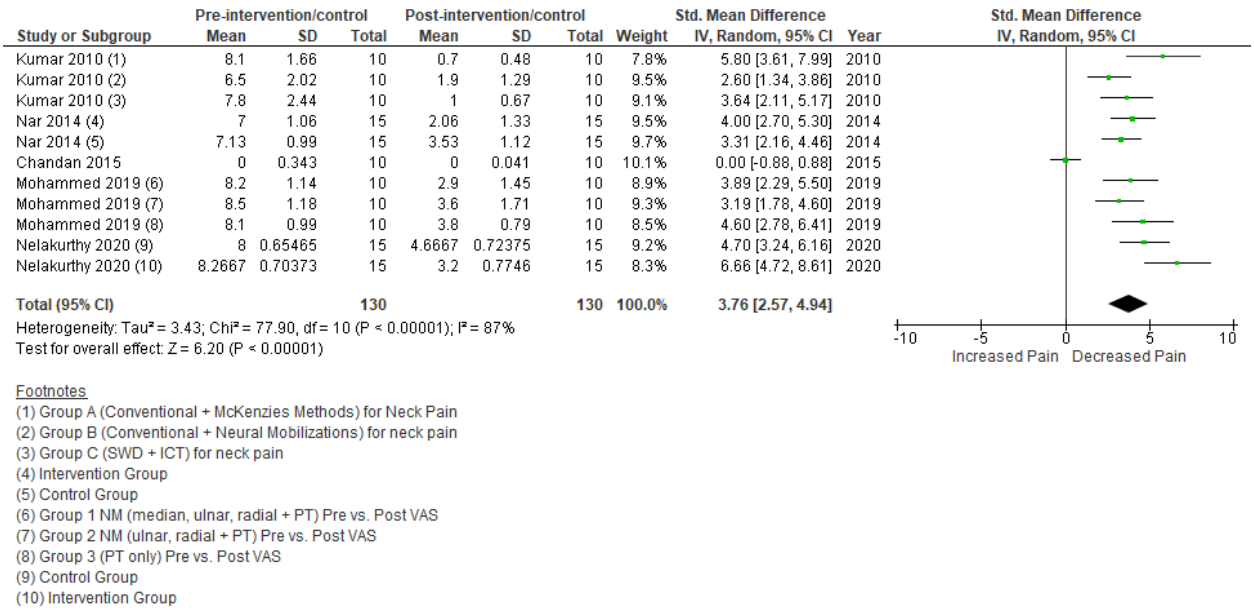


Figure 10. Funnel plot for Post-experimental trial VAS.



Footnotes
(1) Group A (Conventional + McKenzies Methods) for Neck Pain
(2) Group B (Conventional + Neural Mobilizations) for neck pain
(3) Group C (SWD + ICT) for neck pain
(4) Intervention Group
(5) Control Group
(6) Group 1 NM (median, ulnar, radial + PT) Pre vs. Post VAS
(7) Group 2 NM (ulnar, radial + PT) Pre vs. Post VAS
(8) Group 3 (PT only) Pre vs. Post VAS
(9) Control Group
(10) Intervention Group

Figure 11. Forest plot for Pre vs. Post Intervention/Control VAS Scores.

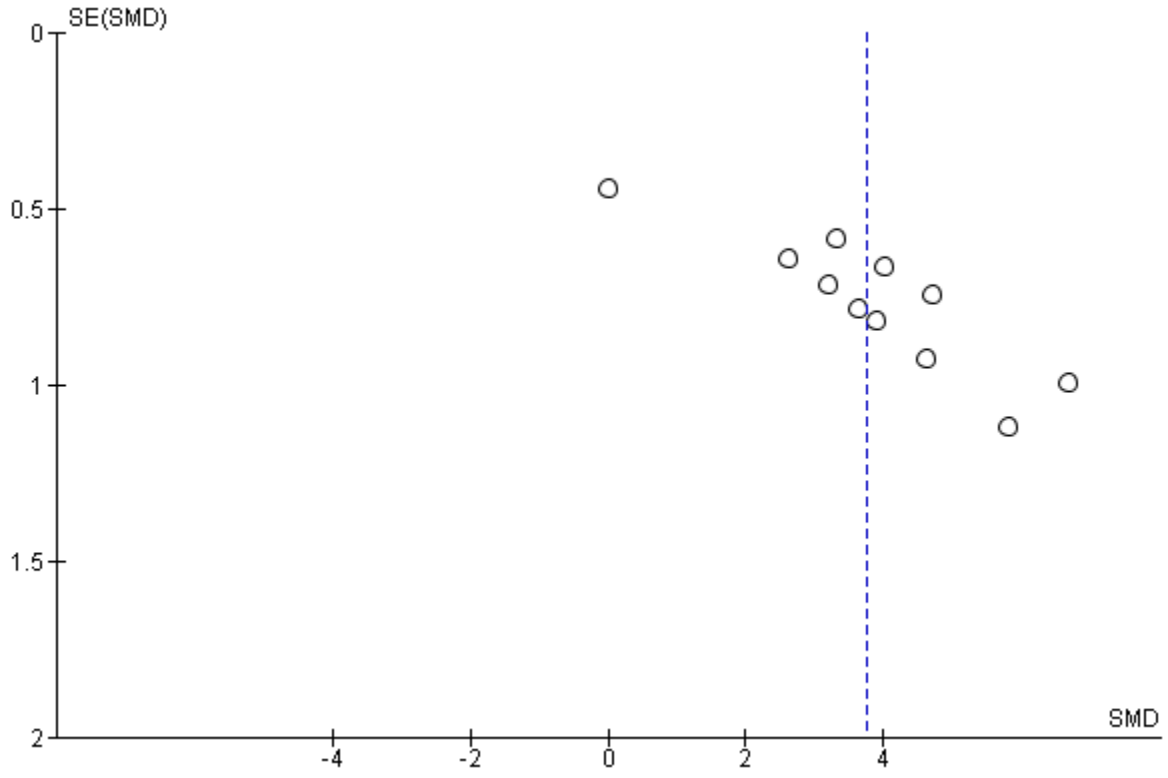


Figure 12. Funnel plot for Pre vs. Post Intervention/Control VAS.

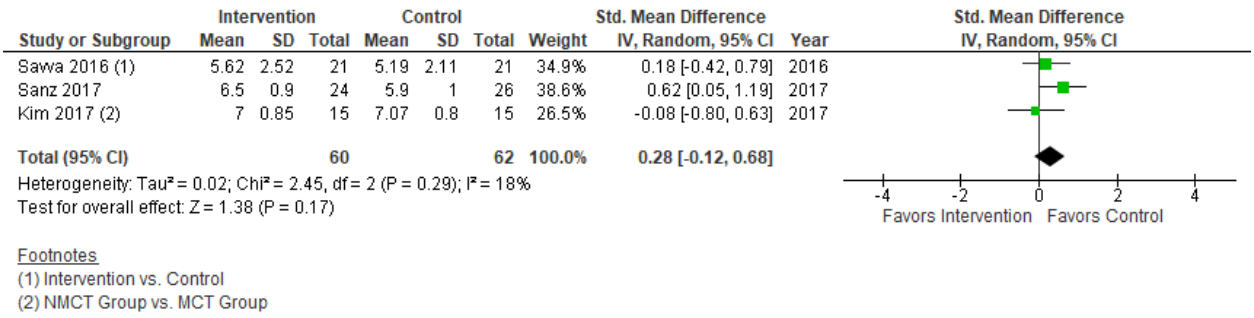


Figure 13. Forest plot for Pre-experimental trial NPRS/NRSP Scores.

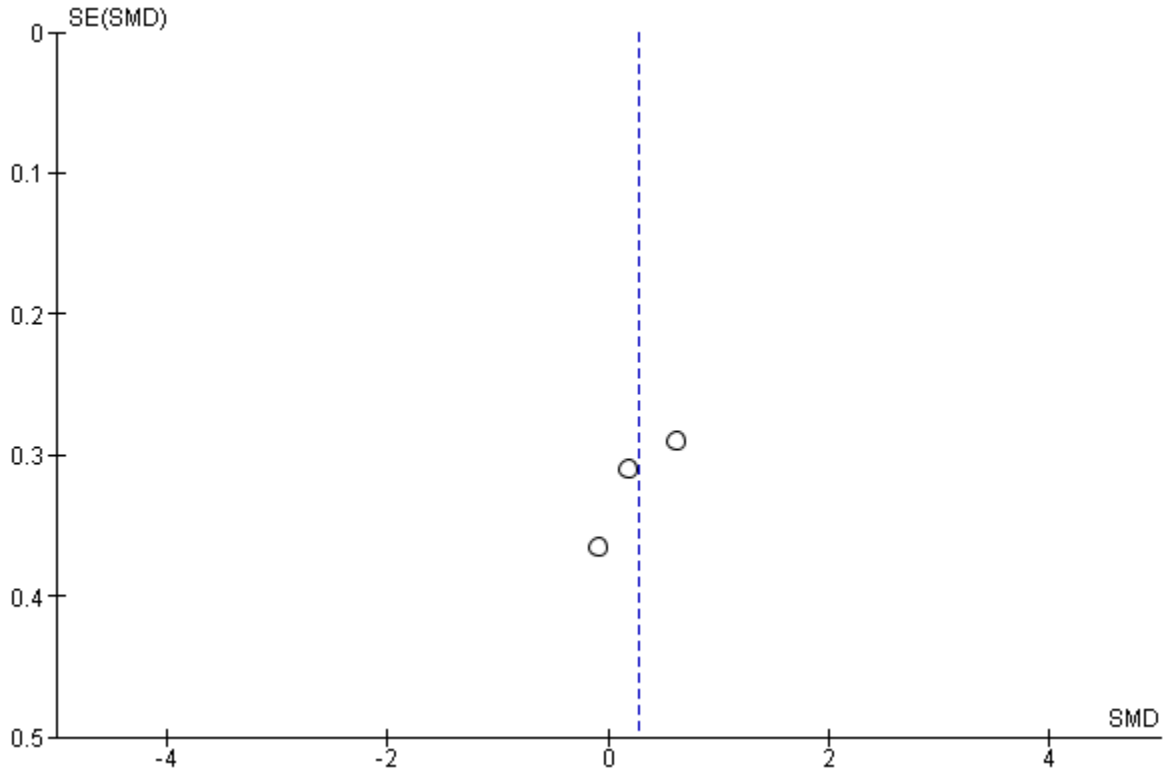


Figure 14. Funnel plot for Pre-experimental trial NPRS/NRSP.

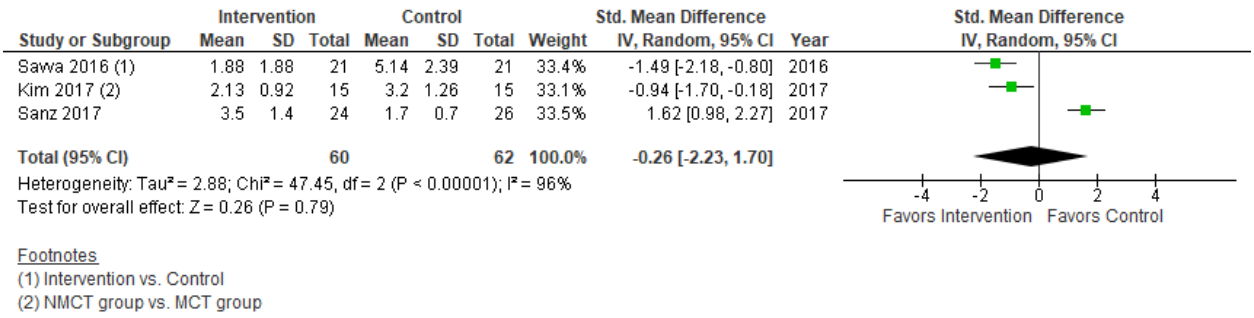


Figure 15. Forest plot for Post-experimental trial NPRS/NRSP Scores.

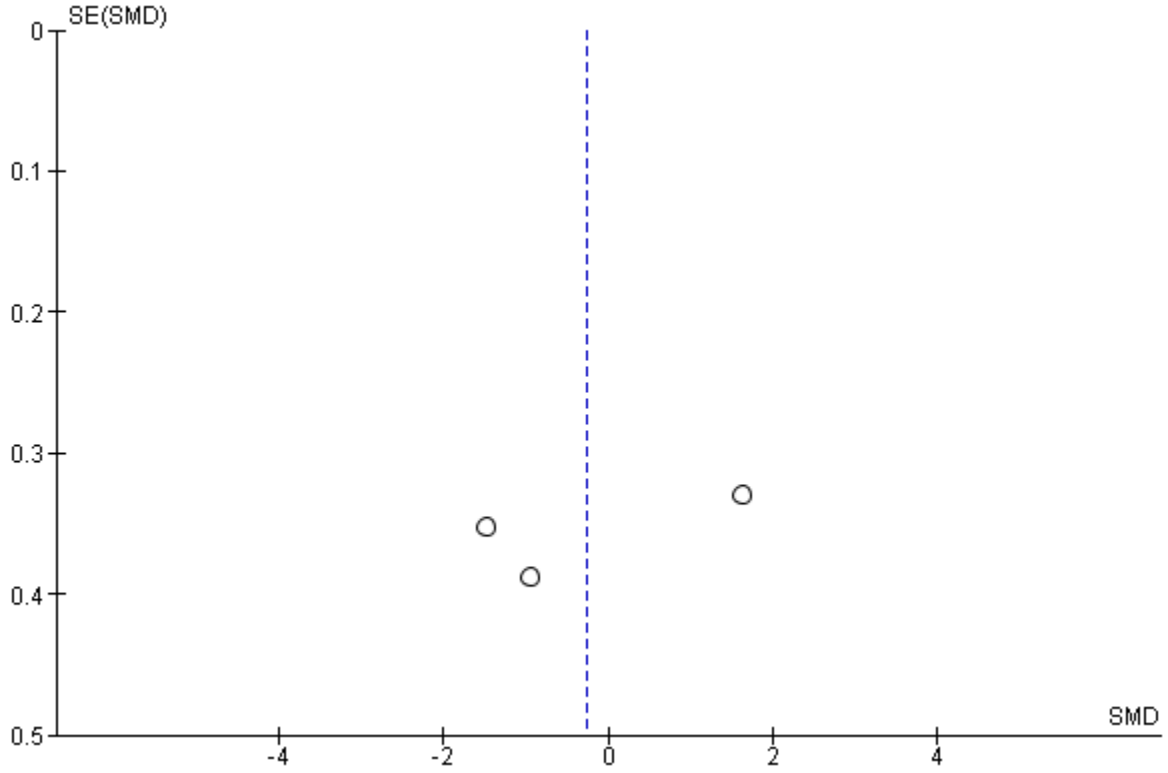


Figure 16. Funnel plot for Post-experimental trial NPRS/NRSP.

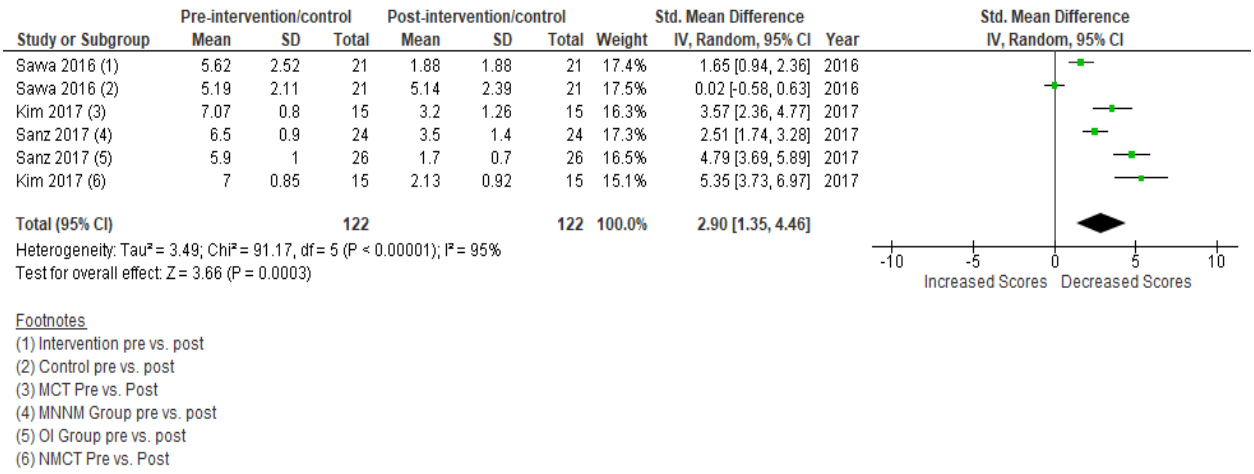


Figure 17. Forest plot for Pre vs. Post intervention/control NPRS/NRSP Scores.

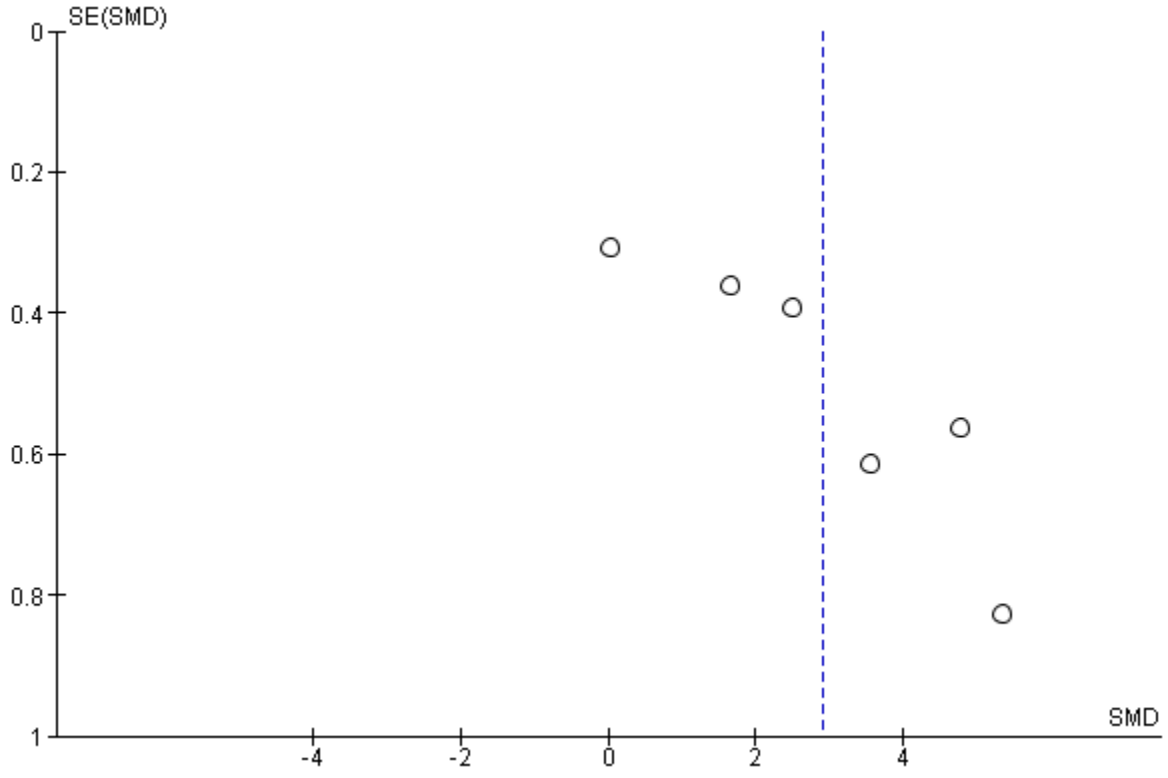


Figure 18. Funnel plot for Pre vs. Post intervention/control NPRS/NRSP.

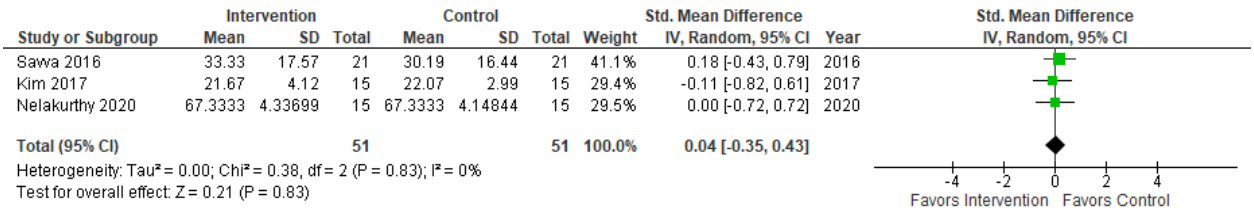


Figure 19. Forest plot for Pre-experimental trial NDI Scores.

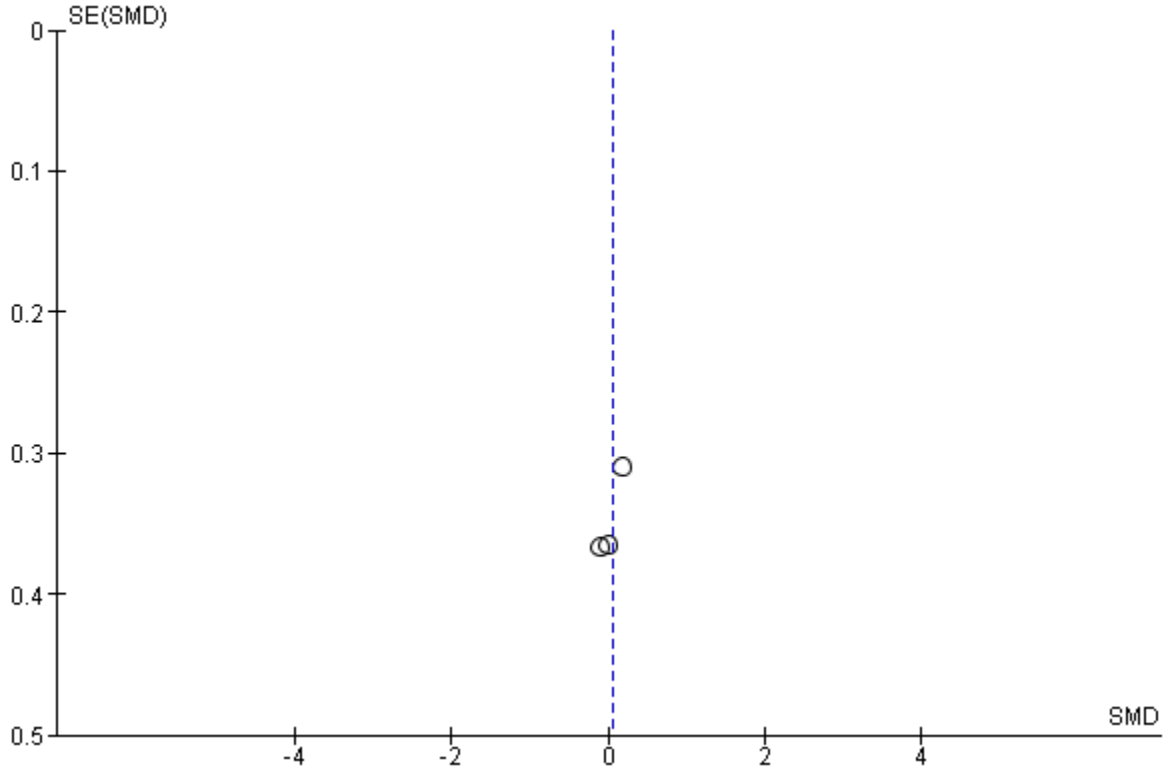


Figure 20. Funnel plot for Pre-experimental trial NDI.

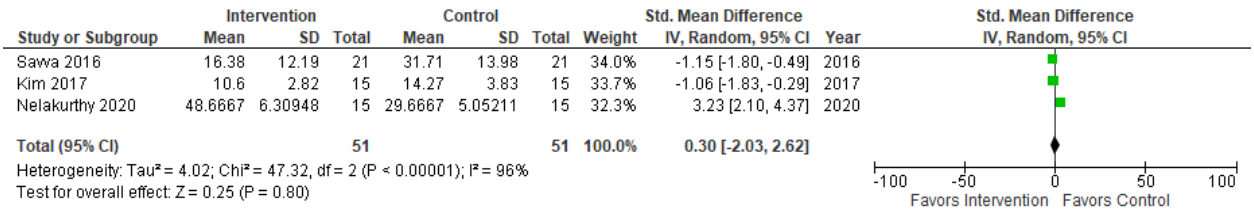


Figure 21. Forest plot for Post-experimental trial NDI Scores.

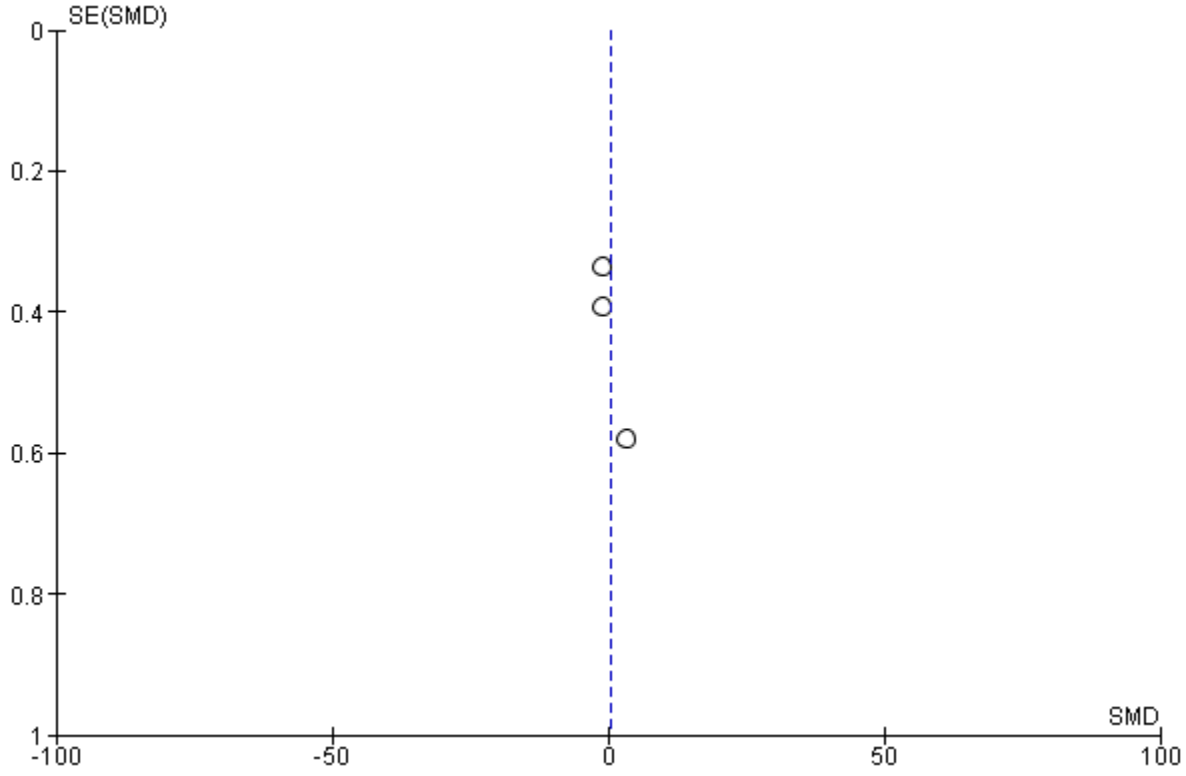


Figure 22. Funnel plot for Post-experimental trial NDI.

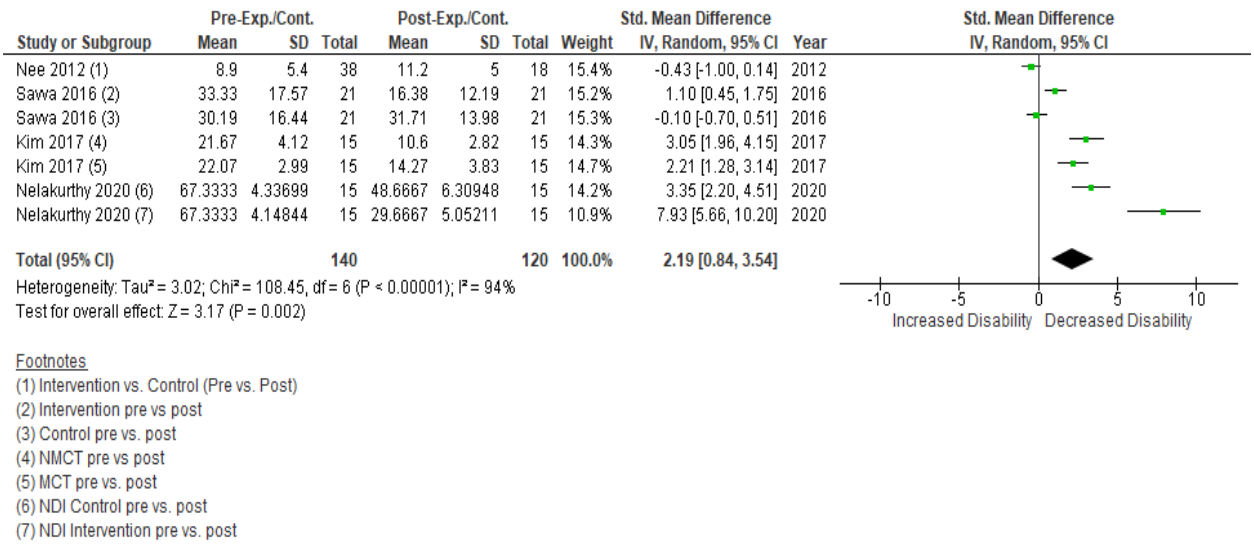


Figure 23. Forest plot for Pre vs. Post intervention/control NDI Scores.

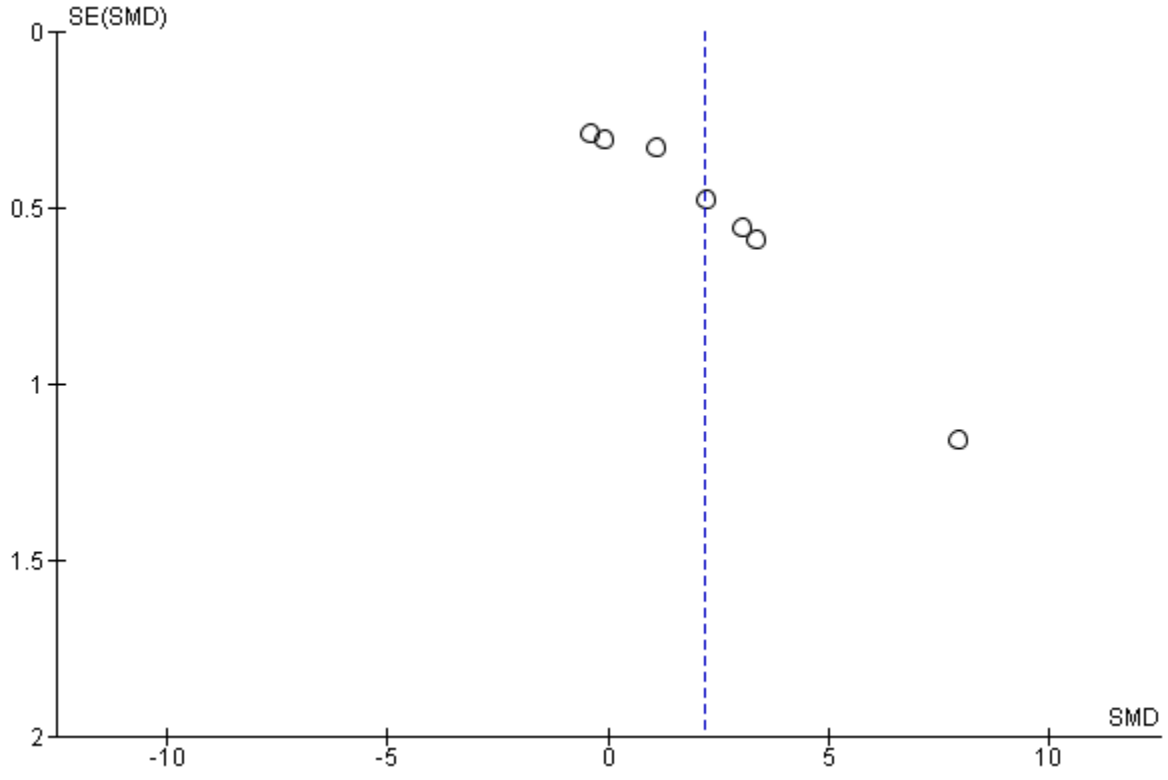


Figure 24. Funnel plot for Pre vs. Post intervention/control NDI.

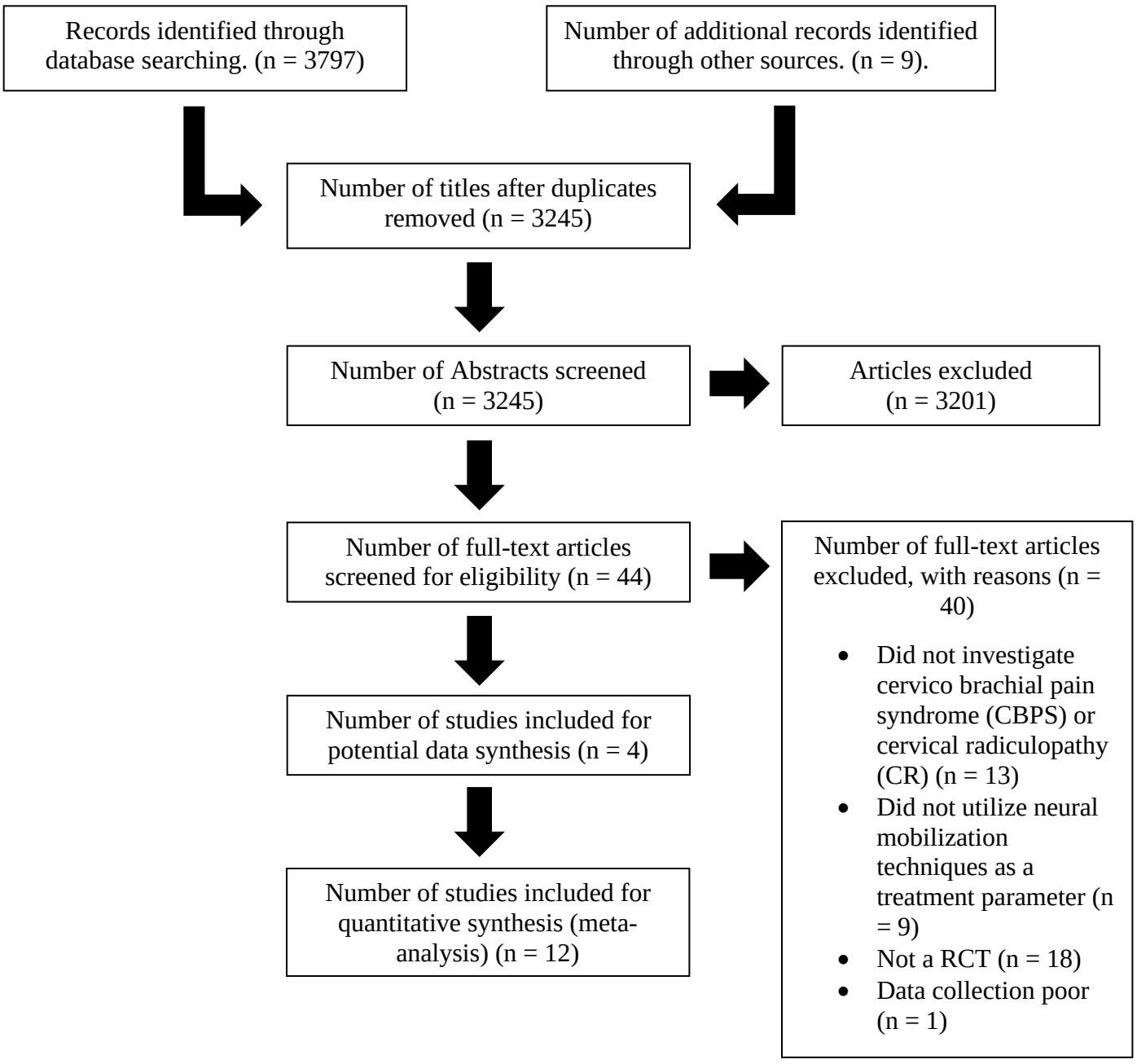


Figure 25: PRISMA flow diagram of selection process.

Table 3.

Summary of Study Demographics & Characteristics.

						Neural Mobilization		Control/Secondary Treatment	
Article	Type of Study	Comparison Groups	CBPS or CR	Total sample size	Sex (Male vs. Female)	Neural Mobilization Sample Size	Intervention Group Age	Control or Secondary Treatment Sample Size	Control or Secondary Treatment Age
Mohammed et al., 2019	Pre test-post test randomized controlled trial	NM ulnar, median, radial nerves & PTP vs. NM ulnar, median nerves & PTP vs. PTP	CR	30	M = 3 F = 27	Group 1 = 10 Group 2 = 10	Overall mean age = 39.53 ± 7.43 (no sig. diff between groups p = .58)	10	Overall mean age = 39.53 ± 7.43 (no sig.diff between groups p = .58)
Sanz et al. 2017	Blinded parallel randomized clinical trial	MNNM vs. 1200 mg/day OI treatment	CBPS	50	M = 18 F = 32	24	32.3 ± 3.7	26	30.8 ± 4.3
Gupta & Sharma, 2012	Repeated test-retest experimental design	MNNM vs. Conventional therapy	CBPS	34	M = 18 F = 16	16	Mean age = 29	18	Mean age = 29.5
Chandan et al. 2015	Randomized trial	MNTM vs CLG	CBPS	20	No data provided	10	No data provided	10	No data provided
Savva et al. 2016	Randomized, controlled, assessor-blinded clinical trial	NM w/ ICT vs. no intervention control	CR	42	M = 21 F = 21	21	Mean ± SD age = 45.2 ± 13.5	21	Mean ± SD age, 49.2 ±8.5
Nelakurthy et al., 2020	Randomized controlled clinical trial	NM with CT vs. CT alone	CBPS	30	No data provided	15	No data provided	15	No data provided
Kumar, 2010	Randomized controlled trial	MM vs. NM vs. CT	CR	30	M = 10 F = 20	10	25-68 years	Group 2 = 10 Group 3 = 10	25-68 years
Marks et al., 2011	Randomized clinical trial	NM vs. CSM	CBPS	20	M = 4 F = 16	10	52.6 (± 12.5)	10	53.7 (± 9.0)
Nee et al., 2012	Randomized controlled trial	MT, NM vs. no intervention	NRNAP	60	M = 22 F = 38	40	47, Mean SD = 8	20	48, Mean SD = 9
Nar, 2014	Experimental study	NM with CT vs. CT	CR	30	M = 9 F = 21	15	49.93 +SD 7.05	15	45.06 +SD 7.46
Kim et al. 2017	Blinded randomized clinical trial	NM with CT vs. CT	CR	30	M = 11 F = 19	15	29.27 (3.34)	15	29.33 (3.07)
Calvo-Lobo et al. 2018	Multicenter, blinded, randomized controlled trial	MNNM vs. CLG vs. Oral ibuprofen	CBPS	105	M = 32 F = 43	24	32.3 ± 3.6	51	33.3 ± 5.0 & 30.8 ± 4.2

Note: NM = neural mobilization; CBPS = Cervico brachial pain syndrome; CR = Cervical radiculopathy; PTP = Physical therapy program; MNNM = Median Nerve Neural Mobilization; OI = Oral Ibuprofen; MNTM = Median Neural Tissue Mobilization; CLG = Cervical Lateral Glide; CT = Conventional therapy; MM = Mackenzie method; CSM = Cervical spine mobilization; NRNAP = Nerve related neck and arm pain; MT = Manual therapy;

Table 4.

Summary of Data Design and Acquisition for Individual Studies.

Study	Measurement variable(s)	Measurement Tool(s)	Method of Acquisition
Mohammed et al., 2019	Pain & Grip Strength	VAS & Hand-held dynamometer	*Pain:* 100mm long scale labeled "no pain" at one end and "worst pain possible" at the other. Patients asked to mark along this line the amount of pain they are experiencing. Given prior to and after study treatment completed for all three groups. *Hand-grip strength:* 3 maximal gripping efforts for 5 sec. each, 15 sec. rest period between trials.
Sanz et al., 2017	Pain, cervical rotational ROM, & upper limb function	NPRS, QuickDASH, CROM	*Pain:* Measured at baseline and 1 hour post-treatment. Measurements taken at baseline, week 4, and week 6 respectively. 11-point scale for patient self-reporting for pain. *Function:* QuickDASH given at baseline and at week 6. Self-reporting questionnaire to measure physical function and symptoms. *CROM:* Measured at baseline and 1 hour after treatment application corresponding to intervention sessions 1 and 30 (baseline and week 6). Measured in degrees for rotation of the cervical spine.
Gupta & Sharma, 2012	Pain, Neck Disability, Cervical related symptoms	VAS, NDI, CBSQ	*Pain, Neck Disability, & Cervical Related Symptoms:* All three self-reported scales/Questionnaires provided at baseline for both groups. All three self-reported scales/questionnaires were then re-taken after completion of 5 treatment sessions.
Chandan et al. 2015	Pain & Disability	VAS, DASH, Pressure algometer	*Pain:* VAS given at baseline, day 0, day 7, and day 14. 10cm horizontal line and patients were asked to mark along this line their perceived level of pain. *Disability:* DASH questionnaire provided at baseline, day 0, day 7, and day 14. Consists of 30 questions corresponding to disability of shoulder, arm, & hand of their severity of perceived level of disability. Scale ranges from "no disability" to "unable". *Pain Pressure:* pain pressure threshold measured along three points of the median nerve. Measured at baseline, day 0, day 7, and day 14. 1st point; just medial to the brachial artery at the elbow joint in the cubital fossa. 2nd point between the head of the pronator teres muscle. 3rd

			point at the wrist medial to the radial artery.
Savva et al., 2016	Pain, disability, function, grip strength, Cervical ROM	NPRS, NDI, PSFS, Hand-dynamometer, CSAROM	All outcomes measures were provided at baseline and at the end of 4 weeks of study period. *Pain:* NPRS used to estimate "current, "best", and "worst" pain intensity over the previous 24 hours. NPRS scores range from 0-10. Higher scores represent greater disability and higher pain levels. *Function:* NDI scores range from 0-100%. Higher scores represent higher levels of disability. PSFS scores range from 0-10. Lower scores represent lower amounts of function. *Grip Strength:* Performed using a hand-held dynamometer. *ROM:* Measured using a universal goniometer. Measurements taken for flexion, extension, ipsilateral lateral flexion, contralateral lateral flexion, ipsilateral rotation, and contralateral rotation.
Nelakurthy et al., 2020	Pain, disability, function,	VAS, NDI, Elbow ROM	*Pain:* VAS provided at baseline and at end of treatment after 2 weeks. *Disability:* NDI provided at baseline and at end of treatment after 2 weeks. *Function:* Elbow ROM measured at baseline and end of treatment after two weeks. Performed utilizing ULTT1 test.
Nar, 2014	Pain	VAS	*Pain:* 10cm horizontal line where patients were asked to mark their perceived level of pain from 0 "no pain" to 10 "worst pain". VAS was given pre-test and post-test after 10 days of treatment.
Nee et al., 2012	Pain, function, disability, & overall change	GROC, NPRS, NDI, & PSFS	*Pain:* Measured using the NPRS format. Patients would record their pain intensity over the past 24 hours for current, highest, and lowest levels of perceived pain. Given to participants at the start of each treatment session. *Function/Disability:* Measured utilizing the NDI and PSFS scales. Provided at the beginning of each treatment session. Used to measure if symptoms were provoked or relieved using the studies treatment sessions. *Overall Change:* Measured utilizing the GROC scale. Allows for patients to report their perceived self-reported improvement on a 15-point scale. Scale ranges from (-7 "a very great deal worse") to (0 "no change") to (+7 "a very great deal better"). Patients that reported a ≥ +4 change

			("moderately better") was considered improvement. Given to patients after each treatment session.
Marks et al. 2011	Pain & Function	VAS & CSAROM	*Pain:* Measured at rest, with active cervical ROM, and while performing neurodynamics. Measures were taken pre-and-post intervention and one week later. *Function:* Measured CSAROM for flexion, extension, rotation, and lateral flexion. Each measurement performed three times.
Kumar, 2010	Pain & Function	VAS & CSAROM	*Pain:* Given to patients at baseline, fifth, and tenth days. Two separate VAS scales were utilized. One for neck pain and one for arm pain respectively. *Function:* Measured through CSAROM at baseline, fifth and tenth days. Measurements include flexion, extension, rotation, ipsilateral and contralateral flexion.
Kim et al. 2017	Pain, Function, ROM & deep flexor muscle endurance.	NPRS, NDI, CROM & deep flexor muscle endurance	*Pain*: NPRS given to patients pre-treatment, four weeks, and eight weeks after the experiment. A single-line 0-10 NPRS scale was used and patients self-reported based on instructions provided. *Function*: CROM measured pre-treatment, four weeks, and eight weeks after the experiment. Motions measured include cervical flexion, extension, side bending and rotation. *Disability*: NDI given to patients pre-treatment, four weeks, and eight weeks after the experiment. Questionnaire with 10 questions based on Oswestry Index with scoring from 0-5. Items include reading, headache, concentration, work, driving, sleeping, leisure life, pain intensity, ordinary life and raising an object.
Calvo-Lobo 2018	Pain, Function & ROM	NRSP, Quick DASH & ICR CROM	*Pain* NRSP given to participants before and 1 hour post-treatment at baseline, 3 weeks and 6 weeks. *Function*: ICR CROM measured pre-treatment and 1 hour post-treatment at baseline and 6 weeks. *Disability*: Quick DASH given to participant's pre-treatment baseline and after the last treatment session at 6 weeks. Only one assessment performed.

Note: VAS = Visual Analog Scale: CROM = Cervical Range of Motion; NRSP = Numeric Rating Scale for Pain; NDI = Neck Disability Index; CBSQ = Cervicobrachial Symptom Questionnaire; DASH = Disability of Arm, Shoulder & Hand; NPRS = Numeric pain rating scale; PSFS = patient-specific Functional Scale; CSAROM = Cervical Spine Active Range of Motion; ULTT1 = Upper Limb Tissue Tension test for median nerve; GROC = Global Rating of Change Scale; ICR = Ipsilateral Cervical Rotation;

Table 5.

PEDro Scale Criteria and Associated Studies

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total out of 10
Kumar S. 2010	**Y**	**Y**	**N**	**Y**	**N**	**N**	**N**	**N**	**N**	**Y**	**Y**	**4/10**
Marks et al., 2011	**Y**	**Y**	**Y**	**Y**	**N**	**N**	**N**	**Y**	**N**	**Y**	**Y**	**5/10**
Nar N., H. 2014	**N**	**Y**	**N**	**N**	**N**	**N**	**N**	**N**	**N**	**Y**	**Y**	**3/10**
Nee et al., 2012	**Y**	**Y**	**Y**	**Y**	**N**	**N**	**Y**	**Y**	**Y**	**Y**	**Y**	**7/10**
Gupta & Sharma, 2012	**N**	**Y**	**Y**	**Y**	**N**	**N**	**N**	**Y**	**N**	**Y**	**N**	**5/10**
Nelakurthy et al., 2020	**Y**	**Y**	**Y**	**N**	**N**	**Y**	**Y**	**Y**	**Y**	**Y**	**Y**	**7/10**
Savva et al., 2016	**Y**	**Y**	**Y**	**Y**	**N**	**N**	**Y**	**Y**	**Y**	**Y**	**Y**	**7/10**
Chandan et al., 2015	**N**	**Y**	**Y**	**Y**	**N**	**N**	**N**	**Y**	**Y**	**Y**	**Y**	**7/10**
Sanz et al., 2017	**Y**	**Y**	**Y**	**Y**	**Y**	**N**	**N**	**N**	**N**	**Y**	**Y**	**6/10**
Mohammed et a., 2019	**Y**	**Y**	**N**	**Y**	**N**	**N**	**N**	**Y**	**Y**	**Y**	**Y**	**6/10**
Kim et al. 2017	**Y**	**Y**	**Y**	**Y**	**N**	**N**	**N**	**Y**	**Y**	**Y**	**Y**	**7/10**
Calvo-Lobo 2018	**Y**	**Y**	**Y**	**Y**	**N**	**Y**	**Y**	**N**	**Y**	**Y**	**Y**	**7/10**

- **Question 1 not included in scoring due to PEDro Scale guidelines (Physiotherapy Evidence Database, 2021).**

Table 6

Downs & Black Scale with Individual Study Evaluations.

Study	Kumar S. 2010	Nar N., H. 2014	Nee et al., 2012	Gupta & Sharma, 2012	Nelakurthy et al., 2020	Savva et al., 2016	Chandan et al., 2015	Sanz et al., 2017	Mohammed et a., 2019	Kim et al. 2017	Calvo-Lobo 2018	Marks et al. 2011
Categorical Question												
Q1	1	1	1	1	1	1	1	1	1	1	1	1
Q2	1	1	1	1	1	1	1	1	1	1	1	1
Q3	1	1	1	1	1	1	1	1	1	1	1	1
Q4	1	1	1	1	1	1	1	1	1	1	1	1
Q5	2	2	2	2	2	2	2	2	2	2	2	2
Q6	1	1	1	1	1	1	1	1	1	1	0	1
Q7	1	1	1	0	1	1	0	1	1	1	1	1
Q8	0	0	1	0	0	0	0	1	0	0	0	0
Q9	0	0	1	1	0	1	0	1	0	0	1	0
Q10	1	1	1	0	1	0	1	1	1	1	1	1
Q11	1	1	1	1	1	1	1	1	1	1	1	0
Q12	1	1	1	1	1	1	1	1	1	1	1	0
Q13	1	1	0	1	1	1	1	1	1	1	1	1
Q14	0	0	1	1	0	1	1	1	1	1	1	1
Q15	0	0	1	0	0	1	0	1	0	0	0	0
Q16	1	1	0	0	1	1	0	1	1	1	1	1
Q17	1	1	1	1	1	1	0	1	1	1	1	1
Q18	1	1	1	1	1	1	1	1	1	1	1	1
Q19	1	1	0	0	1	0	1	0	1	1	0	1
Q20	1	1	1	1	1	1	1	1	1	1	1	0
Q21	1	1	1	1	1	1	1	1	1	1	1	1
Q22	1	1	1	1	1	1	1	1	1	1	1	1
Q23	1	1	1	1	1	1	1	1	1	1	1	1
Q24	0	0	1	0	0	1	0	0	0	0	0	0
Q25	1	1	1	1	1	1	0	1	1	1	0	0
Q26	0	0	1	1	0	0	0	1	0	0	0	0
Q27	1	1	1	1	1	1	1	1	1	1	0	0
Level of Evidence	2	2	4	2	2	2	3	4	3	4	2	2

Modified Downs & Black Scale (Downs & Black, 1998).

Discussion

The primary purpose of this systematic review and meta-analysis was to critically assess the level of evidence of the literature and to determine if upper extremity NM alone or combined with a rehabilitation program is an effective therapeutic intervention in the treatment of CBPS or CR. Twelve studies met the inclusion and exclusion criteria. The primary findings of this systematic review and meta-analysis were individuals with CBPS or CR performing NM with or without secondary rehabilitation protocols did not show a significant difference in pain reduction for VAS, NPRS, NRSP between groups and between studies. Within groups comparisons between baseline and post-study recordings showed promise for clinically significant data for VAS, NPRS and NRSP in pain reduction. The systematic review and meta-analysis also showed no significant difference for functional testing utilizing the NDI scale for NM groups compared to control groups but did show significant differences within groups comparison. With the limited amount of literature investigating pain and functional ability utilizing upper extremity NM, caution should be taken when interpreting the findings of this study.

The systematic review and meta-analysis findings of this study are relevant for medical professionals and individuals diagnosed with either CBPS or CR. As previously mentioned in the literature, incidence for CBPS or CR is "83 per 1000 for the population in its entirety, with an increase in prevalence during the fifth decade of life (203 per 1000) (Sambyal & Kumar, 2013) (Savva, Giakas, Efstathiou, & Karagiannis, 2016)." CBPS and associated cervical radiculopathy (CR) symptoms is one of the most frequent upper extremity and neck related complaints. It is stated by Sambyal & Kumar 2013, "50% of the population will experience neck and upper extremity pain at some point in their lifetime". With relatively high incidence rates especially among older individuals, more effective and correct treatment plans are needed utilizing the most

effective treatment methods to reduce patient costs. NM as found in this study show to be an effective therapeutic intervention however, NM alone may not be the most effective treatment method for CBPS and CR patients.

Cautionary discretion must be taken when comparing the studies obtained due to their difference in protocol, sample size, technique differences, and age of patients included. In a study performed by (Kim, Chung, & Jung, 2017), the authors investigated the effects of neural mobilizations with manual cervical traction on CR patients for pain, disability, ROM and deep flexor endurance. Their results showed a significant decrease in NDI over time for the NM with cervical traction (NMCT) group compared to that of the isolated manual cervical traction (MCT). Their results showed a significantly larger decrease in the NMCT group compared to that of the MCT group (Kim, Chung, & Jung, 2017). In another study performed by (Savva, Giakas, Efstathiou, & Karagiannis, 2016), the authors investigated similar outcomes measures with a different treatment method for the NDI. They investigated the effects of NM and intermittent cervical traction on CR. Their results showed a significant improvement in NDI scores. It is plausible with these two studies resulted in similar results due to the use of NM however, further research is needed to determine if NM alone is an effective therapeutic intervention or if other factors contribute to the similar findings presented.

When looking at VAS, in a study done by Mohammed et al. (2019), their findings resulted in a significant decrease in VAS pain scores within each group with no significant difference in VAS scores between the three groups comparison. Group 1 performed NM for the ulnar, median, and radial nerves with a physical therapy program, Group 2 performed NM for the ulnar and median nerves with a physical therapy program, and group 3 performed a physical therapy program alone (Mohammed, Elsayed, Elbalawy, & Ghally, 2019). Once again, we can

see a difference in protocols and interventions utilized between studies with the physical therapy program remaining the same across all three groups. Compared to a study done by Kumar (2010), similar VAS scores comparisons were seen utilizing a different protocol for control groups and intervention groups. Group A performed conventional method treatment with McKenzie's methods (exercises/manipulation), group B performed conventional method therapy along withNM, and group C was treated with short wave diathermy and intermittent cervical traction. Similar results reported by both studies may be due to the generalizability of the VAS and each patients perceived level of pain. Each patient may register different levels of perceived pain which could in turn sway results of VAS recordings, thus caution must be taken when interpreting the data from studies using VAS as an isolated outcomes measure.

As described above, similar results were seen for NDI and VAS scores between these two studies respectively. Differences in mean ages for both control and intervention, sample size, and protocol utilized are noted. Similar results with different study protocols, age groups and intervention style between respective studies may suggest that NM utilized in the rehabilitation setting provides mixed results dependent on the goal trying to be achieved by the patient.

Limitations

A multitude of limitation must be taken into consideration when reviewing this systematic review and meta-analysis. There is a lack of randomized controlled trials utilizing similar protocols and interventions regarding NM. Secondly, future studies should utilize similar outcomes measures and similar intervention and control protocols to increase the potential of cross-study comparisons. Thirdly, multiple studies used in this systematic review and meta-analysis did not perform NM as a stand-alone treatment. More studies should be investigated using only NM as a treatment method compared to a control group. A further limitation of the

studies utilized for this systematic review and meta-analysis is that there is a lack of sham treatment protocols for control groups. The control groups within this study either utilized a rehabilitation protocol, oral medication, or performed no treatment at all. Another limitation is that a single author extracted all data from the studies used within this systematic review and meta-analysis, which could increase the potential risk-of-bias in this study. Mean age of participants between studies varied which may contribute to increased variability of data obtained. Participants within a strict mean age range may produce better between study comparison data.

Summary

Summary of this systematic review and meta-analysis identified that NM as a rehabilitation technique for CBPS and CR, provided mixed results dependent upon outcome measure investigated, protocol utilized, and treatment group performing the technique. Future studies investigating the effect of NM on CBPS and CR should utilize homogenous protocols, similar intervention techniques, and homogenous patient populations to help determine the best application of NM. Further studies should also attempt to implement a sham treatment protocol for control groups to further strengthen validity of NM on CBPS or CR. This would allow clinicians to determine if NM could provide a clinically significant difference to their patients with CBPS or CR. Further research must be done investigating NM as a clinical therapeutic intervention in treating CBPS and CR patients.

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