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Cervical and Thoracic Spine Disorders

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Impact.....

It is estimated that 14% to 71%(1) of the general population experience an episode of cervical pain at some point during their lifetime.(2-11) and pain recurrence is common.(12) The annual prevalence of cervical pain has been reported to be 30% to 50%.(13) The annual incidence of cervical pain ranged from 10.4% to 21.3%.(14) Cervical pain is usually self-limiting and there are many factors that influence outcomes in patients.(15) Out of the 291 conditions studied in Global Burden of Disease 2010 Study, neck pain was found to rank 21st in terms of overall burden and 4th in terms of overall disability.(16)

Cervical pain accounts for a large portion of direct and indirect costs to the health care system (17) resulting in a need to understand the condition's natural history and what interventions for treatment of these patients are beneficial. Prevention of neck and thoracic spine conditions are also addressed towards the end of this guideline.

Overview……

Recommendations for assessment and treatment of adults with cervical (neck) and thoracic (middle back) spine problems are presented in this clinical practice guideline. Compared with low back pain, there are relatively few quality trials evaluating cervical pain and still fewer that evaluate work-related cervical pain. Therefore, studies that include non-workers' compensation patients were used to develop these recommendations.[i] Industry-sponsored trials were also included.[ii] Most studies did not delineate specific diagnoses for cervical pain as a precise anatomic source for most cervical pain episodes is unknown. The lack of specific pathophysiological correlates has resulted in treatment classifications schemes that have been at least partially validated.(18, 19)

Topics include the initial assessment and diagnosis of patients with acute, subacute, and chronic cervical and thoracic pain problems that are potentially work-related, identification of red flags that may suggest the presence of a serious underlying medical condition, initial management, diagnostic considerations and special studies to identify clinical pathology, work-relatedness, modified duty and activity, and return to work, as well as further management considerations including delayed recovery. The majority of peer-reviewed literature categorizes pain as acute (<1 month duration), subacute (1 to 3 months duration), and chronic (>3 months duration). These definitions have been adopted throughout this document. In instances where a study used a different classification, those articles are grouped into one or more of these three categories for purposes of uniformity.

Algorithms for patient management are included. This guideline's master algorithm schematizes how practitioners may generally manage acute, subacute, or chronic cervical and thoracic spine disorders. The text, tables, and numbered algorithms all expand upon the master algorithm.

Summary of Recommendations and Evidence……

The following is a general summary of the recommendations contained in this guideline:

- The initial assessment of patients with cervical and thoracic spine problems focuses on detecting indications of potentially serious disease, termed "red flags" (i.e., fever, serious neurologic involvement, or major trauma).
- In the absence of red flags, imaging and other tests are not recommended in the first 4 to 6 weeks of cervical and thoracic spine symptoms, as it almost never results in a meaningful change in clinical management. Nonprescription medication or an appropriately selected nonsteroidal anti-inflammatory drug (NSAID), appropriate adjustment of physical activity if needed, and the use of thermal modalities such as heat and/or cryotherapies can safely relieve discomfort. Some utilize manipulation in this phase.

[i]Many trials exclude workers' compensation patients. This necessitates relying on those trials for evidence-based guidance for injured workers. However, readers may infer results may differ between those with compared to those without compensation with most literature suggesting compensation imparts somewhat worse outcomes.

[ii]Many studies that focus on pharmaceuticals and specific devices are industry sponsored. Each study must be evaluated on its own merits, including those not sponsored by industry. In certain areas, this also may have made little difference as the comparisons were between the medication and placebo and the results may be stark. However, in other studies, comparison groups may have been suboptimally treated (e.g., a low-dose of ibuprofen) and produced a bias in favor of the medication or device. In addition, industry-sponsored studies have sometimes been shown to have better results and lower complication rates than studies conducted by independent investigators. In other situations, the industry-sponsored studies are superior and stand on their own merit.

- In the absence of red flags, health care professionals can effectively manage most cervical and thoracic spine problems conservatively.
- An early mechanical evaluation using repeated end-range test movements to determine the presence or absence of a directional preference and pain centralization has been suggested to guide directional exercise treatments that are associated with better outcomes, although the quality studies have only been done on the lower back.
- At the first visit, the physician or other health care provider should assure the patient that cervical and thoracic pain is common, has an excellent prognosis, and in most cases is not debilitating on a long-term basis. Patients with elevated fear avoidance beliefs may require additional instructions and interventions to be reassured of this prognosis. Patients with elevated fear avoidant beliefs are likely candidates for utilization of tools to measure the beliefs. Patients with significantly elevated beliefs, particularly combined with early failure to progress as expected, are considered candidates for early referral for allied health referrals to prevent conversion to a chronic pain syndrome (see Chronic Pain guideline).(20, 21) Theoretically, this reassurance has the potential to decrease the probability of the patient developing a chronic pain syndrome.
- To avoid undue weakness, atrophy, contractures, and debilitation from inactivity, some activity or job modification may be helpful in the acute period. However, bed rest is not recommended for essentially all cervical and thoracic pain and cervical radiculopathy patients other than those with unstable fractures or similar problems with pending neurological catastrophe. Maintaining ordinary activity, as tolerated, leads to the most rapid recovery.
- All patients should be encouraged to return to usual activities and work as soon as possible as evidence suggests this leads to the best outcomes for all spine disorders. This process may be facilitated with temporary modified (or alternative) duty for acute and subacute pain, particularly if job demands exceed patient symptom tolerance. Full-duty work is a reasonable option for patients with acute and subacute pain syndromes with low physical job demands and the ability to control such demands (e.g., alternate their posture) as well as for those with less severe presentations. Full duty work is appropriate for those with chronic neck and thoracic pain syndromes who do not have objective evidence that work would cause a significant risk of substantial harm that is imminent (American's with Disabilities Act), with the patient deciding whether the rewards of work despite symptoms is worth the "cost" of the symptoms.
- Strengthening exercises have the best evidence of efficacy among the exercise regimens, whether for acute, subacute, or chronic cervical and thoracic pain patients. This contrasts with low back pain where aerobic exercise has the greatest evidence of efficacy.
- Non-specific stretching is not recommended as it is not helpful for treatment of cervical and thoracic pain. However, directional exercise and slump stretching exercises may be helpful. Strengthening exercises, including cervical stabilization exercises, are recommended, but not until the acute period of cervical and thoracic pain has subsided.
- There is evidence of efficacy for manipulation/mobilization in combination with exercise for treatment of non-specific neck pain for short-term pain relief and increased range of motion (ROM) compared to manipulation and/or mobilization alone or in combination.
- There is some evidence for efficacy of acupuncture in chronic pain patients.
- Many invasive and non-invasive therapies are intended to cure or manage pain, but no strong evidence exists that they accomplish this as successfully as therapies that focus on restoring functional ability without focusing on pain. In those cases, the traditional medical model of "curing" the patient does not work well. Furthermore, patients should be aware that returning to normal activities most often aids functional recovery.
- Patients should be encouraged to accept responsibility for managing their recovery rather than expecting the provider to provide an easy "cure." This process will promote using activity rather than pain as a guide, and it will make the treatment goal of return to occupational and non-occupational activities more obvious.
- If symptoms persist without improvement, further evaluation is recommended.
- Within the first 3 months of cervical and thoracic spine symptoms, only patients with evidence of severe spinal disease or severe debilitating symptoms and physiologic evidence of specific nerve root or spinal cord compromise confirmed by appropriate imaging studies, can be expected to potentially benefit from surgery.
- Quality evidence exists from trials of lumbar spine patients, and is believed to apply to patients with cervical and thoracic spine pain, indicating that patient outcomes are not adversely affected by delaying surgery for weeks or a few months and continued conservative care is encouraged in patients with stable or improving

neurologic deficits who desire to avoid surgery. However, patients with either moderate to severe neurological deficits that are not improving or trending to improvement at 4 to 6 weeks may benefit from earlier surgical intervention. Those with progressive neurological deficit(s) are believed to have indications for immediate surgery. Those with severe deficits that do not rapidly improve are also candidates for earlier testing and referrals. Those with myelopathy also are candidates for early surgical intervention.

- Nonphysical factors (such as psychiatric, psychosocial, environment including non-workplace and workplace issues, socioeconomic, litigation, or advocagenic problems) should be investigated and addressed in cases of delayed recovery or delayed return to work.
- Physicians can greatly improve patient clinical responses by providing assurance, encouraging activity, and emphasizing that more than 90% of cervical and thoracic spine pain resolves without any specific therapies. While patients may be looking for a clear-cut diagnosis for their axial spine pain, the risk from a suggested "cure" for this assumed diagnosis can result in failed expectations, which may be a worse outcome than their symptoms.
- Physicians should be aware that "abnormal" findings on x-rays, magnetic resonance images, and other diagnostic tests are so common by age 40, they are considered normal. There are higher rates of "abnormalities" in asymptomatic people in the cervical spine compared to the thoracic spine. Bulging disc prevalence continues to increase after age 40, and by age 60 will be encountered in 80% of patients' cervical spines. This requires that a careful history and physical examination be conducted by a skilled physician in order to correlate historical, clinical, and imaging findings prior to assigning the finding on imaging to a patient's complaints. It is recommended that physicians unable to make those correlations, and thus properly educate patients about these complex issues, should defer ordering imaging studies to a qualified consultant in musculoskeletal disorders (MSDs). Without proper education on prevalence, treatment, and prognosis, patients may become fixated on "fixing" their "abnormality" found on imaging (which may in fact be a completely normal condition) and thus iatrogenically increase their risk of developing chronic pain.

Basic Principles and Definitions……

Active Therapy: The term "active therapy" is generally thought of as the patient taking an active role in the treatment of their spine pain via various modalities. Although there is not one specific treatment defined by this term, it may include psychological, social, and educational components in conjunction with therapeutic exercises.(22) Therapeutic exercises could include light aerobic activity, directional exercises, muscle reconditioning (light-weight lifting or resistance training), physiotherapy,[iii] and active physical or occupational therapy.(23)

Acute, Subacute, and Chronic Neck and Thoracic Spine Pain: Acute, subacute, and chronic neck and thoracic spine pain are categorized as less than 1 month, 1 to 3 months, and greater than 3 months duration, respectively.

Adjacent Segment Disease: This theory postulates that if there is disease in one spinal segment, it increases the probability of disease in the neighboring segment. It is most commonly used to indicate the probability of a disc problem in the segment adjacent to a fused or otherwise operated upon segment. Whether this represents acceleration of degeneration by increased mechanical forces from the "stiffened" adjacent segment, and/or that degenerative change is genetically more frequent and/or more anatomically severe in those who have required surgery is controversial.(24, 25)

Aggressive Exercise Therapy: This therapy typically consists of cardiovascular training, strengthening of muscles, and stretching in order to improve spine function.(26, 27) Aggressive exercise therapy is a primary treatment for chronic cervical and thoracic pain and after various spine surgeries, and is frequently initiated in the course of treating subacute cervical and thoracic pain.

Ankylosing Spondylitis: Spondylitis is a chronic inflammation of the spine and the sacroiliac (SI) joints that tend to affect the lumbosacral spine modestly more than the cervical-thoracic spine.

[iii] A large percentage of quality trials, probably a majority, use the term "physiotherapy," which is particularly used in Europe.

Bulging Intervertebral Disc: The intervertebral disc is a fibrocartilaginous material. Its primary function is to allow slight movement between each individual spinal segment and significant ranges of motion when all segments are considered together as one functional unit. A disc also acts as a shock absorber for the spine and is composed of an annulus fibrosus (a broad circumferential ligamentous structure) surrounding the nucleus pulposus (a gel-like substance). Identification of a bulging intervertebral disc involves an assessment that the degree of natural disc bulging is larger than is typical at a given level. Bulging is defined as the symmetrical presence (or apparent presence) of disc tissue "circumferentially" (50 to 100%) beyond the edges of the ring apophyses and may be described as a "bulging disc" or "bulging appearance." It is not considered a form of herniation. Furthermore, "bulging" is a descriptive term for the shape of the disc contour and not a diagnostic category. **Protrusion** is present if the greatest distance, in any plane, between the edges of the disc material beyond the disc space is less than the distance between the edges of the base, in the same plane. The base is defined as the cross-sectional area of disc material at the outer margin of the disc space of origin, where disc material displaced beyond the disc space is continuous with disc material within the disc space. In the cranio-caudal direction, the length of the base cannot exceed, by definition, the height of the intervertebral space. **Extrusion** is present when, in at least one plane, any one distance between the edges of the disc material beyond the disc space is greater than the distance between the edges of the base, or when no continuity exists between the disc material beyond the disc space and that within the disc space. Extrusion may be further specified as **sequestration** if the displaced disc material has lost completely any continuity with the parent disc.(28) Providers should be aware that disc bulging increases as a day progresses and is also magnified if an MRI is performed in a standing position.(29, 30) Other than relatively unusual situations (e.g., large lateral bulging into a narrowed neuroforaminal space or large central bulging into a narrowed spinal canal), bulging is thought to be an asymptomatic aging change in nearly all patients.

Centralization: a pattern of pain response elicited and reported by patients during a form of cervical assessment using various postures, often including end-range positioning, and repeated movements in one direction of testing at a time. When pain referred or radiating away from the spine retreats back toward or to the midline in response to a single direction of sustained or repeated positional spinal testing, that pain is "centralizing" or has "centralized."(31)

Chemonucleolysis: Chemonucleolysis is the process of injecting chymopapain (or other enzyme) into the intervertebral disc to dissolve the gelatinous material within the disc. The disc then shrinks in size. This procedure is less invasive than spine surgery, but though shown to be successful is currently largely unavailable in the U.S.

Chronic Nonspecific Cervical and Thoracic Spine Pain: Cervical and/or thoracic spine pain lasting longer than 3 months (12 weeks) is defined in this document as "chronic." Classification of the types of spine pain patients studied (e.g., chronic vs. subacute) in interventional studies evaluated in this document use this definition regardless of whether other definitions were used at the onset of chronic spine pain (e.g., some use a 6-month duration). Chronic spine pain is labeled as "nonspecific" when it is deemed to be not attributable to a recognized, known specific pathology.(32) The vast majority of chronic spine pain is in the category of non-specific spine pain. There is no scientific consensus that the pain-generating structure can be reliably identified in these pain syndromes. Included in this category are terms used to attempt to describe these patients with specificity that includes "specific" terms such as degenerative disc disease, discogenic spine pain, black disc disease, micro instability, cervical or thoracic spondylosis, facet syndrome, and myofascial pain. There are specific treatments that are used to target these patients and most of these are not supported by evidence from quality randomized controlled trials (RCTs). As the placebo or control populations used in many studies included throughout this document routinely improve, health care providers should not infer that improvement in pain with such treatment is quality evidence in support of a mechanistic theory.

Delayed Recovery: Delayed recovery is an increase in the period of time prior to returning to work or usual activities compared with the length of time expected based on average expectations, severity of the disorder, and treatments provided.

Derangement: A non-specific term purportedly a painful displacement within the spine often used by those performing manipulation. A derangement is considered by some proponents to be "reducible" when a directional

preference and pain centralization are elicited during a mechanical evaluation using repeated end-range test movements.

Directional Preference: The single direction of end-range spinal bending or positioning tests that causes an individual's pain to centralize, abolish, or both. Midline-only pain cannot centralize (it is already central) but often has a directional preference where a single direction of end-range bending or positioning eliminates that midline pain.

Facetectomy: Facet joints of the vertebrae (also called the zygapophysial joints) are synovial fluid lubricated joints located on each side of the posterior (back) of the spine. The joint is formed where each side of the vertebrae overlap one another. A facetectomy is the removal of the bone that forms these joints. This procedure is generally performed only in conjunction with other procedures such as fusion.

Failed Spine (or Back) Surgery Syndrome: Failed spine surgery syndrome (FSSS) is a term that is ill defined and sometimes used to label a heterogeneous set of post-operative conditions that are considered suboptimal results. The common denominator is a spinal surgery resulting in chronic pain and persistent or recurrent disability. The ICD-9 code 722.83 (post-laminectomy syndrome) is frequently used for this condition in the lumbar spine, and 722.81 is used in the cervical spine. While this term indicates that spinal surgery failed to achieve its pre-operative goals, there are patients with chronic pain who after spinal surgery improve with either time or subsequent appropriate treatment. Since physicians try to offer hope to patients, use of this term in discussions with patients or in documents is strongly discouraged (cervical pain, thoracic pain, spine pain, or chronic cervical pain are preferable diagnoses, even if the office visit is coded as 722.81). However, because it is used in the ICD system and scientific literature, it is discussed in this document.

Foramenotomy: The intervertebral foramina are the normal gap through the bone between the vertebrae through which a spinal nerve root exits. A foramenotomy is the removal of part of the bone around the intervertebral foramina to increase the size of this passage.

Functional Capacity Evaluation: A functional capacity evaluation (FCE) is a comprehensive battery of performance-based tests to determine an individual's ability to do work-like tasks and conduct activities of daily living.(33) An FCE may be done to identify an individual's willingness/ability to perform specific tasks associated with a job (job-specific FCE), or his or her willingness/ability to perform physical activities associated with any job (general FCE). The term "capacity" used in FCE may be misleading, as an FCE generally measures performance tolerance (current demonstrated ability) and effort, rather than capacity. FCEs may be utilized for "Medical-Legal" purposes to attempt to address residual physical tolerances and potential for rehabilitation in preparation for judicial determination of loss of earning capacity (see discussion in Chronic Pain guideline).

Functional Improvement (especially Objective Evidence): Evaluation of the patient prior to the initiation of treatment should include documentation regarding pain level, objective physical findings, and current functional abilities both at home and at work. This should include a clear statement regarding what objective or functional goals are to be achieved through use of the treatment. These measures should be tracked during treatment and evidence of progress towards meeting these functional goals should be sought. Examples of documentation supporting improved function would be increased physical capabilities (with focus on job specific activities), and by the use of a validated tool(s), including the Neck Disability Index,(34-41) Bournemouth Neck Disability Questionnaire,(42) Modified Oswestry Questionnaire,(43, 44) Patient Specific Functional Scale, and Roland-Morris Disability Questionnaire.(45, 46) Resolution of physical findings (such as increased muscle tone, radicular symptoms, or weakness), increased range of motion, strength, or aerobic capacity may be physical examination correlates of improved function.

Functional Restoration: Functional restoration, like active therapy, is not one specific set of exercises, processes or therapies, but a blend of various techniques and programs (both physical and psychosocial). The basic principle for all of these individually tailored programs is to help patients cope with pain and return to the functioning level required for their daily needs and work activities.(47) Functional restoration refers to a full-day multidisciplinary program lasting from 3 to 6 weeks.(48) There also are work conditioning and work hardening programs that are utilized(49, 50) (see Chronic Pain guideline for further discussion).

Herniated Intervertebral Disc: A herniated intervertebral disc involves a defect in the annulus fibrosus with rupture of the nucleus pulposus through that opening. This is also sometimes referred to as an "extrusion," particularly in the radiological literature. This herniated disc may cause mechanical pressure on and/or is theorized to chemically irritate a nerve root, causing radicular (nerve root related) pain. The distinction between "bulging," protrusion, and extrusion is detailed in the above definition of a "bulging" disc.

Laminectomy: The lamina is the thin bony area of the vertebrae that covers the posterolateral aspect of the spinal canal. A laminectomy is the complete removal of one lamina to expose or access the spinal canal.

Laminotomy: A laminotomy is the partial removal of the lamina to expose or access the spinal canal.

Myofascial Pain: Proponents believe that pain arising from muscles and fascia can be recognized as distinct from pain arising from ligaments, joints, and discs. However, there is no valid way to determine whether the source of neck or thoracic pain is or is not from muscles or fascial structures. Even though some authors have published on "myofascial neck pain", in this review myofascial pain is considered as non-specific cervical or thoracic pain (see Shoulder Disorders guideline for myofascial pain and trigger points).

McGill Pain Questionnaire: The McGill Pain Questionnaire (MPQ) is a non-standardized instrument that attempts to quantify pain, describing pain not solely in terms of intensity, but also in terms of sensory, affective, and evaluative qualities. It was intended to provide a way of identifying differences among different methods of relieving pain.(51, 52) However, it has been noted that the MPQ may only address affective pain.(53)

Myelopathy: Impairment in the function of the spinal cord from external compression resulting in motor or sensory impairment in the limbs, and/or bowel and bladder control impairment. It is often associated with pathological changes in the spinal cord on MRI imaging. This is a considered a serious neurological event or sequelae.

Neck Disability Index: The Neck Disability Index is a revised form of the Oswestry Low Back Pain Index for the assessment of activities of daily living of cervical pain patients, particularly from whiplash type injuries.(34-39, 41) It contains 10 sections addressing the impact of the cervical pain including – pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping, and recreation.(34) However, the tool is not standardized and is frequently modified, making interpretations difficult.(54)

Passive Modality: Passive modalities refer to various types of treatment given by a provider that usually involve administration of some form of stimulus being applied to the body as opposed to the individual actively doing some sort of therapy (see Active Therapy). Forms of passive modality include massage, hydrotherapy (whirlpools, hot tubs, spas, etc.), ultrasound, and hot/cold compresses.

Percutaneous Discectomy: Percutaneous means "through the skin." In the case of surgery, it typically means a small incision. Discectomy is the surgical removal of an intervertebral disc. Thus, a percutaneous discectomy is the removal of a portion of a spinal disc via a small incision (or puncture wound) through the skin.

Physical or Occupational Therapy: The term "physical therapy" is used in ACOEM's *Guidelines* generically to mean physical medicine, therapeutic and rehabilitative evaluations and procedures. Much of the available research uses this term generically. This rehabilitative therapy may be performed by or under the direction of trained and licensed individuals such as physical therapists, occupational therapists, exercise physiologists, chiropractors, athletic trainers, and physicians. Jurisdictions may differ on the qualifications for licensure to perform these interventions. The *Guidelines* are not meant to restrict physical therapy to being performed only by physical therapists.

Radicular Pain Syndrome: Radicular pain syndrome refers to pain in the extremities (arms, hands, legs, and feet) that is caused by an associated nerve root being affected in or near the spine. Pain is usually substantially worse in the extremity than in the spine. Frequently, there are minor spine symptoms. An example is cervical radiculopathy from a disc herniation, most typically resulting in characteristic symptoms of pain radiating down the upper extremity in those specific nerve root distributions). Radiculopathy may result in numbness or paresthesias in the corresponding dermatome, muscle weakness in the corresponding myotome, and/or loss of muscle stretch reflex

corresponding to the affected root level (see Table 4). The condition may occur with a thoracic nerve root, but is relatively uncommon.

Slump Stretching: The nerve is stretched by rounding the neck and back and flexing the hip to 90° with knee extension (ankle neutral or slightly dorsiflexed).

Spinal Motion Segment: The spine is made up of the vertebrae (bone) and connective tissue (specifically, the intervertebral discs and ligaments). A spinal motion segment, or functional unit of the spine, is considered to be two adjacent vertebrae, the intervening vertebral disc, the two facet joints and the connecting ligaments. If two vertebrae are completely fused together (surgically or otherwise), then the spinal motion of that segment becomes zero, and the overall range of motion for the entire spine is decreased.

Spinal Stenosis: Spinal stenosis is narrowing of the spinal canal with neurological impingement on the spinal cord and nerves. Symptoms include neck and extremity pain. Spinal stenosis may be associated with myelopathic findings if there is significant compression of the spinal cord (see Myelopathy). This condition is most often degenerative, though it may be acquired after significant trauma resulting in spondylolisthesis. Most commonly, spinal stenosis involves a combination of factors that may include facet joint osteoarthrosis with osteophytes, intervertebral disc space narrowing, hypertrophy of the ligamentum flavum and other ligamentous structures, and/or congenital narrowing of the spinal canal.

Spondylolisthesis: Spondylolisthesis is usually classified as isthmic and/or degenerative. Spondylolisthesis is the abnormal alignment of one vertebra in relation to the adjacent vertebral body usually measured in millimeters of displacement between the posterior aspects of the two vertebral bodies. Isthmic spondylolisthesis is a congenital defect. Fractures may also occur in childhood (e.g., non-union of a stress fracture) and produce or contribute to spondylolisthesis, but requires high forces, generally repeated, such as football linemen and female gymnasts. This form of spondylolisthesis rarely progresses once skeletal maturity is attained. It frequently is asymptomatic, but may be rendered symptomatic by adult trauma. Degenerative spondylolisthesis has a different pathophysiology. It occurs as the facet joints and adjacent disc lose their stabilizing ability due to degenerative changes (e.g., facet joint osteoarthrosis and degenerative disc space narrowing), typically in those over age 60. The degree of spondylolisthesis tends to increase with age-related changes, especially as the degree of disc space narrowing advances. It is usually thought to be asymptomatic unless there is neurological impingement (e.g., accompanying spinal stenosis), or the severity is sufficiently great that there is instability. While most commonly degenerative, it may also be acquired from major trauma.

Spondylosis: Spondylosis is the age-related degeneration of the vertebral disc in each segment of the spine or the natural aging degeneration. It is sometimes used synonymously with the term "degenerative disc disease." This process may involve the spinal facets as well as the disc. Cervical spondylosis may also lead to spinal stenosis (a narrowing of the spinal canal) putting pressure on the spinal cord and other nerves.(55) Spondylosis is generally considered to be a normal process of aging and is generally thought to be asymptomatic unless neurological impingement results. This condition is generally insignificant unless the individual has a congenitally narrowed spinal canal (i.e., congenital cervical canal stenosis).

Visual Analog Scale: Visual Analog Scales (VAS) are figures of lines that are used to measure a patient's level of subjective pain. There are different types of VAS pain scales, but nearly all range in value from "0" or "no pain" to "10" or "worst pain" (or 0 to 100). Some have no numeric designation on them; instead a line is drawn between the extreme ends of the line noted as "no pain" and "severe pain" and the patient's "x" on the line is used to measure the fraction or distance between the ends. Some are 0 to 100mm in length. Some have additional verbal anchors such as "mild" and "moderate." Despite these nuances, the performance of these various VAS scales is believed to be valid and reliable.

Initial Assessment. . . . . .

Thorough medical and work histories and a focused physical examination (see General Approach to Initial Assessment and Documentation guideline) are sufficient for the initial assessment of a patient complaining of potentially work-related neck or thoracic spine symptoms. Findings of the medical history and physical

examination may alert the physician to other pathology (e.g., not of spine origin) that can present as spine disorders. In this assessment, certain findings, referred to as red flags, raise suspicion of serious underlying medical conditions (see Table 1). The absence of red flags and conditions rules out the need for special studies, referral, or inpatient care during the first 4 to 6 weeks. During this time, spontaneous recovery is expected, provided any associated workplace factors are mitigated.(32)

There also are potential psychological conditions that may be confounding and/or interacting and should be evaluated, such as PTSD, suicidality, childhood sexual abuse, hallucinations or intoxication, which have been called primary risk factors,(56) and have been reviewed elsewhere.(57) Suicidality though is a potentially fatal complication, which makes it a more severe complication than cauda equina.

Red Flags

Features of the patient's history or examination that indicate the possibility of potentially serious disorders are referred to as "red flags." These include features that suggest the possibility of acute fractures, acute dislocations (e.g., spondylolisthesis), spinal infection, tumor, or serious or progressive neurologic deficit. While recognizing these "red flag" disorders is clearly important, there are no high quality prospective cohort studies to provide the evidence base for this section of the guidelines.

Table 1. Red Flags for Potentially Serious Neck or Thoracic Spine Conditions

Disorder	Medical History	Physical Examination/Diagnostic Testing
SPINAL DISORDERS		
Fracture	Major trauma, such as vehicular accident or fall from height(58) (Boissonnault 05) Minor trauma or strenuous lifting in older or potentially osteoporotic patients Metabolic risks for osteopenia (including renal failure, hyperthyroidism, rheumatic disorders, debility and inheritance)	Percussion tenderness over specific spinous processes Careful neurological examination for signs of neurological compromise
Tumor and Neoplasia	Severe localized pain over specific spinal processes History of cancer Age >50 years Constitutional symptoms, such as recent unexplained weight loss or fatigue Pain that worsens when patient is supine Pain at night or at rest	Pallor, reduced blood pressure, diffuse weakness Tenderness over spinous process and percussion tenderness Decreased range of motion due to protective muscle spasm C8 or T1 nerve root (or ulnar nerve) symptoms or findings, especially in a smoker (Pancoast tumor) Other neurological impairment
Infection	Risk factors for spinal infection: recent bacterial infection (e.g., urinary tract infection); IV drug abuse; diabetes mellitus; or immune suppression (due to corticosteroids, transplant, or HIV) Constitutional symptoms, such as recent fever, chills, or unexplained weight loss	Tenderness over spinous processes Decreased range of motion Vital signs consistent with systemic infection (late): ▪ Tachycardia ▪ Tachypnea ▪ Hypotension ▪ Elevated temperature, high white blood cell count, or inflammatory markers (sedimentation rate, C-reactive protein, etc.) ▪ Pelvic or abdominal mass or tenderness Neurological impairment(s)

Progressive Neurologic Deficit	Severe spine pain Progressive limb numbness or weakness, bowel or bladder control impairment, gait ataxia	Significant and progressive myotomal motor weakness Significant and increased sensory loss – in anatomical distribution Radicular signs Corticospinal tract involvement (gait ataxia, Babinski sign, hyperreflexia, and limb spasticity, etc.) Other neurological impairment(s)
Myelopathy	Ataxic gait, impaired upper limb coordination, poor or reduced finger movements, bladder and/or bowel control impairment (incontinence)	Hyperreflexia, ataxia, clonus, pathologic reflexes (Babinski, Hoffman) Other neurological impairment(s)
EXTRASPINAL DISORDERS		
Pneumonia	Fatigue Dyspnea May have chest pain, usually pleuritic Sputum production Subacute onset without inciting event	Fever, tachypnea Decreased breath sounds. May have rhonchous breath sounds, generally in only 1 or 2 segments, but could be widespread Dullness to chest percussion Purulent sputum

Adapted from van den Hoogen 95; Jarvik 02; Bigos 94.(59-61)

Absence of Red Flags

Absent red flags, cervical and thoracic disorders can usually be classified into one of two working categories:

- **Nonspecific disorders**, including benign, self-limited disorders with unclear etiology, such as regional cervical pain. This includes the overwhelming majority of cervical pain patients' problems, generally over 95% of those with acute cervical pain.
- **Specific disorders**, including potentially degenerative disorders such as herniated discs, spinal stenosis, and other neurological impingements.

It should be noted that there may be overlap between these two categories.

Cervical Pain

More than 90% of patients have no identifiable cause for their cervical pain.(62) Symptoms are pain, usually without radiation to the limb, although some patients have radiation into the interscapular area or upper trapezii. Radiation into an arm or forearm generally signifies radiculopathy, particularly when the radicular pain in the extremity exceeds that in the neck or is the sole complaint. Patients with cervical pain generally have no limb tingling, numbness, or muscle weakness other than weakness associated with pain-producing activities. Some physicians refer to these patients as having incurred "sprains" and/or "strains"; however, these labels are not appropriate. A sprain is a disrupted ligament and a strain is a myotendinous junction disruption. Both imply knowledge of the anatomic cause of cervical pain and a forceful mechanism of injury when the former is untrue for cervical pain patients and the latter may or may not be true. Most cervical "sprains" or "strains" occur doing tasks the individual has done before without difficulty and which do not put a significant biomechanical load on the spine. The event the patient associates with the pain onset usually reflects when the pain first occurred rather than why the pain occurred. Use of those terms also confuses the proper use of those diagnoses elsewhere in the body and becomes problematic in determination of work-relatedness. Therefore, the term "nonspecific" cervical pain should be used to describe these symptoms.(63)

Thoracic Pain

The same pathophysiological mechanisms, conditions, and treatments apply to the thoracic spine as they do for the cervical and lumbar spine with modest differences. Degenerative anatomic changes are very common, if not universal, with age. However, the thoracic spine is considerably less mobile and, as a consequence is believed to

result in a lower prevalence of pain syndromes commonly attributed to degenerative changes, and when these syndromes do occur, they are usually milder conditions. Yet, these conditions are common in the thoracic spine with MRI evidence of herniations (37%), bulging discs (53%), annular tears (58%), deformation of spinal cords by discs (29%), Scheurmann end-plate irregularities or kyphosis (38%) and degenerative findings (56%).(64) There are no quality studies identified for treatment of thoracic spine conditions, and all recommendations are based on consensus analogy to the treatment of the cervical and lumbar spine, but have insufficient evidence.

Radicular Pain Syndromes

Radicular pain denotes pain that is in a specific neurological distribution, nearly always involving only one nerve root. Symptoms are pain, tingling and numbness, and muscle weakness. Corresponding signs, including sensory loss, muscle weakness, and a diminished reflex(es) all in the distribution of that one nerve root, may be present. The diagnosis of radiculopathy is generally not complex in more severely affected individuals. It becomes more difficult with milder symptoms, as historical features and physical examination findings may be less pronounced or many physical examination findings may be largely absent. There is a clinical prediction rule in the diagnosis of cervical radiculopathy. It includes Spurling test, distraction test, upper limb tension test (ULLT1), and ipsilateral cervical rotation of less than 60 degrees.(41) It has been reported that when 3 of the 4 signs are present on exam the specificity is 94%, sensitivity is 24%, and positive likelihood ratio is 6.1. When all 4 physical exam signs are present the specificity is 99%, sensitivity is 39% and positive likelihood ratio is 30.3.(41) These were originally reported in Wainner et al 2003, and have not been validated.(65)

There are multiple possible causes of radicular pain. Most commonly, in the cervical spine in younger individuals this is due to a herniated intervertebral disc. Such a herniation involves a rupture in the annulus fibrosus and extrusion of nucleus pulposus material, also referred to as an extrusion. A combination of a physical displacement of the material along with a purported inflammatory chemical reaction to this material is believed to be responsible for the development of the symptoms of neurological compromise. It is also possible for a severe degenerative arthritic process to result in substantial osteophytic growth around the facet joint and/or intervertebral disc space and cause radicular symptoms. In elderly individuals this cervical spondylosis is the most common cause of radicular neck syndromes.

Uncovertebral joints (also called Joints of Luschka) are formed between uncinate processes above, and uncus below. These are "joints" without joint capsules or synovial fluid. They are located in the cervical region of the spine between C3 and C6. Two lips project upward from the superior surface of the vertebral body below, and one projects downward from the inferior surface of vertebral body above. They allow for flexion and extension and limit lateral flexion in the cervical spine. They can enlarge and be part of the spinal stenosis process at these levels in the cervical spine. There is considerable controversy regarding whether these are pain-generating structures and some therapeutic interventions specifically target these joints.

Zygapophysial (Facet) Joint Degenerative Joint Disease

Facet joints are synovial fluid filled, synovium lined, ligamentously encapsulated joints that are in alignment along the posterior aspect of the spinal column. They are in many ways similar to nearly all other joints in the body (the main exceptions are the intervertebral discs). Not surprisingly, facet joints are prone towards the same maladies that affect other joints, including osteoarthrosis (degenerative joint disease), gout,(66) psoriatic arthritis, and many other arthritides. There appears to be a propensity towards facet joint osteoarthrosis in those with osteoarthrosis elsewhere in the body, sometimes referred to as "systemic osteoarthrosis."

The diagnosis of radiographic facet joint osteoarthrosis is relatively straightforward. Roentgenograms, particularly facet joint (or rotated) views for the lumbar spine and lateral views for the cervical spine, will show evidence of degenerative findings (i.e., sclerosis, joint space narrowing, and cyst formation). However, the diagnosis of pain arising from such degenerative joints is not straightforward. Osteoarthrosis in the spine is extremely common (so common that many physicians do not record these abnormal findings, especially when mild or moderate on imaging, as they are "normal" for age). It appears to be largely asymptomatic. In those with multiple levels affected, there often is not pain at all of those levels. As cervical pain is so common and the overwhelming anatomic cause of cervical pain is unknown, it follows that attempting to diagnose the pain as related to a specific structure such as the facet joints is quite challenging.(67)

Important diagnostic limitations to the use of diagnostic facet blocks are that they are often accomplished involving intra-articular injection(s) of anesthetic agents. Results of the procedure therefore cannot be directly related to the value of neurotomies.(68) Other limitations to the use of diagnostic blocks include single level diagnostic blocks vs. multiple level blocks and the use of corticosteroids. Problems with diagnostic blocks of the dorsal root rami include: 1) the ability to anesthetize the joint; 2) the specificity to not anesthetize adjacent neural structures; and 3) the likelihood ratio of a single diagnostic block.(67-69)

CLINICAL SYNDROMES

The inability of conventional clinical testing and advanced imaging to reliably identify an anatomic pain source for most cervical and lumbar pain has stimulated research attempting to reliably identify and validate clinical syndromes or subgroups based on clusters of clinical examination findings. If homogeneous syndromes are validated, this should enable more effective individualized care than a less specific approach towards all non-specific cervical pain.

One syndrome with perhaps more support than others, especially in the lumbar spine, is "directional preference." A directional preference is often identifiable in a patient's history and examination. Directional preference patients typically describe a history of episodic and intermittent LBP with a directional theme as to what positions, movements and activities commence or worsen their pain (e.g., flexion) and what improves or stops their pain. A presumptive pain generator's directional preference is that single direction of repeated end-range spinal bending tests or static positioning that causes the pain to "centralize," abolish, or both. Pain "centralization" is a pattern of pain response whereby pain referred or radiating away from the spine retreats back toward or to the midline in response to a single direction of sustained or repeated end-range spinal testing. Midline-only pain cannot centralize because it is already central but it also frequently appears to have a directional preference where a single direction of testing will reduce or eliminate the patient's midline pain. After pain centralization or elimination, the pain typically remains improved until or unless the patient moves excessively in the opposite direction of the preferred direction. According to this syndrome's constructs, avoiding moving in a direction that aggravates the pain should be taught, minimized, and avoided especially during the early phase of treatment to speed recovery.

The unique theoretical purpose of these end-range tests, performed in weight-bearing and recumbency, is to load the spine in different bending directions. The most common cervical directional preference is lower cervical extension, yet smaller numbers of pain-generators benefit from other directions of loading: lateral, rotational or flexion movements. Those with an extension directional preference typically worsen with lumbar flexion and improve with extension or simply restoring their lordosis.

This syndrome has been referred to as a "reducible derangement" or a "directional preference syndrome." Its two characteristic clinical findings (directional preference and pain centralization) purportedly have strong interexaminer reliability (Kappa = 0.9, 0.823, 0.7, % agreement: 88-100%), with training.(70-73)

The prevalence of this directional preference syndrome is reportedly high in the lumbar and cervical spine: 70-89% of acute(74, 75, 76, 77) and 40-50% in chronic pain.(78-81) It is commonly elicited in axial, referred, as well as radicular pain.(82-84) There is also suggestive evidence of a concomitant psychosocial benefit by teaching and empowerment with the knowledge and skills to effectively self-treat.(85)

Medical History and Physical Examination . . . . . .

A focused and detailed medical history and physical examination are necessary to assess the patient's medical condition and specific cervical or thoracic complaint. This section reviews the medical history including the questions that should be asked by the examiner.

The context of the appearance of the patient in the clinic is important. Patients with spine disorders generally initiate treatment due to pain, which is often attributed to an ostensible injury. However, acute spinal pain is not usually directly attributable to a discrete, definable pathophysiology Pain is also commonly associated with sensory, affective, cognitive, social and other processes.(86-88) The pain sensory system itself is organized into two parts, often called first and second pain. A-∂ nerve fibers conduct first pain via the neospinothalamic tract to the

somatosensory cortex, and provide information about pain location and quality. In contrast, unmyelinated C fibers conduct second pain via the paleospinothalamic tract, and provide information about pain intensity. Second pain is more closely associated with emotion and memory neural systems than it is with sensory systems.(89-91)

As a patient's condition transitions through the acute, subacute and chronic phases, the central nervous system is believed to undergo reorganization. The temporal summation of second pain produces a sensitization or "windup" of the spinal cord,(92) and the connections between the brain regions involved in pain perception, emotion, arousal, and judgment are changed by persistent pain.(93) According to this theory, these changes cause the CNS's "pain neuromatrix" to become sensitized to pain.(86-88) This CNS reorganization is also associated with changes in the volume of brain areas,(94) decreased gray matter in the prefrontal cortex,(94) and the brain appearing to age more rapidly.(95) As pain continues over time, the CNS remodels itself so that pain becomes less closely associated with sensation, and more closely associated with arousal, emotion, memory and beliefs.(90, 96) Because of these CNS processes, one should be aware that as the patient enters the subacute phase, it becomes increasingly important to consider the psychosocial context of the disorder being treated, including the patient's social circumstances, arousal level, emotional state, and beliefs about the disorder. However, behavioral complications and physiological changes associated with chronicity and central sensitization may also be present in the acute phase, and within hours of the initial injury.(97)

Medical History

No scientific studies of the medical history in patients with cervical pain(98, 99) or thoracic pain are available. Asking the patient open-ended questions, such as those listed below in items 2 through 8, allows the physician to gauge the need for further discussion or specific inquiries to obtain more detailed information.

1. What are your symptoms?
   - Do you have pain or stiffness?
   - Do you have numbness or tingling?
   - For traumatic injuries: Was the area deformed? Did you lose any blood or have an open wound?
   - Is the discomfort located primarily in your thoracic/mid-back? Neck? Arm?
   - Do you have pain or other symptoms elsewhere? (Patients who present with a primary complaint of upper extremity pain may well have radiculopathy from a cervical disc herniation or other cervical spine or cervicothoracic spine pathology.)
   - Do you have clumsiness with your hands or a change in your ability to walk?
   - Have you lost control of your bowel or bladder? Are you soiling your undergarments?
   - Do you have fever, night sweats, or weight loss?
   - When did your symptoms begin? Are your symptoms constant or intermittent? What makes the problem worse or better?
   - What is the day pattern to your pain? Are you better first getting out of bed in the morning, during the morning, mid-day, evening, or while asleep? Are you worse as the day progresses? Do you have a problem sleeping? What position is most comfortable? Is there any pain with cough, sneezing, deep breathing, or laughing?
   - What positions, activities, or movements make your pain worse (more intense or radiate further into periphery)?
   - What positions, activities, or movements make your pain better (less intense or less peripheral radiation, i.e., centralization)?
   - How long can you sit, stand, walk, and bend your back or neck?
   - How much weight can you lift (use items such as a gallon of milk, bag of groceries, etc., as examples)?
2. How did your condition develop?

   Past:
   - Have you had similar episodes previously?
   - Have you had previous testing or treatment? With whom?

   Cause:

- What were you doing when you first noticed the symptoms? (It is important to obtain all information necessary to document the biomechanical forces of injury.)
- What do you think caused the problem?
- How do you think it is related to work?
- Did your symptoms begin gradually or suddenly? Did you notice the pain the day after the event?

Job:

- What are your specific job duties?
- How long do you spend performing each duty on a daily basis?
- Do you have assistance of other people or lifting devices?

Non-occupational Activities:

- What other activities (hobbies, workouts, sports) do you engage in? At home or elsewhere?
- Any physically demanding activities requiring heavy lifting, awkward postures, prolonged sitting or standing?

3. How do these symptoms limit you?
   - What activities of daily living are limited? Are there specific challenges in your home environment (e.g., steep steps)?
   - How long have your activities been limited?
   - Have your symptoms changed over time? How?
4. Do you have other medical problems?
5. What are your expectations regarding your return to work and disability from this health problem?
6. What are your concerns about the potential for further injury to your neck or mid-back as you recover?
7. How do you like your job? Your supervisor and coworkers? What is your relationship with your co-workers and supervisor and how do they treat you?
8. What do you hope to accomplish during this visit?

Indices of functional ability are often incorporated in the history. There are several validated and partially validated tools including the Neck Disability Index,(34-41) Bournemouth Neck Disability Questionnaire,(42) Modified Oswestry Questionnaire,(43, 44) Patient Specific Functional Scale, and Roland-Morris Disability Questionnaire.(45, 46)

Physical Examination

The objective of the physical examination of the cervicothoracic spine is to document a patient's baseline status from which to judge future improvement and to detect nerve root or spinal cord impairment that might suggest the need for specific tests and treatment. The examination begins as soon as the physician introduces him or herself to the patient, particularly including observations of positioning; use or disuse of the neck, shoulders and arms; skin color and signs of distress. Vital signs, such as an elevated temperature, may suggest the presence of an infection or neoplasm. Tachycardia may be a sympathetic nervous system response to the patient's pain or it may be anxiety related. For those undergoing more advanced testing for chronic pain, tachycardia may also be relevant as indicating potential anxiety.

The three primary distributions for spine pain are those that are:

1. Localized to the paraspinal area of the neck, with or without radiation to the shoulder or scapular area.
2. Referred to the paraspinal area of the thoracic spine (that can be from a musculoskeletal source or from internal organs such as heart, lungs, or abdominal aneurysm).
3. In the cervical or upper thoracic spine and accompanied by pain or numbness referred to the extremities in a dermatomal or myotomal distribution and that may suggest nerve root involvement. In addition, there may be lower limb, and/or bowel or bladder control impairment symptoms that suggest spinal cord involvement (myelopathy).(100, 101)

Guided by the medical history, the physical examination includes:

- General observation of the patient, including changes in positions, stance, and gait;
- Regional examination of the cervical and thoracic spine;
- Examination of organ systems related to appropriate differential diagnosis possibilities;
- Neurologic examination;
- Testing for cervical nerve root tension;
- Monitoring pain behavior during range of motion and while seated as a clue to origin of the problem; and
- Head protrusion (lower cervical flexion) and retraction (lower cervical extension) positions and repeated movements to determine symptom response.(102)

The completely objective parts of the cervical and thoracic spine examination are limited to circumferential measurements for atrophy or findings of fasciculations (rarely present visible rhythmic contraction of small portions of a muscle). All other findings require the patient's cooperation, although reflexes and pin-prick in a dermatomal distribution are generally much more objective than subjective.

Determining whether or not there is cervicothoracic nerve root compromise (and if so, the level of compromise) is important. Symptoms correlating with specific dermatomal and myotomal levels of compression and possible motor weakness are shown in Table 2.

Table 2. Symptoms of Cervicothoracic Nerve Root Compromise

Root Level	Pain or Paresthesia	Motor Weakness
C1		
C2	Occipital region	
C3	Ear	Neck rotation, shoulder elevation, diaphragm
C4	Top of Shoulders	Shoulder elevation
C5	Medial scapular border, lateral upper arm to elbow	Deltoid, supraspinatus, infraspinatus
C6	Lateral forearm, thumb and index finger	Biceps, brachioradialis, wrist extensors
C7	Medial scapula, posterior arm, dorsum of forearm, middle finger (3rd digit)	Triceps, wrist flexors, finger extensors, radial wrist extension
C8	Shoulder, ulnar side of forearm, little finger, (5th digit)	Thumb flexors, abductors, intrinsic hand muscles
T1	Upper medial forearm, medial arm	Finger abduction, adduction
T2-T12	Mid to low back pain, radiating around the torso towards the anterior midline	Generally none perceptible on examination unless multiple nerve roots involved

A. OBSERVATION AND REGIONAL NECK EXAMINATION

This section on examination applies to patients presenting to an office-based examiner, and not to those presenting to an emergency room. Shoulder disorders commonly have symptoms that are similar to those of neck and mid back disorders, and distinguishing whether a patient has a neck/mid thoracic problem, a shoulder problem, or both can be challenging. Shoulder pain can occasionally or frequently radiate to at least the mid arm. The reader is referred to the guideline on shoulder disorders for a discussion of the history and physical examination of the shoulder, but patients presenting with complaints suggesting cervical and thoracic spine disorders should routinely have a physical examination of the shoulder.

An important part of the examination is the observation of the patient with cervical and thoracic spine pain. This includes head and upper thoracic posture, stance, and gait. The patient should be asked to walk down the hallway so there is sufficient distance over which to observe the gait and spine posture. In the process, the ease with which the patient stands up and moves the cervical and thoracic spine should be carefully observed. Most patients should be observed over at least 20 feet of ambulation. The examiner should observe whether the spine is maintained in a normal or a flexed posture, and whether there is normal spine motion during gait or "stiff necked" gait. Gait fluidity should be carefully observed. How the patient turns around to return to the examination room is also of interest. Acute cervical and thoracic spine pain usually decreases the mobility of the spine and produces restriction of normal spinal movement during gait.

The disrobed, but modestly covered, patient is examined standing. The neck and spine are viewed from behind, laterally, and anteriorly for alignment. The levels of the shoulders and any lateral spinal curves (scoliosis) if present should be noted. The patient should have the shoulders and knees level so any discrepancy will not be due to a weight shift. The spine is compensated if the first thoracic vertebra is centered over the sacrum. A tape measure end

held over the T1 spinous process can be used as a plumb line to verify this. The upper extremities should be in normal alignment and used normally. Patients with acute cervical or thoracic muscle spasm may demonstrate a list to one side – a compensatory scoliosis, with loss of normal spinal contours. "Spasm" cannot be reliably detected by palpation, but may be seen if it produces a list (deviated posture) or scoliosis.

The patient should perform ranges of motion (ROM) of the neck in all cardinal directions (flexion, extension, axial rotation, and lateral bending.(102, 103) Normal ROM is 50° for forward flexion, 60° for extension, 45° for lateral bending, and 80° for rotation,(103, 104) although ROM may decline with age in certain disorders. Spinal motion is important in terms of symmetry and rhythm. The absolute ROM is not of major diagnostic significance because of wide variance. Asymmetries should be noted. Inquiries regarding which of these positions produced pain, if any, are also of interest and may be useful therapeutically. Initial ROM is thought to be predictive of future limitations and disability.(105) ROM is believed to become normal within 3 months of a whiplash injury.(106)

Qualitative muscle strength testing of the upper extremity muscles should be performed.(103) Both proximal and distal muscle strength should be assessed. When differences are mild, repeated testing may accentuate decrements through revealing earlier fatigue of affected muscle groups. Shoulder girdle strength testing may include resisted supraspinatus (thumb down shoulder abduction or the empty can test), biceps and triceps testing. Distal upper extremity muscle strength screening generally includes resisted wrist extension, flexion, phalangeal flexion, and intrinsic muscles.

The patient generates uniform resistance to pressure that is overcome in a smooth fashion. Patients may demonstrate give-way weakness, which is manifested by either resisted pressure for a few seconds and then sudden release of the muscle or demonstrate a stepwise release of the muscle resulting in a cogwheel or ratcheting effect. Causes of give-way weakness frequently include submaximal efforts, but can be due to other causes including pain, misunderstanding of directions, and attempting to help the examiner. The probability of feigning rises if the directions are repeated and give-way weakness remains. Testing extremity flexion bilaterally and simultaneously may help identify a mechanism for observed give-way weakness.(107-109)

In addition to the soft tissue, bony structures should be palpated. The spinous processes are covered by ligamentous structures, not muscle, and are easily palpated. Localized tenderness may suggest the presence of an isolated process, such as an infection, tumor, or fracture affecting that vertebral body. Tenderness over spinous processes is considered a sign of amplification in patients with non-specific spine pain, although it is also often present among those with fibromyalgia.(107)

Assessment of the neurologic status of the patient is important in the overall cervicothoracic evaluation. The history is the most critical feature and guides the degree to which the neurological testing must be performed. A positive neurologic finding will give objectivity to the patient's subjective complaints. Each nerve root must be examined (Table 2). Abnormalities of motor, sensory, and reflex function are tested. It is worthwhile to review the anatomy of the nerve roots in order to better understand abnormalities discovered during the neurologic examination.

Each nerve root, as it leaves the spinal canal through the neural foramen, is enclosed within a sleeve that contains spinal fluid and small blood vessels about and within the nerve. This sac, referred to as the dural sleeve, provides nourishment to a particular nerve root. Compression and/or traction on the dura may compress the dural sleeve's contents and encroach upon the nerve and its blood supply. It is thought that compression may cause pain along the course of the peripheral nerve, which and may be accompanied by dysesthesias, motor weakness, and decreased reflex function associated with the affected nerve root. The goal of many of the maneuvers done during this phase of the examination is to increase nerve compression to uncover neurologic dysfunction. These maneuvers have been reported to have high positive predictive value and specificity.(41, 110)

Of the possible neurologic abnormalities, true muscle weakness is the most reliable indicator of persistent nerve injury with atrophy and loss of nerve conduction.(111-114) Sensory changes are subjective, take significant time to document, and require the full cooperation and attention of the patient. Reflex changes may have permanently occurred in a previous episode of nerve root compression. Reflexes may not return even with recovery of sensory and motor function. With age, but also with some medical conditions such as diabetes mellitus and hypothyroidism, reflexes diminish and are more difficult to elicit, even without any prior history of nerve compression. The normal

loss of reflexes is generally symmetric.(115, 116) Patients who lose reflexes in both upper extremities on the basis of compression may have spinal stenosis or a large central disc herniation.

In addition to nerve root lesions, upper motor neuron and peripheral nerve disease cause abnormalities that may be discovered during the neurologic exam. With upper motor neuron lesions, the fine control of muscles is lost while the trophic effects of the peripheral nerves remain intact (no atrophy or needle EMG changes occur). Muscle strength is diminished, but in a different pattern from lower motor neuron weakness. Patients develop spasticity of muscles (tonic contractions) and hyper-reflexia. Patients may also develop a positive Hoffmann's reflex (aka finger flexor reflex: flexion of the thumb tip due to tapping the nail or flicking the tip of the third or fourth finger) or Babinski reflex (extension of the large toe and spreading of other toes with stroking of the sole of the foot). Ankle clonus, an involuntary rhythmic plantar flexion motion after rapid dorsiflexion of the ankle may also suggest upper motor neuron compression. Peripheral nerve injuries may cause sensory and/or motor abnormalities, but in the distribution of the peripheral nerve, and not in the pattern of a specific spinal nerve root. Peripheral nerves receive nerve fibers from a number of nerve root levels.

Perhaps the most widely used physical examination sign for cervical radiculopathy is the Spurling's test,(117, 118) which when positive results in a reproduction of distal upper extremity symptoms consistent with the patients symptoms and generally isolated to the distribution of one nerve root. This maneuver, as originally described, involves the patient partially extending the neck and rotating the chin toward the affected extremity while the examiner applies an axial load to the spine to provide further compression of the neuroforamen on that side.(119) Mere production of cervical pain with this maneuver does not signify neurological compromise and appears frequently misrecorded as it must involve pain in that nerve root's distribution.

Table 3. The reliability of neck physical examination tests has been reported below. These data suggest a wide range in reproducibility.

Test	Inter-rater reliability: Kappa*
Range of motion	0.05 – 0.61
Neck and Upper Limb Strength Testing	≤ 0.60
Trigger Point Palpation	0.24 – 0.56
Sensory Exam: Light touch and pin prick	0.16 – 0.67
"Non-Organic" Signs	0.08 – 1.00
Composite exam: inspection, range of motion, palpation, and provocative tests	-0.18 – 0.52

*Kappa values that are higher are more reproducible.
Adapted from Nordin M, Carragee E, Hogg-Johnson S, et al. Assessment of neck pain and associated disorders: results of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders. *Spine*. 2008;33(4S):S101-22.

B. NEUROLOGIC SCREENING

The most important neurologic deficit to recognize is myelopathy from spinal cord compression. Patients may have symptoms of cervical pain, and arm numbness and/or weakness like other patients with neck disorders. However, many also have additional symptoms of gait abnormality, leg numbness and/or weakness, and some have bowel or bladder control impairment.(120)

Physical examination findings that correlate with significant myelopathy are:

1. Hyperreflexia (Grade 3 or greater);
2. Hoffman reflex (observing reflex flexion of the thumb distal phalanx when the distal phalanx of the middle finger is "flicked" or suddenly passively pushed into flexion at the DIP joint);
3. Inverted brachioradialis reflex (during testing the brachioradialis reflex there is a decreased response from the brachioradialis and an abnormal flexion response of the fingers);
4. Ankle clonus (forcefully dorsiflexing the ankle and maintaining pressure on the sole of the foot to maintain ankle dorsiflexion and observing for rhythmic beats of ankle flexion and extension, at least 4 "beats" required for sustained clonus to be abnormal);
5. Babinski sign or reflex – firmly sweeping the pointed end of a reflex hammer from the lateral sole to the base of the toes and observing for an extensor response of the hallux (great toe);

6. Cervical stenosis – while not a physical examination finding per se, it should be recognized that myelopathy is strongly linked to cervical stenosis, particularly congenital.

The neurologic examination most commonly focuses on a few tests that reveal evidence of nerve root impairment, peripheral neuropathy, or spinal cord dysfunction. The most common herniated disc in the cervical spine is the C5-C6 disc with impingement of the C6 nerve root. The clinical features of cervical nerve root compression are summarized in Table 4.

1. **Testing for Muscle Strength**
There are no specific muscle tests for the C1 to C2 nerve roots.

Table 4. Physical Examination Correlates of Cervical Nerve Root Dysfunction

Root Level	Sensory Deficit	Motor Weakness	Reflex
C3	Ear, anterior neck, occiput, posterior temporal area	Not usually detectable	None
C4	Shoulder, posterior upper arm, upper chest	Not usually detectable	None
C5	Lateral shoulder, upper arm	Shoulder abduction, elbow flexion	Biceps
C6	Lateral forearm, **thumb**,* and perhaps index finger	wrist extension (ECRL/ECRB) and elbow flexion (biceps)	Brachioradialis, and possibly biceps
C7	**Middle** finger*	Elbow extension (triceps), wrist flexion, finger extension	Triceps
C8	Distal forearm, ulnar ring, and **little*** finger	Finger flexion	Triceps
T1	Medial upper forearm and arm	middle finger flexion, finger abduction and adduction	None
T2-T12	Unilateral, dermatomal based on nerve root(s) affected	Generally none unless multiple roots affected	None

*These are the most common sensory nerve deficits related to cervical nerve root dysfunction.

2. **Circumferential Measurements**
Muscle atrophy is one of the few purely objective findings and can be measured with bilateral circumferential measurements of the upper arms and forearms at a fixed distance from an anatomic point (e.g., olecranon process). However, the dominant upper extremity usually may have an increase of up to 1cm. in circumference at the forearm and, possibly, also of the upper arm. Additional disparities in circumference are possible based on asymmetrical job physical requirements.

3. **Reflexes**
The biceps reflex primarily tests the C5 root, and to a lesser extent, the C6 root. The brachioradialis reflex tests the C6 root. The C7 root is assessed with the triceps reflex. The Hoffmann pathologic reflex in combination with clonus may indicate an upper motor neuron lesion.

4. **Sensory Examination**
Testing to light touch and pinprick (sharp dull perception) in the forearm and hand is usually sufficient to detect common nerve root compromise, but it may be necessary to perform sensory examination of the area from the neck to the forearm to test for higher nerve root compromise. Decreased sensation over the lateral deltoid muscle is a sign of C5 nerve root or axillary nerve compromise. Loss of sensation in the area of the radial forearm and thumb (and perhaps the index finger) suggests C6 nerve root involvement. Decreased sensation in the middle finger (3rd digit) may be a sign of C7 involvement, although it also is supplied occasionally by the C6 or C8 nerve root. The C8 root may show ring and little finger sensory findings. The ulnar side of the little finger (5th digit) is the purest area of C8 innervation. The T1 nerve root can be tested by evaluating sensation in the upper medial forearm and medial arm. The examiner should determine whether light touch can be felt, and whether the patient can distinguish between sharp and dull stimuli. These findings are more reliable than the report that sensory stimuli feel odd or "different" to the examinee, and yet each sensory stimulus is perceived (felt).

5. **Physical Examination Tests**
Ideally, the treatment of cervical or thoracic pain should be based upon a correct diagnosis. However, for most patients a specific diagnosis that indicates the pain generating structure and the pathophysiology is not possible, and

their diagnosis is non-specific cervical pain. Physical examination rules out major neurologic involvement and provides a baseline from which to judge improvement over time. For a variety of reasons, a patient's response to a single test may not be reflective of the presence of identifiable underlying pathology.

6. **Non-Organic Signs**
Waddell articulated non-organic signs on physical examination of the lumbar spine in patients with probable psychosocial confounders and these signs have also been described in cervical spine patients.(121) However, they are not as well-known as Waddell's lumbar spine signs, and they have not been validated in multiple studies.

Evidence for Physical Examination/Medical History
There is 1 high-quality RCT incorporated into this analysis.(99)

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Bertilson 2003 RCT	8.0	N = 100 neck and shoulder pain; duration not specified	Exam findings with medical history vs. no medical history. Each patient examined by 2 examiners. Exam order was randomized variable.	Fifty-three (53) of 66 (80%) exam tests showed increase in findings, 11 (17%) decrease, 2 (3%) unchanged vs. no history. Highest prevalence of positive findings is for palpable tenderness of spinal processes and lower cervical paraspinal joints.	"Our results indicate that knowledge of history did not influence reliability of the clinical tests but increased the prevalence of positive findings. Bias in the direction as to what was positive was present in all categories of tests, except the sensitivity (pain from pinwheel) and reflex tests."	Suggests history bias on most physical exam maneuvers including ROM, tenderness, hypertrophy observation, strength deficiency, nerve stretch, neck compression/ traction. Usefulness of palpation of spinal processes and lower paracervical paraspinal joints of questionable diagnostic significance.

Early Disability Prevention and Management Issues

See also the Cornerstones of Disability Prevention and Management guideline. As an example of the biopsychosocial model, initial patient management should include alertness to the presence or development of physical and psychosocial factors that may be barriers to recovery and, if not addressed, are thought to increase the probability of the development of delayed recovery or chronic pain.(122-125) Initial flags(126) drawing attention to these potential issues include excessive verbal attention to symptoms or physical features, inquiries about permanent impairment rating during an initial presentation, prior history of disability or impairment, familial members with acquired disabilities, a history of mental health disorders, history of substance(s) abuse, an apparent overreaction on examination, and presence of other non-organic physical examination signs. Besides the issues noted above, some additional yellow flags that the physician should consider include early signs of medication dependence, disproportionate inactivity, fear avoidance, compliance/attendance problems, resistance to transitional work options, and provider shopping.

Management of the patient at this stage of treatment necessitates overcoming these identified barriers in order to facilitate functional recovery and patient autonomy. Education is important, as there is evidence that when physicians view whiplash as a relatively benign condition their patients appear to consequently experience less debility.(127, 128) Therapies that are not resulting in functional recovery or that foster treatment dependence should be avoided. In contrast to the "watch and wait" philosophy, it is increasingly recognized that better outcomes are associated with maintaining work status or early return to work and avoiding or resolving disability at the earliest possible time. Patients should be encouraged to resume/continue normal basic and instrumental activities of daily within pain tolerance to minimize decline in function. These concepts reflect recognition that chronicity of disability is the overriding barrier to ultimate benefit for the injured worker. For example, the managing physician should consider early discontinuation of ineffective treatment and avoidance of interventional procedures of questionable significant functional benefit. For more difficult cases, referral for psychosocial evaluation and/or single-or-interdisciplinary treatment options with a proven record of success may be needed. For providers familiar with these management concepts, early referral (including after the first visit) to a physician well versed in the conservative management of cervicothoracic pain is recommended upon the discovery of these signs.

C. INDICATIONS FOR FURTHER WORKUP

Physical examination evidence of severe or increasing neurologic compromise that correlates with the medical history and test results may suggest a need for immediate referral. Suspicion of tumor, infection, fracture, dislocation, or other related serious conditions, warrants further investigation and usually urgent referral. A medical history that suggests pathology originating somewhere other than in the cervicothoracic spine may warrant examination of the shoulder, anterior neck, esophagus, heart, vascular system, lungs, upper abdomen, or other areas.

Associated Factors, Risk Factors and Work-Relatedness

Episodes of acute cervical and thoracic pain are sometimes due to discrete trauma, (129) including some cases of work-related traumatic accidents. Most commonly these include effects of motor vehicle crashes, falls from height, and accidents involving being struck by an object. However, in the Mayo Clinic study of cervical radiculopathy cases occurring over 15 years, only 15% of cases had a history of physical exertion or trauma preceding the onset of symptoms. (130) Cases of cervical and thoracic pain that arise from crashes and falls occurring at work are not controversial and are considered work-related. Non-specific cervical pain may also arise as a sequel of a motor vehicle crash (e.g., whiplash). In most cases, work-relatedness of this condition is also not controversial. However, there are some cases where work-relatedness becomes more unclear. Where the inciting event was low force, an activity done many times before without incident, and/or the condition continues beyond healing duration of an injury (does not behave like an injury) (131) particularly in the context of a pre-existing condition, work-relatedness is controversial.

Individual Factors

Most cases of cervical and thoracic pain in the population do not arise from an acute injury or event and determining work-relatedness involves a more complex analysis that includes incorporation of the epidemiology on the subject as part of the causal assessment(132) (see Work-relatedness guideline). There is evidence for non-occupational risk factors for either non-specific cervical pain or persistence of pain, including increasing age,(129, 132-153) female gender,(136, 139, 140, 143, 144, 147, 148, 152-169) physical inactivity/lack of exercise,(139, 143, 163, 170) genetics,(171) poor sleep,(172-176) smoking/tobacco,(133, 134, 143, 148, 149, 152, 177-179) obesity,(144, 146, 175, 180-184) poor health,(151) episodes of sick leave,(185) metabolic syndrome,(186) and cardiovascular disorders.(187, 188) Most reports suggest no relationship between exercise and neck pain,(144, 148, 170, 182, 189) although a strong U-shaped relationship reported in low back pain raises concerns about appropriate statistical analyses in the neck pain studies(190) which is a further concern based on some comparable epidemiological evidence of a possible U-shaped relationship in the neck.(191) Prior neck, back pain, or other injury is a commonly reported risk.(132, 138, 143, 146, 147, 152, 155, 159, 192-194) Crystal diseases including gout, calcium pyrophosphate, and hydroxyapatite arthritides also are known to affect the spine.(195-197)

Poor labor market attachment and unemployment predict worse outcomes in those who subsequently sustain whiplash.(198) Lower baseline work activities also are predictive of worse outcome among acute whiplash patients,(157) as are higher baseline pain or disability scores,(135, 140, 157, 199-203) delay in seeking treatment;(140) treatment with physical therapy;(204) compensation or litigation status.(140, 202)

Psychosocial and Work Organizational Factors

Psychosocial factors have been evaluated in many studies, with some reporting that these factors appear to outweigh job physical factors,(205-209) though some have found job physical factors to be modestly stronger.(210) Problems of inadequate recall of prior psychological, drug and alcohol issues have been reported.(211) Robust conclusions regarding relative importance of these factors are suggested to require quality epidemiological studies that include measured job physical factors. Available studies have suggested increased risks with depression,(128, 143, 149, 159, 181, 212-216) anxiety disorders,(149, 214, 215, 217, 218), stress,(219, 220) somatization,(157, 221) sexual abuse, psychiatric problems,(178) psychological stress,(163, 222) low occupational position,(223) workplace bullying,(175) low decision authority,(224), low social support,(152), emotional exhaustion,(175), distress,(212, 225, 226), self-efficacy,(227) high psychological demand,(132, 209, 225, 226, 228) high job strain,(137, 154, 155, 229-233) low job control,(210, 234) low supervisor support,(168, 209, 210, 235, 236) low empowering leadership,(228) low social support,(132, 229, 232, 235, 237) low occupational position,(223) job dissatisfaction,(166, 205, 230, 238, 239) effort-reward imbalance,(206, 208, 240) and generally reduced productivity.(241)

One study of chronic whiplash patients suggested it is frequently accompanied by wider spread of symptoms and is a functional somatic syndrome.(242) However, another study of whiplash patients found no predictive value of psychosocial variables studied(243) while another found childhood personality did not predict subsequent risk.(244) Stress biomarkers have also been identified as potentially predictive.(245, 246) Cultural factors are also reported to influence disability.(247, 248)

Job Physical Factors

The occupational epidemiological literature base underlying cervical disorders is considerably weaker than for the lumbosacral spine.(232) Many studies combined shoulder and cervical pain, resulting in substantial difficulties in applying any of those studies to an individual case of any single disorder.(249, 250) There are no prospective cohort studies reported that have measured job physical tasks while frequently following workers over time to ascertain potential causal relationships. The relatively few longitudinal studies largely relied on self-reported exposures and infrequent assessments of health status, precluding strong conclusions.(133, 145, 152, 155, 166, 171, 185, 192, 205, 209, 231, 233, 251-260) The vast majority of reported studies have utilized retrospective methods, especially cross sectional study designs, and/or recall of job exposures through questionnaires. There is no validated ergonomic job exposure tool for the cervical spine, and available measures are considerably weaker than for the lumbar spine.

The available data on the importance of job physical factors include substantial conflicts. In contrast with beliefs that manufacturing and/or manual work is the greatest risk for neck disorders, National Health Interview Survey data, a large population-based study found the highest prevalence of neck pain was in the military; arts, design, entertainment, sports, media; life, physical, and social science; health care support; and installation, maintenance, and repair.(261)

A number of physical factors have been reported to be associated with cervical pain in the body of available studies. Force was associated with cervical pain in some studies,(134, 146, 210, 262-266) while others have been negative.(267-270) Repetition has been found associated with cervical pain in some studies,(139, 185, 262, 271-278) though some also are negative.(267-269, 279) Posture has been associated with cervical pain in some studies,(134, 139, 210, 230, 262-264, 274, 275, 277, 280-286) while others have reported no association.(287-289) Prolonged sitting(185, 230, 233, 238, 290) and whole body vibration are also suggested contributors and vibration is further reviewed below. High "physical workload" or "mechanical exposure" has also been reportedly associated with increased risk,(155, 166, 171, 209, 291) while lower job physical demands were purported risks in another study,(204) but no relationship with job physical demands in others.(129, 292, 293) These activities are not exclusive to job functions and must be reviewed as they pertain to non-occupational activities as well. Unaccustomed work, hobbies, or sports (although there is some evidence to suggest that cycling may contributes to neck pain(294)) is largely unstudied in the cervical spine.

It has been theorized that the job physical "stressors" do not cause spine disorders, including cervical pain. Rather, when a disorder arises in an individual who does heavy physical work, the work is then more difficult to accomplish and the individual is more likely to file a workers' compensation claim. This is compared to the sedentary worker who develops back pain and may continue to perform work though more carefully without need to file a claim (reporting bias).(295, 296) Prospective cohort studies have been underway for the lumbar spine to attempt to determine which of these theories (or both) are correct. Whether these results apply to the cervical spine is yet to be determined.

There have been postulates that whole body vibration is a risk for spine disorders(156, 249, 266, 297-306) and one author noted a risk for radiculopathy from segmental vibration.(307) However, there are many study weakness issues in the available data which are mostly from older studies, addressed only the lumbar spine and involved remote, higher amplitude exposures to equipment that is believed to be substantially different from that available today, did not control for known confounders, and generally did not control for time spent seated, which may cause fatal confounding.(308) There are far fewer data for cervical, or especially thoracic outcomes,(134, 156, 238, 249) and no consensus there is an increased risk for those spine segments. One study found no relationship with neck pain or problems.(309) Additionally, heavy material handling tasks involving loading or unloading, as well as the requirement for prolonged sitting(185, 230, 233, 238, 290) appear likely to have partially, but may have completely confounded data in the available studies on risks of whole body vibration.(310)

Cervical Radiculopathy
Population-based data from Mayo Clinic indicate that cervical radiculopathy risk peaks among those 50-54 years of age, is more common among men than women, is disproportionately preceded by lumbar radiculopathy in 41% of cases, and is preceded by a specific discrete or traumatic event in only 15% of cases.(130) Other studies have reported associated factors include increased age,(299, 311-313) female gender,(313, 314) male gender,(299) white race,(313) smoking,(312, 315) obesity,(316) degenerative lumbar spine conditions,(311, 317) and degenerative thoracic spine conditions.(312) Some have noted the apparent predominance of cardiovascular risk factors (smoking, diabetes, hypertension, hypercholesterolemia, family history for premature myocardial infarction) for lumbar disc herniations which might also apply to the cervical spine.(318) Lumbar radiculopathy studies should likely be considered for systemic risks such as smoking.

Cervical radiculopathy has been relatively unstudied in occupational epidemiological studies.(249, 319-322) Most researchers have assumed there is some increased risk from heavy lifting, similar to the beliefs about lumbar spine risk resulting from increased intradiscal pressures from lifting. However, quality epidemiological data supporting these theories have not been published and available data conflict. There are studies that have reported no increased risk among workers performing data entry,(284) industrial workers,(271)shipping dockers,(323) and assembly line packers.(270) There are some reports of increased risk in fighter and helicopter pilots,(324) though not all report increase neck issues in these populations.(325) A population-based study from Denmark suggested professional drivers were at increased risk.(156)

Degenerative Cervical Spine Conditions
Similar to disc herniations, degenerative findings in the lumbar and cervical spine are well correlated.(311) Development of degenerative cervical spine conditions on MRIs over 10 years were related to age, but not to sex, smoking, BMI, alcohol or sports/exercise.(150) Other studies have also suggested relationships with age(311, 326) and genetics.(327, 328) Passive coping has been shown to be a strong risk for disabling neck pain.(329) One study of carrying loads on the head in Nigerian traders found a link with spondylosis,(330) although extension of that activity to other typical western occupations is unknown.

No quality epidemiological studies support the theory that degenerative spondylolisthesis, spinal stenosis, or degenerative facet disease are occupational conditions. However, there is a biomechanical theory that physical factors may contribute through degenerative disease in the discs, with theoretically altered biomechanical forces in the facets resulting in or accelerating degenerative facet osteoarthrosis. Yet osteoarthrosis is now recognized to have strong relationships with genetics and age.(331)

Thoracic Spine Pain
There are few studies of either thoracic pain or thoracic radicular pain. MRI data suggest significant correlations between having cervical degenerative findings and also having degenerative thoracic spine conditions,(312) which by extension suggests systemic risk factors operate throughout the spine (see Neck/Cervical above and Low Back Disorders guidelines). One study found approximately two-times higher prevalence of thoracic spine pain in women than in men. That study also reported lower grade male white-collar workers were more likely to report thoracic pain while upper grade female white-collar and professional workers were more likely to report thoracic spine pain.(332)

There is an absence of quality epidemiological prospective data with measured individual, job and psychosocial factors regarding thoracic pain and thoracic radicular pain.(333) It is recommended that the data on lumbar pain be utilized to help guide a tentative assessment of work-relatedness (see Low Back Disorders guideline), although in the absence of data, it should be recognized a clear conclusion of work-relatedness is speculative outside of discrete, significant trauma (see Work-Relatedness guideline).

Follow-up Visits
Patients with potentially work-related acute cervicothoracic disorders are recommended [**Recommended Insufficient Evidence (I)**] to follow-up from every 3 to 5 days for acute severe conditions particularly with lost time injuries. Follow-ups may be needed less frequently, e.g. every 1 to 3 weeks for mild conditions without lost

time and are **Recommended, Insufficient Evidence (I)** to be with a health care provider who can offer counsel regarding activity levels, relative rest, medication use, activity modification, prognosis, fear avoidant belief training, and other concerns.(334) Health care providers should answer all questions and make these sessions interactive so that the patient is fully involved in his or her recovery. If the patient has returned to work, these interactions may be conducted on site or by telephone to avoid interfering with work activities. Subsequent follow-up can occur when there is need for altered treatment; release to modified-, increased- or full-duty; or after appreciable healing or recovery can be expected. Typically, this will be no later than 1 week into the acute pain period. At the other extreme, in the stable chronic cervicothoracic spine pain setting, follow-up may be infrequent, such as every 6 months by consensus.

Diagnostic Criteria

The criteria presented in the Diagnostic Criteria for Non-red Flag Conditions table (Table 5) list the probable diagnosis or injury, potential mechanism(s) of illness or injury, symptoms, signs, and appropriate tests and results to consider in assessment and treatment.

Table 5. Diagnostic Criteria for Non-red Flag Conditions

Probable Diagnosis or Injury	Mechanism	Symptoms	Signs*	Tests/Results
Acute Cervical Pain (Cervical strain/sprain, or Non-specific cervical pain, or "whiplash")	Occurs commonly without an apparent event or may be associated by patient with a normal activity unlikely to cause harm. May be temporally associated with a slip or fall, a motor vehicle accident, lifting, or forceful pushing and/or pulling.	Cervical pain that may or may not radiate to the scapula or deltoid and/or biceps area of the shoulder. Stiffness (decreased motion). Generally without paresthesias.	Exam may be normal or show decreased neck motion and/or superficial tenderness. No neurologic deficit.	**Not recommended in first 4-6 weeks unless history suggests a possible red flag condition.**
Chronic Cervical Pain (non-specific cervical pain or "chronic whiplash, cervical spondylosis, or pain of presumably disc, facet, or muscular/fascial origin)	Persistence of non-radicular cervical pain beyond 3 months.	Persistence of acute symptoms	Exam may be normal or show decreased neck motion and/or superficial tenderness. No neurologic deficit.	Not recommended
Cervical Nerve Root Compression with Radiculopathy	May occur without any obvious inciting event. May be associated with lifting or trauma.	Arm pain with or without cervical pain. Paresthesias (numbness) are common. C5 and C6 nerve root syndromes are most common.	Dermatomal sensory alteration, myotomal strength and reflex alteration. Foraminal closing (Spurling's) and opening (traction) maneuvers increase/create or decrease arm symptoms.	MRI
Spinal Cord Compression with Myelopathy	Nearly always occurs in the setting of congenital cervical stenosis. Symptoms often insidious and may onset without any obvious inciting event.	Chronic cervical pain. May or may not have arm symptoms. Impaired upper and/or lower limb coordination, with or without altered gait. Bowel or bladder control impairment.	Pathologic reflexes (Babinski, Hoffman, etc.) Hyper-reflexia below level of cord compression. Impaired rapid alternating movements and/or gait. Other neurological impairment(s) (e.g., motor, sensory, bowel/bladder dysfunction)	MRI, CT Myelography

*For patients with severe disorders, the physical examation can be quite helpful. However, for most patients with cervical pain, the physical examination findings tend to have low predictability.

DIAGNOSTIC TESTS
ROENTGENOGRAMS (X-RAYS)

This review focuses on patients presenting to office based medical practices, and not on patients presenting to emergency rooms, and especially not to patients presenting by ambulance after major trauma.

X-rays demonstrate bony structure. Standard film views are generally an anterior-posterior (AP) film, and a lateral film. Oblique views give an excellent view of the neural foramena, and can strongly suggest foraminal stenosis. A coned-down or focused view of the odontoid may be included particularly for evaluation of traumatic or rheumatoid arthritis cases. Flexion and extension films are not standard films, but are occasionally used to evaluate spinal instability, particularly in the setting of rheumatoid arthritis, degenerative spondylolisthesis, and fractures. The criteria for cervical instability are a measurement of 4mm[iv] or more of movement of one vertebral body in relation to an adjacent vertebral body, or angular motion at one interspace that is 12 degrees or more greater than the motion at either the level above or below.(104, 335) Depending on the translation forward or backwards this is referred to as anterolisthesis or retrolisthesis.

1. *Recommendation: X-ray for Acute Cervicothoracic Pain with Red Flags or Subacute or Chronic Cervicothoracic Pain*
   X-ray is recommended for acute cervicothoracic pain with red flags for fracture or serious systemic illness,(336) **subacute cervicothoracic pain that is not improving, or chronic cervicothoracic pain.**
   Indications – Patients with red flags (e.g., dangerous mechanism of injury, over age 65 years, paresthesias in extremities). Also indicated for subacute or chronic cervicothoracic pain particularly when not improving as an option to rule out other possible conditions. (336)
   Frequency/Duration – Obtaining x-rays once is generally sufficient. Repeat films are usually reserved for significant changes in clinical status, i.e., significant worsening of existing symptoms or development of new symptoms.
   Harms – Medicalization or worsening of otherwise benign spine condition. Radiation exposure.
   Benefits – Diagnosis of a fracture, cancer or otherwise latent medical condition(s).

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – High

2. *Recommendation: X-ray for Spondylolisthesis*
   Flexion and extension views are recommended for evaluating symptomatic spondylolisthesis in which there is consideration for surgery or other invasive treatment or occasionally in the setting of minimal trauma.(337)
   Indications – Chronic severe mechanical pain suspected to be due to instability.(337) Assessment is to measure the (dis)continuity of the spinolaminar line, along the posterior line of the vertebral bodies, and measured soft tissue diameters at C2 and C7.
   Frequency/Duration – Flexion and extension views are generally needed no more than every few years. An experienced reader with an established protocol is recommended to avoid variation in interpretation.(337) However, after surgical intervention, flexion/extension views may be used to assess extent of successful fusion.
   Harms – Medicalization or worsening of otherwise benign spine condition. Radiation exposure.
   Benefits – Diagnosis of significant spondylolisthesis that is amenable to surgical correction.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

3. *Recommendation: X-ray for Acute, Non-specific Cervicothoracic Pain*
   Routine x-ray is not recommended for acute, non-specific cervicothoracic pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – High

Rationale for Recommendations

[iv]Test says >3.5mm, but since no one can measure 0.5mm, this really means 4mm or more.

There are few quality studies of x-rays, likely due to reliance on the test for many decades. X-rays are believed to be unnecessary for the routine management of cervicothoracic pain outside of the setting of red flags.(335, 336, 338) When red flags are identified, x-rays at the first visit are recommended to assist in ruling out these possible conditions (fracture, neoplasias, infection).(336) A clinical prediction rule was developed for alert and stable acute cervical trauma patients with a recommendation for x-rays if there is a dangerous mechanism of injury, age over 65 years, or accompanying paresthesias in the extremities. In the absence of red flags and if the patient is able to rotate the neck 45° both left and right then radiographs are not indicated.(336) Even when red flags are suspected, judgment is recommended and it should not be mandatory to order x-rays in all cases (e.g., significant typical cervicothoracic pain in the course of a manual patient transfer in a patient with a remote history of cancer). In the event there is cervical pain without any improvement over 4 to 6 weeks, x-rays may be recommended to rule out other possible problems.(335) If an MRI is used as imaging, plain x-ray may not be needed. MRI is a more sensitive and specific test particularly for disc-related concerns.

A prospective study examined inter-rater reliability in interpretation of flexion extension x-rays of the cervical spine. Three orthopedic surgeons, one neurosurgeon, and 3 radiologists blindly read the same 75 flexion extension x-rays for instability. The same x-rays were re-read in a different order from 28 to 183 days later using a computer assistant program. The first read resulted in 12/75 (16%) unanimous agreements. The second reading resulted in 57/75 (76%) unanimous agreements. It was concluded that there was a need for standardization and quantitative definitions of spinal instability and spinal fusion.(337)

X-rays are non-invasive, low to moderately cost, and have a low risk of adverse effects (exposure to ionizing radiation, which has been estimated to be from 0.12 and 0.02 mSv for AP and lateral cervical x-rays respectfully).(339) Thus, x-rays are recommended for discrete clinical situations.

Quality Evidence
There is 1 moderate quality and 1 other study incorporated into this analysis.(336, 337)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: neck, neck pain, cervical, radicular pain or radiculopathies, neck pain diagnosis, diagnostic, diagnosis, sensitivity, specificity, positive and negative predictive value, predictive value of tests, efficacy, efficiency; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, retrospective studies, or prospective studies. We found and reviewed 240 articles in PubMed, 2 in Scopus, 48 in CINAHL, 0 in Cochrane Library and 0 in other sources. We considered for inclusion 2 articles from PubMed, Scopus, CINAHL, Cochrane Library and from other sources.*

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Type of X-rays	CT used	MRI Used	More than one rater	Blinding of rater	Myelography	Surgery Performed	Clinical outcomes assessed	Long term follow-up (mean when noted)	Outcome	Conclusion	Comments
Taylor 2007 Diagnostic	4.0	52	C	29 with fusions. 14 with spondy-lolisthesis, 13 with chronic pain post trauma, 15 degenerative disease	Flexion/ extension	-	-	+	+	-	-	-	-	Agreement without computerized assistance: Kappa = 0.17 (p <0.001). Unanimous agreement between observers on 12/75 (16%); with computerized assistance: Kappa = 0.77 (p <0.001). Unanimous agreement on 57/75 (76%).	"The result of this study suggest that current, commonly used methods to clinically assess flexion-extension X-rays of the cervical spine do no provide reliable clinical information about intervertebral motion abnormalities."	Data suggest current practice of reading flexion extension x-rays has large variability between raters. With 95% confidence interval provided by computer program and computer assistance, inter-rater correlation significantly increases from 16% to 76%. Data suggest more uniform way for interpretation needed as clinical assessments often based on x-ray findings. Data suggest use of computer assistance technology improves inter rater variability on cervical flexion/extension x-rays.
Stiell 2001 Diagnostic	NA	8,924 (151 had important C-spine injury)	C	Alert and stable trauma patients (Glascow 15)	3 views plus flexion extension*	+*	-	+*	-	-	-	+*	-	Using the 3 clinical rules developed: Sn: 100% (95% CI 98%-100%) Sp: 42.5% (95% CI 40%-44%). Potential radiography ordering rate would be 58.2%	"We have derived the Canadian C-Spine Rule, a highly sensitive decision rule for use of C-spine radiography in alert and stable trauma patients."	Canadian C-spine Rule comprises 3 main questions: 1. Is a high-risk factor present (age >/= 65, dangerous mechanism, paresthesias of extremities); 2. Is low-risk factor present that allows safe assessment of ROM (simple rear-end motor vehicle collision, sitting position in ED, ambulatory at any time since injury, delayed onset of cervical pain, absence of midline tenderness.); 3. Is patient able to actively rotate neck 45° to left and right? Suggests using these rules can decrease unnecessary cervical x-rays in alert, stable trauma patients.

?- was not specified in study; *- Not done on all participants; C- cervical, T-thoracic, L- lumbar spine; #- surgery performed in some participants; **- quantified response not reported

MAGNETIC RESONANCE IMAGING (MRI)

Magnetic resonance imaging (MRI) is considered the gold standard in diagnostic imaging for defining soft tissue anatomy due to its greater ability to distinguish soft tissues.(340-343) Thus, MRI is recommended to assess potential nerve root or spinal cord compression, if the patient is a candidate for surgery or radiation therapy, and if no contraindications to MRI exist. Computerized tomography (CT) remains an important analytical tool especially for evaluating bony or calcified structures.(340, 341, 344, 345) MRI may also be useful in the acute trauma setting to evaluate for soft tissue injury in non-communicative patients with a high pre-test probability of significant injury that would need intervention.(340, 344, 345) MRI also can determine if a fracture seen on x-ray is recent (still has marrow edema) or remote (healed and without marrow edema).

1. *Recommendation: MRI for Diagnosing Red Flag Conditions*
   MRI is recommended for patients with:
   1. **Acute cervical pain with progressive neurologic deficit;**
   2. **Significant trauma with no improvement in significantly painful or debilitating symptoms;**
   3. **A history of neoplasia (cancer);**
   4. **Multiple neurological abnormalities that span more than one neurological root level;**(340, 344-347)
      Previous neck surgery with increasing neurologic symptoms;
   5. **Fever with severe cervical pain; or**
   6. **Symptoms or signs of myelopathy.**

   Harms – Medicalization or worsening of otherwise benign spine condition.
   Benefits **–** Diagnosis of a surgically treatable condition or otherwise latent medical condition(s).
   Strength of Evidence – **Recommended, Evidence (C)**
   Level of Confidence – High

2. *Recommendation: MRI for Diagnosing Subacute and Chronic Radicular Syndromes*
   MRI is recommended for patients with subacute or chronic radicular pain syndromes lasting at least 4 to 6 weeks in whom the dermatomal and myotomal symptoms are not trending towards improvement if either injection is being considered or both the patient and surgeon are considering surgical treatment if supportive findings on MRI are found.(343)
   Harms – Medicalization or worsening of otherwise benign spine condition.
   Benefits **–** Diagnosis of a surgically treatable condition or otherwise latent medical condition(s).
   Strength of Evidence – **Recommended, Evidence (C)**
   Level of Confidence – High

3. *Recommendation: Early MRI for Diagnosing Acute Radicular Syndrome*
   MRI is not recommended for acute radicular pain syndromes. Exceptions include progressive neurological deficit (see above) or severe impairment not trending towards improvement and either injection is being considered or both patient and surgeon are willing to consider early surgical treatment if supportive findings on MRI are found.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

4. *Recommendation: Repeat MRI Imaging without Significant Clinical Deterioration in Signs and/or Symptoms*
   Repeat MRI imaging in the absence of significant new radicular or myelopathy symptoms and/or signs is not recommended. An exception would be agreement on the part of the patient and surgeon that surgery will be performed, and the previous MRI is more than 6 months old. Cervical disc herniations are known to resorb spontaneously, and surgery would be predicated on persisting nerve root or cord compression.(348)

   Strength of Evidence **–** **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

5. *Recommendation: MRI for Diagnosing Non-specific Cervicothoracic Pain*

MRI is not recommended for the evaluation of patients with non-specific chronic cervicothoracic pain. MRI may be considered if the purpose is to rule out non-injury-related diagnoses in select patients, such as possible neoplasia, infection, or other neurological illnesses, based on the presence of symptoms or findings that suggest these diagnoses.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

6. *Recommendation: Flexion/Extension, Standing, or Weight-bearing MRI*
Flexion/extension, standing, or weight-bearing MRI is not recommended for cervicothoracic pain or radicular pain syndrome as the clinical utility of this technology has not been adequately established.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

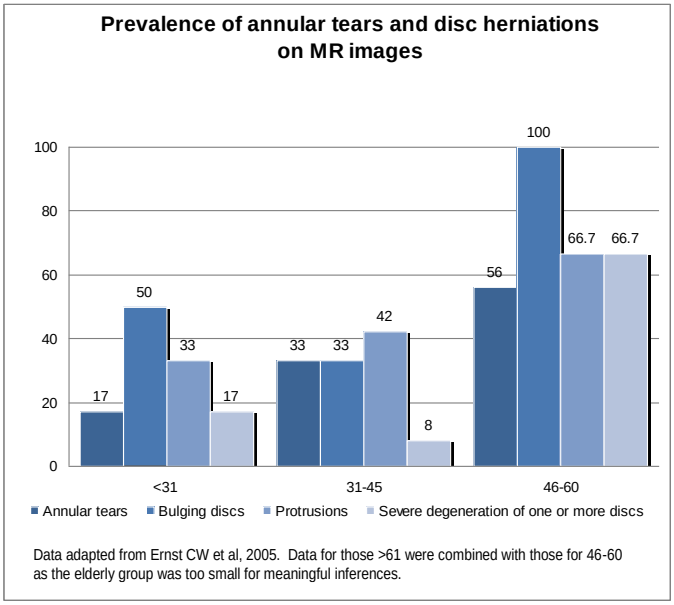
7. *Recommendation: MRI for Acute Whiplash without Neurological Signs*
MRI is not recommended for patients with acute whiplash in whom there is no evidence of dermatomal or myotomal symptoms and signs.

Strength of Evidence – **Not Recommended, Evidence (C)**
Level of Confidence – Moderate

8. *Recommendation: Open MRI*
Open MRIs are not recommended for routine use except in circumstances where the patient is either morbidly obese and exceeds the closed MRI unit's weight specifications, or suffers from claustrophobia that is not alleviated with a low-dose anxiolytic administered prior to the procedure.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Figure 1. Prevalence of Asymptomatic Annular Cervical Tears and Cervical Disc Herniations on MR Images by Three Age Groups



Rationale for Recommendation: Closed MRIs
MRI has been evaluated in quality studies (see evidence table); however, most cases of cervicothoracic pain and radicular pain syndromes spontaneously resolve and require no imaging.(349-351) The sensitivity and specificity of MRI or CT are difficult to define as they require a "gold standard" that is difficult to define in spine pain since the final diagnosis often is based on the same imaging modality being tested. Therefore, these clinical studies may be prone to incorporation bias, artificially inflating the sensitivity and specificity with some assuming MRI has 100%

sensitivity and specificity. Multiple case series have been reported in patients with acute cervicothoracic trauma with neurologic deficits. A retrospective review evaluated MR and CT scans in 113 acute spine trauma patients. The study reported on a total of 166 lesions found on MRI and CT scan. MRI was reported to be superior to CT scan in finding soft tissue injury, ligamentous injury, high-grade stenosis, and spinal cord injuries.(347) A case series evaluated MRI and CT scans in 14 spinal trauma patients. They reported that CT missed 3 epidural hemorrhages (100%) found on MRI, and CT missed 3 of 5 (60%) intervertebral disc injuries found on MRI.(345) It has been shown that MRI is superior to CT scan and x-ray at identifying spinal cord injury and other soft tissue injuries.(340, 344-347, 352, 353)

A study evaluating 52 cervical radiculopathy patients with or without myelopathy reported that MRI was in agreement with the surgical findings 74% of the time. When MRI and CT myelography were conducted on the same patient, the radiographic diagnosis was in agreement with the surgical diagnosis 90% of the time.(343)

A study with 497 asymptomatic patients was conducted. An overall increase of MRI findings related to age ($p < 0.0001$) was reported. Grade 1 or Grade 2 disc degeneration was found in 17% of the discs in asymptomatic men and 12% of the discs in asymptomatic women in their twenties rising to 86% and 89%, respectively, in subjects over 60 years of age.(354) A study evaluated MRI findings in a cohort of high school students with or without cervicothoracic pain. They initially surveyed students about symptoms while they were in high school. Seven years after the first survey was completed another survey was done. The participants with cervicothoracic and shoulder pain on both occasions but without significant changes over the years were chosen as the symptomatic group. Participants without cervicothoracic or shoulder pain at both survey times were the asymptomatic group. Participants had an MRI done at the end of the 7 years follow-up. Pathological changes of the cervical spine seen with MRI in 24 to 27 years old were reported to be equally common in the symptomatic and asymptomatic groups; 20 degenerated discs in the symptomatic group (SG) and 26 in the asymptomatic group (AG); 14 annular tears in the SG, 18 in the AG; 18 disc protrusions in the SG, and 29 in the AG. Disc herniations were the only finding more prevalent in the symptomatic group, 4 in the symptomatic group and 0 in the asymptomatic group.(355)

A prospective study evaluated MRI scans in acute whiplash patients at baseline and after 3 months. Each patient was involved in a RCT evaluating immobilization, active mobilization and advice to act as usual. The initial MRIs were performed on 178 patients and follow up MRIs on 82 (46.1%) patients. The most frequent finding was pre-existing degeneration 139/178 (78%). Bulges or protrusions of one or more discs were present in 35/178 (20%) of the participants. It was determined that 7 had findings on MRI that were "traumatic" in nature (paravertebral bleeding/edema, prevertebral bleeding/edema, edema in the spinal cord, or "traumatic" disc protrusion or bulge). The authors concluded that MRI is not the answer to a diagnosis in the vast majority of patients developing long-lasting pain after a whiplash injury, and early MRI scans do not predict prognosis.(356) Others have reported evidence of fatty infiltrates in the craniocervical flexors being statistically higher on MRI in those with chronic whiplash disorders.(353) However, a prospective, 10-year study has reported MRI findings do not explain persistent symptoms.(357)

Another study evaluated MRI findings in relation to the transverse ligaments of the atlas (alar ligaments). The study evaluated 92 whiplash-injured patients diagnosed as Grade 2 whiplash patients and 30 uninjured individuals who underwent proton density-weighted MRI of the craniovertebral junction at least 2 years after the injury. Twenty out of 117 (17.1%) had Grade 2 or 3 posterior atlanto-occipital membrane lesions. No Grade 3 lesions and only one Grade 2 lesion was found in the uninjured individuals. However, no clinical correlation was made in regard to prognosis or symptoms based in the MRI findings.(358) In another study using the same populations it was reported that the transverse ligament was classified as abnormal in 64% in the injured group and 27% of the uninjured group.(358) The authors failed to explain why the alar ligament should show signs of acute injury (increased signal) 2 to 9 years after the whiplash event in spines that are not clinically unstable. Other investigators did not find MRI evaluation of the alar ligaments clinically helpful due to the high prevalence of "abnormalities" in normal people.(359, 360)

There is no quality evidence for use of MRI within the first 6 weeks of symptom onset. However, rare cases are thought to need MRI and emergent/urgent surgery (see below).(343) Patients presenting with a mild single nerve root deficit, such as an absent deep tendon reflex, should not have early MRI, as their condition usually resolves spontaneously; thus, the test does not alter the course of treatment. Those who have a documented neurologic status

that then objectively deteriorates (particularly a significant increase in weakness or an increased loss of sensation compared with the prior examination) and those with a history of cancer with symptoms suggesting atypical radicular presentation do have an indication for early imaging with MRI.

In the absence of red flags suggesting fracture or serious systemic illness, imaging before 6 weeks produces no clear health outcomes benefit.(355, 356, 361-364) Early imaging would be expected to result in higher overall costs and increased morbidity through the performance of some unnecessary procedures and/or surgeries. Disc degeneration, disc bulging, and endplate changes on MRI have been shown to either not correlate at all or correlate poorly with clinical outcomes, suggesting that MRI is not useful for most patients.(340, 341, 354-356)

Patients should be *a priori* informed that their MRI is highly unlikely to be "normal" as few patients have a normal MRI(354), and there is a considerable rate of resolution of herniations over 6 weeks after an initial MRI documented in the lumbar spine (see Low Back Disorders guideline). A patient handout describing the prevalence of "abnormal findings" on MRI of asymptomatic individuals is helpful. **Physicians lacking the time or knowledge to explain these facts to patients should avoid ordering MRIs**. The discovery of degenerative changes or clinically irrelevant disc herniations in many patients may cause them to focus on the need to "fix" MRI changes that are actually normal for their age or are asymptomatic findings.(354) This may also become a rationale for avoiding participation in the therapeutic activities that promote functional recovery. In addition, lack of understanding of the strengths, indications, and limitations of a technology preclude adequate clinical interpretation of the results. In those cases, consultation with a physician experienced in treating musculoskeletal disorders may be helpful.

A prospective, observational study using MRI preoperatively to predict postoperative recovery in 57 cervical spondylotic myelopathy (CSM) patients found MRI beneficial in predicting outcomes. The study found those with high T2SI and spinal cord failure were found to predict poorer recovery. Patients with low T1SI were predictive of greater impairment, and those with focal T2SI made more significant improvements in walking. However, the evidence of prognostic power for CSM patients is inconsistent.(365)

Open MRIs have lower ability to discern soft tissue without lower costs and are not recommended other than in circumstances where the patient is either morbidly obese and exceeds the closed MRI unit's weight specifications, or suffers from claustrophobia that is not alleviated with a low-dose anxiolytic administered prior to the procedure.

MRI is minimally invasive even when contrast is used, has few adverse effects, but is high cost. MRI changes treatment if it detects unrecognized fracture, systemic disease, or a spinal condition for which surgery is the recommended treatment.

Flexion/Extension, Standing ("Upright" or "Positional") MRIs
There are no quality trials or studies evaluating flexion/extension MRI or standing MRIs in cervicothoracic pain patients (see Low Back Disorders guideline).

Quality Evidence
There are 3 high-(341, 366, 367) and 15 moderate-quality studies(340, 343-347, 352, 354-356, 358, 368-371) incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: magnetic resonance imaging, MRI, MRI scan, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, diagnostic, efficacy, efficiency, sensitivity, specificity, predictive value of tests, positive predictive value and negative predictive value. In PubMed, we found and reviewed 2,442 articles, and considered 8 for inclusion. In Scopus, we found and reviewed 186 articles, and considered 1 for inclusion. In CINAHL, we found and reviewed 68 articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 78 articles, and considered zero for inclusion. We also considered for inclusion 11 articles from other sources. Of the 25 articles considered for inclusion, 17 studies and 8 systematic studies met the inclusion criteria.*

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Type of MRI used	Type of CT used	T1 weighted images	T2 weighted images	X-ray	Myelography	More than one rater	Surgery Performed	Clinical outcomes assessed	Long term follow-up (mean when noted)	Results	Conclusion	Comments
Orrison 1991 Diagnostic	9.0	126	Cranial Lesions	Cranial central nervous system disease	0.064T MRI & 1.5T MRI	High res CT	+	+	-	-	+	-	-	-	0.064T MRI- Sn: 91.3% Sp: 64% ; 1.5T MRI- Sn: 99%, Sp 28% ; HR-CT- Sn: 88%, Sp 72%.	"Low-field and high-field MR imaging were equivalent in the blind diagnoses of neoplasms and white mailer disease, whereas low-field MR and CT were equivalent in the blind diagnoses of contusion, subdural and epidural hematoma, sinus disease, normality, and abnormality. The specificities with low-field MR imaging and CT were substantially better than those with high-field MR imaging."	Low specificity for 1.5T due mainly to diagnoses of white matter disease. 0.064T MRI useful for intracranial disease. Compared to 1.5-T MR and CT in (28/126). (33/126) 1.5-T MR, and (65/126) CT only. *Data suggest high-field MR is more sensitive than low-field MR and CT in diagnosing intra-cranial lesions. CT was more sensitive in identifying skull fractures.
Birchall 2003 Diagnostic	9.0	40	C	Foraminal nerve root impingement in cervical spondylotic radiculopathy	1.5 T Intera scanner	-	+	+	-	+	+	-	-	-	MRI: sensitivity: 88.9%; specificity: 99.1%; positive predictive value: 98.8%; negative predictive value: 91.6%;	"However, the addition of MR myelography increased the diagnostic yield of the MR examination for the detection of foraminal stenotic disease. MR myelography is a	2 radiologist read all images. Used as Gold-Standard MR + MR myelography combined. *Data suggest if only one test can be ordered, conventional MR is superior. MR

															diagnostic accuracy: 94.5%. MR myelography: sensitivity: 84.4%; specificity: 90.1%; positive predictive value: 88.4%; negative predictive value: 87.7%; diagnostic accuracy: 88%.	useful adjunct to conventional MRI in the investigation of cervical spondylotic radiculopathy."	myelography can increase SN and SP of accuracy of diagnosing foraminal stenosis in conjunction with conventional MR scans.
Jackson 1989 Diagnostic	8.5	59	L	Suspected lumbar herniated nucleus pulposus	1.5T T1 and T2 images.	CT rad dose 4.8 rads	+	+	-	+	+	+	-	-	MRI: Sn- 64%, Sp- 87%; CT: Sn- 60%, Sp- 86%; CT-myelography: Sn- 73%, Sp- 79%; myelography: Sn- 56%, Sp- 86%	"Magnetic resonance imaging compares very favorably with other currently available imaging modalities for diagnosing lumbar HNP. Magnetic resonance imaging is painless, has no known side effects or morbidity, no radiation exposure, and is noninvasive. The authors recommend it as the procedure of choice for the diagnosis of most lumbar disc herniations."	All underwent surgical exploration. *Data suggest MR is as accurate as or more accurate in diagnosing lumber disc pathology than CT myelography unless the patient had prior lumbar surgery.

Modic 1986 Diagnostic	7.5	52	C	Cervical radiculopathy with or without myel-opathy	Surface Coil MRI.	CT with metrizamide	?	?	-	+	-	+ #	-	-	Agreement with surgical findings: MRI – 74%; CTM – 85%; myelo – 67%; MRI + CTM – 90%; CTM + myelo – 92%	"In general, SCMR imaging was as sensitive as CTM for identification of disease level, but Not as specific for type of disease. MM was the modality least specific for disease type. The major advantage of CTM was its ability to distinguish bone from soft tissue, for which contrast material is unnecessary. SCMR imaging is a viable alternative to MM and, together with computed tomography, if needed, provides a thorough examination of the cervical region."	No clinical outcomes measures in operated or non-operated patients; 28 of 52 underwent cervical surgery. CT myelogram suggested more accurate diagnosis than either surface coil MR or myelography. Compared to myelography and CT-myelography and surgery (28/52). Did not really compare clinical outcomes. *Data suggest CT-myelography was more specific and accurate compared to MR images as confined by surgery.
Orrison 1995 Diagnostic	7.5	113	C	Acute cervical spine injuries	0.064T MRI	High resolution CT	+	+	+	-	-	-	-	-	166 lesions diagnosed. CT diagnosed 25 posterior fractures, of these MR found 2/25 (8%), and x-ray found 9/25 (36%). MR diagnosed 68 ligamentous or severe soft tissue injury, CT and x-ray diagnosed 0. MR diagnosed 13 complete obliterations of	"The advantages of MR in the acute evaluation of spine injury include improved evaluation of soft tissues, rapid and accurate clearance of difficult spinal studies, and a superior diagnostic capability, particularly in comatose or historically unreliable patients. Using this modality as a "scout" view allows for more effective and efficient use of CT.	MRI diagnosed more soft tissue injury, CT and x-ray diagnosed more bone fractures. Cervical, thoracic, and lumbar spine injuries. *Data suggest MR images are superior in image soft tissue injury in spine trauma patients. CT is superior in imaging fractures of the spine.

															subarachnoid space, CT diagnosed 1/13 (8%).	Lowfield-strength scanners allow for patient care to be maintained in a manner similar to CT. Cost effectiveness can be established by limiting both the MR and CT examinations to those areas and types of scans with the highest probability of clinical benefit."	
Kulkarni 1987 Diagnostic	6.5	27	C, T, L	Acute spinal cord injury	MRI with surface coil	High resolution CT	+	+	?	-	-	-	+	?	MR showed cord injury in 19/24; CT showed cord injury in 1 patient.	"Neurologic recover, determined in 16 patients, was insignificant in patient with intraspinal hemorrhage; however, patient with cord edema or contusion recovered significant neurologic function. MR at 1.5 T is extremely useful in the diagnosis of acute cord injury and also demonstrates potential in predicting neurologic recover."	MR useful in diagnosing cord injury, soft tissue and ligamentous injury. Reported patterns of injury seen on MRI suggestive of certain neurological outcomes. Ages 2-43 years old. *Data suggest MR imaging can be helpful in identifying spinal cord lesions in neurologically compromised individuals.
Tarr 1987 Diagnostic	6.5	14	C ,T,L	Recent spinal trauma	0.5T MRI	CT	+	+	+	-	-	+ #	-	-	7/7 (100%) posterior element fractures were diagnosed with CT, 4/7 (57%) diagnosed with MRI. 14/14	"In summary, we have found MR to be a useful noninvasive adjunctive imaging modality for evaluation of acute and subacute spine	In acute spinal cord trauma MRI superior in diagnosing and characterizing disc and spinal cord injury. Posterior element fractures better diagnosed with CT.

															(100%) vertebral body fractures diagnosed by CT and MRI. MRI provided more definitive evidence of spinal canal narrowing in 4/4 cases. 2/5 (40%) disc injuries diagnosed by CT, 5/5 (100%) diagnosed with MRI. 0/3 epidural hematomas diagnosed by CT, 3/3 diagnosed by MRI.	trauma patient. Most MR suites are not well equipped to image patients with multisystem injuries and complex life support equipment."	When both boney and soft tissue injuries suspected in acute spinal cord injury patients, both CT and MRI will give more clinical information than either test alone. Small numbers for cervical, thoracic, and lumbar spine. *Data suggest MR imaging is useful imaging modeling for evaluation of acute subacute spine trauma patients. CT scans were superior at fracture identification, especially in posterior element fractures.
Mirvis 1988 Diagnostic	6.5	21	C	Acute cervical spine trauma	1.5T MRI	CT and CT myelography	+	+	+	+ #	+	-	+	3 months	MR showed direct cervical cord injury in 15 patients. MR showed focal edema. Sagittal orientation better for demonstrating spinal cord lesions than axial images. MRI did not show 5 vertebral fractures found on x-ray and CT scan.	"Preliminary experience with MR imaging of acute cervical spine trauma suggests that it should be the study of choice on symptomatic patient who are otherwise clinically stable. CT may still be require in selected patient to evaluate complex fractures."	MRI helpful in soft tissue and cord injury diagnoses. CT and/or x-ray superior to MRI in vertebral fractures. Compared CT-myelography (13/21), plain x-ray (21/21), and intra-operative spinal sonography (7/21). *Data suggest MR images can identify spinal cord lesions in the cervical spine of neurologically compromised patients. At least as well if not

																	better than CT-myelography.
Matsumoto 1998 Diagnostic	5.5	497	C	Asymptomatic Japanese patients	1.5T MRI 0.5T MRI	-	+	+	-	-	+	-	-	-	Positive MRI findings increased with age (p <0.0001). Grade-1 or 2 disc degeneration seen in 17% of discs in men and 12% in women in their 20s increasing to 86% and 89%, respectively, in their 80s. Grade-2 disc protrusions with spinal cord compression in 38 (7.6%) subjects. Foraminal stenosis in 5.9%.	"The frequency of degenerative findings on MRI of cervical intervertebral discs of asymptomatic subjects increased with age. These findings should be taken into consideration when reading MR images of patients with various cervical disorders."	High frequency of degenerative findings in asymptomatic subjects. These increased with age, suggesting including these findings when interpreting MRI findings and clinical signs and symptoms. Asymptomatic individuals. Most worked non-physically demanding jobs. Only 12/497 were classified as manual workers. *Data suggest findings of cervical disc degeneration in asymptomatic subjects in sedentary/light work jobs increases significantly with increasing age.
Siivola 2002 Diagnostic	5.5	31	C	Neck & shoulder pain (SG) Asymptomatic controls (AG)	1.5T MRI	-	+	+	-	-	+	-	+	7 years	Degenerated discs: SG-20, AG-26; Annular tears: SG-14, AG-18; Disc protrusions: SG-18, AG-29; Disc Herniations: SG-4 AG-0.	"The study found that abnormal MRI findings were common in both study groups. Disc herniation was the only MRI finding that was significantly associated with neck pain. These findings indicate that patho-physiological changes of cervical spine verified on	Pathological changes of cervical spine in 24-27 years old equally common in symptomatic group (SG) and asymptomatic group (AG). Disc herniations only more prevalent in SG. 7 year follow-up study. Aged from 24-27 years. Data suggest pathological changes seen by MRI in group aged 24-27 equally common in

																MRI seem to explain only part of the occurrence of neck and shoulder pain in young adults."	symptomatic and asymptomatic subjects. Disc herniation was the only variable associated with neck pain.
Kongsted 2008 Diagnostic	5.5	178	C	Acute whiplash injury	Open 0.2T MRI; baseline and repeated at 3 months	-	+	+	-	-	-	-	+	3 and 12 months	Baseline findings: 139/178 (78%) had pre-existing degeneration (reduced signal intensity, reduced disc height.) Bulges or protrusions in 35/178 (20%). 42/178 (24%) had no abnormal findings. MRI at 3 months: (96 total participants): 39/96 (41%) had no abnormal MRI findings. 3 with no abnormal findings at baseline had abnormalities at 3 months 3/42 (7%); 1 had mild degeneration, 1 with Modic Type I and 1 with minor anterolisthesis. 40% reported considerable neck pain and/or	"In conclusion, MRI is not the answer to a diagnosis in the vast majority of patients developing long-lasting pain after a whiplash injury, and early MRI scans do not predict prognosis. It may be relevant to focus future trials upon imaging of the upper cervical spine including functional imaging."	Traumatic findings visible with standard cervical MRI rare following whiplash injury. No distinct symptomatology or prognosis related to findings on MRI. It was not reported what other interventions participants were doing during follow-up period. MRI does not appear to add diagnostic value in stable acute whiplash patients. MR scans were done. 96 had MR at 3 months. *Data suggest MR scans in acutely injured cervical spine patients did not predict outcomes. Repeat scan at 3 months post injury did not add to useful information.

															headache. At 12 months was 44%. Headache more frequent in group with traumatic MRI findings (OR 2.8 0.4-17). Pre-existing degeneration not associated with 3-month outcome. Moderate/severe pre-existing degeneration associated with reduced risk of lasting pain.		
Benzel 1996 Diagnostic	5.0	174	C	Acute spinal trauma without clinically obvious injury, impaired ability to communicate	0.064T MRI	-	+	+	+	-	-	+ #	+	2 mo	62/174 (36%) had MRI evidence of soft tissue injury. All 62 classified as having "lack of excess mobility" on flexion and extension films at follow-up.	"The T2-weighted sagittal images were most useful in defining acute soft-tissue injury; axial images were of minimal assistance. Posttraumatic soft-tissue cervical spine injuries and disc herniations (most likely preexisting the trauma) are more common than expected. A negative MR image should be considered as confirmation of a negative or "cleared" subaxial cervical spine. Diagnostic and patient management algorithms may be	MRI is useful in assessing soft tissue injury in patients who have an impaired ability to communicate. In acutely injured, x-ray did not show disruption of spinal integrity or equivocal physical exam for soft tissue injury. *Data suggest MR images can assist in diagnosing acute soft tissue trama in patients with negative cervical x-rays following trauma.

																appropriately tailored by this information. Thus, MR imaging is useful for early acute posttrauma assessment in a very select group of patients."	
Sekhon 2007 RCT/Diagnostic	5.0	20	C	Patients who had undergone cervical arthroplasty	1.5T MRI	-	-	+	-	-	+	+	-	-	No significant difference in pre- and post-op imaging quality for Bryan and Prestige LP discs. PCM and Prodisc-C had statistically significant quality deterioration after surgery.	"Cervical arthroplasty prostheses have varying articulations, materials, kinematics, and methods to achieve fixation. Optimally, the device and local anatomy would be well visualized with all imaging methods without significant artifact. With current designs, many questions can be resolved with standard radiographs and CT. Neural imaging will be required when neurologic symptoms are present, which is best performed by MRI. Titanium and ceramic materials are the most MRI compatible materials in use today, and will afford the greatest versatility and visibility in	Findings purportedly may assist in surgeon's choice of which product to use if MRI image quality after surgery is considered. 5 patients of each of the four-types of disc replacements. *Data suggest implants made with titanium uses cobalt or chrome result in better post-operative MR images.

																postoperative imaging studies. CT myelography will necessarily retain a role in postoperative imaging with devices made of stainless steel or Co-Cr alloys."	
Beers 1988 Diagnostic	4.5	14	C	Acute cervical cord injury	0.5T MRI & 1.5T MRI	CT	+	+	+	-	-	-	+	?	MRI showed hyperintensity &/or cord swelling in all 12 patients with clinical neurological findings.	"These observations indicate that following acute cervical spine trauma, MR is a valuable technique in assessing injury to the spinal cord, surrounding soft tissues, vertebra, and disks."	MRI showed soft tissue injuries well. Sometimes able to identify fractures, but not as well as radiographs or CT scan. Small numbers. 12/14 had neurological deficits from injury. Scans done within 7 days from injury. Not all scans done in same manner. Different protocols used based on availability and clinical presentation. *Data suggest in severe acutely injured patients cervical MRI can help image the cervical spine and aid in diagnoses.
Krakenes 2002 Diagnostic	4.5	122	C	Grade 2 whiplash injury with normal x-rays. Looking at atlanto-occipital ligaments	1.5T MRI	-	+	-	-	-	+	-	-	-	Grade 0 atlanto-occipital membranes ligaments in 71, 22/71 (31%) in symptomatic group (AG), 49/71 (69%) in whiplash group (WG). Grade	"Whiplash trauma can cause permanent damage to the alar ligaments, which can be shown by high-resolution proton density-weighted MRI. Reliability of classification of alar ligament lesions	Hyperintensity in atlanto-occipital ligament reported more frequently in whiplash group than in control group. No clinical correlations made to outcomes based on MRI findings. No explanation made for findings in

															1: 20/23 (87%) in WG, 3/23 (13%) in AG. Grade 2: 8/9 (89%) in WG, 1/9 (11%) in AG. Grade 3: 11/11 in WG, 0/11 in AG.	needs to be improved."	asymptomatic group. 92 injured and 30 uninjured. MRI performed ≥2 years after injury. No clinical outcomes. *Data suggest MR image can identify possible Alar ligament injury ≥2 years after whiplash injury.
Krakenes Acta Radiol 2003 RCT/Diagnostic	4.5	122	C	Grade 2 whiplash injury with normal x-rays; looking at transverse ligaments	1.5T MRI	-	+	-	-	-	+	-	-	-	Injured group had 23% increased signal throughout entire cross-section of transverse ligament. Grade 1: 20/23 in whiplash group (WG), 2/23 in asymptomatic group (AG). Grade 2: 16/19 in WG, 3/19 in AG. Grade 3: 5/5 in WG, 0/5 in AG.	"In conclusion, by use of high-resolution protonweighted MR sequences we found structural changes in the transverse ligament concomitant with ligament sprain several years after whiplash trauma. The grading of such lesions is difficult, and our study has revealed several pitfalls. Further development of MR technology and more experience in image reading should improve the grading consistency. The reported protocol has the potential to become an important tool to differentiate between normal and sprained transverse ligaments."	Hyperintensities in transverse ligaments reported more frequently in symptomatic whiplash than control group. No clinical correlations made based on MRI findings. No explanation made for findings in asymptomatic group Similar to Krakenes 2002, but looking at transverse ligaments. 92 injured and 30 uninjured individuals. No clinical outcomes. *Data suggest MR images can identify possible tranverse ligaments injury 2-5 years after whiplash injury.
Krakenes	4.5	122	C	Grade 2 whiplash injury	1.5T MRI	-	+	-	-	-	+	-	-	-	27% of injured whiplash	"In classifying injured ligaments	Similar to Krakenes 2002 and 2003, but

Neuro-radiology 2003 RCT/Diagnostic				after 12-16 weeks. Looking at whiplash trauma causing damage to tectorial and posterior atlanto-occipital membrane.										patients had grade 2-3 lesions of tectorial membrane and 17% of posterior atlanto-occipital membrane. K = 0.30 (.19-.41) under 2nd grading for J.K. vs G.M. with p <0.01 and disagreement at 51.3%. K = 0.53 (.42-.65) under 1st vs. 2nd grading for J.K. with p <0.01 and disagreement at 30.8%. Dichotomising groups showed no improved agreement. GM and HN more lesions JK with p <0.05.	and membranes there will be equivocal cases. Hence, a one-step difference in grading does not necessarily indicate real disagreement. The weighted K coefficient was used and, as expected, considerably better values were found when degree of disagreement was taken into consideration. Dichotomising the groups did not improve intra- and interobserver agreement. Thus, a classification of these membrane lesions into four grades (0–3) seems appropriate. ”	looking at posterior atlanto-occipital membranes. 92 injured, 30 uninjured. No clinical outcomes. *Data suggest MR images can identify possible posterior atlanto-occipital membranes 2-5 years after whiplash injury.
Cooley 2001 Diagnostic	4.0	106	C	“History of cervical complaints to warrant a MRI scan”	1.5T MRI	-	+	-	-	-	+	-	-	-	1847 discs scanned, 1173 (64%) had normal findings, 477/1847 (26%) bulges, 185/1847 (10%) disc protrusions, 12/1847 (1%) disc extrusions.	“Interexaminer and intraexaminer agreement were good to very good concerning measurements and fair to good concerning disk assessments. Different disk displacement types demonstrated	Inter and intrarater reliability using MRI for cervical disc pathology are reliable. No clinical outcomes considered. Retrospective review, no clinical outcomes measured. 3 reviewers looked at films.

															When measuring disc displacement a ruler vs. digitizer showed correlation of .96 ($p < .01$).	obvious mean size differences. No significant mean difference in measurements between the ruler and the digitizer was noted."	*Data suggest MR images have the most inter- and intra-rater reliability issues distinguishing between transitional disc types.

? = was not specified in study; *= which levels done on participants not well described; C = cervical, T = thoracic, L = lumbar spine; # = surgery performed in some participants; ** = quantified response not reported

ELECTROMYOGRAPHY

Electromyography (EMG) is a physiological test that assesses the function of the motor unit (including the neuron's anterior horn cell, its axon, the neuromuscular junctions and muscle fibers it supplies).(372, 373) It differs from surface EMG, which is discussed below. EMG technically refers to the needle electromyogram and the term "EMG" is usually misused as a euphemism for an electrodiagnostic exam that includes both needle EMG and peripheral nerve conduction testing. Among spine patients, EMG has been used primarily to evaluate radiculopathy.(374)

1. *Recommendation: EMG with Upper Extremity Symptoms*
   Electrodiagnostic studies, which must include needle EMG, are recommended where a CT or MRI is equivocal and there is ongoing upper extremity pain that raise questions about whether there may be a neurological compromise that may be identifiable (i.e., upper extremity symptoms consistent with radiculopathy, spinal stenosis, peripheral neuropathy, etc.). Also, may be helpful for evaluation of chronicity and/or aggravation of a pre-existing problem.
   Indications – Failure to resolve or plateau of suspected radicular pain without resolution after waiting 4 to 6 weeks (to provide for sufficient time to develop EMG abnormalities as well as time for conservative treatment to resolve the problems), equivocal imaging findings such as CT or MRI, and suspicion by history and physical examination that a neurologic condition other than radiculopathy may be present instead of, or in addition to radiculopathy.
   Harms – Medicalization or worsening of otherwise benign spine condition. Pain. Hematoma. Misinterpretation if not done by an appropriately trained person.
   Benefits – Diagnosis of neurological compromise.
   Strength of Evidence – **Recommended, Evidence (C)**
   Level of Confidence – High

2. *Recommendation: EMG without Upper Extremity Symptoms*
   Electrodiagnostic studies are not recommended for patients with acute, subacute, or chronic neck pain who do not have significant upper extremity pain or numbness.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

Rationale for Recommendations

Needle EMG may help determine if radiculopathy and/or spinal stenosis is present, and can help address acuity.(375) EMG requires full knowledge of the anatomy and precise innervation of each muscle to properly perform and interpret the test results. Needle EMG also requires the skills of an experienced physician who can reliably spot abnormal motor potentials and recruitment patterns. Nerve conduction studies are usually normal in radiculopathy (except, for example, for motor nerve amplitude loss in muscles innervated by the involved nerve root in more severe radiculopathy). Nerve conduction studies rule out other causes for upper limb symptoms (generalized peripheral neuropathy, pronator syndrome, etc.) that can mimic radiculopathy.

An abnormal EMG that persists after anatomic resorption of the herniation(376) and that correlates with the patient's symptoms is generally considered proof the symptoms are due to radiculopathy. Thus, the EMG study documents that management for chronic neuropathic pain appears appropriate.

As imaging studies (especially CT and MRI) have progressed, the need for EMG has declined. However, EMG remains helpful in certain situations. These include ongoing pain suspected to be of neurological origin, but without clear neurological compromise on imaging study. EMG can then be used to attempt to rule in/out a physiologically important neurological compromise. An abnormal study confirming radiculopathy permits a diagnosis of neuropathic pain (helping with pain management decisions). This test should not be performed in the first month unless there is a desire to document pre-existing neurological compromise, as it requires time (generally at least 3 weeks) to develop the needle EMG abnormalities. EMG is minimally invasive, and has no long-term adverse effects (although it is somewhat painful), and it is costly. To result in reliable measures, it must be performed by a practitioner well skilled in the appropriate anatomy and testing procedures. Post-operative changes may persist in normal individuals without clinical significance, thus also requiring careful interpretation.

Evidence for the Use of Electromyography
There are no quality studies regarding the use of electromyography.

We searched PubMed and Google Scholar without limits on publication dates. We used the following search terms: Surface Electromyography, sEMG, neck pain [MESH] and Diagnostic to find 99 articles. We reviewed 99 articles and included 0 articles.

SURFACE ELECTROMYOGRAPHY

Surface electromyography (sEMG) has been used to diagnose spine pain, especially in the lumbar spine (377-393) and involves the recording of summated muscle electrical activity by skin electrodes (such as those used in an electrocardiogram or EKG). Unlike traditional needle EMG (see above), no needle is used to explore specific portions of specific muscles for motor unit potentials.

Recommendation: Surface EMG for Diagnosing Cervical or Thoracic Pain
Surface EMG is not recommended to diagnose cervical or thoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – High

Rationale for Recommendation
There are no quality studies demonstrating that use of surface EMG results in improved diagnosis or evaluation of patients with cervical or thoracic pain. Available studies in the lumbar spine have methodological weaknesses, including poor descriptions of patients, small sample sizes, types of machine, electrode placement, and analysis of the output making outcomes difficult to compare across studies.(379, 383, 389, 393, 394)

The American Association of Neuromuscular and Electrodiagnostic Medicine's position is that there are no clinical indications for the use of sEMG in the diagnosis and treatment of disorders of nerve and muscle, although potential future uses are possible.(395, 396) Surface EMG is not invasive, has few adverse events, is moderately costly, but has a lack of quality evidence of benefits for the clinical evaluation or treatment of spine disorders and thus is not recommended.

Evidence for the Use of Surface Electromyography
There are no quality studies regarding the use of surface electromyography.

We searched PubMed and Google Scholar without limits on publication dates. We used the following search terms: Surface Electromyography, sEMG, neck pain [MESH] and Diagnostic to find 99 articles. We reviewed 99 articles and included 0 articles.

DISCOGRAPHY

Discography is a diagnostic test that attempts to determine if chronic spinal pain is originating from the intervertebral disc.(397-405) A needle is inserted into the middle (nucleus pulposus) of a disc and x-ray dye is injected. Images are then made, often with both x-rays and computed tomography (CT).(397, 400, 401, 406, 407) Discography is usually used in patients with chronic spinal pain without significant extremity pain.(401) This procedure is fairly painful and sedation is required.(400, 401, 408-410) Unlike in the lumbar spine, extravasation of contrast out of the disc is not considered a significant finding in cervical discography.(402, 411-413)

Discography proponents believe that discs with more severe degrees of degeneration are more likely to be painful.(397, 398, 400) If a patient does not experience pain on injection, that disc is considered unlikely to be the source of chronic spinal pain. If a patient experiences pain that is mild or that is clearly different in location or character to his or her chronic pain, that disc is also considered unlikely to be the source of chronic spinal pain.(400, 401, 405, 414) However, if the patient experiences significant pain that is identical in location and character to the patient's chronic pain ("concordant pain"), proponents believe that discography can identify the pain-generating structure responsible for chronic spinal pain.(397-400, 407, 415, 416)

Discography has known complications including discitis, epidural abscess secondary to discitis, herniated cervical disc, and quadriplegia.(401, 413, 417-419) Discography has been shown to result in accelerated degeneration in the normal control discs that are injected in the lumbar spine,(420) and there is a suggestion that this is also true in the cervical spine.(421) The technique of discography is not standardized. There is no universally accepted definition of what constitutes a concordant painful response. There are no published intra-rater or inter-rater reliability studies on cervical discography. Discography is important to the subsequent discussions of spinal fusion for "degenerative disc disease," and artificial disc replacement, as many North American surgeons (but not European surgeons) use discography results in surgical planning.(422) If discography can accurately identify a disc as the pain-generating structure, then surgical procedures on that disc may logically lead to patient improvement.(402, 423) If discography can produce pain, but cannot accurately identify that disc as the pain generating structure, then surgery on that disc is presumably unlikely to be helpful.(408, 418, 422) Due in part to recognition that discography is not a highly accurate test,(408, 411, 418, 422, 424) attempts have been made to modify the test to attempt to increase the accuracy, including measurement of pressures where pain occurs,(398, 407, 423) as well as injection of anesthetics.(400, 417, 425)

Recommendation: Discography for Assessing Acute, Subacute, or Chronic Cervicothoracic Pain or Radicular Pain Syndromes

Discography, whether performed as a solitary test or when paired with imaging (e.g., MRI, CT), is not recommended for acute, subacute, or chronic cervicothoracic pain or radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

Discography has not been evaluated in high-quality studies for cervicothoracic pain. There is considerably greater evidence in the lumbar spine which suggests low positive predictive value of discography (see Low Back Disorders Guideline). There are several case series reports and a few comparisons between discography findings and findings on MRI. One case series evaluated 71 chronic cervicothoracic pain patients who had concordant pain responses with discography and then underwent anterior cervical discectomy and fusion. The authors reported 93% excellent or good outcomes and 7% fair or poor surgical outcomes.(425) This is contrasted with another case series that evaluated 22 patients who had concordant pain responses to discography and then underwent anterior cervical discectomy and fusion. Excellent surgical outcomes were reported in 5%, 41% had a good outcome, 27% had a fair, and 27% had a poor surgical outcome. This study also reported a 13% complication rate including one patient who developed quadriplegia and concluded that discography's benefit in diagnosis did not outweigh the complication rates.(418)

A retrospective case series evaluated 42 surgical patients – all had cervical discography prior to surgery. The diagnoses given at discography were compared to diagnoses given after exploratory surgery. The overall diagnostic accuracy for cervical discography compared to surgical findings was 55%. Of 12 disc protrusions seen at surgery, 8 were identified by discography (66%). Of the 24 cases of spondylosis diagnosed at time of surgery, 12 were identified by discography (50%).(422)

A moderate-quality retrospective study evaluated concordant pain responses in chronic cervicothoracic pain patients without a comparison group and reported that out of 807 discs injected during discography 404 (50%) had concordant pain responses.(401) A study of 72 chronic cervicothoracic pain patients versus 72 controls with no cervicothoracic pain was conducted to evaluate sensitivity and specificity of discography and reported a sensitivity of 65% and specificity of 50%.(411) Thus, with a pre-test probability of 50%, these results suggest the positive predictive value would be 56.5%.

There are a few studies comparing cervical discography to MRI.(412, 413) Parfenchuck et al(413) examined 52 cervicothoracic pain patients who had failed conservative treatment. They performed spinal MRI from C2-T1 and noted abnormalities. They then performed discography on all patients. Of the 62 painful discs on discography, 45 were abnormal on MRI, constituting a sensitivity of 73% and false negative rate of 27% for MRI to detect discs that are painful with discography. Of the 42 asymptomatic discs on discography, 28 were normal on MRI constituting a

specificity of 67% and false-positive rate of 33% for MRI for abnormalities on discs that are not painful on discography.

Another study examined 20 patients, 10 who had chronic cervicothoracic pain and 10 lifelong asymptomatic subjects. All 20 underwent discography at C3-C4 through C6-C7 after MRI. Disc morphology and provoked responses were recorded at each level. MR examinations were judged to be normal in 1 of the 10 asymptomatic patients (5 of the 40 discs injected in the asymptomatic patients were painful on injection). The study examined 80 discs in the 20 subjects. Of the 31 discs reported as normal on MRI, 27 had annular tears of varying degree. The authors concluded that MRI at the time did not reliably detect annular defects.(412) Seventy percent of the asymptomatic subjects had painful disc injections (4 or 5 on a 0 to 10 pain intensity scale), and 2 out of 10 had pain intensity 6 noted on injection. These studies may describe how likely a given finding on imaging is to be associated with pain on injection, but cannot determine whether the pain response is a true-positive or a false-positive response. Thus, these studies are not capable of guiding further therapy.

In low back pain, the estimated positive predictive value appears to be at or below 50%, suggesting the test is not helpful in the lumbar spine.(426) These studies have not found that discography reliably indicates which particular disc is the source of the patient's pain. Validity of those findings through improved operative successes is not consistently present.(427) Studies on imaging have shown that most imaging findings do not correlate with an individual's pain status(426) (see Low Back Disorders guideline).

Discography is invasive and has adverse effects. Temporary complications include headache, nausea, and worsened cervicothoracic pain. Uncommon, but serious reported complications include meningitis, epidural abscess, arachnoiditis, intrathecal hematoma, intradural injection of contrast, and acute disc herniation.(417, 418, 428) Discography results in a patient exposure to radiation of 1.5 to 4.0 rads.(429) Most concerning is the recent report that in long-term follow-up lumbar discography of the discs that are normal (the "negative control" discs) results in more rapid disc degeneration and an increased incidence of disc herniation.(211) Discography requires that one or two normal discs be injected and be painless on injection, so that the disc that is painful during injection can be identified. If discography iatrogenically damages the normal control discs, and does not lead to improved treatment outcomes, then there is clear evidence that discography should not be performed. A similar study has not been performed for cervical discography; however, Nassr reported a case series that is perhaps analogous. At the time of anterior cervical discectomy and fusion, surgeons traditionally verify they are about to operate on the correct level (remove the correct disc) by inserting a metal needle in the disc at the start of the operation, and then taking an intra-operative x-ray to verify the correct disc has been identified. Nassr reported a series of cases in which surgeons inserted a needle in the wrong disc (always the disc above the disc that was to be operated upon). In the short-term (2 years) follow-up, the "normal" disc above the level to have surgery showed faster than expected degenerative change.(421) Discography is also costly and has not been found to provide information that has sufficient positive or negative predictive value to warrant its addition to the clinical examination or other testing currently under use. It is not currently recommended, although there are potential modifications to the procedure being further studied.

A recent systematic review did not find any high quality evidence to support cervical discography, and did not find any studies that show discography could improve clinical outcomes in patients considering cervical surgery.(98)

Evidence for the Use of Discography
There are 13 moderate-quality studies and 2 other studies(401, 402, 408-413, 416-418, 422, 423, 425, 430) incorporated in this analysis. (There are also 20 studies included that focus on lumbar studies.(80, 367, 426, 431-447))

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: discitis, discography, diagnostic, efficacy, efficiency, sensitivity, specificity, predictive value of tests, positive predictive value and negative predictive value. In PubMed we found and reviewed 18 articles, and considered 15 for inclusion. In Scopus, we found and reviewed 30 articles, and considered zero for inclusion. In CINAHL, we found and reviewed one article, and considered zero for inclusion. In Cochrane Library, we found and reviewed 5 articles, and considered zero for

inclusion. We also considered for inclusion zero articles from other sources. Of the 15 articles considered for inclusion, 15 studies met the inclusion criteria.

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Injected Medications	Intradiscal Local Anesthetic	Sedation Used	Fluoroscopy/imaging	Pressure Readings	MRI	CT	CT Myelography	X-ray	More than one rater	More than one level	Surgery Performed	Long term follow-up (mean when noted)	Results	Conclusion	Comments
Schellhas 1996 Diagnostic	6.0	20	C	10- chronic neck and head pain, 10- asymptomatic	Contrast	+**	-	+	-	+	+	-	-	+	+	-	No	MR exams judged normal in only 1 of 10 asymptomatic patients. Examined 80 discs in 20 subjects. Of 31 discs reported as normal on MRI, 27 had annular tears of varying degree. Concluded MRI did not reliably detect annular defects.	"Significant cervical disc anular tears often escape magnetic resonance imaging detection, and magnetic resonance imaging cannot reliably identify the source(s) of cervical discogenic pain."	Participants with chronic cervicothoracic pain (work comp or legal claims excluded). Interobserver agreement for MRI and discography in asymptomatic patients 88.75 % and 91.25% respectively. Lack of study details. Failed to show asymptomatic annular tears is clinically significant. Not all study aspects of done in all participants. Videotaping not done in all patients, Not all had intradiscal anesthetic injected. 10 asymptomatic and 10 chronic neck/head pain patients. 2 of 11 normal discs on MRI in 10 chronic pain patients had concordant pain

																				with discography. 3 discs in asymptomatic patients had significant pain with discography. Data suggest both false negative and false positive results on MRI and cervical discography.
Parfenchuck 1994 Diagnostic	6.0	52	C	Chronic neck pain	Contrast	+	?	+	-	+	+	-	-	-	+	-	No	59/104 (56.7%) discs abnormal on MRI. 45/63 (71.4%) painful discs on discography abnormal on MRI. MRI in detecting abnormal discs: Sn-78%, Sp-67%, False Neg 27%, False Pos 33%.	"Our results suggest that several MRI patterns correlate well with positive or negative cervical discography responses while other patterns are equivocal. Magnetic resonance imaging is a useful adjunct to cervical discography but there are some MRI patterns that cannot be considered pathologic, and discography is required to diagnose discogenic pain syndrome."	Leakage of contrast occurred in all discs irrespective of clinical symptoms. Complication rate 4%. Sensitivity and specificity show MRI is a good diagnostic tool for disc abnormalities without major complications. Complication rate of discography is 4%. No mention of sedation. Data suggest MRI correlates reasonably well but does have discrepancies with cervical discography.

Shinomiya 1993 Diagnostic	6.0	144	C	Cervical spondylitic myelopathy or cervical spondylitic radiculopathy or Cervical amyotrophy	Contrast	-	-	+	-	+	+	-	-	-	+ *	-	No	Neck pain group 47/72 (65%) had provocative pain; 22/72 (30.6%) had epidural space leakage of contrast. No neck pain group, 36/72 (50%) had provocative pain; 29/72 had epidural space leakage of contrast	"The results demonstrated that this provocations technique appeared unreliable for diagnosing symptomatic disk levels."	Non-painful group had other neurological symptoms. High rate of provocative pain in group without neck pain (50%) combined with modestly higher pain response in neck pain group (65%) concerning. Both groups significant pain response to discography. Retrospective study design. No sedation used/reported. 65% in neck pain group had provocative pain where 50% in control group had provocative pain. Data suggest cervical discography was unreliable. Given retrospective nature of study, further studies are needed.
Simmons 1975 Diagnostic	5.5	507	C, T, L	Chronic pain	Saline and contrast	-	+	+	- #	-	-	-	-	-	+	+	3 years	If improved after surgery, considered positive. Cervical clinical exam: 43%; x-ray: 46.5%; myelography: 45.6; miscography: 91%. Lumbar clinical exam: 44.2%; x-ray: 71.5%; myelography:	"On the basis of a review of 507 patients, discography was a reliable diagnostic procedure in determining the symptomatic level in discogenic disease of the cervical and lumbar spine."	Retrospective record review. No control group. Diagnostic values unclear as patients already scheduled for surgery. No positive discography patients refused surgery to ascertain non-surgical outcomes. Discography done in cervical, thoracic and

																		45.6%; discography: 82.2%		lumbar spine. Data suggest discography can aid in determination as to what level of spine to operate on.
Holt 1964 Diagnostic	5.5	50	C	Asymptomatic patients	Contrast	-	+	+	-	-	-	-	+	-	+	-	No	Was pain in every disc injected with contrast; 10 of 148 discs injected did not leak contrast.	"Cervical discography is a painful and expensive procedure and is without diagnostic value."	Used 50% sodium diatrizoate as contrast material, which is more irritating than non-ionic contrast. Population used likely had high burden of psychological conditions which complicates findings with discography. Results suggest in this population approach unhelpful diagnostically. Done on only volunteers with no history of spine pain. Only looked at extravasation of contrast, not pain. Sedation was used. Data suggest extravasation in cervical discography is not indicative of pain generating discs.
Ohnmeiss 1999 Diagnostic	5.5	187	L	LBP	Contrast	-	?	+	-	-	+	-	-	-	+	-	No	Pain limited to low back and buttocks was frequently associated with lack of disc pathology	"[A]lthough aching pain was the most prevalent in entire study group, patients with discogenic pain used significantly	Study to ascertain areas of referred pain during discography in lumbar spine. Data may be helpful if repeated in diagnosing pain generators with

																	(58.3%) Anterior thigh pain was seen with L4-L5 disc.	more symbols indicating aching sensation. Pain of a burning sensation was indicated more frequently in the discogenic pain group. Pain drawings appear to be a helpful diagnostic tool for identifying lumbar discogenic pain."	using discography. "Mild" sedation used. Data suggest pain diagrams in low back pain patients who had failed conservative therapy could be helpful in identifying discogenic pain when compared to lumbar discography results.
Connor 1993 Diagnostic	5.5	31	C	Neck pain, suboccipital headache, and periscapular discomfort	Contrast	-	-	+	-	-	+	+	-	-	+ *	+	38 months after surgery	1/22 (5%) had an excellent outcome after surgery 9/22 (41%) had a good result 6/22 (27%) had a fair result; 6/22 (27%) had a poor result; 4/31 (13%) had a major complication; 3/31 (10%) had a minor complication	"In view of these findings, we believe that diagnostic cervical discography does not provide the degree of clinical predictive value necessary to substantiate the potential risks inherent to the procedure."	Complication rate of 13% considerably higher than other publications. Minimum follow-up period 24 months. Longer-term follow-up suggests results not strong. No patient with radiculopathy. No sedation was used. 26/31 had concordant pain and were positive, 88% were C5-6 and C6-7. 22/26 had anterior fusion. 13% complication rate including quadriplegia. Data suggest that cervical + discography did not correlate with positive surgical outcomes.

Grubb 2000 Diagnostic	5.5	173	C	Chronic pain, failed medical management	Saline and contrast	-	+	+	-	-	+	-	-	-	+	+	No	Of 807 discs injected 404 (50%) had concordant pain responses. Many had evidence of multilevel disease.	"Discography is a safe and valuable diagnostic procedure showing characteristic pain patterns that may have clinical significance. In more than half of the studies, three or more levels were identified as pain generators, suggesting that treatment decisions based on information from fewer discs injected during discography may be tenuous."	50% concordant pain yet concluded it is a useful diagnostic procedure. Retrospective record review over 12 years time of clinical data. Patients failed conservative therapy first before discography. Used mild IV sedation. Did all level they could access. 2.3% complication rate. Data suggest multidiscography may be helpful, but due to retrospective record review nature of study conclusions need further study.
Roth 1976 Diagnostic	5.0	71	C	Medically intractable cervical-discogenic syndrome	2% local anesthetic	+ 100% had positive results	-	+	-	-	-	+	+	-	+ *	+	No	60.6% classified as excellent results, 32.4% as good, 1.4% as fair, and 5.6% as poor.	"Analgesic discography is the most effective test for diagnosis and location in the painful-disk syndrome."	No comparison group. Reported 100% positive response rate on injection. No sedation used. They use analgesia if concordant pain was experienced. Data suggest analgesia and relief of symptoms may be more diagnostic than concurrent pain by injection.
Ohnmeiss 2000 Diagnostic	5.0	161	C	Neck pain, or shoulder pain, and arm pain	Contrast	-	+	+	- #	+	+	+	-	-	+ *	-	No	60% of normal appearing discs on	"There was good agreement between the	No blinding, no comparison groups. Lack of baseline

																	imaging painless with discography. 25% of normal appearing discs on imaging had non-concordant pain on discography. 77.8% of disrupted discs on imaging painful with discography	radiographic appearance of the disc and the pain provocation results. Discs that were painless but disrupted were found among older patients. Among such patients, discography may be particularly helpful in differentiating clinically significant abnormalities from those associated with aging."	characteristics makes it difficult to apply to clinical management of a patient group. Results suggest more positive results with more abnormal appearing discs. No mention of sedation. Data suggest MRI findings correlate with cervical discography, but there are false negatives and false positives.
Whitecloud 1987 Diagnostic	5.0	34	C	Neck pain, and/or shoulder pain, and/or occipital headache, and/or periscapular pain	Contrast	+	?	?	-	-	-	-	+	-	+ *	+	27 months after surgery	10/34 (32%) classified as having excellent surgical outcome. 13/34 (38%) had good, 4/34 (12%) had fair, 6/34 (18%) had poor. **24 who had excellent or good outcomes 20 had a single level fusion, where only 1 of 10 who had fair or poor had a single level fusion.	"Cervical discography should be used as a last diagnostic modality in the treatment of patients presenting with chronic neck, shoulder and upper extremity discomfort. Discography should be proceeded by a CT evaluation with or without contrast or magnetic nuclear resonance evaluation."	No control group. Patients had neck pain with normal myelogram prior to discography and surgery. No patients included who did not have surgery to follow their outcomes. No radicular symptoms. Retrospective record review. 37/40 in litigation or workers' comp cases. Given a "mild analgesic," never injected more than 0.5cc of solution. Data suggest cervical discography could

																			be helpful in determining surgical levels prior to use of MRI scan.
Klafta 1969 Diagnostic	4.5	42	C	Chronic neck pain	Contrast	-	-	+	-	-	-	-	+ *	+	+ *	+	?	4/6 (67%) disc protrusions seen at surgery seen on discography. 9/21 (43%) of spondylosis seen on surgery seen on discography. Overall diagnostic accuracy of discography 19/36 (53%). Myelography accurate in 26/36 (72%).	"Cervical discography is a safe procedure of limited value and should only be judged in relation to the clinical picture, roentgenograms, and myelograms. Cervical discography was valuable in the demonstration of degeneration of the disc. Myelography could not do this. Discograms demonstrated degeneration of the disc in all cases of spondylosis, although the degree of degeneration could not be accurately ascertained."	Diagnostic accuracy reported for discography in study 53% when compared to findings seen during surgery. No long-term follow-up to assess clinical outcomes from surgery. Retrospective record review. Data suggest cervical discography can be helpful but can also lead to false positive and false negative diagnoses.
Slipman 2005 Diagnostic	4.0	41	C	Neck pain	Contrast	-	-	+	- #	-	+	-	+	-	+ *	-	No	Unilateral symptoms provoked as often as bilateral. C7-T1 disc only one to produce midline pain.	"In conclusion, these results confirm the observations of prior investigators that cervical internal disc disruption can	Study to ascertain areas of referred pain during discography. Data suggest pain distributions potentially related to cervical discs. No sedation used.

																		elicit axial and peripheral symptoms. The particular patterns of pain generation allow the discographer to pre-procedurally anticipate disc levels to assess. With these data, the number of disc punctures that are required can be limited rather than routinely assessing all cervical discs."	Only patients who had pain ≥6/20, concordant pain completed pain diagram. Data suggest that certain discs case pain in certain areas.
Zeidman 1995 Diagnostic	N/A	1,357	C	Degenerative disc disease and severe neck pain	Saline & Contrast	+**	-	+	-#	-	-	-	?	-	+*	-	No	Discitis in 0.16%, 0.07% prevertebral abscess, 7 of 1357 had disc space infections	"This study demonstrates significant complications from diagnostic discography procedures occurring in less than 0.6% of the patients and 0.16% of the cervical disc injections."	Retrospective record review; main purpose to evaluate complication rates related to discography.
Simmons 1969 Diagnostic	N/A	31	C	Chronic pain with or without neurological signs	Saline & Contrast	-	?	+	-	-	-	?	+	-	+*	+	1 week	30/31 (96.8%) had a "good" result after surgery. Clinical exam: 9/31 (29.0%) correct in identifying level for pain generation; myelography:	"Until a good theory is proposed to explain pain production from cervical disc disease and until a method of investigation is outlined on this principle,	No control group. Multiple sub-analyses that complicate interpretation. Paper contained more than one study result. No intermediate or long-term follow-up completed for discography study

																		7/21 (33.3%) correct; discography 30/31 (96.8%) correct.	diagnostic disc puncture is the best method for investigation of disease of the cervical discs."	group. Complicated study design. Multiple studies/case series/opinions.
LUMBAR STUDIES																				
Carragee 2000 Prospective case series	6.5	47	L	Patients with single level discectomy for sciatica previously.	Contrast	-	+	+	+	-	-	+	-	+	+	+	1 mo	Asymptomatic subjects with normal psychometric testing had painful disc injections at levels that had previous surgery in 40% studied. Symptomatic patients with normal psychometric testing with painful discs on discography 43%. 70% of symptomatic patients with abnormal psychometric scores had painful disc injections.		Results suggest positive discography in patients with emotional stress or abnormal psychometric testing be interpreted with caution.
Carragee 2004 Prospective control study	7.5	50	L	Asymptomatic cases and controls	Contrast	-	+	+	+	+	-	-	+	-	+	-	4 years	Psychometric scores at start of study predicted future LBP (p <.01) Chronic non-lumbar pain weakly associated with future LBP (p = 0.06). Painful disc injection		Results suggest patients with a history of somatization distress and non-lumbar chronic pain be carefully screened when considering invasive procedures.

																	did not predict future LBP.		
Carragee 2000 Prospective study	5.0	26	L	10 asymptomatic, 10 chronic neck and arm pain but no back pain, 6 primary somatization disorder	Contrast	-	+	+	+	+	-	-	+	-	+	-	1 year	Positive pain response to discography reported in 10% of asymptomatic group, 40% in cervical pain group, and 83% in somatization group.		Subjects with other chronic pain issues and somatization disorders more likely to have positive pain response to lumbar discography regardless of clinical history of LBP. Suggests caution in interpreting results.
Madan 2002 Prospective study	4.0	73	L	Underwent LBP surgery. A = 41 surgery without discography. B = 32 discography screening before surgery	Contrast	-	-	+	+	+	-	-	+	-	+	+	2.8 years	Group A and Group B had satisfactory outcomes; 75.6% and 81.2% respectively.		According to study provocative discography has limited efficacy in improving clinical outcome scores after low back surgery for discogenic back pain.
Carragee 2006 Prospective study	5.0	62	L	30 with positive single-level discogram, 32 with spondylolisthesis.	Contrast	-	-	+	+	+	-	-	+	-	+	+	2 years	Highly effective success criteria: 72% in spondylolisthesis group and 27% in presumed discogenic group. Minimal effective success: 91% in spondylolisthesis , 43% in discogenic		Despite removal of pain generator as diagnosed by discography, approximately half continued with significant pain and impairment. Complete removal of supposed pain source in spondylolisthesis group frequently completely removed pain.
Jackson 1989	9.0	124	L	Chronic pain patients who underwent	Contrast	-	-	+	-	-	+	+	-	+	+	+	No	Discography Sn- 81%, Sp- 31%. CT-		Discography less accurate than CT, CT myelography,

Prospective Study				surgical exploration														discography: Sn- 92%, Sp- 81%. Disc Injection: Sn- 43%, Sp- 89%.		and myelography. CT-discography accurate, especially in patients with possible foraminal or recurrent herniated discs.
Walsh 1990 Prospective study	7.5	17	L	7 with LBP, 10 asymptomatic patients	Contrast	-	+	+	+	-	-	-	+	-	+	-	No	False positive rate: 0%. Sp- 100%.		Discography revealed abnormal findings in 65% of discs in symptomatic group in all 7 patients. Small sample size precludes strong conclusions.
Collins 1990 Prospective study	5.0	29	L	Chronic pain, failed conservative therapy	Contrast	-	-	+	-	+	+	-	-	-	+	+ ^	No	Discography correlated with MRI in 90% of discs.		All with a symptomatic level at discography had evidence of degeneration on MRI. Results suggest disc levels that appear normal on MRI should not undergo discography. MRI can lead to a reduction of disc levels requiring injection.

Birney 1992 Prospective study	7.0	90	L	Incapacitating LBP or radicular pain; 20 had prior surgery at one or more of investigated levels.	Contrast	-	-	+	?	+	-	-	-	+	+	+ ^	No	MRI degeneration: Sn- 93%, Sp- 100%. MRI herniation: Sn- 100% Sp- 93%. Discography degeneration: Sn- 100% Sp- 100%. Discography herniation: Sn- 88% Sp- 100%.		MRI described as a sensitive and specific tool for diagnosing degeneration and herniation. No clinical outcome data presented to evaluate if either test selected patients with better outcomes after surgery. MRI appears valid tool in diagnosing disc degeneration and herniation.
Schneiderman 1987 Prospective study	6.0	36	L	Chronic LBP	Contrast	-	-	+	-	+	+	-	+	-	+	-	No	MRI 99% accurate in predicting whether disc would be normal or abnormal on discography.		Suggests no reason to do discography if MRI does not show any abnormalities. No clinical correlation or outcomes discussed.
Osti 1992 Prospective study	6.0	33	L	LBP	Contrast	-	-	+	+ #	+	-	-	-	+	+	-	No	All discs identified as abnormal on MRI abnormal on discography. 6/60 (10%) of normal discs on MRI showed degeneration on discography. 27/39 (69%) of discs with typical pain with discography had abnormal signals on MRI.		MRI is a diagnostic tool for degenerative disc disease, since no clinical correlations or outcomes reported it is difficult to assess clinical relevance of findings.

Linson 1990 Prospective Study	6.5	50	L	Chronic LBP failed conservative therapy	Contrast	-	-	+	-	+	-	-	-	-	-	-	No	6% negative correlation. 5 discs read by MRI as normal were read on discography as abnormal. 1 disc read as abnormal on MRI was read as normal on discography.		30/57 (53%) discs read as degenerative by discography had reproduction of back pain with injection. MRI is a valid diagnostic tool for degenerative disc disease.
Gibson 1986 Prospective study	5.5	22	L	Mechanical back pain	Contrast	-	+	+	-	+	-	-	-	-	-	-	No	44/50 (88%) of discs evaluated as degenerative by both MRI and discography.		MRI is a valid diagnostic tool for diagnosing degenerative disc disease.
Ito 1998 Prospective study	7.0	39	L	Chronic LBP failed conservative measures	Contrast	-	-	+	-	+	+	-	-	+	+	-	No	23% concordant pain with discography, 33% non-concordant pain, 45% no pain with discography. Detecting concordant pain reproduction on MRI: Radial tears, Sn- 87% Sp- 66%. Degeneration: Sn- 9%, Sp- 100%. Concentric and transverse tears: Sn- 52%, Sp- 80%. Disruption of outermost		Results state there are many degenerated discs seen on T2 MRI without pain reproduction on discography.

																	annulus: Sn-35%, Sp-90%.		
Carragee 2002 Prospective study		108	L	3 groups: 1) 13 with good results from cervical spine surgery; 2) 12 continued pain after cervical surgery; 3) 52 chronic LBP seeking discography for possible surgery	Contrast	-	-	+	+	+	-	-	+	+	+	-	No	23% Group 1 positive discograms; 50% Group 2 had positive discograms; 73% of Group 3 positive discograms. Disc degeneration with annular disruption 43% in Groups 1 & 2, 50% in Group 3. Discography: Sp- 74%, PPV- 31%.		Failure to find a definitive spinal lesion that consistently causes chronic LBP illness without associated co-morbidities suggests social, emotional, neurophysiological variables exert a strong permissive effect.
Laslett 2005 Prospective study	6.0	69	L	Chronic LBP patients seeking out discography	Contrast	Local anesthetic	-	+	+	-	+	-	-	+	+	-	No	Sensitivity, specificity, and positive likelihood ratios for centralization: 40%, 94%, 6.4. In presence of severe disability: 46%, 80%, 3.2. In presence of distress: 45%, 89%, 4.1. With moderate, minimal or no disability: 37%, 100%. With no or minimal		Report of centralization in non-distressed and not severely disabled chronic LBP patients suggest discography not necessarily indicated if a McKenzie centralization exam is positive; since expected results of discography already known (positive pain provocation.)

																	distress: 35%, 100%.		
Derby 2005 Prospective study	4.0	106	L	16 asymptomatic patients; 90 chronic LBP who failed conservative therapy	Contrast	Local anesthetic	+	+	+	-	+	-	-	+	+ *	-	-	In asymptomatic patients: Grade 3 annular tears exhibited in 32/55 (58%). 141/199 (71%) of discs in symptomatic patients had Grade 3 annular tears. All discs in asymptomatic group classified as negative.		Pain tolerance regardless of clinical status influenced pain provocation with discography. Mental and physical distress influences outcomes with discography need to be considered when choosing patients to send to discography. Higher grade annular tears more likely painful on discography than lower grade tears. About 50% Grade 4 tears painful with discography both high and low pressure. Leaves 50% of Grade 4 tears not painful. Annular tears can be a pain generator, but only up to 50% of time in study.
Carragee 2006 Retrospective case series	5.0	121	L	69 with no clinically significant LBP; 52 with chronic LBP considering additional treatment	Contrast	-	-	+	+	-	-	-	-	-	+	-	-	Positive injections correlated with annular disruption, abnormal psychometric findings, and chronic pain states. 17/69 (25%) in experiment group had positive low-pressure discography.		Using low-pressure guideline of 15-25 psi unlikely to eliminate all or most false-positive injections in patients with pain sensitivity risk factors. In patients without psychological distress, chronic pain, or previous surgery low-pressure discography likely

																	14/52 (27%) of chronic LBP patients had positive low-pressure discography.		more accurate, but these are not typically patients referred for procedure.
Manchikanti 2001 Prospective study	5.0	50	L	25 chronic LBP patients with somatization disorder and 25 without	Contrast	-	-	+	-	-	-	-	-	-	+	-	No	14/25 (56%) in non-somatization group and 12/25 (48%) in somatization group judged positive.		No differences in positive outcomes with discography based on a diagnosis of somatization disorder.
Jackson 1989 Prospective study	9.0	59	L	Patients with chronic LBP who underwent testing and then surgical exploration						+	+	+		+	+	+	-	MRI: Sn-64%, Sp-87%; CT: Sn-60%, Sp-86%; CT-Myelography: Sn- 73%, Sp-79%; Myelography: Sn- 56%, Sp-86%		MRI compared well to other diagnostic modalities in study. It is a good choice for imaging when considering more invasive treatment for herniated lumbar discs.

? = was not specified in study; * = which levels done on participants not well described; C = cervical, T = thoracic, L = lumbar spine; # = exact pressure measurement not reported; ** = quantified response not reported; ^ = surgery done on some participants, but not all

MRI DISCOGRAPHY
MRI is sometimes paired with discography for evaluation of the intervertebral discs.

Recommendation: MRI Discography for Evaluating Herniated Discs
MRI discography is not recommended for evaluating herniated discs.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation
There is no quality evidence supporting this combined test. The role of discography combined with MRI for evaluating herniated discs has not been determined. MRI discography is invasive, has adverse effects, and is costly. Therefore, it is not recommended.

Evidence for the Use of MRI Discography
There are no quality studies incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: MRI discography, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, diagnostic, efficacy, efficiency, sensitivity, specificity, predictive value of tests, positive predictive value and negative predictive value. In PubMed, we found and reviewed 26 articles, and considered zero for inclusion. In Scopus, we found and reviewed 22 articles, and considered zero for inclusion. In CINAHL, we found and reviewed one articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 5 articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the zero articles considered for inclusion, zero randomized controlled trials and zero systematic studies met the inclusion criteria.*

SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY (SPECT)
Single photon emission computerized tomography or SPECT is a nuclear tomographic imaging technique using gamma rays.(448) SPECT scanning is a less invasive modality that has been used, for example to attempt to make the diagnosis of facet joint arthritis.(449)

Recommendation: SPECT for Cervical and Thoracic Pain and Related Disorders
SPECT is not recommended for the evaluation of patients with cervical or thoracic pain and related disorders.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There is no quality evidence with patient-related outcomes that SPECT is helpful in improving care of acute, subacute, or chronic cervical pain, thoracic pain, or radicular pain syndromes or other spine-related conditions. Some data suggest SPECT may outperform bone scanning. Additional studies are needed to determine if SPECT adds something to the diagnosis, treatment and outcomes beyond that obtained by a careful history, physical examination, plain x-rays, and clinical impression before it can be recommended for evaluating, e.g., facet arthropathies.

Evidence for use of Single Photon Emission Computerized Tomography (SPECT)
There are 2 moderate-quality studies incorporated into this analysis.(450, 451) There is 1 low-quality study in Appendix 1.(449)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Single-photon emission computed tomography, single-photon emission computerized tomography, SPECT, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, diagnostic, efficacy, efficiency, sensitivity, specificity, predictive value of tests, positive predictive value and negative predictive value. In PubMed, we found and reviewed 49 articles, and considered 3 for inclusion. In Scopus, we found and*

reviewed 7 articles, and considered zero for inclusion. In CINAHL, we found and reviewed 3 articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 1 articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 3 articles considered for inclusion, 3 studies and zero systematic studies met the inclusion criteria.

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Type of SPECT	CT used	MRI Used	More than one rater	Blinding of rater	Myelography	Surgery Performed	Clinical outcomes assessed	Long term follow-up (mean when noted)	Results	Conclusion	Comments
Seitz 1995 Diagnostic	5.5	35	C	Persistent neck pain after trauma. Injuries included motor vehicle accidents, sport-related trauma, falls, and minor blunt head trauma.	SPECT	+	+	+	-	-	-	-	-	16 (46%) with cervical images demonstrated abnormal activity; 14 (88%) underwent subsequent CT (4 patients), MRI (8) or x-ray (2), which confirmed fractures in 7 patients. In final diagnosis, sensitivity 100% for detention of recent fracture with specificity of 78%. In 19 with normal SPECT results had final diagnosis, 12 had cervical strain, 5 a healed fracture, 1 degenerative osteoarthritis, and 1 an identified congenital abnormality.	"This study documents the normal cervical spine bone SPECT anatomy and demonstrates the importance of SPECT in the diagnostic and treatment approach in patients with persistent cervical pain after recent or remote trauma."	Data suggest use of SPECT in cervical spine trauma patients can assist in identifying occult fractures and recent fractures. Patients with abnormal SPECT scan may recover slower than those with normal SPECT scans.

Matar 2013 Diagnostic	4.0	72	C, L	Chronic neck or back pain.	dual-headed, hybrid SPECT/CT γ-camera	+	+	?	-	-	-	+	-	25 cervical and 49 lumbar spine scans. In cervical spine group, 13 (52 %) had evidence of facet joint arthropathy as likely pain generator. In lumbar spine group, 34 (69.4 %) had evidence of facet joint arthropathy as likely pain generator.	"Hybrid SPECT/CT imaging identified potential pain generators in 92% of cervical spine scans and 86% of lumbar spine scans. The scan precisely localised SPECT positive facet joint targets in 65 % of the referral population and a clinical decision to inject was made in 60% of these cases."	Data suggest in patients with chronic neck or back pain, SPECT can show facet pathology. But no outcome measures given on patients with certain findings.

FUNCTIONAL CAPACITY EVALUATIONS

The functional capacity evaluation is a set of tests, observations and practices that are combined to attempt to ascertain the ability of the patient to function most commonly either in one discrete job (e.g., return to work after injury) or potentially in a wide variety of different employment settings without targeting one in particular. A functional capacity evaluation is used to infer the work capacity.(452) A FCE may also be used to ascertain a baseline from which to develop a treatment program, to target specific work return to work needs.(453-455) The goals of FCEs include:

1. Determine individual's readiness to work after injury or illness at Maximum Medical Improvement (MMI),
2. Assist with goal-setting and treatment planning for rehabilitation or to monitor the progress of a patient in a rehabilitation program,
3. Estimate potential vocational status and provide a foundation for effective vocational rehabilitation,
4. Provide information to assist in disability determinations,
5. Provide information for hiring decisions (post-offer or fit-for-duty testing),
6. Assess the extent of disability in litigation cases, and
7. Provide information regarding a patient's level of effort and consistency of performance.

1. *Recommendation: FCEs for Chronic Disabling Cervical or Thoracic Pain*

   FCEs are a recommended option for evaluation of disabling chronic cervical or thoracic pain where the information may be helpful to attempt to objectify worker capability, function, motivation and effort vis-à-vis either a specific job or general job requirements. There are circumstances where a patient is not progressing as anticipated at 6 to 8 weeks and an FCE can evaluate functional status and patient performance in order to match performance to specific job demands, particularly in instances where those demands are medium to heavy. If a provider is comfortable describing work ability without an FCE, there is no requirement to do this testing.

   Harms – Medicalization, worsening of LBP with testing. May have misleading results that understate capabilities.

   Benefits – Assess functional abilities and may facilitate greater confidence in return to work.

   Strength of Evidence **– Recommended, Insufficient Evidence (I)**

   Level of Confidence – Moderate

2. *Recommendation: FCEs for Chronic Stable Cervicothoracic Pain or Post-operative Recovery*

   There is no recommendation for or against FCEs for chronic stable cervicothoracic pain or after completion of post-operative recovery among those able to return to work.

   Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

   Level of Confidence – Low

3. *Recommendation: FCEs for Acute Cervicothoracic Pain, Acute or Subacute Radicular Syndromes, or Post-Surgical Cervical or Thoracic Pain*

   FCEs are not recommended for evaluation of acute cervicothoracic pain, acute or subacute radicular syndromes, or post-surgical cervicothoracic pain problems within the first 12 weeks of the post-operative period.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

   Level of Confidence – High

Rationale for Recommendations

FCEs are one of the few means to attempt to objectify limitations and are frequently used in workers' compensation systems, particularly as the correlation between pain ratings and functional abilities appears weak.(456-462) Yet, obtaining objective data regarding spine problems is somewhat more challenging than for extremity-related impairments due to the degree of reliance on the patient's subjective willingness to exert or sustain major activities (e.g., standing, walking, sitting) that are critical for job performance. Because their reliability and validity have not been proven, FCEs should be utilized to evaluate work ability about what a patient was willing to do on a given day. They should not be used to override the judgment about the work ability of a patient with a back problem.

Many commercial FCE models are available. There is research regarding inter-and intra-rater reliability for some of the models (complete discussion is beyond the scope of this guideline). The validity of FCEs, particularly predictive validity, is more difficult to determine, since factors other than physical performance may affect return to work.(463, 464) An FCE may be done for one or more reasons, including identifying an individual's ability to perform specific job tasks associated with a job (job-specific FCE) and physical activities associated with any job (general FCE), or to assist in the objectification of the degree(s) of impairment(s). The type of FCE needed, and any other issues the FCE evaluator needs to address, should be specified when requesting a FCE.

The term "capacity" used in FCE may be misleading, since an FCE generally measures an individual's voluntary performance rather than his or her capacity. Physical performance is affected by psychosocial as well as physical factors. The extent of an individual's performance should be evaluated as part of the FCE process through analysis of his or her level of physical effort (based on physiological and biomechanical changes during activity) and consistency of performance. Perhaps more importantly, the objective findings identified in the musculoskeletal evaluation should correlate with any identified functional deficits. The individual's performance level, especially as it relates to stated levels of performance, should be discussed in the FCE report. A properly performed and well-reported FCE will highlight such discrepancies. This is particularly important in cervicothoracic evaluations where there may be greater degrees of impairments at stake and where there are somewhat fewer metrics available than for the distal upper extremity.

FCE test components may vary depending on the model used, but most contain the following:

- Patient interview including:
  - Informed consent
  - Injury/illness and medical history
  - Current symptoms, activities and stated limitations
  - Pain ratings/disability questionnaires
- Musculoskeletal examination (e.g., including Waddell's non-organic signs)
- Observations throughout the session (e.g., demonstrated sitting tolerance, pain modifying behaviors)
- Material handling tests (lifting, carrying, pushing, pulling)
- Movement tests (walking, crouching, kneeling, reaching, etc.)
- Positional tolerance tests
- Dexterity/hand function
- Static strength (varies among models)
- Aerobic fitness (usually submaximal test-also variable among models)
- Job specific activities as relevant
- Reliability of client reporting (e.g., non-organic signs, pain questionnaires, placebo tests, etc.)
- Physical effort testing (e.g., Jamar Dynamometer maximum voluntary effort, bell curve analysis, rapid exchange grip, competitive test performance, heart rate, observation of clinical inconsistencies, etc.)

FCE test length may vary between FCE models, although most 1-day FCEs are completed in 3 to 4 hours. Two-day tests, where the patient is seen on 2 consecutive days, may be recommended when there are problems with fatigue (e.g., chronic fatigue syndrome), delayed onset of symptoms, unusually complex job demands to simulate, and questions about symptom validity. Test length for 2-day tests is generally 3 to 4 hours on the first day, and 2 to 3 hours on second day.

Interpretation of FCE results is complicated in that it is a measure of voluntary performance. Before beginning testing, the patient is counseled to avoid doing anything to knowingly reinjure him or herself. Thus "fear avoidance" may cause testing to seriously underestimate actual ability and result in a report that the patient had "self-limited performance due to pain," suggesting a low pain tolerance, when in reality the patient was doing what he or she was instructed.

The best studies on the ability of FCEs to predict safe re-entry to the workplace following rehabilitation of work-related back pain/injury suggest that FCEs are not able to predict safe return to work (concurrent validity).(465-467) In a prospective cohort study of 1,438 consecutive work-related back patients, all underwent a FCE prior to return to work. In the control group, the FCE was used to write return-to-work guidelines, while in the study group it was ignored and the worker was returned usually to full duty. Ignoring the FCE reportedly improved outcomes in

a 1994 study, although the results have not been duplicated(468) and the quality of an FCE is believed to be heavily dependent on the skill, knowledge and experience of the FCE evaluator.(469)

Evidence for the Use of Functional Capacity Evaluation
There are 2 moderate-quality studies incorporated into this analysis.(454, 470)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Functional capacity evaluation, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, diagnostic, efficacy, efficiency, sensitivity, specificity, predictive value of tests, positive predictive value and negative predictive value. In PubMed, we found and reviewed 27 articles, and considered 2 for inclusion. In Scopus, we found and reviewed 6 articles, and considered zero for inclusion. In CINAHL, we found and reviewed one article, and considered zero for inclusion. In Cochrane Library, we found and reviewed zero articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 2 articles considered for inclusion, zero randomized controlled trials and zero systematic studies met the inclusion criteria.*

Author/Year Study Type	Score (0-11)	Population/Case Definition	Investigative Test	Gold Standard/ Comparative Test	Results	Conclusion	Comments
Harcourt 2003 Diagnostic	4.0	N = 50 with neck, midback, or lower back pain, with or without radiculopathy	Subjective and objective Numerical Outcome Measure Assessment (SONOMA)	N/A	Pearson correlation coefficients statistical significant ($p < 0.0001$): VAS (0.92), ADL (0.93), subjective analysis total (0.92), muscle strength (0.80), ROM (0.86), pressure pain thresholds (0.55), objective analysis total (0.87), and combined total (0.96). Kendall correlation coefficients joint dysfunction (0.68) and additional findings (0.68) statistical significant ($p < 0.0001$).	"[T]he SONOMA tool represents the first outcome measure tool that evaluates pain perception, activities of daily living or function, and physical parameters separately and combines values for a reliable and diversified depiction of the clinical picture. A very high correlation coefficient of .96 ($p < 0.0001$) demonstrates the reliability of this simple and practical tool. It is simple and practical for both the patient and the doctor."	Data suggest SONOMA had reasonable interrater reliability. However, this was not correlated with any outcome data or compared to other questionnaires.
Law 2013 Diagnostic	4.0	N = 54 divided into patient group (n = 26): neck pain during past 3 months vs. normal group (n = 260: non-neck pain past 6 months.	Electronic Cervical Range of Motion (CROM) Goniometer	N/A	Cervical Active ROM statistical significantly smaller in patient group vs. normal group in 3 planes of cervical movement. Saggital Plane (89.09±14.38 vs. 123.96±15.12; $p < 0.001$), Coronal Plane (69.04±12.54 vs. 89.19±13.10; $p < 0.001$), and Transverse Plane (134.42±18.91 vs. 161.58 ± 9.36; $p < 0.001$). Total Cervical AROM significantly smaller ($p < 0.001$) in patient group (292.56±35.08) vs. normal group (374.73±30.86).	"The ACRON cervical goniometer was found to be reliable for measuring cervical mobility in 3 planes for both normal and patient subjects. Construct validity of the goniometer was supported as the test's result documented significant difference in CROM between the control and the neck pain groups."	Data suggest reasonable interrater and intra-rater reliability with the specific ACRON system. This was not compared to any other diagnostic test. Data also suggest overall greater active ROM in the asymptomatic group.

DIAGNOSTIC FACET BLOCKS (INTRA-ARTICULAR AND NERVE BLOCKS)
See Injection Therapies.

MYELOSCOPY
Endoscopic examination of the epidural space is termed "myeloscopy." This procedure theoretically can be used solely for diagnostic purposes. It is most often performed in conjunction with adhesiolysis (see Adhesiolysis). The other method for performing adhesiolysis does not involve myeloscopy.(471-474)

Recommendation: Myeloscopy for Diagnosing Acute, Subacute, or Chronic Cervical Pain, Thoracic Pain, Spinal Stenosis, Radicular Pain Syndromes, or Post-surgical Spine Pain
Myeloscopy is not recommended for diagnosing acute, subacute, or chronic cervical pain, spinal stenosis, radicular pain syndromes, or post-surgical back pain problems.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
Currently, while there are studies suggesting different levels of neurological impingement are identified with myeloscopy, there are no quality controlled studies identifying the utility of this diagnostic procedure for improving long-term outcomes. A few reported studies have used this procedure in conjunction with adhesiolysis (see surgical treatments section of this Guideline). Myeloscopy has not been shown to be beneficial in large scale, medium- to long-term studies sufficient.(472, 473) It is invasive, has likely complications, and is costly. Well-designed multi-center studies are needed prior to recommending this procedure.

Evidence for the use of Myeloscopy
There is 1 other study in Appendix 1.(474)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: myeloscopy, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, diagnostic, efficacy, efficiency, sensitivity, specificity, predictive value of tests, positive predictive value and negative predictive value. In PubMed we found and reviewed 2 articles, and considered 1 for inclusion. In Scopus, we found and reviewed 0 articles, and considered zero for inclusion. In CINAHL, we found and reviewed 0 articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 0 articles, and considered zero for inclusion. We also considered for inclusion 1 article from other sources. Of the 2 articles considered for inclusion, zero randomized trials and zero systematic studies met the inclusion criteria.*

ULTRASOUND (Diagnostic)
There are two uses for ultrasound technology – one is therapeutic (see Ultrasound in the heat therapies section), and the other is for diagnoses. Ultrasound projects high-frequency sound waves through tissue and records the echoes through a 2-dimensional imaging system. Ultrasound is seldom used for diagnostic purposes in the spine other than for unusual specific purposes such as detection and guided drainage of superficial abscesses.(475-481)

Recommendation: Ultrasound for Diagnosing Cervical or Thoracic Pain
Diagnostic ultrasound is not recommended for diagnosing cervical or thoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – High

Rationale for Recommendation
Ultrasound has not been shown to result in improved patient outcomes or diagnoses other than minor applications. Ultrasound is not invasive, does not have adverse effects, and is moderately costly. There are other imaging techniques, which are currently shown to be useful for diagnosis in patients with spine pain. For most imaging purposes, CT and MRI are superior.

Evidence for the Use of Ultrasound
There are no quality studies incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Neck, cervical, vertebral, vertebrae, spine, disc, discs, disks, disk, radiculopathy, radiculopathies, radicular, Efficacy, Efficiency, Diagnostic, diagnosis, pain, Cervicalgia, Neck pain, cervical pain, Radicular pain, Herniated disk, Cervical Radiculopathy, Postoperative neck pain, Postoperative cervical pain, Sensitivity, Specificity, Predictive Value of Tests, Positive predictive value, Negative predictive value, intervertebral disc, displacement, displacements, displaced, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 2540 articles, and considered 2 for inclusion. In Scopus, we found and reviewed 4 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 18 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 30 articles, and considered 0 for inclusion. We also considered for inclusion 3 articles from other sources. Of the 5 articles considered for inclusion, 0 randomized trials and 1 systematic studies met the inclusion criteria.*

THERMOGRAPHY

Thermography is a diagnostic test that has been used to assess spine pain and radicular pain syndromes and other conditions.(482-484)

Recommendation: Thermography for Diagnosing Acute, Subacute, or Spine Pain or Radicular Pain

Thermography is not recommended for diagnosing acute, subacute, or chronic spine pain, or radicular pain.

Strength of Evidence – **Not Recommended, Evidence (C)**
Level of Confidence – Moderate

Rationale for Recommendation

There are 2 moderate quality studies suggesting thermography is unhelpful for diagnostic purposes.(485, 486) Thermography is not invasive, has little potential for adverse effects, but is costly. Thus, there is no convincing evidence that thermography is an effective test for assessing spine pain.

Evidence for the Use of Thermography

There are 2 moderate-quality incorporated into this analysis.(485, 486) There is 1 low-quality study in Appendix 1.(487)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: neck, neck pain, cervical, radicular pain or radiculopathies, neck pain diagnosis, diagnostic, diagnosis, sensitivity, specificity, positive and negative predictive value, predictive value of tests, efficacy, efficiency; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, retrospective studies, or prospective studies. We found and reviewed 12 articles in PubMed, 44 in Scopus, zero in CINAHL, 10 in Cochrane Library and zero in other sources. We considered for inclusion 3 from PubMed, zero from Scopus, zero from CINAHL, and zero in other sources. Of the 3 articles considered for inclusion, 3 diagnostic studies and zero systematic studies met the inclusion criteria.*

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Type of Thermography	CT used	MRI Used	More than on rater	Blinding of rater	Myelography	Surgery Performed	Clinical outcomes	Long term follow-up (mean when noted)	Results	Conclusion	Comments
So 1990 Diagnostic	6.5	14	C	Cervical radiculopathy (n = 14) vs. Control group (n = 20).	Telethermography unit (Bales Scientific MCT 7000)	-	-	-	+	-	-	-	-	Electro-physiologic studies supported diagnosis of cervical radiculopathy of 10/14 (71%) patients. 6/14 (43%) had an abnormal thermographic study. False positive rate 10% at 2.5 SD and 0% at 3 SD. 5 had abnormal electrophysiologic studies and normal thermographic studies. 5/14 (36%) had an abnormally increased interside temperature difference (3 SD above normal mean) in skin regions. 8/14 (57%) had agreement of 2 diagnostic tools on		Thermo-graphy appeared infereior to electromyography in evaluating cervical radiculo-pathy

														presence or absence of abnormalities.		
Dibai Filho 2012 Diagnostic	5.5	36 females	C	Neck pain (n = 18) vs. Control group (n = 18). Upper trapezius muscle temperature	FLIR Systems (Stockholm, Sweden) T360 Thermographic Camera	-	-	+	+	-	-	-	-	Correlation between NDI score and temperature of upper trapezius muscle for NDI (score) × TULT (°C)/ × TURT (°C)/ × TAUT (°C): r = −0.082/ r = −0.075/ r = 0.137; (p = 0.635/0.665/ 0.424).	"Women with neck pain, diagnosed with mild disability by NDI, did not present with reduction or asymmetry of upper trapezius muscle temperature when compared with a group without neck pain."	No difference in temperature between women with or without neck pain

FLUOROSCOPY
Fluoroscopy is live (real-time) x-ray imaging which can define abnormalities that may be visualized on movement, but that are not apparent on static films. It has been used for evaluation of the cervical and thoracic spine.

Recommendation: Fluoroscopy for Evaluating Acute, Subacute, or Chronic Cervical and Thoracic Pain
Fluoroscopy is not recommended for evaluating acute, subacute, or chronic cervical and thoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation
The main use for fluoroscopy is to guide procedures (e.g., facet injections, radiofrequency procedures, etc.) that are discussed individually elsewhere. While this test for evaluating cervical and thoracic pain was previously used to image the spine, it has been largely supplanted by other studies. Because continual x-ray exposure is needed to obtain the images, exposure to radiation is far higher with this procedure than with static x-rays. Fluoroscopy is not invasive, has low risk of adverse effects, but is costly and involves considerable radiation exposure. There are no evidence-based indications for fluoroscopy outside of its use in the performance of specific diagnostic tests or procedures and other infrequent indications.

Evidence for the Use of Fluoroscopy
There are no recent quality studies of the value of fluoroscopy in the evaluation of LBP or radicular pain syndromes or other back-related conditions.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: neck, neck pain, cervical, radicular pain or radiculopathies, neck pain diagnosis, diagnostic, diagnosis, sensitivity, specificity, positive and negative predictive value, predictive value of tests, efficacy, efficiency; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, retrospective studies, or prospective studies. We found and reviewed 88 articles in PubMed, 4 in Scopus, 6 in CINAHL, 4 in Cochrane Library and 0 in other sources. We considered for inclusion 0 articles from PubMed, Scopus, CINAHL, Cochrane Library and from other sources.*

VIDEOFLUOROSCOPY
Videofluoroscopy involves recording a videotape of fluoroscopic images of the spine that has been used for diagnostic purposes. Videofluoroscopy has been used for evaluation of the cervical and thoracic spine, particularly searching for possible spinal instability. After evidence interpreted as consistent with instability is found, surgery is typically proposed.

Recommendation: Videofluoroscopy for the Assessment of Acute, Subacute, or Chronic Cervical and Thoracic Pain
Videofluoroscopy is not recommended for the assessment of acute, subacute, or cervical and thoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation
There are no studies demonstrating improved clinical outcomes attributable to videofluoroscopy. There are no validated criteria for the utilization of videofluoroscopy to evaluate spine conditions. Other diagnostic tests have been shown to be effective in the evaluation of these patients. Videofluoroscopy is not invasive, has little potential for adverse effects, but is costly. It involves considerable radiation exposure. The clinical relevance of instability demonstrated via videofluoroscopy has not been established.

Evidence for Use of Videofluoroscopy
There are no quality studies regarding the use of videofluoroscopy.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: neck, neck pain, cervical, radicular pain or radiculopathies, neck pain diagnosis, diagnostic, diagnosis, sensitivity, specificity, positive and negative predictive value, predictive value of tests, efficacy, efficiency; controlled clinical trial, controlled trials, randomized controlled trial, randomized

controlled trials, random allocation, random, randomized, randomization, randomly; systematic, retrospective studies, or prospective studies. We found and reviewed 60 articles in PubMed, 159 in Scopus, 2 in CINAHL, 1 in Cochrane Library and 0 in other sources. We considered for inclusion 0 articles from PubMed, Scopus, CINAHL, Cochrane Library and from other sources.*

Initial Care

EDUCATION

In this guideline, "education" refers to formal, structured education programs separate from the education about diagnosis, treatment options, and prognosis that occurs at the time of office evaluation of the patient by a health care provider. Components of educational programs are quite variable and may include any or all of the following components: physical training, exercise, behavior modification, stress management, lifestyle change, education on anatomy, biomechanics, and "optimal posture."(488-492) While the primary thrust of these programs is rehabilitation, a secondary aim used to justify the costs of this intervention is the prevention of subsequent musculoskeletal pain episodes.(493) A recent case series found adherence to exercise was more likely if there was greater self-efficacy, clarification of patients' doubts by the provider, and supervision while the patient was learning the exercises.(494)

1. *Recommendation: Educational Programs for Select Patients with Subacute or Chronic Cervicothoracic Pain or Chronic Radicular Pain Syndromes*
   Educational programs are recommended for treatment of select patients with subacute or chronic cervicothoracic pain or radicular pain syndromes.
   Indications – Select patients with subacute or chronic cervicothoracic pain or radicular pain syndromes who require additional treatment and are motivated to adhere to the associated exercise components of the program on discharge.
   Duration/Frequency – Two to 6 weeks(488, 489, 495) with re-evaluation of participation and symptomatology during that time. If a positive outcome, can be extended for an additional 4 to 6 weeks.(489, 493, 496) Frequency of contact up to 3 times a week.(497, 498)
   Indications for Discontinuation – Resolution of symptoms, non-compliance with prescribed program, no improvement on follow up during initial implementation.
   Benefits – Potential for improved adherence and faster recovery
   Harms – Negligible. Possible reduced self-reliance.
   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

2. *Recommendation: Educational Programs for Acute Cervicothoracic Pain*
   Educational programs are not recommended as a sole treatment for acute cervicothoracic pain as other treatments are effective and it may be ineffective as a solitary treatment.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

3. *Recommendation: Educational Programs for the Prevention of Cervicothoracic Pain*
   There is no recommendation for or against the use of educational programs and education for prevention of cervicothoracic pain.
   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendations

There are quality studies that included educational programs. However, there are no trials that solely used an educational program, thus efficacy as a sole intervention is not demonstrated. An educational program has been used as the control group compared with another active intervention. Also, problematic is that trials do not describe these programs well. The advice/educational program groups often do not have all statistics performed on them for intragroup outcomes.(488, 496, 499, 500) This large programmatic variability also leads to difficulties in comparing the results between many of the RCTs. The more successful programs appear to have greater reliance on aerobic and endurance exercises and cognitive-behavioral principles than on education or flexibility exercises.(498)

A moderate-quality trial compared supervised exercises vs. advice alone in chronic whiplash associated disorder patients. The authors reported overall improvement in pain, functionality, and disability in both groups at the 12 month follow up. Employment status had greater improvement in the advice alone group than the supervised exercise group.(488) Another moderate-quality trial compared advice from a general practitioner to advice and exercise therapy as part of physiotherapy. At the 12-month follow-up, the advice-only group scored significantly better on work activities compared to patients treated by physiotherapists.(489) A moderate-quality trial evaluated the difference between general practitioner care and advice vs. manual therapy versus physiotherapy. The authors found greater benefits from manual therapy and physiotherapy for pain and recovery, but all groups had equal improvement at 12-month follow-up.(501) Another moderate-quality trial evaluating the difference between a supervised exercise program and an advice/home based exercise program reported better improvement in Self-Efficiency Scale, Tampa Scale, and Pain Disability Index at 3-month follow-up in the supervised group. Improvement in advice/home-based program was found as well, especially in the disability index score.(498)

There is evidence suggesting that educational programs may be associated with short-term improvements for chronic cervicothoracic pain and that such programs are more effective in a supervised setting than in a non-supervised setting.(488, 498) No quality evidence supports using educational programs for prevention as opposed to treatment.(13, 493) Even though there is little risk, there are no quality data to suggest a benefit of educational programs in preventing cervicothoracic pain.(493) Educational programs are not invasive, have low risk of adverse effects, but are expensive and consequently should be used in select patients who are likely to both achieve benefits and adhere to the program components after discharge.

Evidence for the Use of Education
There is 1 high-(488) and 6 moderate-quality(490, 493, 496, 498, 500, 501) RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.(502)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: cervicalgia, neck pain, neck, cervical pain, cervical radiculopathy, radicular pain, herniated disk, postoperative neck pain, postoperative cervical pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 752 articles, and considered 2 for inclusion. In Scopus, we found and reviewed 54 articles, and considered 1 for inclusion. In CINAHL, we found and reviewed 0 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 1 articles, and considered 0 for inclusion. We included 0 articles from other sources. Of the 3 articles considered for inclusion, 1 randomized trial and 2 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Stewart 2007 RCT Sponsored by the NSW Motor Accidents Authority. No mention of COI.	8.5	N = 134 whiplash associated disorder Grades I- III	Exercise and advice vs. advice alone for 6 weeks.	Influence of exercise at 6 weeks: p = 0.005 pain intensity, p = 0.003 pain bothersomeness, p = 0.006 patient specific pain. At 12 months, effects no longer significant or smaller. Exercise and advice more effective in reducing disability, improving SF 36, and greater global perceived effect compared with advice alone. Exercise group perceived treatment as more credible than advice group, p <0.0001 for all 4 questions.	"The results of this randomized controlled trial indicate that exercise and advice produced better outcomes than advice alone for people who have sustained a whiplash injury and have ongoing pain and disability that persist beyond three months."	Study done on WAD patients only. Exercise intervention group had more contact with providers. Showed that the higher the baseline pain and disability, the more response to treatment. A large portion (53%) in control group received therapies outside the study at 12 months, but analyses concluded it did not affect results. No effect at 6 weeks or 12 months on work status. No effect of duration of symptoms on outcomes.
Pillastrini 2009 RCT No mention of COI or sponsorship.	7.0	N = 71 nursery school teachers	Exercise program and brochure (Group E) vs. brochure only (Group C).	No effect from just ergonomics brochure but improvement in exercise group seen at 2 months.	"An exercise program, 'can be decisive in the prevention and management of low back and neck complaints and in reducing consequent LBP functional disability.'"	Statistical difference in baseline neck pain with higher pain in experimental group shown to increase recovery effect. No mention of duration of symptoms data on prevention; cannot confirm or deny.
Bunketorp 2006 RCT Sponsored by Vårdal Foundation for Health Care Sciences and Allergy Research, local Research and Development Council of Göteborg and Southern Bohuslän, and Swedish Association of Insurance Medicine. No mention of COI.	6.5	N = 47 subacute disorders following whiplash trauma	Home-training group vs. supervised training group for 3 months.	Of supervised group, 68%r eported higher self-efficacy levels compared to home group, 36%. 73% of supervised group reported a lessened degree of disability compared to home group, 40%. No difference between groups for lower VAS scores. No differences between groups for sick leave or use of analgesics.	"[S]upervised training was significantly more favourable than home training and promoted more rapid improvement in self-efficacy, fear of movement/ (re)injury, and pain disability in the short term."	Appears difference at baseline in number of controls that have sick leave 1-30 days with 36% in supervised group and 56% in home training group. At-home group continued to show improvement 3-9 months after intervention period; supervised group did not. Supervised group had contact 2x a week for 3 months where fear-avoidance training also conducted, in addition to baseline pamphlet given to both groups. Exercises mainly stretching and strengthening with some low impact aerobics.
Bernaards 2007 RCT No mention of sponsorship or COI.	6.5	N = 466 computer workers with frequent or long-term neck and upper limb symptoms	Work style group (WS) vs. work style and physical activity group (WSPA) vs. usual care group for 6 group meetings.	Current pain (0-10) for WS vs. WSPA vs. usual care group (mean±SD) at baseline/6/12 month follow-up: 3.9±2.3; 3.7±2.3; 3.5±2.1/ 3.6±2.4; 3.5±2.4; 3.3±2.3/ 3.0±2.3; 3.1±2.2; 3.2±2.4 (p <0.05). Worst pain (0-10): 5.3±2.4; 5.1±2.2; 5.1±2.3/ 4.8±2.4; 5.0±2.6; 4.5±2.6/ 3.8±2.4; 4.1±2.7; 4.4±2.9 (p <0.05).	"The combined intervention was ineffective in increasing total physical activity. Therefore we cannot draw conclusions on the effect of increasing physical activity on the recovery from neck and upper limb symptoms. There was no significant intervention effect over time	Long-term study. Increased physical activity did not occur which made this more a study of work activity vs. control group. No stratification of acute, subacute, chronic neck pain and their outcomes.

					for pain and recovery in the arm/wrist/hand region. In the neck/shoulder region, all pain measures reduced significantly in the WS group compared to the usual care group."	
Taimela 2000 RCT No mention of sponsorship. COI, COI category 12.	6.0	N = 76 chronic neck pain >3 months	Stabilization, postural and dynamic neck muscle exercises vs. home stretching and stabilizing vs. home neck exercise program education.	Self-experienced total benefit highest in ACTIVE group vs. HOME and CONTROL p <0.001. ACTIVE group had increased general health (p = 0.022) vs. controls, as well as reduction of symptoms in neck (p = 0.002) No significant difference in neck pain at 12 month follow-up; p = 0.066, but tendency was for HOME therapy group.	"The multimodal active treatment including exercises offer benefits in chronic neck trouble including improved self-experienced working ability."	Mixture of exercises in all 3 groups. More exposure to providers in ACTIVE group than HOME and CONTROL group.
Andersen 2008 Med Sci Sports Exerc RCT No mention of COI. Supported by funding from the Ministry of Culture Committee on Sports Research N200310016 and National Board of Health under Ministry of Interior and Health.	5.5	N = 549 workers with neck/ shoulder pain	Specific resistance training (SRT) vs. all-round physical exercise (APE) vs, reference intervention with counseling (REF) for 1 year.	Two physical training groups reduced neck pain intensity during 1st half of intervention. SRT group went from 5.0±0.2 to 3.4±0.2, p <0.0001. APE group from 5.0±0.2 to 3.6±0.2, p <0.001. No change in REF group. Pain intensity did not change during 2nd half of intervention. Shoulder controls developed less shoulder pain when compared to REF over a 1-year period.	"SRT and APE resulted in clinically relevant reductions of neck pain in those with symptoms and prevention of should pain in those without symptoms, although only minor gains in muscle strength were found."	SRT group training at work during working hours. Unequal exposure to trainers between groups. Specific resistance training group was only one to keep a training diary on type/intensity of exercise. All-round physical exercise group was a broad mixture of different exercises. Low compliance and lower training intensity may have disrupted stronger or more significant findings.
Hoving 2006 RCT Sponsored by grants from Netherlands Organization for Scientific Research and Fund for Investigative Medicine of the Health Insurance Council. No mention of COI.	5.0	N = 183 non-specific neck pain >2-weeks duration	Manual therapy (6 weekly sessions of low velocity mobilization, exercises) vs. physical Therapy (12 sessions over 2 weeks of exercises, traction, stretching, massage) vs. general practice (education of favorable prognosis, ergonomics, analgesics)	Perceived 100% Recovery: At 13 weeks, difference between MT and GP of 29.5 (95% CI 12.9, 46.1), At 52 Weeks 15.4 (-1.3, 3.21). No differences in Severity Physical Dysfunction, Pain Intensity, Neck Disability Index scores, Main functional limitation scores between any of the groups at 13 or 52 weeks.	"[A]fter MT had speeded up recovery in the short term, GP and PT treatment caught up in the long term, and differences between the three treatment groups at 12 months of follow-up were small and no longer statistically significant."	Follow-up study to Hoving 2002. Co-interventions common in all groups (more of same or cross-over therapy). Outcomes measures of Global Perceived Recovery of unknown reliability. Study results suggest all groups improve, with no significant differences between interventions at 3 months or 1-year.

FEAR AVOIDANCE BELIEF TRAINING

The Fear Avoidance Belief Model was developed in the 1980s to attempt to explain differences between patients who had resolution of acute cervicothoracic pain vs. those who progressed to chronic cervicothoracic or low back pain.(1518-1520) Waddell developed a questionnaire to investigate these fear avoidance beliefs in a clinical setting.(1521) Fear Avoidance Belief Training (FABT) was developed from a model to help individuals overcome fears that result in avoidance of activities and become self-fulfilling and self-reinforcing. Thus, FABT hopes to prevent the development of chronic cervicothoracic pain.(199, 1520, 1522-1524) Studies have been conducted to investigate the predictive ability of different measures, including clinical questionnaires, in the development of various measures of chronic cervicothoracic pain, including lost time and disability.(199, 1520, 1522) Interventions have involved specific training to directly address patient's fears, whether expressed or not, and address a de-emphasis on anatomical abnormalities, encouraging active management by the patient and education. FABT has been most frequently accomplished in the setting of physical rehabilitation programs, although it is not specific to any discipline. It is suggested that all health care providers be familiar with these principles and frequently remind patients of the main teaching points in these principles in the course of treatments for cervicothoracic pain.

Recommendation: Fear Avoidance Belief Training for Acute, Subacute, or Chronic Cervicothoracic Pain
FABT is recommended for acute, subacute, or chronic cervicothoracic pain, particularly if there are any suggestions of fear avoidance belief issues.

Indications – Acute, subacute, or chronic cervicothoracic pain.

Frequency/Duration – The most important intervention may be that all health care providers be aware of these principles and intervene with appropriate training and education at the first appointment. A typical program consists of 2 to 3 appointments for a total of approximately 6 appointments for acute and subacute cervicothoracic pain. Patients with more severe or chronic cervicothoracic pain problems may require up to 12 appointments. This training is most commonly accomplished in the context of physiotherapy physical therapy appointments.

Indications for Discontinuation – Resolution of fear avoidance beliefs or failure to respond.

Harms – None reported.
Benefits – Improved exercise compliance and earlier functional restoration

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

There are no randomized trials evaluating FABT as an independent intervention. There are cohort studies evaluating fear-avoidance behavior and the impact it has on chronicity of cervicothoracic pain.(1520, 1522) There are multiple trials in cervicothoracic pain that include FABT as a component of an intervention or have an "act as usual group" with a poor explanation of the advice given.(199, 489, 496, 498, 508) The data suggest that FABT is beneficial and should be started during the first visit for acute cervicothoracic pain.(508, 1520, 1522)

FABT has been evaluated in acute, subacute, and chronic low back pain patients with quality studies.(1525) All of these studies demonstrated that those with elevated fear avoidance beliefs (FABs) benefited from the intervention (1526-1528) with one exception – that exception was in Norway among individuals on disability pensions, thus applicability to the U.S. or to acute, subacute, or even chronic cervicothoracic pain settings seems remote (1529) (see Low Back Disorders guideline).

FABT is moderate cost as a sole intervention, but low cost for educational information in addition to other provider visits. Thus, FABT is recommended for acute, subacute, or chronic cervicothoracic pain patients with elevated FABs at baseline with or without referred pain.

Evidence for the Use of FABT

There are 2 high-(489, 508) and 6 moderate-quality(199, 496, 498, 1523, 1524, 1530) RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.(1531)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Fear Avoidance Belief Training, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies,

radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 961 articles, and considered zero for inclusion. In Scopus, we found and reviewed 42 articles, and considered 2 for inclusion. In CINAHL, we found and reviewed zero articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed zero articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 11 articles considered for inclusion, 11 randomized trials and zero systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Kongsted 2007 RCT Sponsored by an unrestricted grant from Danish Insurance Association and from PTU, Karen Elise Jensens Foundation and the IMK Foundation. Professional Organizational funds were received. No COI.	8.5	N = 458 age 18-70 years from emergency units and general practitioners within 10 days after a whiplash injury	Immobilization in semirigid collar for 2 weeks then active mobilization, max of 2 treatment sessions per week during 4 weeks (N = 156) vs. act-as-usual: information about whiplash injuries and need to stay active, resume normal activities (N = 153) vs. active mobilization: consisting of Mechanical Diagnosis and Therapy (MDT) based on repetitive movements directed by pain response for max of 2 times a week for 3 weeks of 6 weeks; for 3 weeks after accident, instructed to do light repetitive rotational movements within pain free ROM every 10 waking hours (N = 149). Follow-up for 1 year.	No statistically significant difference between the 3 treatment groups at 1 year (p = 0.2-0.6).	"Almost similar outcomes regarding pain intensity, disability, and work capability were observed across the 3 treatment groups, indicating that advice to "act as usual" is as effective as prescribing immobilization or a structured mobilization program."	Median number of consults with physiotherapist was 2. Duration of pain <10 days, assessed up to 12 months. Collar group significant increased risk for altered working ability and increased disability compared to other groups. Participants considered high-risk for developing chronic WAD.
Scholten-Peeters 2006 RCT Sponsored by Professional Organization funds (not specified). No COI.	8.0	N = 80 patients aged 18-55 years with whiplash-associated disorders from a car accident and symptoms present in last 48 hours.	Education (advice on graded activity) by GPs (N = 42) vs. education and exercises (graded activity performed at physical therapist office: progressive loading, stabilization, coordination, strength, endurance, length, ROM, posture, and balance by physiotherapist (N = 38) for 9 months. Follow-up at 8, 12, 26, and 52 weeks after trauma maximum.	No differences between 2 groups for all primary outcomes at 12 weeks. At 52 weeks, GP scored better on work activities, ($p \leq 0.01$). Physiotherapy better cervical ROM, $p \leq 0.05$ at 12 weeks. PT more effective on neck pain; initial pain intensity >75mm on VAS at 12 weeks, ($p = 0.0013$).	"Treatment by GPs and PTs were of similar effectiveness."	Broad range of exercises for varied amounts of time making it difficult to standardize treatments or assess if 1 modality more efficient than another. Some sub-group analyses suggest greater amount of pain with a greater response to therapy, but post hoc.
Bunketorp 2006 RCT	6.5	N = 49 subacute whiplash-associated	Home training group consisting of neck pain pamphlet aimed at	68% of supervised group reported higher self-efficacy levels compared to home	"[S]upervised training was significantly more favourable than home training and	Appears difference at baseline in number of controls that have sick leave 1-30 days with 36% in

Sponsored by Vårdal Foundation for Health Care Science and Allergy Research, local Research and Development Council of Göteborg and Southern Bohulslän, and Swedish Association of Insurance Medicine. No mention of COI.		disorders following a whiplash-type trauma. Mean age of 31 years.	reducing fear and anxiety and advice about self-management by being physically active; encouraged to participate in low intensity aerobic exercise at least 20 minutes twice a week (N = 25) vs. supervised training group: twice a week with sessions lasting 1-1.5 hours focused on neck and shoulder muscles (N = 24) for 3 months. Follow-up for 6 months after study.	group, 36%. 73% of supervised group reported a lessened degree of disability compared to home group, 40%. No difference between groups for lower VAS scores. No differences between groups for sick leave or use of analgesics.	promoted more rapid improvement in self-efficacy, fear of movement/(re) injury, and pain disability in the short term."	supervised group and 56% in home training group. At-home group continued to show improvement 3 to 9 months after intervention period; supervised group did not. Supervised group had contact twice a week for 3 months where fear-avoidance training also conducted, in addition to baseline pamphlet given to both groups. Exercises mainly stretching and strengthening with some low impact aerobics.
Ferrari 2005 RCT Sponsored by the University of Alberta Hospitals Foundation and the Division of Emergency Medicine, University of Alberta. No COI.	6.0	N = 112 patients aged 18 years or older with Grade I, II whiplash injury evaluated in emergency department (ED)	Educational pamphlet (summary of evidence based treatment based on *The Whiplash Book*) (N = 55) vs. no additional education (usual ED care: information sheet about neck sprain or whiplash symptoms, possible treatments, and signs to prompt return to hospital) (N = 57). Follow-up at 2 weeks and 3 months post injury.	No significant differences in recovery, pain, function, or loss of work. More in intervention group hired lawyers (p = 0.08).	"An evidence-based educational pamphlet provided to patients at discharge from the emergency department is no more effective than usual care for patients with grade 1 or 2 whiplash-associated disorder."	Study suggests provision of educational pamphlet with evidence based information provided no benefit to this subset of patients. Sample may be underpowered to make general assumptions for other populations.
Brison 2005 RCT Sponsored by Emergency Health Services Branch of Ontario Ministry of Health and Physical Medicine Research. Foundation and Other funds received to support study. No COI.	6.0	N = 405 patients aged 16 years or older evaluated in ED within 24 hours of rear-end motor vehicle accident	Educational video (20 minute presentation of best available evidence regarding posture, early return to daily activities, ROM exercise, and pain-relief methods) with usual care of whiplash injuries (N=206) vs. usual care alone (N=199). Follow-up at 2, 6, 12, 24, and 52 weeks post initial ED visit.	Education vs. no Education: both groups had high prevalence of WAD symptoms (88.9% vs. 89.8%). No statistically significant differences between groups for pain or persistent whiplash associated disorders at 2,6,12, 24, or 52 weeks.	"The presence of persistent WAD symptoms following simple rear-end MVCs was high in this sample. The video group demonstrated a trend toward less severe WAD symptoms."	No controls on usual care or limit on co-interventions. Subjects enrolled after usual care started several days after accident in many cases (mailed to home). Compliance to watching video71%. Study suggests additional educational video of marginal benefit (trend).
Kasch 2008 RCT Sponsored by an unrestricted grant	6.0	N = 688 age 18-70 years with acute whiplash injury from rear or frontal end car collision and	High risk: risk score ≥ 4 based on active neck mobility, 11-box VAS present neck pain/headache, female gender, and number of	No difference in handicap or outcomes (see Kongsted 2007; 2008). Reduced active neck mobility, high intensity of neck pain, headache, and multi non-painful symptoms	Active WAD. High-risk and low-risk block randomization. 1) neck immobilization for 2 weeks, then physiotherapy. 2) Active mobilization: 2 times a week for 6 weeks. 3) Act as	Results described in other publications (see Kongsted 2007; 2008).

from Insurance and Pensions in Denmark. No mention of COI.		whiplash associated disorders (WAD) within 3 days of post-injury	non-painful symptoms (N = 458) vs. low risk (N = 230). Follow-up for 12 months.	carry a 10 times raised risk for development of WAD.	usual verbal information. Duration: Active 5 days after injury. Asses: Base, 3, 6, and 12 months.	
Taimela 2000 RCT No mention of sponsorship. Conflict of interest category: 12.	5.0	N = 76 age 30-60 years with non-specific chronic neck pain for more than 3 months.	ACTIVE (N = 25) stabilization, postural and dynamic neck muscle exercises two sessions per week for 45 minutes for 12 weeks vs. HOME (N = 25) lecture about neck pain and written information about stretching and stabilizing exercises plus practical training for home exercises vs. CONTROL (N = 26) 1 lecture on neck pain and home neck exercise program education. Treatment period 12 weeks. Follow-up for 12 months.	Self-experienced total benefit highest in ACTIVE (mean score 4.6) vs. HOME (mean score 3.8) and CONTROL (mean score 3.3) (p <.001). ACTIVE group had increased general health (p = .022) vs. the other groups, as well as reduction of symptoms in neck (p=.007) at 12 months. No significant difference in neck pain at 12 month follow-up (p = .066), but tendency was for HOME therapy group.	"[T]he multimodal active treatment including exercises offer benefits in chronic neck trouble including improved self-experienced working ability."	A mixture of exercises in all 3 groups. More exposure to providers in ACTIVE group than HOME and CONTROL group.
Rolving 2014 RCT Sponsored by the Danish Working Environment Research Fund. No COI.	4.5	N = 83 on sick leave due to non-specific neck pain for 4-16 weeks, age range 18-60	General Physical Activity (GPA), physically active for a minimum of three to four hours per week, walking or swimming (N = 43) vs. Specific Strength Training plus GPA (SST group), specific exercise program to train the neck and shoulder muscles, use of rubber bands, 3X15 reps of each exercise, 3 times per week, 15-20 minutes (N = 40). Both groups: diary of training and pain. Follow-up: baseline, 3 months.	Score (range) measured on NRS scale: GPA v. SST: baseline vs. 3 months: 6 (3-8) vs. 7 (6-8), (p<0.01). Neck extension measured in Newton: 75.5 (50.0-112.8) vs. 98.1 (54.9-192.3), (p<0.01), in favor of SST; Neck flexion: 46.1 (27.5-87.3) vs. 60.8 (36.3-112.8), (p<0.01), in favor of both groups; shoulder abduction: 54.9 (40.2-68.7) vs. 58.9 (36.3-75.5), (p<0.01). Score (range) measured for Fear Avoidance Belief: GPA vs. SST: baseline vs. 3 months: 18 (13-22) vs. 25 (23-28), (p <0.01), in favor of SST.	"This study indicates that in rehabilitation of subjects severely disabled by non-specific neck pain, there is no additional improvement on pain or muscle strength when neck exercises are given as a home-based program with a minimum of supervision. However, strength training of the painful muscles seems to be effective in decreasing fear-avoidance beliefs."	Both groups improved over time, however no difference between groups were found.

Activity Modification and Exercise

REST AND RELATIVE REST

Rest and relative rest have long been used for the treatment of cervical pain, particularly acute cervical pain.(503) Use of rest is believed to have evolved from consideration of increased pain on a short-term basis experienced during activity by those with cervical pain, without consideration of whether there might be adverse short or longer-term implications. Prescriptions of rest have also implied that compliant patients were those that spent a greater proportion of time resting their neck and wearing cervical collars to presumably recover sooner. Rest is often prescribed in the form of wearing a cervical collar.

1. *Recommendation: Rest and Immobilization for Acute Cervicothoracic Pain*
   Rest and immobilization are moderately not recommended for the management of acute cervicothoracic pain.
   Strength of Evidence – **Moderately Not Recommended, Evidence (B)**
   Level of Confidence – High

Rationale for Recommendation
Quality studies have been reported with many studies having shown that maintaining activity and active forms of treatment are superior to neck immobilization and rest in the first 14 days after neck injury.(504-508) A higher quality study found that the patients randomized to wearing a neck collar had poorer outcomes in working ability and disability compared to active groups at 12 months.(508) Though rest is non-invasive, it is costly and associated with high morbidity, and therefore not recommended.

2. *Recommendation: Rest for Subacute and Chronic Cervicothoracic Pain*
   Rest is not recommended for the management of subacute and chronic cervicothoracic pain as it is suspected to be as ineffective for these situations as it is for acute cervicothoracic pain.(498)
   Strength of Evidence **– Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – High

3. *Recommendation: Rest for Radicular Pain Syndromes*
   Rest is not recommended for the management of radicular pain syndromes.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – High

Rationale for Recommendations
Multiple quality trials showed increasing, rather than decreasing activity was associated with improvement in neck and cervicothoracic pain.(509) Early mobilization was shown to be more effective than rest in acute cervical pain and interventions with exercises resulted in marked improvement over controls or less active interventions.(509-511) A study comparing anterior fusion surgery, physical therapy with multiple treating clinicians and a lack of standardized treatment, and 3 months of cervical collar in patients with cervical radiculopathy referred for surgery showed that the cervical collar group was the slowest to recover, but at 12 months all three groups had similar recoveries.(512)

It is suspected that rest is as unhelpful as it is for lumbar radiculopathy (see Low Back Disorders guideline). A recent study comparing semi rigid neck collar, physiotherapy, and usual activity in patients with cervical radiculopathy found that patients in either the neck collar or physiotherapy groups did equally well at 6 weeks and 6 months.(342)

Cervicothoracic braces, while non-invasive and generally low cost are not recommended. Bed rest, while not studied in cervicothoracic pain, is costly primarily due to lost time, and can have documented adverse effects beyond those associated with deconditioning, such as pulmonary emboli.(513) Studies document that compliance is poor, which likely results in underestimation of the magnitude of the adverse effects of this intervention. Bed rest is strongly not recommended as a treatment strategy for management of acute cervicothoracic pain. However, bed rest for unstable fractures is recommended.

Evidence for the Use of Rest and Relative Rest
There is 1 high-(508*)* and 5 moderate-quality(342, 504, 510-512) RCTs incorporated into this analysis. There are 3 low-quality(505-507) RCTs in Appendix 1.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: rest, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed, we found and reviewed 14 articles, and considered zero for inclusion. In Scopus, we found and reviewed 279 articles, and considered zero for inclusion. In CINAHL, we found and reviewed 19 articles, and considered two for inclusion. In Cochrane Library, we found and reviewed 14 articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 6 articles considered for inclusion, zero randomized trials and zero systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Kongsted 2007 RCT Sponsored by Danish Insurance Association and from PTU, Karen Elise Jensens Foundation and the IMK Foundation. No COI.	8.5	N = 458 recruited from emergency units and general practitioners within 10 days after whiplash injury, mean age 33 for neck collar, 34 for act-as-usual, 33 for active mobilization.	Immobilization in collar for 2 weeks then active mobilization, Mechanical Diagnosis and Therapy (MDT) based on repetitive movements directed by pain response, 2 sessions/wk for 4 weeks (n = 156) vs. act-as-usual patients given info on how to act when they have whiplash (n = 153) vs. active mobilization, Mechanical Diagnosis and Therapy (MDT), light repetitive movements, move neck in ROM (n = 149). Follow-up at baseline and after 3, 6, and 12 months post injury.	"At the 1-year follow-up, 48% of participants reported considerable neck pain, 53% disability, and 14% were still sick listed…no significant differences were observed between the 3 interventions group."	"Immobilization, 'act-as-usual,' and mobilization had similar effects regarding prevention of pain, disability, and work capability 1 year after a whiplash injury."	Median number of consults with physiotherapist was 2. Duration of pain <10 days, assessed up to 12 months. Looking at per-protocol analysis, collar group had significant increased risk for altered working ability and increased disability compared to other groups. Participants considered high-risk for developing chronic WAD.
Rosenfeld 2000 RCT Sponsored by Swedish National Health Insurance. COI: category 14.	7.5	N = 97 whiplash injury caused by motor vehicle collision, mean age 39 for group 1, 33 for group 2, 32 for group 3 and 38 for group 4.	Group 1: Active treatment within 96 hours, participants instructed to perform gentle, active, small range and amplitude rotational movements of neck, first in one direction, then other (n = 21) vs. Group 2: standard treatment within 96 hours, participants given leaflet providing information about injury mechanisms, advice on suitable activities, and instructions on postural correction (n = 23) vs. active treatment with delay of 14 days after trauma and instructed to perform gentle, active, small range and amplitude rotational movements of neck, first 1 direction, then other (n = 22) vs. standard treatment given after 14 days, participants given leaflet on	Change in Pain (VAS score) level at 6 month follow-up comparing all 4 groups: -30 vs. 0.74 vs. -15 vs. -7.1. No pain at follow-up (%): 38 vs. 17 vs. 23 vs. 5. Reduction in pain was greater for those receiving active treatment than in those receiving standard treatment (p <0.001).	"In patients with whiplash-associated disorders caused by a motor vehicle collision treatment with frequently repeated active submaximal movements combined with mechanical diagnosis and therapy is more effective in reducing pain than a standard program of initial rest, recommended use of a soft collar, and gradual self-mobilization. This therapy could be performed as home exercises initiated and supported by a physiotherapist."	Active group had more contact with health care providers than standard treatment group. Unsure of how well compliance was for 6 months of observation in groups. Active treatment based on McKenzie Principles done several times a day with some additional exercises given at 6 weeks.

			injury mechanisms, advice on suitable activities, and instructions on postural correction (n = 22). Follow-up at baseline and 6 months.			
Borchgrevink 1998 RCT Sponsored by The Association of Norwegian Insurance Companies. No mention of COI.	6.5	N = 201 whiplash neck sprain injuries, mean age 37.2±13.2 for act-as usual, and 36.0±11.8 for immobilized.	Act-as-usual group instructed to act as usual and received no sick leave or collar (n = 82) vs. Immobilized group received 14 days of sick leave and immobilized with soft neck collar for 14 days. Instructed to alternate use of soft collar during day with 2 hours on/2 hours off and to use continuously during night (N=96). Follow-ups at baseline, 2 and 6 weeks, and 6 months after accident.	Symptoms after 6 months: headache (p <0.01), neck pain (p <0.01), and neck stiffness (p <0.001). Severe symptoms at intake and 6 months later: headache at intake (Group 1 = 10% vs. Group 2=20%), 6 months later (Group 1 = 12% vs. Group 2 = 21%). Neck pain at intake (Group 1 = 17% vs. Group 2 = 26%), 6 months later (Group 1 = 11% vs. Group 2 = 15%). Symptoms during the 6 months of follow up: at intake pain factor Group 1 (1.99+/-0.13) Group 2 (2.10+/-0.12), 6 week pain factor Group 1 (1.98+/-0.14) Group 2 (2.01+/-0.13).	"The outcome was better for patients who were encouraged to continue engaging in their normal, pre-injury activities as usual than for patients who took sick leave from work and who were immobilized during the first 14 days after the neck sprain injury."	Outcome better for patients encouraged to continue engaging in pre-injury activities as usual than for patients who took sick leave from work and who were immobilized during 1st 14 days after neck sprain injury. Both groups instructed in self-training of neck from 1st day of treatment. Saw improvement only in subjective measure, no objective measures. Suggest a large psychological component had significant difference at baseline in education, headache pain, and severe neck pain.
Persson 1997 RCT Sponsored by Einar Bjorkelunds Foundation, The Land and Sea Foundation, and the Neurosurgery Institution Foundation, University of Lund. No mention of COI.	6.0	N = 81 cervicobrachial pain >3 months from C-root compression spondylotic spurs +/- disc bulging, mean age 45 for surgery, 48 for physiotherapy, and 49 for cervical collar.	Anterior cervical discectomy and fusion (Cloward) (n = 27) vs. rigid cervical collar for 3 months vs. physiotherapy ("decided by the physiotherapist according to preferences and symptoms," 30-45 minute sessions, 1-2/wk, may have included TENS, moist heat, U/S, cold, massage, traction, gentle mobilization, heat relaxation, stretching, flexibility, isometric neck strengthening (n = 27). Follow-up at baseline, 14-16 weeks and 12 months after treatment.	ACDF surgery vs. physiotherapy vs. cervical collar; mean present pain intensity VAS (average baseline/ 14-16 weeks/12 months): ACDF (47/27/30) vs. PT (50/41/39) vs. collar (49/48/35). Surgery superior to collar at 14-16 weeks (p <0.01). No differences at study end between groups. Subjective estimation of restored (surgery/PT/ collar) vs. improved vs. unchanged vs. improved vs. worse: N = 2/3/2, 5/11/9, 11/4/9, 8/9/6. At 12 months, no difference between any group for pain intensity or function (SIP) and mood (MACL) outcomes.	"In treatment of patients with long lasting cervical radicular pain, it appears that a cervical collar, physiotherapy, or surgery are equally effective in the long term."	Some baseline differences. Compliance unclear and 5/27 collared treated surgically. PT unstructured and individualized, precluding assessment of program elements or ability to replicate PT in composite. 8/27 had second surgery. Unclear how 1-year data analyzed with crossovers and most co-intervention procedures.
Kuijper 2009 RCT	6.0	N = 205 symptoms and signs of cervical radiculopathy < 1	Semi-hard collar and taking rest for 3 to 6 weeks (n = 69) vs. 12 twice weekly sessions	In wait and see group, neck pain did not decrease significantly 1st 6 weeks.	"A semi-hard cervical collar and rest for three to six weeks or physiotherapy accompanied	Clinical diagnosis based on pain in arm distal to elbow, provocation of pain

Sponsored by Non-Profit Foundation, Dr Eduard Hoelen Stichting, Wasswnaar, Netherlands. No COI.		month duration, mean age 47.0±9.1 for collar, 46.7±10.9 for physiotherapy, and 47.7±10.6 for control.	of physiotherapy and home exercises for 6 weeks (n = 70) vs. continuation of daily activities as much as possible without specific treatment, control group (n = 66). Follow-ups at baseline, 3 and 6 weeks, and 6 months.	Treatment with collar resulted in weekly reduction on VAS of 2.8mm (-4.2 to -1.3), amounting to 17mm in 6 weeks; physiotherapy gave weekly reduction of 2.4mm (-3.9 to -0.8) resulting in decrease of 14mm after 6 weeks. Compared with wait and see, neck disability index had significant change with use of collar and rest and non-significant effect with physiotherapy and home exercises.	by home exercises for six weeks reduced neck and arm pain substantially compared with a wait and see policy in the early phase of cervical radiculopathy."	with neck movement, or diminished DTRs, or sensory changes in a dermatomal pattern, or muscle weakness. Duration of symptoms <1 month. Patients in all groups had similar outcomes at 6 months. Data suggest collar and exercise similar at 3 and 6 weeks and outcomes better than wait and see.
Provinciali 1996 RCT No mention of sponsorship or COI.	4.0	N = 60 whiplash injury (recruited within 2 months after injury), mean age for group A was 40.3±15.1, and 40.9±23.1 for group 2.	Experimental multimodal treatment (Group A) consisting of postural training, manual technique and psychological support (n = 30) vs. control treatment (Group B) using physical agents only i.e., electrical and sonic modalities (n = 30). Each participant underwent 10, 1 hour sessions over a 2 week period. Follow-up at baseline, 15 days later after rehabilitation intervention, and 6 months after baseline.	Greater improvement in the multimodal group than passive modalities group in ROM, pain, self-rating scores and return to work. Return to work was 38.4+/-10.5 days in multimodal group vs. 54.3+/-18.4 days in passive modalities group (p <0.001).	"When analyzing the results, we found that the neck movements were improved both in patients given a multimodal treatment, including active mobilization (Group A), and in those treated with physical agents (Group B). However, a difference between the two groups was observed when considering the outcomes expressed by subjective symptoms such as pain, emotional changes and postural disturbances."	Lack of study details in paper lowered score. Return to work was assessed and more active group had significantly better outcomes. The more active the patient is the better the outcomes in therapy. Data suggest active exercises appear beneficial for acute whiplash patients.

SLEEP PILLOWS AND SLEEP POSTURE

Pillows and certain sleep postures are believed by some to be superior. The controversy appears largely driven by two different issues. One is a theory that a straight spine while sleeping is beneficial and the second is commercial. This theory holds that specific sleep postures that maintain the nocturnal alignment of the spine will reduce cervical pain incidence, persistence, and/or severity. Recommendations include sleeping on the side, sleeping with a pillow specifically designed for patients with cervical pain, and use of brand-name pillows and mattresses.(514-516)

1. Recommendation: Sleep Posture for Acute, Subacute, or Chronic Cervicothoracic Pain

The sleep posture most comfortable for the patient is recommended for treatment of acute, subacute, or chronic cervicothoracic pain. If a patient habitually chooses a particular sleep posture, it may be reasonable to recommend altering posture to determine if there is a reduction in pain or other symptoms.

Indications – Acute, subacute, or chronic cervicothoracic pain that results in nocturnal awakening, particularly if not amenable to other treatments.

Indications for Discontinuation – Non-tolerance.

Harms – Negligible.

Benefits – Better sleep and potentially reduced pain.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Level of Confidence – Low

2. Recommendation: Neck Pillows for Acute, Subacute, or Chronic Cervicothoracic Pain

There is no recommendation for or against the use of specific commercial products (e.g., neck pillows) as there is no quality evidence that they have roles in primary prevention or treatment of acute, subacute, or chronic cervicothoracic pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

Level of Confidence – Low

Rationale for Recommendations

Changing sleep posture is low cost and not invasive, although there is the potential for increased symptoms. Most of the studies done on neck pillows are lower quality; very few are RCTs. One moderate quality RCT suggested some differences between types of pillows that would need further investigation prior to a recommendation. (Gordon 10) No long-term studies have been reported.(517) A study evaluated neck pillows as part of a rehabilitation program where exercise seemed to be the main component with benefit, but the neck pillow may have had some role in the outcomes, although the trial is confounded by multiple co-interventions.(518) There are two non-randomized trials(512, 519) in patients that trended toward benefit of neck support while sleeping. Another study(520) suggested some improvement with use of any neck pillow. Among those who had 4 weeks of inpatient rehabilitation with one group receiving a neck pillow, follow-up in 12 months showed overall better maintenance of improvement among those who received the pillow in the hospital.(521) There has not been a cost analysis done to show the true cost of the pillow for the improvement seen in some studies.

Evidence for the Use of Sleep Pillows and Sleep Posture

There are 3 moderate-quality RCTs incorporated into this analysis.(515, 518, 521) There are 2 low-quality(520, 522) crossover trial or RCT in Appendix 1.

Sleep Pillows and Sleep Posture - A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: bedding and linens, sleep posture, neck pillows, sleep pillows, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed, we found and reviewed 12 articles, and considered 3 for inclusion. In Scopus, we found and reviewed 19 articles, and considered two for inclusion. In CINAHL, we found and reviewed one articles, and considered one for inclusion. In Cochrane Library, we found and reviewed zero articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 5 articles considered for inclusion, one randomized trial and two systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Helewa 2007 RCT No mention of sponsorship or COI.	7.0	N = 151 chronic neck pain >2 months, but <12 months; mean age 53.1±12.2 for control group, 51.6±12.8 for pillow only group, 47.6±14.7 for exercise only group, 47.1±15.0 for pillow and exercise.	Thermal massage, moist hot or cold pack per preference 20 minutes, then 5 minutes effleurage massage (n = 37) vs. thermal massage and neck support neck support pillow for sleep (n = 38) vs. thermal massage and neck exercise (postural instructions, manually resisted isometric exercises (n = 38) vs. all 3 interventions (n = 38). Follow-ups at baseline and weeks 3, 6 and 12.	Statistical difference between pillow plus exercise group present by 12 weeks (p=0.0285). Not significant differences between other 3 groups.	"[S]ubjects with chronic neck pain should be treated by health professionals trained to teach both exercises and the appropriate use of a neck support pillow during sleep; either strategy alone will not give the desired clinical benefit."	The apparently low magnitude of exercise may result in suboptimal results.
Gordon 2010 RCT No mention of sponsorship. No COI.	5.0	N = 106 side-sleepers, not receiving treatment for cervicothoracic problems; Mean age 49.0±14.3 years.	Polyester pillows + Foam regular pillow + Standard Dunlopillo latex pillows + Feather pillows vs. Control or own pillow. At baseline using own pillow for 1 week, over 9 weeks using each treatment-pillow for 7 nights, returning for 1 week to own pillow between using trial pillow. Each subject served as own control.	Those using own pillow reported 33.9 %, 19.6%, and 17.9% any walking cervical stiffness, walking headache and walking scapular arm pain, respectively.	"'Own' pillows did not guarantee symptom-free walking, and thus were a questionable control."	Allocation not described although this appears to be a cross-over trial (not stated). Control was use of "own pillow" although no data on types used. Data suggest improvement of symptoms with latex pillows, worse with feather pillows over own pillow.
Bernateck 2008 RCT No mention of sponsorship or COI.	4.0	N = 149 chronic cervico-brachialgia; mean age 50.9±7.4 for group 1, and 51.9±5.9 for group 2.	Group 1, Physical Therapy only (n = 73) vs. Group 2, Physical Therapy plus neck pillow (n = 76). Follow-up at baseline, and months 1, 3, 6, 9, and 12 after end of treatment.	No significant difference between groups during 4-week treatment. Neck support pillows group showed significant (p <0.05) level of improvement in cervical spine pain 1 to 12 months after treatment.	"[I]ndividuals with cervicobrachialgia and its typical complaints (pain radiation and sleep disturbances cause by pain) should receive comprehensive physiotherapy and an individual selected sleeping neck support."	Cervicobrachialgia patients without radiculopathy or inflammatory disease. No know mechanism of injury. Unsure of duration of pain in each group. Patients admitted for inpatient rehab in both groups. During 12-month follow-up, no mention of co-interventions or neck pillow compliance.

MATTRESSES

Mattresses of all types have been used according to personal preference and there are strong advocates particularly regarding therapeutic value of firm mattresses.

1. Recommendation: Mattresses for Treatment of Acute, Subacute or Chronic Cervical and Thoracic Pain

There is no recommendation for or against the use of mattresses for treatment of acute, subacute, or chronic cervical or thoracic pain other than to raise provider awareness that the dogma to order patients to sleep on firm mattresses appears wrong regarding the lumbar spine. By analogy, sleeping on the floor may be incorrect as well.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

2. *Recommendation: Other Sleeping Surfaces for Treatment of Acute, Subacute, or Chronic Cervical and Thoracic Pain*

There is no recommendation for or against the use of optimal sleeping surfaces (e.g., bedding, water beds, and hammocks) for treatment of acute, subacute, or chronic cervical and thoracic pain. It is recommended that patients select mattresses, pillows, bedding, or other sleeping options that are most comfortable for them. Individuals with spine pain may report better or worse pain and associated sleep quality with different sleeping surfaces. In cases where there is pain sufficient to interfere with sleep, recommendations by the provider for the patient to explore the effect of different surfaces in the home is appropriate. This could include switching to a different mattress, sleeping on the floor with adequate padding, and use of a recliner. Any recommendation in this regard should be preceded by adequate exploration of varied sleep positions/posture that could improve sleep quality.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendations

There are no quality studies in cervical spine patients. One quality study of chronic LBP patients reported a medium firm mattress was superior to a firm mattress,(523) but it neither discussed sleep position nor prior mattress firmness which may be important issues. Another trial suggested a waterbed or foam mattress is superior to a hard mattress.(524) Mattress selection is subjective and depends on many factors including personal habits and the weight/size of an individual. For these reasons, individuals must evaluate which mattress is best suited to provide some relief to their particular problem and it is not appropriate for providers to order mattresses or bedding for patients. However, providers should be aware that the dogma that a more firm mattress is superior to a less firm mattress currently appears wrong.

Evidence for the Use of Mattresses

There are no quality studies incorporated into this analysis.

EXERCISES

Exercises have long been considered among the most important therapeutic options for the treatment and rehabilitation of musculoskeletal disorders including cervical and thoracic pain.(525-527) Research has shown that aerobic exercises can reduce pain for up to 30 minutes after exercise.(528) However, despite a plethora of literature, the vast numbers of possible permutations and combinations of exercises impairs the ability to identify specific exercises that demonstrate particular benefit, particularly as trials nearly always include various combinations of exercises and are frequently unstructured.(488, 496, 501, 506, 529-532)

Similar to low back pain, the spectrum of patients with neck pain makes up a heterogeneous population with many different variables contributing to an individual patient's presentation. There is some preliminary evidence that patients with differing clinical presentations of cervical pain do not benefit equally from all types of therapeutics.(493, 529, 533, 534) The resulting theory is that some patients with specific disorders or presentations are more likely to benefit from different types of exercise programs.(13, 19, 488, 493, 499, 529, 533, 535-544) These classification systems, while suggesting possible improved outcomes from treatment based on syndromes (e.g., mobility, centralization, exercise and conditioning, pain control and headache),(19) await full validation studies.

There are many different types of exercise that have been assessed in many different settings with heterogeneous populations of patients. Outcome measures used are similarly heterogeneous (e.g., pain, composite scores such as the Neck Disability Index (NDI), modified duty, lost time, or disability ratings). There are an increasing numbers of studies suggesting longer-term benefits from exercise programs beyond 4 to 6 months.(499, 527, 529, 535, 536, 545-552)

Many studies have also combined exercise with manual therapy and some evidence suggests superior outcomes with that approach.(499, 533, 537, 553-555) A study created an algorithm for individualizing a therapy program compared to no intervention and reported better outcomes with the individualized therapy.(533)

There are few studies evaluating exercise as an intervention to prevent cervicothoracic pain. One study reported strength resistance training and overall increased physical activity helped prevent the development of cervicothoracic and shoulder pain over a 1-year period.(493)

There are also different programs with varied sequences and combinations of exercises. Taken in composite, the evidence of a beneficial effect of exercise for the treatment of cervicothoracic pain is moderately strong, but individually the evidence for any one exercise is weaker. Exercises can be segregated into different categories, but for purposes of this discussion, these three broad categories or "domains" of exercise will be utilized: aerobic, stretching/flexibility/centralizing, and strengthening/stabilization.

One major issue is motivation to exercise. Most RCTs evaluating exercise programs have supervised sessions where participants are accountable for doing the exercises or are able to do the exercises as part of a paid working day,(488, 498, 556) and also often keep exercise journals. One study did not inform participants of a planned 36 month follow-up and found that 17 to 25% of participants reported they were still complying with the exercise program and 35 to 40% were performing no exercises.(552)

Yet, formal supervision is not always necessary while performing exercises. Scholten-Peeters suggested even general practitioner care with advice on graded activity can be as beneficial as formal treatment with a physical therapist where the focus is education, graded activity and exercise.(489)

General Exercise Approaches and Recommendations
Exercise is commonly recommended as a prescription for a healthy lifestyle. Specific exercise regimens are often used as treatments for acute, subacute, and chronic cervicothoracic pain. An exercise prescription should address specific treatment goals and be time limited with transition to an independent exercise program as part of a healthy lifestyle. The purposes of supervised exercise therapy are symptom reduction, functional improvement, and educating the patient so that he or she can independently manage the program. Evaluation of an exercise prescription involves consideration of five critical components:

1. Stage of (theoretical) tissue healing (acute, subacute, chronic);
2. Severity of symptoms (mild, moderate, severe);
3. Degree and type of deconditioning (flexibility, strength, aerobic, muscular endurance);
4. Centralization pain response; and
5. Psychosocial factors (e.g., medication dependence, fear-avoidance, secondary gain, mood disorders).(549) (Vonk 09)

General Exercise Approach: Acute Cervicothoracic Pain
Stretching, aerobic, and directional centralizing exercises are recommended. Pain control modalities may be needed as a complement to exercise. Classification-based exercise management may be beneficial in selection of specific exercises.(506, 510) The recommended frequency is 1 to 3 sessions a week for up to 4 weeks as long as objective functional improvement and symptom reduction is occurring.(557)

General Exercise Approach: Subacute Cervicothoracic Pain
For patients with no prior treatment, the treatment plan is similar to acute cervicothoracic pain. For those who failed acute treatment, a trial of more intensive reconditioning that includes strengthening exercises is recommended. Particular attention should be paid to psychosocial factors that may impair compliance with exercise recommendations among those with subacute cervicothoracic pain, as it is believed that it is possible to reduce the risk of cervicothoracic pain becoming chronic. The frequency is 2 to 3 sessions a week for 4 weeks, as long as there

is objective functional improvement, symptom reduction, patient compliance, and efficacy. Progress should be reassessed after 6 to 8 sessions. Visit frequency depends on work status, symptom severity, comorbidities, and functional status.(488, 498) As the participants learn the exercises it may be reasonable to move from individualized therapy sessions to group session of 3 to 4 patients.(498)

General Exercise Approach: Post-operative Exercising
Post-operative progressive exercise programs should first emphasize flexibility and aerobic exercises and then progress to strengthening. Treatment frequency of 1 to 3 sessions a week progressing to 2 to 4 sessions a week is recommended depending on patient compliance, objective functional improvement, and symptom reduction. Reassessment should occur after 6 to 8 sessions with continuation based on demonstration of functional improvement. The upper range is 12 sessions.

General Exercise Approach: Chronic Episodic Cervicothoracic Pain and Radicular Pain
For patients with mild symptoms or a flare-up of symptoms, the treatment focus is on education regarding home management and exercise. Individuals with mild symptoms and minimal functional limitations may receive a therapy evaluation and one follow-up visit to adjust the home therapy program. For individuals with a moderate to severe flare-up with mild to severe disability, treatment should consist of a progressive exercise program first emphasizing strength and endurance exercises with treatment frequency of 1 to 3 visits a week up to a maximum of 8 to 12 visits.(558) Reassessment should occur after visit 6, with continuation based on patient compliance, objective functional improvement, and symptom reduction.

General Exercise Approach: Chronic Cervicothoracic Pain and Radicular Pain
For patients with mild symptoms and minimal disability, treatment should consist of a therapy evaluation to instruct the patient in a home-based exercise program, with 1 to 2 follow-up visits. For patients whose prior treatment failed and who have moderate symptoms and some functional deficits but no previous exposure to exercise therapy, treatment would be the same as for a patient with subacute symptoms (outlined above). If the patient failed prior exercise therapy, consider 6 additional exercise visits, or consider an interdisciplinary approach (see Chronic Pain guideline for managing patients with severe chronic pain or disability). It is recommended patients exercise 3 to 5 times a week.(493, 559)

General Exercise Approach: Cervicothoracic Pain Prevention
Some studies have attempted to determine whether exercise may prevent neck pain.(560, 561) A detailed, evidence-based and validated exercise prescription for this purpose is not yet possible.

Evidence for the Use of Other Exercises
There are 2 high-(489, 562) and 37 moderate-quality (one with two reports)(342, 490, 493, 498-501, 518, 536, 547, 549, 550, 556, 557, 559, 563-585) RCTs incorporated into this analysis. There are 12 low-quality RCTs and 2 other studies in Appendix 1.(576, 586-598)

AEROBIC EXERCISES
Theoretical benefits of aerobic exercise include improved aerobic capacity, improved blood flow, less depression, and higher pain thresholds and pain tolerance. These exercises include walking, running, bicycling, and many other activities. Whether there is benefit from weight-bearing vs. non-weight bearing aerobic exercises remains unclear. However, an exercise test is not believed to be necessary for the evaluation and treatment of the vast majority of cervicothoracic pain patients. For most patients, a structured, progressive walking program on level ground or no incline on a treadmill is recommended. For patients who desire aerobic exercises, there are no specific data, although there are indications that imply that there is a direct correlation between benefit and the amount of aerobic activity that results in higher MET expenditure. Therefore, the activity that the patient will adhere to is believed to be the one most likely to be effective, given that compliance is a recognized problem. Similar to other exercises, there is gathering evidence suggesting specific exercises may be helpful for specific presentations although those data have not yet been fully validated.(599)

1. *Recommendation: Aerobic Exercises for Acute, Subacute, or Chronic Cervicothoracic Pain*
   Aerobic exercise is recommended for treatment of acute, subacute, or chronic cervicothoracic pain.

Indications – All patients with acute, subacute, and chronic cervicothoracic pain are believed to benefit from aerobic exercises, especially those with whiplash-associated injury.(338, 557) Those with significant cardiac disease, or significant potential for cardiovascular disease should be evaluated prior to institution of vigorous exercises. It is recommended that the American College of Sports Medicine's *Guidelines for Exercise Testing and Prescription, 9th ed.*,(600) be followed for health screening and risk stratification.

Frequency/Duration – For patients with chronic cervicothoracic pain, there is no quantified prescription available, however, based on analogy to the quality evidence for treatment of LBP, walking at least 4 times a week at 60% of predicted maximum heart rate is recommended. For acute or subacute cervicothoracic pain patients, a graded exercise program is generally desired, often using distance or time as minimum benchmarks – e.g., start with 10 to 15 minutes twice a week(498) for 1 to 2 weeks and increase in 10 to 15 minute increments per week until at least 30 minutes walking a day is achieved. Studies that included exercises less frequently did not show any benefit.(601) However, vigorous exercise is generally not indicated until after a solid fusion has been accomplished.

Indications for Discontinuation – Aerobic exercise should be adjusted, reduced, or discontinued when there is intolerance (rarely occurs) or development of other disorders. Nearly all patients should be encouraged to maintain aerobic exercises on a long-term basis for both prevention of cervicothoracic pain and to maintain optimal health.
Benefits – Improvement in spine pain, improved cardiovascular fitness.
Harms – None reported in quality studies. Increased pain with onset of exercise. Theoretical risk of myocardial infarction and angina in a severely deconditioned patient.

Strength of Evidence **– Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

2. *Recommendation: Aerobic Exercises for Acute Post-operative Cervical Pain*
Aerobic exercise is recommended for acute post-operative cervicothoracic rehabilitation of patients.
Benefits – Improvement in spine pain, improved cardiovascular fitness.
Harms – None reported in quality studies. Increased pain with onset of exercise. Theoretical risk of myocardial infarction and angina in a severely deconditioned patient.

Strength of Evidence **– Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendations
While many studies included some aerobic exercises(488, 493, 538, 545) as part of a battery of exercises, there are no quality RCTs that solely or largely evaluated aerobic exercise as an intervention in any group. The studies that included aerobic exercises did report benefits; however, due to the scarcity of details on types of aerobic exercises or a tendency for the aerobic exercises to be a part of the intervention or also be included in the control group's treatment,(548) there is less data on the benefit of aerobic exercises in cervicothoracic pain compared to low back pain. In addition, there is no quality evidence for post-operative cervicothoracic rehabilitation. A study evaluating bicycling showed a decrease in pain up to 2 hours after the therapy sessions, but the decrease in pain was not long lasting.(602)

Evidence for the Use of Aerobic Exercise
There is 1 high-(488) and 24 moderate-quality(490, 493, 498, 510, 535, 539, 541, 545, 548, 599, 601, 603-614) RCTs incorporated into this analysis. There are 5 low-quality studies in Appendix 1.(615-619)

DIRECTIONAL EXERCISE
Directional exercise has been used for treatment of cervical pain.(76, 620)

Recommendation: Directional Exercises for Treatment of Acute, Subacute, Chronic, or Radicular Cervical and Thoracic Pain
Directional exercises are recommended for patients found to have directional preference (i.e., centralization or abolishment of pain in a direction).(621) This has been described in the lumbar spine and adapted to the rest of the spine including the cervical spine.(620) For chronic pain, directional exercises are generally not the primary or sole exercise treatment as aerobic and strength deficits are usually present.

Indications – For acute, subacute, or chronic cervical and thoracic pain, directional preference exercises are recommended.
Frequency/Duration – Exercise frequency is determined by the stage of recovery. They are initially performed every two hours (8-10 repetitions) to fully centralize and abolish the pain, along with posture modifications that also honor patients' directional preference and protect the patient from symptoms returning when not exercising. Once the pain is eliminated even for a short period of time, the same exercises and posture changes should continue proactively to attempt to prevent the pain from returning. Proactive exercise remains important in maintaining a pain-free status as the opposite direction of spinal movement and positioning are progressively re-introduced. The duration of this sequence is typically a few days or weeks.

Indications for Discontinuation – Directional exercises should be discontinued if there is worsening pain in the course of treatment or failure to improve.

Benefits – Often rapid elimination of the pain and earlier return to function.
Harms –Similar to all therapies, risk of increased pain.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendations
There are no quality studies of directional exercise for treatment of the cervical spine. There is one low quality study in chronic cervical pain patients suggesting efficacy.(620) There is evidence of efficacy for using directional exercise to treat the lumbar spine and thus, directional exercise is recommended for treatment of the cervical spine.

Evidence for the Use of Directional Exercise
There is 1 low-quality RCT in the Appendix.(620)

STRETCHING AND FLEXIBILITY
Stretching exercises include active movements to improve joint mobility and centralize symptoms, and to increase the length of a target muscle group.(622) Stretching exercises also have been utilized for both treatment as well as prevention, and are used in some manufacturing settings as part of an injury prevention program. Generally, most stretching exercises are actively performed by a patient. However, it is also possible to perform such exercises passively or with assistance of a provider. The latter should be performed carefully to not exceed the patient's natural range of motion and incur an injury.

1. *Recommendation: Stretching for Acute or Subacute Cervicothoracic Pain*
   Specific stretching exercises are recommended for treatment of acute or subacute non-specific cervicothoracic pain.

   Indications **–** Acute or subacute cervicothoracic pain under the direction of health care professional.

   Frequency/Duration – For pain that centralizes during an exam using repeated end-range test movements, single directional end-range exercises are believed to be preferred (see Directional exercise).(70)
   Three to 5 times a day for acute cervicothoracic pain; 2 to 3 times a day for subacute or chronic cervicothoracic pain. Stretching exercises shown to be beneficial include extension, flexion, and rotation held for 30 seconds, repeated 3 times daily, 5 times a week.(536)

   Indications for Discontinuation – Increased pain during course of treatment; failure to improve.
   Benefits – Shorter recovery time.
   Harms – Increased pain especially short term, and particularly if stretch in a direction of worsening (see Directional Exercise). Theoretical risk of muscle strain from over-stretching.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

2. *Recommendation: Stretching for Chronic Cervicothoracic Pain*
   Stretching is recommended for treatment of chronic cervicothoracic pain.
   Benefits – Shorter Recovery Time
   Harms – Increased pain especially short term, and particularly if stretch in a direction of worsening (see Directional Exercise). Theoretical risk of muscle strain from over-stretching.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – Moderate

3. *Recommendation: Stretching for Prevention of Cervicothoracic Pain*
There is no recommendation for or against stretching exercises as an isolated prescription or program for purposes of preventing cervicothoracic pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendations
There is quality evidence suggesting that stretching exercises may be of assistance particularly in those with subacute or chronic cervicothoracic pain.(536, 545, 559, 623) Stretching exercises shown to be beneficial include extension, flexion, and rotation held for 30 seconds, repeated 3 times daily, five times a week.(536) Studies report that stretching programs decreased pain and disability in chronic non-specific cervicothoracic pain over their baseline up to 12 months.(499, 536, 538, 557, 623, 624) Follow-up 3 years later in one cohort showed they maintained the improvement over baseline,(552) however; the stretching only control group was not included in the 36 month follow up. Other shorter term studies evaluated stretching as an intervention group and report mixed results.(625) Many other RCTs used stretching as a control group activity and did not find much benefit over baseline measures.(626) As with many other RCTs evaluating exercise and cervicothoracic pain, stretching is often a component of a mixed exercise intervention program.(498, 538, 545, 559, 627, 628) A study evaluated relaxation and stretching compared to dynamic exercises and found no significant improvement over baseline; however, compliance was low.(629)

There are concerns that over-stretching may result in additional injuries to patients. Aggressive stretching requires a health care provider for each session and thus costs are considerably greater than those for self-performed stretching exercises. While these treatments are not invasive, there are concerns that the potential for harm outweighs the potential for benefit. There are many other interventions with evidence of efficacy. Stretching exercises actively performed by patients for purposes of treatment and rehabilitation of cervicothoracic pain are low cost when performed as a home exercise program, are not invasive, and have low potential for adverse effects. They may help alleviate the stiffness that occurs with cervicothoracic pain that is thought to contribute to increased pain. These exercises are recommended.

Evidence for the Use of Stretching and Flexibility
There are 12 moderate-quality RCTs incorporated into this analysis.(497, 498, 545, 557, 559, 604, 627, 629-633) There are 6 low-quality(622-624, 634-636) RCTs and 1 other study in Appendix 1.(637)

STRENGTHENING AND STABILIZATION EXERCISES
Strengthening exercises theoretically may be used for purposes of improving or regaining prior maximum strength. Such improved strength would result in the ability to perform the same task at a lower percentage of maximum voluntary contraction, which in theory improves the individual's margin of safety.(638, 639) However, quality evidence to support the theory is sparse.(293, 488, 599, 608, 610, 611, 614, 640-642) A caution is that in the process of strengthening, sustaining a strain is possible. Another issue is that long-term compliance is required and is difficult to achieve. Fear avoidance belief training appears important in the management of patients with cervicothoracic pain (see Fear Avoidance Belief Training).(489, 496, 498) Inclusion of these principles in the course of exercise training or supervision appears to be beneficial. This would also strengthen the education of the patient about cervicothoracic pain and if there is a team treating the patient, all team members should have the same advice about exercise.

1. *Recommendation: Strengthening and Stabilization Exercises for Acute, Subacute, or Chronic Cervicothoracic Pain*
Strengthening, endurance, and aerobic exercises are moderately recommended for treatment of acute, subacute, or chronic cervicothoracic pain.

Indications – Acute, subacute, or chronic cervicothoracic pain.

Frequency/Duration – Home program frequency is 3 to 5 times a week for subacute or chronic cervicothoracic pain.(7, 493, 541, 556, 558, 599, 643) Supervised treatment frequency and duration is dependent of symptom

severity and acuity and the presence of comorbid conditions. Studies that had lower weekly participation in exercise programs failed to find benefits compared to controls.(629) Improvement of symptoms overall may be somewhat independent of exact exercise program type.(529, 541, 599, 606, 607) It appears in the literature that exercise programs that include both aerobic and strengthening often have better success in long-term compliance.(536, 547, 558) It is recommended that a program for strengthening include aerobic exercises as well.

Indications for Discontinuation – Resolution, failure to improve, noncompliance; development of injury in the course of exercise generally requires short-term reductions in exercise prescriptions.
Benefits – Improvement in spine pain, improved strength and fitness.
Harms – Increased pain, especially short-term. Theoretical risk of musculoskeletal injury.

Strength of Evidence – **Moderately Recommended, Evidence (B)**
Level of Confidence – High

2. *Recommendation: Fear Avoidance Belief Training*
Inclusion of fear avoidance belief training during the course of rehabilitation is recommended.
Benefits – Improvement in exercise and activity compliance, with resultant improved LBP, improved fitness.
Harms – None reported.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – High

Rationale for Recommendations
Many quality trials have evaluated strengthening exercises for chronic cervicothoracic pain,(7, 488, 489, 493, 499, 529, 535-537, 540, 541, 545-547, 549, 556, 558, 559, 607, 625, 629, 644-647) however, these exercises are often part of a program that includes strengthening, stretching, and some aerobic exercises. The longer the exercise program, the longer lasting the outcomes appear to be.(529, 536, 559, 646) The more dynamic the program the more improvement reported compared with very low intensity exercises.(493, 552, 559) It has also been shown that the greater the pain reported by the patient and greater the disability the more robust the benefits are of strengthening programs.(489, 535) More intense exercises regimens that include both concentric and eccentric muscle contraction with high intensity (8 to 12 lifts) and high volume (9 sets per session) have shown to have greater effect.(493, 535, 541, 607)

Studies that included fear avoidance belief training in their design showed that the intervention group had better outcomes.(489, 496, 498) These studies were not designed to specifically evaluate fear avoidance or behavioral support, but included them in their study protocols for the intervention groups.

Evidence for the Use of Strengthening and Stabilization Exercise
There are 1 high-(489) and 36 moderate-quality(7, 493, 496, 498, 499, 529, 536, 537, 541, 545-547, 549, 552, 556, 558, 604, 606-608, 610, 611, 614, 625, 629, 631, 640-642, 644, 645, 647-651) RCTs incorporated into this analysis. There are 11 low-quality(506, 615-617, 636, 646, 652-656) RCTs and 3 other studies(293, 637, 657) in Appendix 1.

AQUATIC THERAPY (Including Swimming)
There are no quality studies evaluating aquatic therapy in patients with cervical pain of any duration. Aquatic therapy involves the performance of aerobic, and/or flexibility, and/or strengthening exercises in a pool to minimize the effects of gravity, particularly where reduced weight-bearing status is desirable. However, this is less applicable with cervical pain patients than back or lower extremity pain patients.

Recommendation: Aquatic Therapy (Includes Swimming) for Acute, Subacute, or Chronic Cervicothoracic Pain
There is no recommendation for or against the use of aquatic therapy for acute, subacute, or chronic cervicothoracic pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There are no quality trials evaluating aquatic therapy exercises in cervicothoracic pain patients. Practitioners are cautioned that, unlike with low back pain patients, swimming may lead individuals to use prolonged awkward neck

positions during the activity that may exacerbate cervical pain symptoms. Other therapies have been shown to be efficacious.

Evidence for the Use of Aquatic Therapy
There are no quality studies incorporated into this analysis.

YOGA
Yoga for purposes of treating cervicothoracic pain has not been reported in quality trials.(630, 658, 659) Yoga involves postures, stretches, breath control, and relaxation. There are many different types of yoga that are practiced. In the cervical literature a variation of yoga called Qigong, has been evaluated. This review focuses on the exercise aspects of yoga and does not endorse or support spiritual elements or specific religious beliefs.

Recommendation: *Yoga for Acute, Subacute, or Chronic Cervicothoracic Pain*
There is no recommendation for or against yoga for acute, subacute, or chronic cervicothoracic pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
Moderate-quality RCTs that evaluated Qigong with other exercises found no significant difference although both groups improved.(546, 647) Since yoga has low or no risk, and may encourage exercise and activity, it may be an option for motivate patients with chronic cervicothoracic pain.

Evidence for the Use of Yoga
There are 5 moderate-quality RCTs incorporated into this analysis.(546, 630, 647, 659, 660) There are 4 low-quality RCTs in Appendix 1.(661-664)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: stair climbing, elliptical training, indoor rower, stairmaster, stationary bicycle, treadmill, jogging, walking, cycling, running, cross country skiing, cross country running, Nordic walking, inline skating, rowing, kick boxing, skipping rope, jump rope, circuit training, jumping jacks, 5BX, XBX, aerobic exercise, aerobics, aerobic exercises, exercise, cardio exercise, cardio exercises, aerobic programs, aerobics programs, aerobic exercise therapy, endurance training, tolerance training, exercise tolerance, strengthening exercise, weight lifting, weight bearing, lifting, stretching, muscle stretching, stretching exercises, stretching exercise, muscle stretching exercise, stretch, flexibility, passive stretching, static stretching, relaxed, isometric, static active stretching, specific stretching, PNF, cervical stabilization exercises, stabilization, postural exercises, neck stabilization, neck stabilization, specific neck stabilization, stabilization training, active neck stabilization, aquatic therapy, pool therapy, swimming, aqua therapy, hydrotherapy, Ai Chi, Aqua running, Bad Ragaz Ring Method, watsu, deep water exercise, shallow water exercise, yoga, hatha yoga, qigong, breath control, relaxation, relaxation control, therapeutic exercise, warm-up exercise, exercise intensity, abdominal exercises, pilates, walking, plyometrics, home maintenance, physical fitness, sports, yoga pose, athletic training, exercise positions, isokinetic, isometric and isotonic training, circuit training, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 687 articles, and considered 124 for inclusion. In Scopus, we found and reviewed 2,373 articles, and considered 11 for inclusion. In CINAHL, we found and reviewed 111 articles, and considered 1 for inclusion. In Cochrane Library, we found and reviewed 13 articles, and considered 0 for inclusion. We also considered for inclusion 37 articles from other sources. Of the 173 articles considered for inclusion, 139 randomized trials and 34 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Aerobic Exercise / Endurance Training						
Acute Pain						
Lange 2013 Clin J Pain RCT Sponsored by the Royal Danish Air Force. No COI.	5.0	N = 55 F-16 pilots who have experienced an acute neck injury in the previous 3 months, the mean age 31 for training group and 33.5 for control group	Training Group receiving 24 weeks of intervention and exercises, focusing on strength, endurance and coordination, 3x a week for 20 minutes per session (n = 27) vs. Control Group (n = 28). Assessments at baseline and after 24 weeks of treatment.	At 24 weeks follow-up, training group exhibited significant change in pain scores for last 3 months over control group: Difference between means (95% CI): 1.3 (0.4 to 2.2), (p = 0.01). Pain scores in last 7 days significant for training vs. control: Difference between means (95% CI): 0.8 (0.1 to 1.5), (p = 0.04). Training group had decreased prevalence of neck pain over control during previous 3 months: OR (95% CI) - 4.0 (1.3-13.0), (p = 0.02).	"[W]e found a high prevalence of self-reported neck and shoulder pain and clinical signs and symptoms among F-16 pilots. Twenty-four weeks of targeted training combining deep neck muscle training with neck and shoulder strength training proved effective in reducing neck pain in F-16 pilots with repeated whiplash-like exposures."	Few meaningful differences were seen between groups.
Lange 2014 Aviat Space Environ Med Single Blind RCT No mention of sponsorship or COI.	5.0	N = 55 F-16 pilots who have experienced an acute neck injury in previous 3 months, mean (IQR) age 33.5 (29-36) for neck pain in previous 3 months training group and 33 (30-34) for no neck pain in previous 3 months group	Group with neck pain within previous 3 months (n = 30) Vs. Group with no neck pain within the previous 3 months (n = 25). Both groups consisted of some participants who received 24 weeks of deep cervical muscle intervention focusing on coordination, endurance and strength, 3 times a week for 20 minutes per session. Assessments at baseline and after 24 weeks of treatment.	No significant results reported between neck pain and no neck pain group. Significant results reported for the training group over the control group (from primary outcome analysis above) for the Romberg test with closed eyes only: Training Group- 650 ± 405 mm² vs. Control Group- 761 ± 311 mm², (p = 0.02).	"Impaired postural control and steadiness may only be quantifiable in individuals experiencing acute neck pain of certain intensity, and there may be a ceiling effect in the ability to improve these parameters. For individuals with highly developed physiological capacity, a battery of tests with more stringent demands should be considered, e.g., increased number of repetitions, prolonged duration of the tests, or testing with eyes closed."	Paper is reporting significant secondary outcomes to study listed above. Group training is same as above, but group analysis was based on those with or without pain in previous 3 months. Few meaningful differences were seen between groups.
Subacute Pain						
Stewart 2007 RCT Sponsored by the NSW Motor Accidents Authority. No mention of COI.	8.5	N = 134 with whiplash associated disorder Grades I- III. Mean age 43.3 years	Aerobic Exercise and advice (n = 66) vs. Advice alone for 6 weeks (n = 68). Follow-up at 6 weeks and 12 months.	Influence of exercise at 6 weeks: (p = 0.005) pain intensity, (p = 0.003) pain bothersomeness, (p = 0.006) patient specific pain. At 12 months, these effects no longer significant or smaller. Exercise and advice more effective in reducing disability, improving SF 36, and greater global perceived effect compared with advice alone. Exercise group perceived treatment as more credible than advice group, (p <0.0001) for all 4 questions.	"The results of this randomized controlled trial indicate that exercise and advice produced better outcomes than advice alone for people who have sustained a whiplash injury and have ongoing pain and disability that persist beyond three months."	Study done on WAD patients only. Exercise intervention group had more contact with providers. Showed that higher baseline pain and disability, more response to treatment. Large portion (53%) in control group received therapies outside study at 12 months, but analyses concluded it did not

						affect results. No effect at 6 weeks or 12 months on work status. No effect of duration of symptoms on outcomes.
Rosenfeld 2003 RCT Sponsored by local research committee in southern Elfsborg County, the Swedish National Health Insurance, and Vårdal Foundation. No COI.	7.5	N = 97 with whiplash injury caused by motor vehicle collision. Mean age 35.4 years	Group 1 Active, < 96 hours (n = 21) Vs. Group 2 Standard, < 96 hours (n = 23) vs. Group 3 Active, >2 weeks (n = 22) Group 4 Standard, > 2 weeks (n = 22). Follow-up at 6 months and 2 years.	Active vs. Standard (Tx at <96 hours, >2 weeks); Mean improvement in Pain Intensity at 6 months: 27% vs. 6%, 11% vs. 8.5%; at 3 years 17% vs. 5% ; 11% vs. 8.5 %; Mean Sick Days at6 months:11.2 vs. 40.2 at 3 years 10 vs. 20.5; statistical analysis unclear as presented in tables.	"In patients with whiplash-associated disorders, active intervention is more effective in reducing pain intensity and sick leave, and in retaining/regaining total range of motion than a standard intervention. Active intervention can be carried out as home exercises initiated and supported by appropriately trained health professionals."	One therapist had intervention up to six weeks. Mean number of sessions 3.95. Compared timing. Looked at sick days because of neck pain
Bunketorp 2006 RCT Supported by Vardal Foundation for Health Care Sciences and Allergy Research, local Research and Development Council of Goteborg and Southern Bohuslan, and the Swedish Association of Insurance Medicine. No mention of COI.	6.5	N = 47 with subacute disorders following whiplash trauma. Mean age 36.4 years	Home-training group (n = 19) vs. Supervised training group for 3 months (n = 21). Follow-up at 3 months and 9 months.	Of supervised group, 68%reported higher self-efficacy levels compared to home group, 36%. 73% of supervised group reported a lessened degree of disability compared to home group, 40%. No difference between groups for lower VAS scores. No differences between groups for sick leave or use of analgesics (p>0.05)	"[S]upervised training was significantly more favourable than home training and promoted more rapid improvement in self-efficacy, fear of movement/ (re)injury, and pain disability in the short term."	Appears to be difference at baseline in number of controls that have sick leave 1-30 days with 36% in supervised group and 56% in home training group. At-home group continued to show improvement from 3 to 9 months after intervention period; supervised group did not. Supervised group had contact twice a week for 3 months where fear-avoidance training also conducted, in addition to baseline pamphlet given to both groups. Exercises mainly stretching and strengthening with some low impact aerobics.
Ask 2009 RCT No mention of sponsorship or COI.	6.0	N = 25 with subacute whiplash-associated disorders. Mean age: motor control and endurance/ strength groups: 38.3 and 35.6.	Motor control group (n = 11) received physiotherapy focused on motor control. Vs. Endurance/Strength group (n = 14) received physiotherapy focused on endurance and strength of neck muscles. Follow-up at 12 months.	Differences between groups was not statistically significant at 6-weeks or 12-months. Neck Disability Index Change, Motor vs. Endurance/Strength – 6-weeks: 9.0 vs. 7.0 (p = 0.912); 12-months: 4.0 vs. 4.0 (p = 0.783).	"In conclusion, the findings of our study suggest that the changes associated with motor control training and endurance/strength training of neck muscles were similar when prescribed to a most likely high-risk patient group."	Small sample size (n = 25). No meaningful differences between groups.

Chronic Neck Pain						
Rosenfeld 2000 RCT Supported by the Swedish National Health Insurance. No mention of COI.	7.5	N = 97 with whiplash injury caused by motor vehicle collision. Mean age 35.4 years	Group 1 Active, <96 hours (n = 21) vs. Group 2 Standard, < 96 hours (n = 23) vs. Group 3 Active, >2 weeks (n = 22) vs. Group 4 Standard, >2 weeks (n = 22). Follow up at 2 weeks and 6 months.	Active vs. standard (Tx at <96 hours, > 2 weeks); Mean improvement in Pain Intensity at 6 months: 27% vs. 6%, 11% vs. 8.5%; at 3 years 17% vs. 5% ; 11% vs. 8.5 %; Mean Sick Days at 6 months:11.2 vs. 40.2 at 3 years 10 vs. 20.5; statistical analysis unclear as presented in tables.	"In patients with whiplash-associated disorders caused by a motor vehicle collision treatment with frequently repeated active sub maximal movements combined with mechanical diagnosis and therapy is more effective in reducing pain than a standard program of initial rest, recommended use of a soft collar, and gradual self-mobilization. This therapy could be performed as home exercises initiated and supported by a physiotherapist."	Active group had more contact with health care providers than standard treatment group. (Potential contact bias)Unsure of how well compliance was for 6 months of observation in groups. Active treatment based on McKenzie Principles done several times a day with some additional exercises given at 6 weeks.
Evans 2002 RCT Sponsored by Consortium for Chiropractic Research. No COI.	7.5	N = 191 with chronic neck pain.	See Bronfort et al, 2001	See Bronfort et al, 2001	See Bronfort et al, 2001	See Bronfort et al, 2001
Ylinen 2003 RCT Supported by Social Insurance Institution, Helsinki, Finland. No mention of COI.	7.5	N = 180 female office workers with chronic, non-specific neck pain. Age range 25-53 years.	Endurance Training Group (dynamic neck exercises) (n = 60) vs. Strength training group performed high-intensity isometric neck strengthening (n = 60) vs. Control (n = 60). Both training groups performed dynamic exercises for shoulders and upper extremities with dumbbells. All advised to do aerobic and stretching exercises 3x a week. Follow-up at 2, 6, 12 months.	Neck VAS scores (baseline/12 months): controls (58/-16) vs. endurance (57/-35) vs. strength (58/-40). Neck and shoulder pain and disability index scores followed a similar pattern: controls (38/-12) vs. endurance (36/-22) vs. strength (35/-23). Endurance and strength groups showed significant improvement for all measures compared to control (p <0.001). No significant difference between strength and endurance.	"Both strength and endurance training for 12 months were effective methods for decreasing pain and disability in women with chronic, nonspecific neck pain. Stretching and fitness training are commonly advised for patients with chronic neck pain, but stretching and aerobic exercising alone proved to be a much less effective form of training than strength training."	Trial included aerobic exercises plus stretching when aerobic exercise plus strengthening may be preferable for chronic pain. Significant overlap in specific exercises between groups.
Ylinen 2010 RCT Supported by the Social Insurance Institution, Finland. No mention of COI.	7.5	N = 180 female office workers with chronic non-specific neck pain. Age range 25-53 years.	Endurance group (EG) dynamic muscle and stretching exercises (n = 60) vs. Strengthening group (SG) dynamic, isometric, and stretching exercise (n = 60) vs. Control group (CG) stretching exercises only (n =	Neck pain decreased in all groups compared to baseline. However, endurance (-35 (95% CI -42 to -28) p = 0.44)) and strength groups (-40 (95%CI -48 to -32) p = 0.013) improved significantly vs. control group (-16 (95% CI -22 to -9) (p = 0.10)).	"[S]trength and endurance exercises, when accompanied by stretching exercises, were shown to be an effective treatment for headache and arm pain associated with neck pain."	Secondary analysis of Ylinen 2003. Data suggest addition of strength and endurance training exercises to stretching of neck musculature may be beneficial. Conclusions

			60). Follow-up took place 12 months after baseline.			weakened by multiple baseline differences.
Salo 2010 RCT 1-year follow-up of previous study by Ylinen 2010 No mention of funding/support. No COI.	7.5	N = 180 female office workers with chronic non-specific neck pain. Age range 25-53 years.	Endurance group (EG) dynamic muscle and stretching exercises (n = 60) vs. strengthening group (SG) dynamic, isometric, stretching exercise n = 60) vs. control group (CG) stretching exercises only (n = 60). Follow-up 12 months after baseline.	By 12 month follow-up, changes in total 15 dimensions scores for quality of life improved significantly in both treatment groups compared to baseline. Effect size for strengthening group 0.39 (95% CI 0.13 to 0.72) and endurance training 0.37 (95% CI 0.08 to 0.67) (p>0.05).	"[T]welve months of neck strength or endurance training significantly improved HRQoL compared to control group among females with chronic neck pain."	Secondary analysis of Ylinen 2003. Data suggest intervention is related to improved quality of life scores. However, no direct correlation to neck pain or clinical outcome has been established.
De Hertogh 2009 RCT Supported by Faculty of Physical Education and Physiotherapy, Vrije Universiteit Brussel and research grant from University College of Antwerp, Health Care Sciences. No COI.	7.0	N = 37 with neck pain and recurrent headache for minimum of 2 months. Mean age 43.2 years	Usual care (UC) (n = 19) vs. Usual care plus manual therapy (UCMT) (n = 18). Follow-up at 7, 12 and 26 weeks.	Number of responders vs. unresponders not significantly different between groups. Headache impact scores similar for both UC 56.8+/- 6.46 and UCMT 55.21 +/- 9.75, 95% CI -5.76 to 8.94. Values not significant (p>0.05)	"We were unable to demonstrate differences in treatment effects between both treatment groups at the follow-up measurements (week 7, 12, and 26)."	Study discontinued prematurely due to low enrollment, lack of power. No differences found between groups in limited analysis.
Pillastrini 2009 RCT No mention of sponsorship or COI.	7.0	N = 71 nursery school teachers. Group C mean age 43.5 years, Group E mean age 44.7	Exercise program and brochure (Group E) (n = 35) vs. Brochure only (Group C) (n = 36). Follow-up assessments at 2 months.	No effect from just the ergonomics brochure but improvement in exercise group seen at 2 months. Improvements significant in favor of Exercise group. RMDQ 1.9 vs. 3.8 (p <0.0001), ODI 3.8 vs. 8.3 (p <0.0001), LBP 3.7 vs. 5.4 (p <0.0001).	"An exercise program, 'can be decisive in the prevention and management of low back and neck complaints and in reducing consequent LBP functional disability.'"	Statistical difference in baseline neck pain with higher pain in experimental group shown to increase recovery effect. No mention of duration of symptoms or prevention data.
Jordan 1998 RCT No mention of sponsorship or COI.	6.5	N = 119 with chronic neck pain >3 months' duration. Age range-20-58	Intensive training (n = 40) vs. Physiotherapy (n = 39) vs. Manipulative treatment 2x a week for 6 weeks (n = 40). Follow-up at 4 and 12 months.	Pain ratings decreased (baseline/completion/12 month): intensive training (12/6/6) vs. physiotherapy (12/6/8) vs. chiropractic (13/6/6). Disability ratings were similar: (8/5/5) vs. (9/4/6) vs. (8/4/5). Endurance in groups was (baseline/completion): intensive (60/120s) vs. physiotherapy (70/110s) vs. chiropractic (60/90s).	"There was no clinical difference between the three treatments. All three treatment interventions demonstrated meaningful improvement in all primary effect parameters."	Intensive training at 5-6 minutes did not include substantial aerobic exercise and included bicycling which may result in a postural issue; program appears to have primarily consisted of strengthening exercises. Study is of heterogeneous group of interventions; endurance lowest in chiropractic group. No significant differences between groups.
Nikander 2006	6.5	N = 180 female office workers	Strength training: elastic rubber band for neck flexor	Metabolic equivalents (MET)-hours in the strength program correlated	"[T] he described specific exercise protocols were	Suggests stretching had minimal impacts on neck

RCT Study supported by Social Insurance Institution, Helsinki, Finland. COI: Professor Ma¨ lkia¨ has a decision-making position in SciReha Company.		with chronic neck pain (at least 6 months duration) and disability, but continuing interest in working. Age range 25-55 years	muscles 15 times directed forward, obliquely towards right and left, and directly backwards while sitting (n = 60) vs. endurance training: exercises for neck flexor muscles by lifting head up from supine position 3 sets of 20 reps (n = 60) vs. Control group: stretching exercises (n = 60). Training groups participated in 12-day rehab period to learn exercises properly; perform exercises at home 3x a week for 1 year.	negatively with the reductions in neck pain and somewhat favored the strength training over the endurance training. Mean VAS (baseline/12 months): Strength (57±20/18±22) vs. endurance (57±21/23±22) vs. control (58±20/42±23). Mean disability scores (baseline/12 months): strength (35±13/12±13) vs. endurance (38±14/16±16) vs. control (38±15.26±16). No significant differences between groups (p>0.05).	associated with decreases in chronic neck pain and disability. The effective dose of training was feasible and safe to perform among female office workers."	pain, in addition to evidence that strengthening is superior to endurance training for these groups of workers. Baseline leisure time physical activity was somewhat higher in the strength group.
Falla 2006 RCT Supported by grant from National Health and Medical Research Council of Australia. No mention of COI.	6.5	N = 58 females with chronic non-severe neck pain. Cranio group 37.7 years and Endurance group 38.1 years	Endurance strength training of cervical flexor muscles (n = 29) vs. Referent exercise intervention for 6 weeks (n = 29). Follow-up after 6 week exercise intervention.	Endurance strength training group had a greater increase in MVC force (10.1±17.3 N) compared to cranio-cervical flexion group (1.8±10.6 N), (p <0.05). Endurance group had significant improvement in reduction of MSF values and rate of change across all force levels compared to cranio-cervical group, (p <0.05). Both intervention groups had reduction in average pain intensity and NDI score, but not significant.	"This study demonstrated that an endurance-strength exercise regime for the cervical flexor muscles is effective in reducing myoelectric manifestations of sternocleidomastoid and anterior scalene muscle fatigue as well as increasing cervical flexion strength in a group of female patients with chronic neck pain."	All participants received personal instruction and supervision once a week. Intervention done for 6 weeks. While improvement in strength and reduction in muscle fatigue found, no difference in pain or disability measures between intervention groups at end of training.

Jull 2002 RCT No mention of industry sponsorship. COI: Although one or more authors have received or will receive benefits for personal or profession use from a commercial party related directly or indirectly to subject of this manuscript, benefits will be directed solely to research fund, foundation, educational institution, or other nonprofit organization with which authors have been associated. One or more of the authors have received or will receive benefits (*e.g.*, royalties, stocks, stock options, or decision-making position) for personal or professional use from a commercial party related directly or indirectly to subject of manuscript.	6.0	N = 200 with chronic cervicogenic headaches (1 a week for at least 2 months). Age range 18-60 years.	Manipulation (MT) (combination low and high velocity mobilization) (n = 51) vs. Therapeutic exercise (ExT) (low load endurance training of cervicoscapular musculature) (n = 52) vs. Both Manipulation plus therapeutic exercise (MT + ExT) (n = 49) vs. No treatment (no physical treatments) 8-12 intervention sessions over 6 weeks (n = 48). Follow-up at 7 weeks, 3, 6 and 12 months.	MT, ExT, and MT + ExT all significantly reduced (Mean differences compared to baseline) headache frequency (2.07, 2.37, 2.02), intensity (3.01, 3.26, 3.37), and neck pain index (10.69, 11.03, 12.13) after treatment compared with controls at 7 weeks ($p < 0.001$). Differences still significant at 12 months. ($p < 0.05$)	"The trial provided evidence that manipulative therapy and a specific therapeutic exercise regimen were effective for cervicogenic headache, although there was no statistical evidence of an additive effect when the two therapies were used simultaneously."	Study excluded workers' comp patients. Some baseline differences. Lack of details regarding Control group treatments other than physical treatments.
Hagberg 2000 RCT No industry sponsorship. No mention of COI.	6.0	N = 77 female industrial workers with nonspecific neck-shoulder pain. Endurance group mean age-39.8. Strength group mean age-37.9 years.	Isometric Shoulder Endurance Training (n = 38) vs. Isometric Shoulder Strength Training (n = 31). Treatment was 12 weeks of training	Endurance group showed significant pain increase at each follow-up date ($p < 0.05$), whereas strength group did not. ROM was also significantly improved in both groups compared to baseline ($p < 0.05$). However, no significant differences between groups ($p > 0.05$)	Authors concluded that "physical training programs for neck-shoulder pain may include isometric shoulder muscular strength exercise in addition to isometric shoulder endurance training, rather than endurance training only," however this conclusion is not entirely warranted as design limits conclusions to value of each exercise compared individually and does not allow for conclusions on aggregate exercise interventions. Lack of a	Study aggregated various potential shoulder and neck pain without identifying workers' specific conditions, thus whether results are applicable to any one condition is unclear. Study suggests endurance training had better effects on pain ratings, but strength training had better effects on job ratings of perceived exertion.

					non-interventional control or other control among whom strength would be unexpected to increase somewhat limits conclusions. Not clear whether results are generalizable to other populations of workers performing other types of work or to asymptomatic populations.	
Takala 1994 Crossover Trial No mention of support or COI.	6.0	N = 45 females (20-55 years) with frequent neck symptoms. Age range- 20-55 years	Gymnastics for 10 weeks. Group A-Gymnastics intervention for 10 weeks (n = 22) vs. Group B- Control Group (n = 22). Follow-up at 3 months.	Difference between groups for increase in mean pressure pain threshold after 1st intervention, 4.0 for group A vs. 3.3 for group B (p = 0.008). During spring, treatment group had a decrease of 9mm in pain ratings on VAS, (p = 0.042) compared to baseline.	"[N]o major effects on neck pain are seen after group gymnastics performed once a week."	Exercises only once a week for 45 minutes for 10 weeks, so not enough exercise to make an impact. Patients' symptom duration unknown.
Andersen 2008 Med Sci Sports Exerc RCT No mention of sponsorship or COI.	5.5	N = 549 office workers with chronic neck and shoulder pain.	Specific Resistance Training (SRT) vs. All-round Physical Exercise (APE) vs. Reference intervention with counseling (REF) for 1 year.	Two physical training groups reduced neck pain intensity during 1st half of intervention. SRT group went from 5.0±0.2 to 3.4±0.2, (p <0.0001). APE group from 5.0±0.2 to 3.6±0.2, p <0.001. No change in REF group. Pain intensity did not change during 2nd half of intervention. Shoulder controls developed less shoulder pain when compared to REF over a 1-year period.	"In conclusion, SRT and APE resulted in clinically relevant reductions of neck pain in those with symptoms and prevention of should pain in those without symptoms, although only minor gains in muscle strength were found."	In SRT group, all training done at work during working hours. Unequal exposure to trainers between groups. (Potential contact bias).Specific resistance training group only one to keep training diary on type and intensity of exercise. All-round physical exercise group a broad mixture of different exercises. Had overall low compliance and lower training intensity that likely disrupted any stronger or more significant findings.
Waling 2000 RCT Supported by a grant from The Swedish Council for Work Life Research. No mention of COI.	4.0	N = 103 females with work-related trapezius myalgia. Mean age 38.2 years.	Strength training (n = 29) vs. Endurance training (n = 28) vs. Coordination training (n = 25) vs. No-exercise control (n = 21). Follow-up at 10 weeks.	At 10 weeks, exercise groups vs. controls had decreased pain at present, at worst, and decreased pain with palpation of trigger points, however difference not significant (p <0.05). No significant difference between exercise groups in any measures (p <0.05)	"[T]his study indicates that training reduces the pain of work-related trapezius myalgia but that the type of training might be of less importance."	No mention of blinding or co-interventions. Exercises appear beneficial in chronic myofascial syndrome in working women <45 years of age.
Ahlgren 2001 RCT	4.0	N = 126 females with trapezius myalgia. Mean age 38.2 years.	Strength training (ST) (n = 29) vs. Endurance Training (ET) (n = 28) vs. Co-ordination (CO) (n = 25) vs.	Pain before and after intervention period with non-training group as reference group: VAS at present (mm): ST (23±17/11±16), ET	"Women with trapezius myalgia improved their physical performance in relation to training performed	Either strength, endurance or coordination prescribed to decrease pain in

Sponsored by the Swedish Council For Work Life Research. No mention of COI.			Non-training (NT) (n = 20). Assessments taken immediately following training period at 10 weeks.	(32±22/19±14), CO (34±20/24±25), NT (32±23/30±21). VAS in general (mm): ST (36±15/22±18), ET (43±20/31±17), CO (40±15/30±17), NT (42±22/38±24. VAS at worst (mm): ST (72±14/54±27), ET (70±17/59±21), CO (76±12/67±19), NT (75±17/74±19). All groups except non-training group had a significant difference from pre- and post-intervention ($p < 0.05$). Only strength training group had a significant difference ($p < 0.05$) with VAS at worst from the other groups.	and rated less pain after 10 weeks of strength-, endurance-, or co-ordination training or neck/shoulder muscles, while a non-training group did not. The type of training was not found to be different in reducing perceived pain at present and in general. However, strength training more effectively reduced the perception of worst possible pain...Our study...failed to find a distinction between different types of training regarding their effect on neck/shoulder pain."	women with trapezius myalgia. Strength training should be at least 75% of maximal volume contraction to affect pain. Study included 1-hour sessions, 3 times a week, for 10 weeks.
O'Leary 2012 RCT Sponsored by National Health and Medical Research Council, an NHMRC of Australia Research Training Fellowship, Health Practitioner Research Fellowship from Queensland Health and University of Queensland. No COI.	4.0	N = 60 with chronic mechanical neck pain or MNP, aged 18-55	Endurance training (ETr) warm-up 3 submaximal reps, plus 3 trials of maximal contractions with 60 seconds rest between each trial (n = 20) vs. coordination training (CTr) 5 incremental stages of increasing craniocervical flexion range in supine position (n = 20) vs. active mobility training (MTr) measured in 4 directions; flexion, extension, right/left axial rotation from upright neutral position of head and neck (n = 20). Follow-up for 26 weeks.	ETr/CTr/MTr: greater endurance by ETr group vs. CTr or MTr at 10 weeks, $p < 0.01$, and greater than MTr at 26 weeks, $p = 0.03$, but not CTr group, ($p = 0.06$)/greater reduction in AS activity in CTr vs. ETr and MTr groups, for 30mmHg stage of the test at 10 ($p < 0.03$) and 26 weeks, ($p < 0.01$)/significant main effect for time, ($p < 0.01$) sustained over both follow up periods, for measure of NDI, but no significant group effect, ($p = 0.30$), or group by time interaction, ($p = 0.60$).	"Changes in motor performance in individuals with MNP in response to an exercise program were dependent on the specific mode of exercise performed, with minimal improvement in other domains of motor performance."	Methodological details sparse. Reproducibility of interventions is questionable. High degree of subjectivity in activities. All groups improved over study period.
Non Specific Pain						
Sihawong 2014 RCT Sponsored by Social Security Office of Thailand and Chulalongkom University Centenary Academic Development Project. No COI.	4.5	N = 567 with lower-than-normal neck movement or neck flexor endurance; mean age 37.2±10.1 for intervention group and 36.9±10.7 for control group.	Intervention group, exercise program consisting of muscle strengthening and endurance training, repeat exercise twice a week at home on Wednesday and Sunday (n = 285) vs. Control group, no treatment (n = 282). Follow up at baseline and 3, 6, 9, and 12 months.	Mean ± SD for Neck flexion ROM (degrees): intervention vs. control: 3 month: 29.1±8.0 vs. 21.1±5.0, ($p < 0.001$); 6 month: 36.2±8.7 vs. 30.4±5.0, ($p < 0.013$); 9 month: 38.3±9.4 vs. 30.4±5.0, ($p < 0.002$); 12 month: 39.3±7.7 vs. 33.4±8.3, ($p < 0.025$). Incidence of neck pain: 12.1% (32/264) in intervention groups; 26.7% (72/270) in control group at 12 month follow up.	"The exercise programme reduced incident neck pain and increased neck flexion movement for office workers with lower-than-normal neck flexion movement."	Possible randomization failure. Data suggest exercise intervention may be superior to control for pain prevention.
Specific Stretching and Flexibility Exercises						
Acute Neck Pain						

Ylinen 2003 RCT Sponsored by Social Insurance Institution. No mention of COI.	7.5	N = 180 female office workers with chronic, non-specific neck pain.	See Ylinen 2003 above	See Ylinen 2003 above	See Ylinen 2003 above	See Ylinen 2003 above
Evans 2002 RCT Sponsored by Consortium for Chiropractic Research. No COI.	7.5	N = 191 with chronic neck pain	See Bronfort et al, 2001	See Bronfort et al, 2001	See Bronfort et al, 2001	See Bronfort et al, 2001
Rosenfeld 2003 RCT Sponsored by local research committee in southern Elfsborg County, Swedish National Health Insurance, and Vårdal Foundation. No COI.	6.0	N = 102 with acute whiplash injury; baseline VAS mild to moderate (30-39 on 100 scale)	See Rosenfeld 2003 above	See Rosenfeld 2003 above	See Rosenfeld 2003 above	See Rosenfeld 2003 above
Subacute Neck Pain						
Bunketorp 2006 RCT Sponsored by Vårdal Foundation for Health Care Science and Allergy Research, local Research and Development Council of Göteborg and Southern Bohuslän, and Swedish Association of Insurance Medicine. No mention of COI.	6.5	N = 47 with subacute whiplash-associated disorders	See Bunketorp 2006 above	See Bunketorp 2006 above	See Bunketorp 2006 above	See Bunketorp 2006 above
Chronic Neck Pain						

Zaproudina 2007 RCT No mention of sponsorship or COI.	7.5	N = 105 with chronic neck pain (cNP). Mean age 41.5 years	Traditional bone setting (TBS) (n = 35) vs. Conventional physiotherapy (PT) (n = 35) vs. Massage (M) (n = 35). Five treatments. Physiotherapy included massage, stretching, and exercise therapy (text states 1 session lasting 45 minutes, thus frequency of appointments conflicts with other text indicating 5 treatment sessions.) Follow-up at 1, 6 and 12 months.	Neck pain decreased and NDI scores improved in all groups 1 month after treatment (p <.001). Improvement of NDI and persons' satisfaction significantly better after TBS. Neck spine mobility in rotation movements tended to improve significantly better and frons-knee distance improved more after TBS; 1 year later, both NDI and neck pain significantly better after TBS than in reference groups. A significant improvement reported by 40 to 45.5% in PT and M groups and by 68.6% in TBS group.	"The traditional Finnish Kalevala-type bone setting appears to be effective in cNP. Two thirds of subjects experienced TBS beneficial, which seems to be safe and able to improve disability and pain in cNP. Subjective and *partially objective benefits of TBS were in those patients* greater than after PT and M interventions, and the effects lasted at least for 1 year."	Description of study and methods unclear, as appears to be multiple co-interventions, lengths of treatments differ, so inconclusive.
Rendant 2011 RCT No mention of sponsorship or COI.	6.0	N = 123 with chronic neck pain. Mean age: Qigong group-44.7 years; Exercise Therapy = 44.4 years; Waiting List = 47.8 years	Qigong (n = 42) vs. Exercise therapy (n = 39) vs. Waiting list for 6 months (n = 41). Follow-up at 6 months.	Significant difference between qigong and control group in VAS scores after 6 months (-14.2 95% CI -23.1 to -5.4; (p = 0.002)). No difference between qigong and exercise therapy at 3 months (1.3 95% CI -8, 1 to 10.8; p = 0.002) and 6 months (-0.7 95% CI -9, 1 to 7.7; (p = 0.872)).	"[P]atients with chronic neck pain who had received qigong, improved in a statistically significant more compared to waiting list control after 6 months of intervention. Improvements in the qigong group were comparable with those in the exercise group."	No blinding. Compliance to treatment unclear. Data suggest no difference between qigong and exercises. Statistically significant improvement of both groups at 3, 6 weeks over wait list group, although clinical significance is uncertain, as there was no differences in analgesic consumption.
Viljanen 2003 RCT Supported by a grant from the Finnish work environment fund. No COI.	5.0	N = 393 female office workers with chronic non-specific neck pain. Mean age-45 years	12 weeks dynamic muscle training (n = 135) vs. Relaxation training (n = 128) vs. Ordinary Activity, control group (n = 130). Follow-up at 3, 6 and 12 months.	No statistical difference (p>0.05) between all 3 groups in regards to pain intensity, range of motion for flexion and extension, muscle strength, or neck disability.	"Dynamic muscle training and relaxation training do not have more favorable effects on chronic neck pain over advising patients to be active."	Very low compliance. During 12 weeks of intervention, dynamic and relaxation groups had 39% and 42% compliance with exercise sessions respectively. At 12 months, dynamic and relaxation groups doing exercises for an average of 31 and 20 minutes per week respectively A low level of activity in intervention groups makes them similar to control.
Michalsen 2012 RCT	5.0	N = 77 with chronic neck pain; mean age 47.9±7.9 years.	Yoga class 90 minutes weekly and practice postures at home 10-15 minutes 2-3x a week for 8-10 weeks (n = 38) vs. Self-care manual	Mean±SD for Neck Disability Index for Yoga vs. exercise: 23.1±4.1 vs. 26.0±6.5 for week 4 [95% CI,-2.3 (-5.0, 0.4)], (p = 0.092); and 18.4±4.0 vs. 24.5±6.0 [95% CI,-4.6 (-6.8,	"In conclusion, this study suggests that Iyengar yoga might be an effective and safe treatment option in chronic neck pain. However, as the	High dropout rate. Comparison group had some unmeasured amount of exercise intervention.

Sponsored by Carl and Veronica Carstens Foundation, Germany. COI, Rainer Lüdke is affiliated the company that sponsored the study. No COI for other authors.			describing stretching, strengthening, and joint mobility, exercises were required to be practiced at home 10-15 minutes at least 3 times a week (n = 39). Outcomes assessed at baseline, week 4 and week 10. 70 days follow up.	2.3)] (p <0.001) for week 10. Mean±SD for Neck Pain and Disability Questionnaire for Yoga vs. exercise: 59.3±25.8 vs. 75.0±36.1 for week 4 [95% CI,-10.9 (-21.88, 0.0)], (p = 0.049); and 35.0±18.1 vs. 71.3±42.1 [95% CI,-25.9(-41.7, 10.0)] (p = 0.001) for week 10.	control treatment was not comparable with regard to time intensity, attention, and social interaction, the value of Iyengar yoga should be further evaluated in comparative effectiveness trials including exercise forms with similar intensity and group setting and longer observation periods."	
Randlov 1998 RCT Supported by the Danish Rheumatism Association. No mention of COI.	4.5	N = 77 females (18-65 years) with chronic neck/ shoulder pain ≥6 months.	Intensive neck/shoulder training program (n = 36) vs. Program of lesser intensity but similar duration (n = 41). Follow-up at 3 months and 12 months.	No statistical difference between groups, but did improve from baseline. ADL 25% improvement in light group through 12 months, 38% improvement in intensive group at 12 months. Pain scores light group returned to baseline by 12 months after a 25% decrease, intensive group pain scores decreased by 20% at 12 months compared to baseline.	"The type of low-tech dynamic training used in either of our two programmes resulted in both subjective and objective improvements in patients suffering from chronic neck/shoulder pain, but there were no statistically significant differences in outcome between the two approaches."	Good description of exercises. Females only, no diagnoses for conditions. Unsure of all baseline characteristics. Co-interventions not recorded.
Skoglund 2011 RCT Crossover Crossover No mention of sponsorship or COI.	4.5	N = 37 office workers working with computers. Mean age 48 years.	Qigong (n = 37) vs. Waiting list (n = 37). Follow-up assessments after 6 weeks.	The change in neck disability for Qigong, as measured by von Korff was -0.29 (95% CI -0.52 to -0.07).	"…The observed health improvements were limited to reduced neck disability. A longer training period could be beneficial in future studies."	Small sample size. Lack of details, control of co-interventions. Data suggest no differences between groups except in a disability perception score. No analysis of timing of intervention provided (Qigong 1st or 2nd).

Monticone 2012 RCT No mention of sponsorship. No COI.	4.5	N = 80 with chronic neck pain; mean age: 49.6 years	Physiotherapy including passive and active mobilization aimed to improve postural control, strengthening, and stretching (PT group; n = 40) vs. Physiotherapy plus cognitive-behavioral therapy (PTcb group; n = 40); 12 months' follow up.	Mean±SD for Neck Pain and Disability Scale (NPDS) for PTcb vs. PT groups: 48.93±21.86 vs. 56.66± 21.57 before treatment; 32.39±22.66 vs. 43.53±22.35 after treatment; and 30.88±17.02 vs. 47.01±16.79; after 12 month follow up; [95% CI, -8.06 (-18.3; 1.06)]. Mean±SD for numeric rating scale (NRS) Scale for PTcb vs. PT groups: 4.84±2.72 vs. 5.50±.2.69 before treatment; 2.32±2.34 vs. 3.78±2.30 after treatment; and 2.83±2.14 vs. 4.04±2.11; after 12 month follow up; [95% CI, -0.44(-1.75; 0.87)]. Mean±SD for SF-36 "physical pain" for PTcb vs. PT groups: 51.36±18.37 vs. 49.80±19.73 before treatment; 62.57±20.02 vs. 49.80±19.73 after treatment; and 61.01±23.95 vs. 52.94±23.65; after 12 month follow up; [95% CI, -9.03 (-20.99; 1.20)].	"In conclusion, both groups showed improvements in disability, pain and quality of life, but there were no clinically significant between-group differences. Despite growing interest in the bio-psychosocial model of chronic pain and the results of cognitive-behavioral approaches to the treatment of chronic LBP, further evidence is needed before suggesting that psychosocial factors should also be treated in patients with chronic NP."	No meaningful differences between groups.
Non Specific Pain						
Hakkinen 2007 RCT Sponsored by grant from Jyvaskla Central Hospital. No mention of COI.	4.0	N = 125 employed females motivated for exercise and treatment, and neck pain >6 months, age range 25-53.	Group 1: manual therapy 8 sessions for 30 minutes, 2x a week then switched to stretching instructions 10 minutes per session 5x a week after week 4 follow-up) (n = 62) vs. Group 2: stretching instructions 10 minutes per session 5x a week then switched to Manual therapy 8 sessions (30 minutes) 2 x a week (n = 63). Follow-up for 4 weeks.	Spontaneous neck pain (VAS) at (baseline/4 weeks/ 12 weeks) (mean(SD)) Group 1: 50(22)/-26(-33 to-20)/-19(-27 to -12) Group 2: 49(19)/-19(-27 to-12)/-19(-25 to -13) ($p = 0.06$) at 4 weeks and ($p = 0.91$) at 12 weeks. No significant difference between groups, there is a pain reduction in group 1 and 2, ($p < 0.001$).	"In conclusion, manual therapy and stretching were equally as effective as short-term treatments for chronic neck pain. The significant decrease in pain reported by the patients in this study may have reduced inhibition of the motor system and thus, in part, improved neck function. However, the changes in neck muscle strength were minor, showing that these treatments alone are not effective methods of improving muscle strength."	Data suggest only notation is different between groups
Strengthening and Stabilization Exercises						
Acute Neck Pain						
Lange 2013 Clin J Pain RCT Sponsored by the Royal Danish Air Force. No COI.	5.0	N = 55 F-16 pilots with acute neck injury last 3 months, mean age 31 for training group; 33.5 for control group	See Lange 2013 above	See Lange 2013 above	See Lange 2013 above	Few meaningful differences seen between groups.

Lange 2014 Aviat Space Environ Med Single Blind RCT No mention of sponsorship or COI.	5.0	N = 55 F-16 pilots who have experienced an acute neck injury in the previous 3 months, mean age 31 for training group and 33.5 for control group	See Lange 2014 above	Lange 2014 above	Lange 2014 above	Paper reports significant secondary outcomes to study listed above. Group training same as above, but group analysis based on those with or without pain in previous 3 months. Few meaningful differences seen between groups.
Subacute Neck Pain						
Bunketorp 2006 RCT Supported by Vardal Foundation for Health Care Sciences and Allergy Research, local Research and Development Council of Goteborg and Southern Bohuslan, and Swedish Association of Insurance Medicine. No mention of conflict of interest.	6.5	N = 47 with subacute disorders following whiplash trauma.	See Bunketorp 2006 above	See Bunketorp 2006 above	See Bunketorp 2006 above	See Bunketorp 2006 above
Ask 2009 RCT No mention of sponsorship or COI.	6.0	N = 25 with subacute whiplash-associated disorders. Mean ages Motor control and Endurance/Strength groups: 38.3 and 35.6 years.	See Ask 2009 above	See Ask 2009 above	See Ask 2009 above	Small sample size. No meaningful differences between groups.
Chronic Neck Pain						
Vonk 2009 RCT Supported by Dutch Health Care Insurance Board (CVZ). No mention of COI.	6.5	N = 139 patients with non-specific chronic neck pain. Age range: 18-70 years.	Conventional Exercise up to 18 treatments or 9 weeks (n = 71) vs. Behavioral Graded Activity (n = 68). Outcomes assessed at baseline and 4, 9, 26, 52 weeks. Follow-up at 12 months.	No differences in primary outcomes between groups found for recovery in complaints, daily functioning, or any physical outcomes.	"[T]his study showed no differences in effectiveness between BGA and CE in the management of patients with chronic neck pain."	Mean number of treatments 6.6 in BGA group, 11.2 in CE group. Types and amounts of exercises varied greatly within each group making it difficult to understand outcomes in

						terms of which therapies work for which patients.
Evans 2012 RCT No sponsorship or COI.	6.5	N = 270 patients with chronic neck pain. Age range (mean): 18-65 (46.3 ±10.7) years.	Exercise therapy (ET) supervised high-dose 20 session 1-hour strengthening program (n = 89) vs. Exercise therapy + spinal manipulation (ET + SMT) 15-20 minute sessions with chiropractor (n = 91) vs. Home exercise and advice (HEA) attended 2 1-hour sessions and given booklet and laminated exercise cards (n = 90). Outcomes assessed at weeks 4, 12, 26, and 52.	Mean pain outcomes weeks 4, 12, 26, 52 for ET+SMT vs. ET vs. HEA: 4.0±1.9, 2.3±1.8, 3.3±2.2 and 3.4±2.3 vs. 3.7±2.0, 2.6±1.9, 3.1±2.3 and 3.1±2.2 vs. 4.1±1.8, 3.6±2.1, 3.7±2.3 and 3.6±2.3 (mean difference -1.27, 95% CI -1.96 to -0.58; (p <0.001). ET treatments vs. HEA at week 12). Mean from pain outcomes at weeks 4, 12, 26, 52 for ET+SMT vs. ET vs. HEA: 21.4±9.8, 14.5±9.5, 17.3±11.3 and 18.0±11.3 vs. 20.4±10.8, 16.0±11.3, 16.8±13.4 and 17.5±13.3 vs. 21.9±10.0, 19.6±10.5, 19.4±10.7 and 19.3±10.9 (mean difference -4.66, 95% CI -7.80 to -1.52; (p <0.001). Disability scores significant at short-term (weeks 4 and 12) (p = 0.028), but not long-term (weeks 26 and 52) (p = 0.086).	"Our study found that groups receiving high-dose supervised ET with and without spinal manipulation performed similarly, reporting less pain, greater global perceived effect, and more satisfaction than the low-dose home exercise group, particularly in the short term. The supervised exercise groups also demonstrated greater gains in blinded assessment of neck endurance and strength, supporting the patient-self report measures. The results of qualitative interviews suggest that personal attention played an important role in the supervised exercise groups."	Data suggest differences in pain, disability, global perceived effect, and satisfaction at 12 weeks favoring manipulation groups. Clinical significance appears minimal.
von Trott 2009 RCT Sponsored by The Karl and Veronica-Carstens-Foundation. No mention of COI.	6.0	N = 117 elderly patients with long-term chronic neck pain. Age: 55 and older.	Qigong, 24 sessions of 45 minutes, over 3 months (n = 38) vs. Exercise Therapy, 24 sessions of 45 minutes, over 3 months (n = 39) vs. Waiting list control for 3 months (n = 40). Follow up at 6 months.	After 3 months, no difference between qigong and waiting list group for average neck pain, Δ = 11.0mm (CI, –24.0 to 2.1; (p = 0.099)) or between qigong and exercise group, Δ = 2.5mm (CI, -15.4 to 10.3; (p = 0.697)). No difference between groups after 3 and 6 months.	"In this confirmatory study, we found qigong ineffective to improve long-term neck pain and disability in elderly patients."	Average age 76. 100% had "concomitant diseases." Exercise group had flexibility, strengthening, and cervical rotations as basis of therapy.
O'Leary 2007 RCT Sponsored by Physiotherapy Research Foundation and National Health and Medical Research Council of Australia (NHMRC). COI: D. Falla supported by fellowship awarded by NHMRC, and P. Hodges supported by an	5.5	N = 48 females with chronic neck pain. Age mean±SD: 41.2±11 years.	Cranio-cervical flexion (CCF) Exercise (n = 24) vs. Cervical Flexion (CF) Exercise (n = 24). 12 month follow up.	Means (SD) for VAS (cm)-REST before and after for CCF group vs. CF group: 0.77 (1.07) and 0.57 (1.01) vs. 1.09 (1.52) and 0.85 (1.43). Means (SD) for VAS (cm)-ACT before and after for CCF group vs. CF group: 1.4 (1.03) and 0.98 (0.92) (p <0.05) vs. 1.55 (1.15) and 1.42 (1.07). Means (SD) for PPT (kPa) - Neck 1 before and after for CCF group vs. CF group: 106.38 (42.16) and 128.3 (39.6) vs. 109.2 (44.56) and 117.21 (49.79; (p <0.05)), (p = 0.03). Means (SD) for PPT (kPa) - Neck 2 before and after	"[R]esults suggest that specific CCF exercise can be prescribed with the intention of providing immediate reduction of neck pain. Patients may find exercise of this nature an effective pain relieving modality potentially as a substitute for, or as a conjunct therapy to, other self-applied pain relieving modalities such as medication or heat."	85% of participants had C2/C3 as their most symptomatic segments. CCF works more on upper segments.

NHMRC Principal Research Fellowship.				for CCF group vs. CF group: 111.13 (40.49) and 126.7 (41.27; p<0.05) vs. 117.04 (48) and 120.64 (56.76).		
Blangsted 2008 RCT Sponsored by Ministry of Culture Committee on Sports Research, and National Board of Health under ministry of Interior and Health. No COI.	5.5	N = 549 with MSD symptoms in neck and shoulders (higher than one year prevalence). Mean age: 46.0 years.	Specific resistance training (n = 70) vs. All-round physical exercise (n = 66) vs. Reference for 1 year (n = 83). Follow up at 1 year.	Significant difference between those who did physical activity and reference group for improvements in intensity, (p = 0.0318), and duration, (p = 0.0565), of symptoms.	"Different physical-activity interventions were successful in reducing neck-shoulder symptoms, and SRT was superior to APE in the primary prevention of such symptoms."	Groups had different amounts of contact with therapists. (Potential contact bias) APE had a broad mixture of exercises with poor documentation of effort.
Viljanen 2003 RCT Sponsored by Finnish Work Environment Fund. No COI.	5.0	N = 393 female office workers with chronic non-specific neck pain. Mean age: 45 years old.	12 weeks of dynamic muscle training (n = 135) vs. Relaxation training (n = 128) vs. Plus 1 week of reinforcement training six months after baseline vs. Ordinary Activity, control group (n = 130). Follow-up at 3, 6 and 12 months.	Mean(SD) for pain intensity at 3, 6, and 12 months for dynamic muscle training group vs. relaxation training group vs. control group: 2.9 (2.6), 2.9 (2.8) and 3.1 (2.5) vs. 2.9(2.4), 3.0 (2.7) and 3.3(2.6) vs. 2.7(2.5), 2.9(2.8), and 3.2(2.5). Mean(SD) for neck disability at 3, 6, and 12 months for dynamic muscle training group vs. relaxation training group vs. control group: 15(14.6), 15 (15.4) and 19(15.5) vs. 14(12.5), 15 (14.5) and 19(14.7) vs. 14(13.8), 14 (13.8) and 17(13.7).	"Dynamic muscle training and relaxation training do not have more favorable effects on chronic neck pain over advising patients to be active."	Low compliance. During 12 weeks of intervention, dynamic and relaxation groups had 39% and 42% compliance with exercise sessions respectively. At 12 months, dynamic and relaxation groups doing exercises for an average of 31 and 20 minutes per week respectively. Low level of activity in intervention groups makes them more like control.
Monticone 2012 RCT No mention of sponsorship. No COI.	4.5	N = 80 with chronic neck pain. Mean age: 49.6 years	See Monticone 2012 above	See Monticone 2012 above	See Monticone 2012 above	No meaningful differences between groups.
Ylinen 2007 Eura Medicophys RCT No mention of sponsorship or COI.	4.5	N = 118 females with chronic non-specific neck pain.	See Ylinen 2003 and 2006 above	See Ylinen 2003 and 2006 above	See Ylinen 2003 and 2006 above	See Ylinen 2003 and 2006 above
Kjellman 2002 RCT Sponsored by grants from Arbetsmarknadsförsäkringar (AMF). No mention of COI.	4.5	N = 77 with complaints of neck pain. Age range: 18-65 years.	General exercises (n = 23) vs. McKenzie method, or mechanichal diagnosis and therapy for 8 weeks (n = 28) vs. Control group treated with ultrasound at the lowest intensity for 4 weeks (N = 26). Follow up at 6- and 12-months.	After treatment, all groups had significant improvement for pain intensity, (p <0.0001) m, and NDI score, (p <0.01-0.001), after 4 weeks. Greater improvement in McKenzie group at 3 weeks and 6 months compared to control group, (p <0.05).	"[T]he study did not provide a definite evidence of treatment efficacy in patients with neck pain, however, there was a tendency toward a better outcome with the two active alternatives compared with the control group."	Included smoking status, work status, satisfaction with work, and exercise status in baseline. Also had patients' rate expectations and fulfillment of expectations. Mixture of acute, subacute, and

						chronic patients. Mixture of diagnoses and interventions had high variability of exercises. Number of visits varied between groups.
Zebis 2011 RCT Sponsored by Danish Working Environment Research Fund. No COI.	4.5	N = 537 from industrial occupations with high prevalence of neck and shoulder pain. Mean age 42 years.	Strength training, 3 session per week lasting 20 minutes (n = 282) vs. Control (n = 255). Follow up at 20 weeks.	74% of the training group and 92% of control group completed the study. Participants that were non-cases at baseline the odds ratio of the training group compared to the control group for being cases at follow-up was 0.6 (95% CI 0.2 to 1.5) for neck and 0.6 (95% CI 0.3 to 1.3) for shoulder. Pain intensity in the neck decreased significantly in the training group compared to control -0.6 (95% CI -1.0 to -0.1) and in shoulder -0.2 (95% CI -0.5 to 0.1).	"[S]pecific strength training reduced the overall level of neck pain among industrial workers…[A] high percentage of daily activities were performed with static work postures and bent neck…high intensity strength training was effective in reducing neck pain in this job group."	Cluster randomization ratio appeared effective. Lack of details for control of co-interventions, withdrawal, study design, intended intervention 3x times a week, compliance started at 1x a week. Data suggest strength training of work 20 minutes week may prevent neck/shoulder complaints and reduce pain in those with neck/shoulder pain. May not be applicable to worksites outside those requiring prolonged static position of head and neck.
Jull 2009 RCT Sponsored by grant from the National Health and Medical Research Council of Australia. No mention of COI.	4.5	N = 46 with chronic neck pain, mean age for C-CF training group 39.6±12.22, and Strength training 37.1±10.3.	Exercise interventions, low and higher load strength training 6 weeks duration, plus personal instruction and supervision by one of 10 experienced physiotherapists 1x per week (n = 23) vs. C-CF training, low load training of cranio-cervical flexor muscles followed established protocol (n = 23). Follow-up for 6 weeks of training program.	ROM for CCFT and relative latencies during arm movement task not different between groups, ($p > 0.05$). No difference in DCF EMG amplitude in strength-training group, ($p > 0.05$). Significant reduction in average pain intensity (NRS), C-CF training, ($p < 0.001$); strength training ($p < 0.05$), NDI score, C-CF training, ($p < 0.001$); strength training, ($p < 0.001$), but no between-group differences, both ($p > 0.05$).	"[S]pecific low load C-CF training but not strength training enhanced the pattern of deep and superficial muscle activity in the CCFT."	Both groups improved over the 7 week study period.
Ahlgren 2001 RCT Sponsored by Swedish Council for Work Life Research. No mention of COI.	4.0	N = 126 females with trapezius myalgia.	See Ahlgren 2001 above	See Ahlgren 2001 above	See Ahlgren 2001 above	See Ahlgren 2001 above
Waling 2000 RCT Sponsored by grant from The Swedish for	4.0	N = 103 females with work-related trapezius myalgia. Mean age 38.2 years.	See Waling 2000 above	See Waling 2000 above	See Waling 2000 above	See Waling 2000 above

Work Life Research. No mention of COI.						
Ylinen 2006 RCT Supported by Social Insurance Institution, Helsinki, Finland. No mention of COI.	4.0	N = 180 females with chronic neck pain. Age range 25-53 years.	See Ylinen 2006 above	See Ylinen 2006 above	See Ylinen 2006 above	See Ylinen 2006 above
Falla 2007 RCT Sponsored by National Health and Medical Research Council of Australia. No mention of COI.	4.0	N=58 females with chronic, non-severe neck pain >3 months; neck disability index score ≤15, mean (±SD) age 37.7 (±9.9) for craniocervical flexor exercise group; 38.1 (±10.7) endurance-strength exercise group.	See Falla 2007 above	See Falla 2007 above	See Falla 2007 above	Methodolical details sparse.
Non-Specific Neck Pain						
Scholten-Peeters 2006 RCT No mention of sponsorship or COI.	8.0	N = 80 with whiplash-associated disorders. GP group mean age 33.8 years. Physiotherapy group mean age 31.9 years.	Education by general practitioner (n = 42) vs. Education and exercises by physiotherapist for 9 months maximum (n = 38). Follow-up assessments taken at 4, 12, 20, 28, 36, 44 and 52 weeks.	No differences between 2 groups for all primary outcomes at 12 weeks. At 52 weeks, GP better on work activities, 46.3 vs. 22.8 ($p \leq 0.01$). Physiotherapy had better cervical ROM, ($p \leq 0.05$) at 12 weeks. PT more effective on neck pain with an initial pain intensity of >75mm on VAS at 12 weeks, ($p = 0.013$).	"In conclusion, physiotherapy and "enhanced" GP care were of similar effectiveness in the treatment of patients with WAD grade 1 and 2."	Variable exercises for varied amounts of time making it difficult to standardize treatments or see if one modality more efficient than another. Did some subgroup analyses that show greater amount of pain with a greater response to therapy.

Bronfort 2001 RCT Sponsored by Consorium for Chiropractic Research. No mention of COI.	7.5	N = 191 with chronic neck pain. Mean age 44.3 years.	Spinal manipulation plus low-technology exercise (n = 63) vs. MedX (n = 60) vs. Spinal manipulation for 11 weeks (n = 64). Follow-up assessments at 3, 6 and 12 months.	After 11 weeks, SMT/exercise produced greater gains in strength endurance, and ROM than SMT alone ($p < 0.05$) and more improvement in flexion endurance and in flexion and rotation strength than group treated with MedX ($p = 0.03$). Finally, MedX group showed greater gains in extension strength and flexion-extension ROM than SMT group ($p < 0.05$).	"[T]he use of strengthening exercise, whether in combination with spinal manipulation or in the form of a high-technology MedX program, appears to be more beneficial to patients with chronic neck pain than the use of spinal manipulation alone. The effect of low-technology exercise or spinal manipulative therapy alone, as compared with no treatment or placebo, and the optimal dose and relative cost effectiveness of these therapies, need to be evaluated in future studies."	Study suggests manipulation alone is inferior to active exercises. A 2-year follow-up noted that differences at 1 year persisted at 2 years. Benefits tend to extinguish over time, potentially suggesting lack of compliance with exercise regimens although they documented no differences between patients who continued home exercise program over those who did not. All patients had 20 1-hour visits over 11 weeks. All received a HEP.
Evans 2002 RCT Sponsored by Consortium for Chiropractic Research. No COI.	7.5	N = 191 with chronic neck pain.	See Bronfort et al, 2001	See Bronfort et al, 2001	See Bronfort et al, 2001	See Bronfort et al, 2001
Griffiths 2009 RCT No mention of sponsorship or COI.	7.5	N = 74 with chronic neck pain >3 months. Mean age 51.3 years.	General exercise (posture correction and ROM exercises) (n = 37) vs. Specific exercise (only specific neck stabilization exercises) for 6 weeks (n = 37). Follow-up at 6 weeks and 6 months.	The NPDS score improved in both groups, 9.3 in the general group vs. 10.6 in the specific group at 6 weeks. And 9.0 vs. 14.7 at 6 weeks. NPDS not significant between groups at 6 weeks and 6 months and not clinically important <12 points.	"Adding specific neck stabilization exercises to a general neck advice and exercise program did not provide better clinical outcome overall in the physical therapy treatment of chronic neck pain."	Used 11 different therapists. Study listed out diagnoses for neck pain, although they were not able to look at subgroups by diagnosis.
Ylinen 2003 RCT Sponsored by Social Insurance Institutionn, Helsinki, Finland. No mention of COI.	7.5	N = 180 female office workers with chronic, non-specific neck pain.	See Ylinen 2003 above	See Ylinen 2003 above	See Ylinen 2003 above	See Ylinen 2003 above

Ylinen 2007 J Rehabil Med RCT Sponsored by grant from Jyväskylä Central Hospital. No mention of COI.	7.5	N = 125 females with non-specific neck pain.	Manual therapy vs. stretching for 4 weeks.	Group 1 (manual therapy) at 4 weeks had average neck pain decreased by -26 (-33 to -20) on VAS, Neck stiffness -27 (-33 to -21), Headache -22 (-29 to -14). Group 2 (stretching only) at 4 weeks had neck pain decrease -19 (-27 to -12), neck stiffness -19 (-26 to -13), Headache -17 (-23 to -12) (SEE TABLE 2). Only measures statistically different between group 1 and 2 at 4 weeks were neck and shoulder pain and disability index p = 0.013, and neck stiffness p = 0.01. No statistical difference between groups at 12 weeks after crossing over of treatment protocols between groups but still decreases in each area studied compared to baseline.	"Both stretching exercise and manual therapy considerably decreased neck pain and disability in women with non-specific pain. The difference in effectiveness between the 2 treatments was minor. Low-cost stretching exercises can be recommended in the first instance as an appropriate therapy intervention to relieve pain, at least in the short-term"	As stretching exercises are thought to have little if any benefit for chronic spine pain, this may be a placebo control group. Alternately, most patients would presumably have been treated with stretching exercises previously, which would produce a bias in favor of manual therapy. High interventional variability.
Sjogren 2005 Crossover Trial Sponsored by Chydenius Institute, University of Jyva¨skyla,¨ Palokka Health Center, and personal grants from Finnish Work Environment Fund, Juho Vainio Foundation, and Academy of Finland. No mention of COI.	7.5	N = 53 with headache, neck and shoulder pain. Mean age 46.6 years.	Physical Exercise Intervention for 15 weeks. Then no-intervention for 15 weeks (n = 36) vs. No activity for 15 weeks. Then exercise intervention for 15 weeks (n = 17).	Decrease in headache during 5-week period 0.64 (0.28-1.00) (p = 0.001) or 49% decrease. Decrease in neck symptoms during the exercise program. 0.42 (0.11-0.72) (p = 0.002). No effect on shoulder symptoms.	"Light resistance training on a daily basis at the workplace with guidance can promote coping strategies in regards to the intensity of headache and neck symptoms, as well as increase the upper extremity extension strength of symptomatic office workers."	No washout time period between cross over. Participants able to do exercises as part of paid work time. Had both symptomatic and asymptomatic participants. No mention of smoking status, duration of symptoms, any prior treatments.
Andersen 2011 Pain J RCT Lars Andersen received a grant from Danish	7.5	N = 198 with frequent neck/shoulder pain. Mean ages for 2-minute, 12-minute, and Control groups: 44, 42, and 43 years.	2-minute group performed progressive resistance training with elastic tubing 5x weekly 10minutes/week (n = 66). vs. 12-minute group performed progressive resistance training with elastic tubing 5x weekly 60min/week (n = 66). vs. Control group received	Change in Pain Intensity (0-10) compared to control – 2-minute: -1.4 (-2.0 to -0.7, (p <0.0001)); 12-min: -1.9 (-2.5 to -1.2, (p <0.0001)). Total tenderness compared to control– 2-minute: -4.2 (-5.7 to -2.7, (p <0.0001)); 12-minute: -4.4 (-5.9 to -2.9, (p <0.0001)). No statistical	"In conclusion, as little as 2 minutes of daily progressive resistance training for 10 weeks results in clinically relevant reductions of pain and tenderness in healthy adults with frequent neck/shoulder symptoms."	Study population not generalizable. Data suggest both interventions are superior to control for pain.

Rheumatism Association.			weekly emailed information on various aspects of general health (n = 66). No long-term follow-up.	difference between 2-minute and 12-minutes.		
Andersen 2012 Pain Physician J RCT No sponsorship or COI.	7.5	See Andersen 2011, Pain Journal	See Andersen 2011, Pain Journal	See Andersen 2011, Pain Journal	See Andersen 2011, Pain Journal	See Andersen 2011, Pain Journal.
Walker 2008 RCT No COI or sponsorship.	6.5	N = 98 with primary complaints of neck pain with or without unilateral upper extremity symptoms, mean age 48.8(14.1) for MTE group, and 46.2(15.0) for MIN group.	Manual Physical Therapy and Exercise (MTE), 1 to 3 manual interventions; thrust and nonthrust joint mobilization muscle energy, stretching (n = 50) vs, Minimal Intervention (MIN), general practitioner care, posture advice, maintain neck motion (n = 48). Follow-up at 3 and 6 weeks, and 1 year.	Mean (95% CI) for NDI: MTE vs. MIN: baseline: 15.5 (13.9-17.1) vs. 17.0(15.5-18.6); 1 year: 5.5(3.4-7.7) vs. 10.6(8.5-12.7), (p = 0.01). Mean (95% CI) for VAS cervical pain score: MTE vs. MIN: baseline: 53.7(47.9-59.6) vs. 51.1(45.3-56.9); 1 year: 17.7(11.0-24.4) vs. 24.5(17.8-31.2), (p = 0.016). Mean (95% CI) for upper extremity VAS pain: MTE vs. MIN: baseline: 25.6(18.8-32.3) vs. 18.2(11.4-25.0); 1 year: 9.2(3.2-15.2) vs. 12.5(6.5-18.5), (p = 0.0371).	"An impairment-based MTE program resulted in clinically and statistically significant short- and long-term improvements in pain, disability, and patient perceived recovery in patients with mechanical neck pain when compared to a program comprising advice, a mobility exercise, and subtherapeutic ultrasound."	Data suggest manual therapy plus exercise is superior to manual therapy for treatment of pain and disability.
Chiu 2005 Spine RCT Institutional funds received in support of work. No COI.	6.0	N = 145 with non-specific neck pain greater than 3 months duration. Mean age 43.8 years.	Exercise (n = 78) vs. No exercise (n = 67). Exercises include activation of muscles, dynamic strengthening, 2 sessions per week for 6 weeks. Both groups received infrared irradiation; 6 month follow-up.	Exercise vs. control at 6 weeks, 6 months; Disability (NPQ): 1.1 vs. 1.2, 1.0 vs. 1.0; Pain (VNPS): 3.8 vs. 3.9, 3.0 vs. 3.1; Strength (6 directions): 8.5-12.2 vs. 8.2-12.1, 9.2 -14.6 vs. 9.0 - 13.9. There were no significant differences between groups (p <0.05).	"The results showed that after a 6 weeks training program, patients in the exercise group were significantly better in disability scores, subjective report of pain, isometric neck muscle strength in most of the different directions, and satisfaction than those in the control group at week 6."	Baseline measures indicate mild severity 1.4 of 4.0 on disability index. Statistics reported on % changes in mean rather than actual change, were not different. Only mild improvement seen in both groups.
Hagberg 2000 RCT No sponsorship or COI.	6.0	N = 77 female industrial workers with nonspecific neck-shoulder pain.	See Hagberg 2000 above	See Hagberg 2000 above	See Hagberg 2000 above	See Hagberg 2000 above

Lansinger 2007 RCT Sponsored by foundation funds. No COI.	6.0	N = 122 with long-term non-specific neck pain. Mean age 44 years.	Patients randomly assigned to qigong (n = 60) Vs. Exercise Therapy for 3 months (n = 62). Follow-up assessments immediately following intervention and at 6 and 12 months.	No differences between two groups for neck pain frequency and ROM. However, neck pain frequency was approaching significance in favor of Qigong group 33 vs. 47 (p = 0.101). Compared to baseline, both groups improved in ROM rotation compared to baseline (p = 0.028).	"[P]atients with long-term NP effectively reduced their NP and neck disability after a 3-month intervention with supervised qigong or exercise therapy and that this improvement was maintained over the 1-year follow-up."	Each group given ergonomic instructions and pamphlet including written information about NP. Exercises more strengthening, no true aerobic exercises described. Compliance not well documented. Unsure of all co-interventions that were "discouraged."
Andersen 2008 Med Sci Sports Exerc RCT Sponsored by Ministry of Culture Committee on Sports Research and National Board of Health under Ministry of Interior and Health. No mention of COI.	5.5	N = 549 office workers with neck/shoulder pain.	See Andersen 2008 above	See Andersen 2008 above	See Andersen 2008 above	See Andersen 2008 above
Taimela 2000 RCT No mention of sponsorship or conflict of interest.	5.0	N = 76 with non-specific chronic neck pain. Age range 30-60 years old.	ACTIVE stabilization, postural and dynamic neck muscle exercises (n = 25) vs. HOME stretching and stabilization (n = 25) vs. CONTROL home neck exercise program education (n = 26). Outcomes measured at baseline, 3 months, and 12 months 12 months; 1 year follow-up.	Mean self-experienced benefit of the treatment on ACTIVE group vs. HOME group vs. CONTROL group 3 months after treatment: 4.6 vs. 3.8 vs. 3.3 (p <.001). And 12 months after treatment: 4.2 vs. 3.8 vs. 3.4 (p<0.001). VAS pain intensity score at 3 months on ACTIVE vs. HOME vs. CONTROL groups: 22mm vs. 23mm vs. 39mm (p=0.018). No statistically significant at 12 months.	"Regarding self-experienced benefit, the multimodal treatment was more efficacious than activated home exercises that were clearly more efficacious than just advising. No major differences were noted in objective measurements of cervical function between the groups, but the content validity of these assessments in chronic neck trouble can be questioned."	A mixture of exercises in all 3 groups. More exposure to providers in ACTIVE group than HOME and CONTROL group so potential for contact bias.
Jay 2013 RCT No mention of sponsorship and no COI.	4.5	N = 198 generally healthy adults with frequent neck/shoulder muscle pain, mean age 43.1 years.	2-minutes daily progressive resistance training with elastic tubing (n = 66) vs. 12-minutes (n = 66) vs. Control group receiving weekly information on general health (n = 66); 10-week follow-up.	RTD increased by 16.0% and 18.2% in 2 groups. Changes in rapid force development and self-reported pain pre- to post-intervention, r = 0.27, (p <0.01). An increase in maximal muscle strength of 5.7% and 5.1% in 2 groups, respectively.	"Small daily amounts of progressive resistance training in adults with frequent neck/shoulder pain increases rapid force development and, to a less extent, maximal force capacity."	Secondary analysis. Both intervention arms were statistically significantly better than the control group at 10 weeks.

Sihawong 2014 RCT Sponsored by Social Security Office of Thailand and Chulalongkom University Centenary Academic Development Project. No COI.	4.5	N = 567 with lower-than-normal neck movement or neck flexor endurance; mean age 37.2±10.1 for intervention group and 36.9±10.7 for control group.	See Sihawong 2014 above	See Sihawong 2014 above	See Sihawong 2014 above	Possible randomization failure. Data suggest exercise intervention may be superior to control for pain prevention.
Dziedzic 2005 RCT Sponsored by The Arthritis Research Campaign and West Midlands R & D NHS. No mention of COI.	4.0	N = 350 with non-specific neck pain; mean age 51 years.	Advice and exercise (n = 115) vs. Advice and Exercise plus Manual Therapy (n = 114) vs. Advice and exercise plus pulsed shortwave diathermy (PSWD; n = 121); Maximum 8 therapy visits over 6 weeks. Assessments at 6 weeks and 6 months.	Mean±SD Northwick Park for advice and exercises alone vs. advice and exercises plus manual therapy vs. advice and exercises plus PSWD group: 11.5±15.7 vs. 10.2±14.1 vs. 10.3±15.0, at 6 months; 10.1±12.6 vs. 8.7±12.1 vs. 7.7±10.8 at 6 weeks. No statistically significant.	"The addition of pulsed shortwave or manual therapy to advice and exercise did not provide any additional benefits in the physical therapy treatment of neck disorders."	Advice-and-exercise-only group had significantly lower number of visits and duration of treatment, and also less medication use and fewer doctor visits likely biasing against that group.
Kietrys 2007 RCT Sponsored by UMDNJ – School of Health Related Professions, with additional support from TheraBand Academy. No mention of COI.	4.0	N = 72 computer operators with no history of acute cervical or back pain.	Resistance exercise vs. stretching exercise vs. control; deep breathing and seated ankle pumps for 4 weeks.	After 4 weeks, no difference between groups for on Pain Impact, but was on perceived reduction in discomfort ($p < .001$) when comparing control to both intervention groups.	"[E]ither the stretching or strengthening exercise programs were effective in reducing perceived discomfort, when compared to a control group. Otherwise, satisfaction was not different between groups."	Questionable symptom duration or type as well as baseline comparability differences. Used a working population and at-work intervention.
Yoga						
Chronic Neck Pain						
von Trott 2009 RCT Sponsored by Karl and Veronica-Carstens-Foundation. No mention of COI.	6.0	N = 117 with long-term chronic neck pain. Age: 55 and older	See von Trott 2009 above	See von Trott 2009 above	See von Trott 2009 above	See von Trott 2009 above

Michalsen 2012 RCT Sponsored by the Carl and Veronica Carstens Foundation, Germany. COI, Rainer Lüdke is affiliated the company that sponsored study. No COI for other authors.	5.0	N=77 with chronic neck pain; mean age: 47.9±7.9 years	See Michalsen 2012 above	See Michalsen 2012 above	See Michalsen 2012 above	See Michalsen 2012 above
Tobbackx 2013 RCT/ crossover Sponsored by Belgian Acupuncture Federation and the European Federation of Oriental Medicine. No mention of COI.	4.5	N = 39 with chronic whiplash associated disorders; age between 18 and 65.	Acupuncture; neck, lower back, arms and legs; 20 minutes (insertion and removal of needles) (n = 20) vs. Relaxation; guided imagery (n = 19).	Mean ± SD for local pressure pain sensitivity: trapezius: pre-acupuncture vs post-acupuncture: 3.92±1.72 vs. 3.16±1.60, (p = 0.001); pre-relaxation vs. post relaxation: 4.13±1.74 vs. 4.10±1.88, (p = 0.001); trapezius CPM (conditioned pain modification): pre-acupuncture vs. post-acupuncture: 3.84±1.76 vs. 2.84±1.32, (p = 0.001); pre-relaxation vs. post-relaxation: 3.95±1.82 vs. 3.77±1.60, (p = 0.001). P-values all in favor of acupuncture.	"In conclusion, it was shown that one session of acupuncture treatment results in acute improvements in pressure pain sensitivity in the neck and calf of patients with chronic WAD. Acupuncture had no effect on conditioned pain modulation or temporal summation of pressure pain. Both acupuncture and relaxation appear to be well-tolerated treatments for people with chronic WAD. Further work is required to examine whether acupuncture activates endogenous analgesia in patients with chronic WAD."	Group 1 not as healthy as Group 2. Data suggest acupuncture superior to relaxation.
Non Specific Neck Pain						
Cramer 2013 RCT Sponsored by Karl and Veronica Carstens Foundation. No COI.	6.5	N = 51 with chronic non-specific neck pain for at least 5 days a week lasting >12 weeks, pain intensity >40mm (100mm VAS scale), mean age (±SD) 46.2 (±11.2) for yoga group and 49.5 (±9.5) for exercise group	Yoga Group treated with 90 minute Iyengar yoga sessions weekly for 9 weeks along with a home practice manual (n = 25) vs. Exercise group receiving self-directed home manual for stiffness and neck pain for 10 minutes a day (n = 26). Assessments at baseline and 9 weeks.	Yoga group reported significantly less neck pain intensity compared with the exercise group; Mean difference: 13.9mm (95% CI, 26.4 to 1.4), p = 0.03. Functional disability (p = 0.006), mental health (p = 0.027), social functioning (p = 0.027), emotional role functioning (p = 0.005), mental component score (p = 0.016), bodily pain (p = 0.001), ROM flexion (p = 0.036), and ROM extension (p = 0.025) improved significantly for yoga group compared with the exercise group.	"Yoga was more effective in relieving chronic nonspecific neck pain than a home-based exercise program. Yoga reduced neck pain intensity and disability and improved health-related quality of life. Moreover, yoga seems to influence the functional status of neck muscles, as indicated by improvement of physiological measures of neck pain."	Data suggest directed Yoga may be better than home exercises.

Lansinger 2007 RCT Sponsored by Vardal Foundation, Ekhaga Foundation, Development Council of Göteborg and Southern Bohuslän, Swedish Association of Registered Physiotherapists: Minnesfonden and Renée Eanders Hjälpfond. No COI.	6.0	N = 122 with long-term non-specific neck pain. Mean age 44 years.	See Lansinger 2007 above	See Lansinger 2007 above	See Lansinger 2007 above	See Lansinger 2007 above
Other Exercises						
Acute Neck Pain						
Scholten-Peeters 2006 RCT No sponsorship or COI.	8.0	N = 80 with grade 1 or 2 whiplash-associated disorders resulting from motor accident presenting negative symptoms within 48 hours,mean (SD) age 33.8 (10.3) for GP care group; 31.9 (9.0) physiotherapy group	See Scholten-Peeters 2006 above	See Scholten-Peeters 2006 above	See Scholten-Peeters 2006 above	See Scholten-Peeters 2006 above
Lauche 2013 RCT Sponsored by the Karl and Veronica Carstens Foundation and WELEDA AG. No COI.	6.5	N = 61 with chronic non-specific neck pain for previous 3 months with minimum of pain 5 days a week, VAS neck pain >45mm, mean	Cupping massage treatment group, two sessions at home per week for 10-15 minutes recommended (n = 30) vs. Progressive muscle relaxation group, two sessions at home per week for 20 minutes (n = 31). Assessments after	No significant statistics reported between groups in regards to affective pain perception, pain on motion or disability. Vitality and Inner Peace (Assessment of Physical Wellbeing) statistically significant for cupping massage over progressive muscle relaxation: (p = 0.049) and (p = 0.02).	"[C]upping massage is no more effective than progressive muscle in reducing chronic non-specific neck pain. Both therapies can be easily used at home and can reduce pain to a minimal clinically relevant extent. Cupping massage may however be better than PMR in	No meaningful differences between treatment arms were seen in outcome analyses.

		age 54.5 for CM group and 53.7 for PMR group	intervention and 12 weeks post randomization.		improving well-being and decreasing pressure pain sensitivity but more studies with larger samples and longer follow-up periods are needed to confirm these results."	
Dusunceli 2009 RCT No mention of sponsorship or COI.	5.5	N = 60 with neck pain lasting > 6 weeks, mean (SD) age 53.4 (6.8) for group 1, 52.50 (5.80) for group 2 and 50.2 (4.8) for group 3	Group 1: physical therapy agents including transcutaneous electrical nerve stimulation, continuous ultrasound and infra-red irradiation (n = 17); vs. Group 2: physical therapy agents + isometric and stretching exercises (n = 19); vs. Group 3: physical therapy agents + neck stabilization Exercises (n = 19). Assessments at baseline, 1, 3, 6, 9 and 12 months.	Compared with baseline, all groups showed significant decrease in VAS scores during first 6 months. However, this improvement was maintained only in group 3 at 9 and 12 months, with a significant difference among the groups ($p < 0.05$). During study, improvement in disability was marked in group 3 with respect to Neck Disability Index, Beck Depression Scale and range of motion in frontal plane ($p < 0.05$).	"In conclusion, this study shows that a combination treatment of NSE + PTA is the more effective intervention for the management of neck pain, with some advantages in the outcomes for pain and disability over the combination of ISE + PTA, or PTA alone. However, further controlled studies of NSE without PTA on large populations are required in order to establish its definitive effectiveness."	Interventions poorly described. Differences between groups poorly analyzed.
Subacute Neck Pain						
Bunketorp 2006 RCT Sponsored by the Vardal Foundation for Health Care Sciences and Allergy Research, Research and Development Council of Goteborg and South Bohuslan, and the Swedish Association of Insurance Medicine. No mention of COI.	6.5	N = 47 with subacute disorders following whiplash trauma lasting >6 weeks, but <3 months; mean age (SD) 39 (11) for supervised group and 35 (12) for home training group	See Bunketorp 2006 above	See Bunketorp 2006 above	See Bunketorp 2006 above	See Bunketorp 2006 above
Bernaards 2007 RCT	6.5	N = 466 computer workers with frequent or long-term neck and upper limb symptoms, the mean (SD) age 43.8 (8.5) for work style	Work style group (WS) (n = 152) vs. Work style and physical activity group (WSPA) (n = 156) vs. Usual care group for 6 group meetings (n = 158).	Current pain (0-10) for WS vs. WSPA vs. usual care group (mean±SD) at baseline/6/12 month follow-up: 3.9±2.3; 3.7±2.3; 3.5±2.1/ 3.6±2.4; 3.5±2.4; 3.3±2.3/ 3.0±2.3; 3.1±2.2; 3.2±2.4 ($p < 0.05$).	"The combined intervention was ineffective in increasing total physical activity. Therefore we cannot draw conclusions on the effect of increasing physical activity on	Long-term study. Increased physical activity did not occur which made this more a study of work activity vs. control group. No

No mention of sponsorship or COI.		group, 43.6 (8.7) for work style and physical activity group, and 44.4 (8.5) for usual care group	Assessments at baseline, 6 months and 12 months.	Worst pain (0-10): 5.3±2.4; 5.1±2.2; 5.1±2.3/ 4.8±2.4; 5.0±2.6; 4.5±2.6/ 3.8±2.4; 4.1±2.7; 4.4±2.9 (p <0.05).	the recovery from neck and upper limb symptoms. There was no significant intervention effect over time for pain and recovery in the arm/wrist/hand region. In the neck/shoulder region, all pain measures reduced significantly in the WS group compared to the usual care group."	stratification of acute, subacute, chronic neck pain and their outcomes.
Rosenfeld 2003 RCT Sponsored by Institutional and Foundational funds. No COI.	6.0	N = 102 with acute whiplash injury, baseline VAS mild to moderate (30-39 on 100 scale), mean (SD) age 39 (16) active group 1, 33 (11) standard group 2, 32 (12) active group 3, 38 (14) standard group 4	See Rosenfeld 2003	See Rosenfeld 2003	See Rosenfeld 2003	See Rosenfeld 2003
Kuijper 2009 RCT No sponsorship or COI.	6.0	N = 205 symptoms and signs of cervical radiculopathy <1 month duration, the mean (SD) age 47.0 (9.1) for collar group, 46.7 (10.9) for physiotherapy group, and 47.7 (10.6) for controls group	Semi-hard collar and taking rest for 3 to 6 weeks (n = 69) vs. 12 weekly sessions of physiotherapy and home exercises for 6 weeks (n = 70) vs. Continuation of daily activities as much as possible without specific treatment (control group) (n = 66). Follow up at 3 weeks, 6 weeks and 6 months.	In wait and see group, neck pain did not decrease significantly 1st 6 weeks. Treatment with collar resulted in weekly reduction on VAS of 2.8mm (-4.2 to -1.3), amounting to 17mm in 6 weeks; physiotherapy gave a weekly reduction of 2.4mm (-3.9 to -0.8) resulting in decrease of 14mm after 6 weeks. Compared with wait and see, neck disability index had a significant change with use of collar and rest and a non-significant effect with physiotherapy and home exercises.	"A semi-hard cervical collar and rest for three to six weeks or physiotherapy accompanied by home exercises for six weeks reduced neck and arm pain substantially compared with a wait and see policy in the early phase of cervical radiculopathy."	Clinical diagnosis based on pain in arm distal to elbow, provocation of pain with neck movement, or diminished DTRs, or sensory changes in a dermatomal pattern, or muscle weakness. Duration of symptoms <1 month. Patients in all groups had similar outcomes at 6 months. Data suggest collar and exercise similar at 3 and 6 weeks and outcomes better than wait and see.
Pool 2010 RCT Sponsored by Netherlands Organization for Health Research and Development (ZonMW) grant. No COI.	6.0	N = 146 with sub-acute, nonspecific neck pain, between 18 and 70 years of age.	Behavioral graded activity program or BGA, with 2 day training course, maximum of 18 sessions for 30 minutes (n = 71) vs. Manual therapy or MT, consisted of manipulation and specific mobilization techniques, 6 session for 30-45 minutes, within 6 weeks (n = 75). Follow-up for 52 weeks.	At 52 weeks, mean difference of 0.99 (0.15-1.83) points for the NRS, and for the NDI as a mean difference of 2.42 (0.52-4.32). Or, the success rate at 52 weeks, based on the GPE was, 89.4% for the BGA program and 86.5% for MT, but the difference was statistically insignificant.	"Based on this trial it can be concluded that there are only marginal, but not clinically relevant, differences between a BGA program and MT."	No meaningful differences between groups at 52 weeks. Intervention reproducibility would be difficult.

Kim 2012 RCT Sponsored by Development of Acupuncture, Moxibustion, and Meridian Standards Health Technology project of Korea Institute of Oriental Medicine. No mention of COI.	6.0	N=40 participants who worked with computers for at least 20 hours per week and hat work-related neck pain for 3 months. Mean age was 26.75 years.	Cupping Treatment- Both wet and dry cupping was applied for 2 weeks (N=20) Vs. Heating Pad Treatment for 2 weeks (N=20). Follow-up at 3 and 7 weeks.	Cupping group significantly lower NRS at 3 weeks, 28.55 vs. 48.3 (p = 0.025) and 7 weeks, 28.75 vs. 50.3 (p = 0.005) compared to heating pad group. MYMOP2 was also significantly lower at 3 weeks 2.27 vs. 3.09 (p = 0.127) at 7 weeks, 2.03 vs. 3.03 (p = 0.0035) and NDI score at 3 11.57 vs. 19.26 (p = 0.0039) and 7 weeks, 10.19 vs. 20.63 (p <0.0001) compared to heating pad group.	"In conclusion, the results of this pragmatic study suggest that 2 weeks of cupping therapy with an exercise program may be effective in reducing pain and improving neck function in VDT workers. Future studies testing the efficacy of cupping and using an appropriate sham device will be helpful in evaluating the specific effects of cupping."	No meaningful differences between groups.
Chronic Neck Pain						
Young 2009 Phys Ther RCT Sponsored by Saunders Group. No mention of COI.	8.5	N = 81 with unilateral upper extremity discomfort or pain along with testing positive for 3-4 clinical tests including Spurling's, distraction, upper-limb tension, and Ipsilateral cervical rotation <60°; mean age (SD) 47.8 (9.9) MTEX Traction group, 46.2 (9.4) MTEX group.	Manual therapy defined as high-velocity, low-amplitude thrust manipulation or non-thrust manipulation; Exercises included strength training intermittent cervical traction (n = 45) vs. Manual therapy exercise and sham traction. Manual therapy HVLA both cervical and thoracic (n = 36). Assessments at baseline, 2 and 4 weeks.	Improvements seen in both groups in pain and neck disability index. No significant difference between groups	"The results suggest that the addition of mechanical cervical traction to a multimodal treatment program of manual therapy and exercise yields no significant additional benefit to pain, function, or disability with cervical radiculopathy."	Data suggest cervical traction does not change outcomes in patients with cervical radiculopathy undergoing a multimodal program.
Chiu 2005 Clin Rehabil RCT Sponsored by Area of Strategic Development Fund of the Hong Kong Polytechnic University and Health Services Research fund of Hong Kong Government. No mention of COI.	7.0	N = 218 with chronic neck pain lasting >3months, the mean age (±SD) 43.31 (±9.77) for control group, 42.79 (±9.77) for TENS group and 43.28 (±9.69) for exercise group	TENS group: TENS applied to acupuncture sites (Ex21, GB21 and LI11) for 30 minutes plus infrared (IR) for 20 minutes and neck care advice (n = 73) vs Exercise group with IR plus intensive neck exercise program, twice a week for 6 weeks, active exercises, resistance (n = 67) vs. Control group receiving IR plus neck care advice, twice a week for 6 weeks (N = 78). Follow up assessments at 6 weeks and 6 months.	At 6 weeks assessment, Lowest Northwick Park Neck Pain Questionnaire scores showed significant results of improvement over the control for TENS, (p = 0.034) and Exercise Group, (p = 0.02); significant improvements in isometric neck muscle strength after 6 months in exercise group, (p <0.001) and in TENS group, (p = 0.009) over control group. Numbers of patients taking sick leave at 6 months: 5.5% TENS (p = 0.03) vs 3% exercise (p = 0.01) vs 9% for controls.	"After the 6-week treatment, patients in the TENS and exercise group had better and clinically relevant improvement in disability, isometric neck muscle, strength, and pain."	Study's main results suggest exercise superior to TENS or infrared for chronic neck pain. TENS placed over acupuncture sites for neck pain.

Vonk 2009 RCT Sponsored by Dutch Health Care Insurance Board. No mention of COI.	6.5	N = 139 with non-specific chronic neck pain lasting >3months, mean age (SD) 41.7 (10.9) for CE therapist group and 44.8 (7.0) for BGA therapist group.	See Vonk 2009 above	See Vonk 2009 above	See Vonk 2009 above	See Vonk 2009 above
Salter 2006 RCT Sponsored by Medical Research Council Studentship and the Department of Health. No COI.	6.5	N = 24 with chronic neck pain of various diagnoses (cervicalgia, spondylosis, whiplash, wry neck torticollis, neck sprain and stiff neck), the mean age (SD) 45.5 (16.4) for GP care only group and 50.8 (17.1) for Acupuncture group	Acupuncture (up to 10 sessions; both fixed and variable components) (n = 10) vs. General Practice (GP) care (medication, massage, exercise chiropractic, surgery, physiotherapy, and hydrotherapy) (n = 14). Assessments at baseline and 3 months.	Northwick Park Questionnaire scores at baseline and 3 months: GP care (38.4 decreased to 25.7) vs. acupuncture (34.3 to 22.7). Medication use at baseline and 3 months among the GP group was unchanged (42.9% to 41.7%), but decreased from 40% to 11.1% in the acupuncture group. No statistically significant p-values reported.	"We found a trend towards higher levels of satisfaction among those patients referred to acupuncture, compared to those receiving usual GP care alone…The results of this pilot have provided useful data on key features of a full-scale trial of acupuncture for chronic neck pain."	Usual care group may have been equivalent to "more of the same" which is a recognized biased study design. It appears that a large trial was planned.
Gam 1998 RCT Sponsored by Kebo Care A/S. No mention of COI.	6.0	N = 67 with myofascial trigger points (MTrP) in neck and shoulder (duration >3 months), age 18-60	Ultrasound plus exercise plus massage (n = 18) vs. Sham ultrasound plus exercise plus massage (n = 22) vs. Control group (n = 18). Ultrasound at frequency of 100 Hz, pulse = 2 :8, intensity was 3 W/cm2 ; massage was transverse friction on MTrP followed by myofascial technique for 10 minutes; 6 exercise addressed strengthening neck/shoulder region. Assessments at baseline, 1, 2, 3, 4, 5, and 6 weeks.	Active treatment groups superior to no treatment group at 6 weeks and controls offered active treatment at that time. Exercise compliance 68% at 6 months. P-value statistics not reported.	"The over-all conclusion of the present study is that US give no pain reduction, but apparently massage and exercise reduces the number and intensity of MtrP, but this reduction had little impact on the patient's neck and shoulder complains."	Control group's worse ratings week after randomization and treatment initiation, as well as higher medication tablets consumed, suggests wait-list control group bias. Considerable baseline differences and controls had substantially longer duration of symptoms (12 vs. 7.5 months for placebo ultrasound vs. 4 months active ultrasound), concerning for potential randomization failure. Utilization of massage in 1st 2 groups a co-intervention and limits conclusions regarding utility of ultrasound or massage.
Andersen 2008 Med Sci Sports Exerc RCT Sponsored by Danish Medical	5.5	N = 549 workers engaging in repetitive and monotonous tasks facing chronic neck, shoulder pain >30 days in last year, mean age (± SD) 45 (±9) for GFT	See Andersen 2008 above	See Andersen 2008 above	See Andersen 2008 above	See Andersen 2008 above

Research Council and Danish Rheumatism Association. No mention of COI.		group, 44 (±9) for SST group, and 42 (±8) for reference group.				
Blangsted 2008 RCT Sponsored by Ministry of Culture Committee on Sports Research and National Board of Health under Ministry of Interior and Health. No mention of COI.	5.5	N = 549 with MSD symptoms in neck and shoulders (>1 year prevalence), mean (SD) age 47.3 (9.3) for men; 45.5 (10.4) for women in specific resistance training group, 43.1 (9.5) for men and 44.4 (8.0) for women in all around physical exercise group and 46.3 (9.0) for men and 43.9 (9.7) for women in reference group	See Blangsted 2008 above	See Blangsted 2008 above	See Blangsted 2008 above	See Blangsted 2008 above
Cleland 2010 RCT Sponsored by Foundation for Physical Therapy and Orthopaedic Section of American Physical Therapy Association. No mention of COI.	5.5	N = 140 with primary report of neck pain, mean age (SD) 39.2 (10.5) for manipulation + exercise group and 40.6 (12.0) for exercise only group.	Thoracic spine manipulation plus stretching and strengthening exercises (n = 70) vs. Stretching and strengthening exercise alone (n = 70). Assessments at baseline, 1 week, 4 weeks and 6 months.	Outcomes measured by NDI scores (p = 0.79) and NPRS score (p = 0.22) over time were not dependent upon the combination of a patient's treatment group or on the status of the clinical prediction rule.	"The results of the current study did not support the validity of the previously developed CPR. However, the results demonstrated that patients with mechanical neck pain who received thoracic spine manipulation and exercise exhibited significantly greater improvements in disability at both the short- and longterm follow-up periods and in pain at the 1-week follow-up compared with patients who received exercise only."	Larger dropout rate in exercise only group. Baseline differences present and impacts are unclear. Data suggest clinical prediction rule did not work; but manipulation groups modestly better than non-manipulation groups.
Koes 1992 a,b 3 reports of 1 RCT Sponsored by the Dutch Ministry of Welfare, Health, and Cultural Affairs and the Dutch National Health Insurance	5.0	N = 256 with chronic back and neck pain lasting >6 weeks (mean duration 1 year), mean age 43 for manipulative therapy group, 42 for physiotherapy group, 43 for placebo group, and 43 for general practitioner group.	Manual therapy, manipulation and mobilization of spine (n = 65) vs. Physiotherapy, exercises, massage and/or physical therapy (n = 66) vs. Placebo therapy (n = 64). Assessments at baseline, 3 weeks, 6 weeks, 12 weeks, 6 months and 12 months.	At 12 months, manipulative therapy marginally superior to physiotherapy in "improvement," but not for all other measures and time intervals. No p-value statistics reported between groups.	"[M]anipulative therapy and physiotherapy are better than general practitioner and placebo treatment. Furthermore, manipulative therapy is slightly better than physiotherapy after 12 months." In a second report, "a substantial part of the effect of manual therapy and physiotherapy appeared to be due to nonspecific (placebo) effects." The third report concluded "the subgroup	Value of this type of trial diminished today as therapies may have been heavily relied upon that have been subsequently shown ineffective. Lack of treatment visits in GP group both appear to have provided major bias against it suggest GPs unfamiliar with spine pain management and may not have been standardized. Other

Council. No mention of COI.					analysis suggests better results of manual therapy compared to physiotherapy in chronic patients (duration of present complaints of 1 year or longer) and in patients younger than 40 years old)."	interventions varied and not well defined. Placebo unblinded for provider, potentially influencing advice on how to treat ongoing symptoms, thus influencing outcomes. Heterogeneous nature of largely unstructured interventions prevents strong conclusions regarding efficacy.
Pillastrini 2009 RCT No mention of sponsorship or COI.	5.0	N = 71 nursery school teachers with low back and neck pain, the mean (± SD) age 43.5 (± 7.9) for control group and 44.7 (± 7.4) for experimental group	Exercise program with physical therapist and ergonomic brochure (Experimental) (n = 35) vs. Ergonomic brochure alone (Control) (n = 36). Assessments at baseline and 2 months.	Neck pain improved in 37.2% of subjects in the exercise group compared to 5.6% in control group (p = 0.0041). VAS scores decreased by 0.86±1.96 for neck pain in the exercise group.	"[S]ix-session extension-oriented exercise program, conducted in the occupational setting, can be decisive in the prevention and management of low back and neck complaints."	Statistical difference in baseline neck pain with higher pain in experimental group shown to increase recovery effect. No mention of duration of symptoms data on prevention.
Randlov 1998 RCT Sponsored by Danish Rheumatism Association. No mention of COI.	4.5	N = 77 females with chronic neck/ shoulder pain ≥6 months, ages 18-65 years	See Randlov 1998 above	See Randlov 1998 above	See Randlov 1998 above	See Randlov 1998 above
Cen 2003 RCT No mention of industry sponsorship and COI.	4.5	N = 31 with episodes of neck pain and loss in range of motion for a period exceeding one year, the mean (±SD) age 47 (±11) for Group A, 48 (±13) for Group B, 51 (±7) for Group C.	Traditional Chinese therapeutic massage (TCTM) (n = 10) vs. A home based, self-administered exercise program (N = 10) vs. Control group without treatment (head tilt, trapezius stretch, neck flexion, shoulder rolls and neck rolls (n = 11). Assessments at baseline, 6 weeks and 12 weeks.	TCTM group showed significant reduction in pain over other groups (p <0.05). After 6 weeks treatment and follow up, significant improvement in ROM (p <0.05). TCTM alone appeared equally effective to TCTM plus exercise.	"Traditional Chinese Therapeutic Massage provided significant benefit to those suffering from neck pain. Further studies need to address the combination of the treatments using TCTM and the therapies in mainstream medicine."	Pain for >1 year. Exercise group included 10 minutes moist heat and stretching exercises. Massage group 3 30-minute sessions for 6 weeks. Exercise group contacted by phone once a week; no contact with control. By comparing to an exercise program that is not been shown effective, in essence there are 2 controls. Massage may be helpful as component of therapy, but study does not support it over exercise.
Joghataei 2004	4.5	N = 30 with history of neck pain for more than	Cervical traction, electrotherapy and exercise	No differences in grip strength after 10 sessions (p = 0.65)	"The application of cervical traction combined with	Claims double blind, but manipulation group

RCT Sponsored by University of Social Welfare and Rehabilitation Sciences. No mention of COI.		one month and unilateral C7 radiculopathy following herniated disc or cervical spondylosis, mean (±SD) age 46.93 (±5.32) for control group and 47.53 (±5.6) for experimental group	(Experimental) (n = 15) vs. Electrotherapy and exercise only (Control) (n = 15). Assessments at baseline, after 5 sessions and after 10 sessions.		electrotherapy and exercise produced an immediate improvement in hand grip function in patients with cervical radiculopathy."	could not be blinded. Follow-up timing unclear as timed with treatments not time. Baseline differences in strength make primary outcome uninterpretable.
Falla 2013 RCT Sponsored by Danish Medical Research Council and Gigtforeningen Denmark. No COI.	4.5	N = 46 females with cervical pain limiting daily activity for at least 1 year, mean (SD) age 39.1 (8.7) for intervention group and 38.6 (9.0) for control group	Training group participating in 8-week exercise program for neck flexor and extensor muscles (n = 23) vs. Control group (n = 23). Assessments at baseline and 8 weeks.	Significant between-group difference in change in NDI score observed (interaction between group and time: F = 4.4; (p □□0.05)). A significant reduction in reported neck pain and disability (NDI) observed for intervention group post-treatment (pre: 18.2 ±7.4; post: 14.1 ± 6.6; SNK: (p □□0.01)) but not for the control group (pre: 17.5 ± 6.3; post: 16.6 ± 7.4). Effect size of this primary outcome was 0.65. Similarly, average intensity of neck pain over last 4 weeks lower for patients in training group (pre: 5.3±2.8; post: 3.6±2.4; SNK: (p □□0.001)) but did not change for control group (pre: 5.1 ±2.0; post: 4.9±2.3).	"This study investigated the immediate effectiveness of specific exercise for patients with chronic neck pain. In addition to assessing the effect on pain and perceived disability, we evaluated the effect on the specificity of neck muscle control. The results show that an 8-week specific exercise programme is efficacious for improving the directional specificity of neck muscle activity and reducing pain in the immediate term. Future studies are relevant to evaluate whether this type of training has further benefits such as a reduction in neck pain recurrence in the long term."	Data suggest intervention may be superior to control
Lluch 2014 Randomized Trial No mention of sponsorship or COI.	4.0	N = 18 with chronic idiopathic neck pain ≥3months, pain intensity on NRS ≥ 3/10, mean age (± SD) 44.3 (±14.3) for exercise group and 39.7 (±13.2) for mobilization group	Treatment group receiving active assisted plus cranio-cervical flexion exercise (n = 9) vs Treatment group receiving passive mobilization plus assisted cranio-cervical flexion group (n = 9). Assessment at baseline and post intervention.	Pressure pain threshold percentage values statistically significant for exercise group over mobilization group- Exercise: 17.3±18.8% vs. Mobilization: 0.7±17.7%; f = 6.1, (p = 0.02).	"Both an exercise and mobilization intervention induced immediate pain relief and reduced pressure pain sensitivity over the cervical spine in patients with chronic neck pain. Despite a reduction of pain for both intervention groups, only participants in the exercise intervention improved their performance on the CCFT. These findings highlight the importance of active intervention for improved motor control."	Small sample size (N=18). Short follow up (Pre & post intervention on same day.
Non Specific Neck Pain						
Sjogren 2005 Crossover Trial	7.5	N = 53 with headaches, neck or shoulder symptoms. Mean age: 45.7 years.	See Sjogren 2005 above	See Sjogren 2005 above	See Sjogren 2005 above	See Sjogren 2005 above

Sponsored by Chydenius Institute, University of Jyväskylä, Palokka Health Center, and personal grants from Finnish Work Environment Fund, Juho Vainio Foundation, and Academy of Finland. No mention of COI.						
Ylinen 2007 J Rehabil Med RCT Sponsored by grant from Jyväskylä Central Hospital. No mention of COI.	7.5	N = 125 females with non-specific neck pain. Mean age: 45.5 years.	See Ylinen 2007 above	See Ylinen 2007 above	See Ylinen 2007 above	See Ylinen 2007 above
Bosmans 2011 RCT Sponsored by the Netherlands Organization for Research and Development (ZonMw). No COI.	7.0	N = 146 with subacute nonspecific neck pain. Mean/DS age; 44.5 ± 12.0, 45.6 (11.1)	BGA program, described as a time-contingent increase in activities from baseline toward predetermined goals, (N = 71) vs. MT consists of specific spinal mobilization techniques plus exercises. (n = 75). 52 weeks follow up period.	Improvement in disability and pain in BGA group statistically larger than MT group; group difference for Continuous improvement -2.4 (-4.5 to -0.22, 95% CI); improvement NDI scores ≥ 4, 0.13 (0.00 to 0.26); pain continuous improvement -0.88 (-1.7 to -0.02); improvement ≥ 3, 0.19 (0.05 to 0.33); and QALYs gained, -0.02 (-0.06 to 0.02).	"In conclusion, significant improvements in pain and disability were found in primary care patients with nontraumatic neck pain, although substantial investments should be made to reach a 0.95 probability that BGA is cost effective in comparison with MT for these outcome measures."	Data suggest cost effectiveness greater for manipulation although there was no statistical difference in the primary outcome measured of "global perceived effect," limiting conclusion of economic efficacy.
Hoving 2002 RCT Sponsored by Netherlands Organization for Scientific Research and Fund for Investigative Medicine of	7.0	N = 183 with non-specific neck pain for at least 2 weeks, 18 to 70 years of age, or mean age of 45 years.	Manual therapy, or specific mobilization Techniques, once per week (n = 60) vs. Physical therapy, or exercise therapy, twice per week (n = 59) vs. Continued care by general practitioner; including, analgesics, counseling, and education (n = 64). Follow-up for 6 weeks.	At 7 weeks, twice as high for manual therapy group or 68.3% as for continued care group or 35.9%. 13% (6 of 47), 29% (12 of 42), and 26% (12 of 46) absent due to neck pain. At 7 weeks, success rates 70.7% for manual therapy, 50.8% for physical therapy, and 34.6% for continued care.	"In daily practice, manual therapy is a favorable treatment option for patients with neck pain compared with physical therapy or continued care by a general practitioner."	Minimal differences between groups were observed

Health Insurance Council. No mention of COI.						
Fritz 2014 RCT Sponsored by DJO, LLC. No mention of COI.	7.0	N = 86 with neck pain symptoms extending caudal to the superior edge of the scapula or distal to the acromioclavicular joint and a NDI score ≥ 10, mean (SD) age 44.9 (±11.3) for exercise group, 48.1 (±10.0) for mechanical traction group, and 47.6 (10.9) for over-door traction group	Exercise group received an active exercise program commonly used for patients with neck pain (n = 28) vs. Mechanical traction group With same intervention as exercise group with additional mechanical cervical traction during treatment sessions (n = 31) vs. Over-door traction group receiving the same exercise interventions plus traction using a Chattanooga Overdoor Traction Device (n = 27). Assessments at baseline, 4 weeks, 6 months and 12 months.	Intention-to-treat analysis found lower Neck Disability Index scores at 6 months in the mechanical traction group compared to the exercise group (mean difference between groups, 13.3; 95% confidence interval: 5.6, 21.0) and over-door traction group (mean difference between groups, 8.1; 95% confidence interval: 0.8, 15.3), and at 12 months in the mechanical traction group compared to the exercise group (mean difference between groups, 9.8; 95% confidence interval: 0.2, 19.4).	"We found that adding mechanical traction to a standard exercise program, particularly with an in-clinic, motorized device, for patients with cervical radiculopathy led to greater improvements in disability and neck and arm pain. These improvements were particularly notable at the longer-term follow-ups. Further research is needed to identify the most effective nonsurgical treatments for patients with cervical radiculopathy, and whether clinical decision making can be enhanced by consideration of more narrow subgrouping strategies."	Data suggest exercise plus traction superior to exercise alone
Walker 2008 RCT No sponsorship. No mention of COI.	6.5	N = 98 with primary complaint of neck pain with or without unilateral UE symptoms. Age: ≥18 years.	See Walker 2008 above	See Walker 2008 above	See Walker 2008 above	See Walker 2008 above
Bronfort 2012 RCT Sponsored by National Institutes of Health's National Center for Complementary and Alternative Medicine. No mention of COI.	6.0	N = 272 with non-specific neck pain of 2 to 12 weeks duration. Age range: 18-65 years.	Spinal manipulation (SMT) (n = 91) vs. Medication (n = 90) vs. home exercise advice (n = 91). Outcomes measured at 2, 4, 8, 12, 26, and 52 weeks.	At 12 weeks, pain scores improved in both the SMT and HEA groups, but difference between groups not significant (p = 0.087). Difference between HEA and medication group not significant. SMT group used far less medications long-term vs. medication group (p <0.001).	"…[S]MT seemed more effective than medication according to various measures of neck pain and function. However, SMT demonstrated no apparent benefits over HEA."	High loss to follow-up at 52 weeks limits long-term conclusions. Data suggest in short term, no clinically significant differences between groups, all of which demonstrated improvement. 90% of medication group were taking NSAID, opioid, acetaminophen, and muscle relaxants.
Jensen 2009 RCT Sponsored by AFA Försäkringar. No COI.	6.0	N = 275 with non-specific neck and back pain. Mean age: 42 years.	Orthopaedic manual therapy program (OMTP) (n = 98) vs. Multidisciplinary rehabilitation programme (MDP) for 5 months (n = 157). 7 years follow up.	Patients with <60 sick days had significant effect of treatment, (p <0.001) with MDP having less sickness during study period. If >60 sick days, treatment groups not different.	"In conclusion, full-time workplace-oriented multidisciplinary programme is a cost effective form of rehabilitation for individuals suffering from non-specific neck/back pain."	Follow up for 7 years after intervention. Many varied exercises in each group that were individualized. Large differences between neck

						and back pain between groups.
Ma 2010 RCT Sponsored by Grant of Science and Technology of Guangdong Province. No mention of COI.	5.5	N = 43 with myofascial pain syndrome and trigger points on one of the upper trapezius muscles that restricts ROM for 6 months to 5 years, mean age (± SD) 42.3 (±5.1) for group 1, 42.2 (±5.3) for group 2 and 42.6 (± 4.9) for group 3.	Group 1 mini scalpel-needle release therapy in conjunction with self neck-stretching exercises (n = 15) vs. Group 2 received acupuncture needling treatment and performed self-neck-stretching exercises (n = 15) vs. Group 3 control group with only self neck-stretching exercises (n = 13). Follow up at 2 weeks and 3 months.	Miniscapel VAS scores significantly decreased at 2 weeks ($p < 0.01$), 3 months ($p < 0.01$) follow-up. Contralateral bending ROM of cervical spine ($p < 0.01$) at 2 weeks and 3 months. Acupuncture group also had significant improvements in VAS scores ($p < 0.05$) at both follow-ups and in contralateral ROM of cervical spine ($p < 0.05$) at both follow-ups. Neck stretching also improved at 3 months follow-up ($p < 0.05$).	"[T]his study supports the hypothesis that [miniscalpel-needle] release and acupuncture needling treatment effectively reduced myofascial pain, increased the pain threshold at [trigger points] area, and increased contralateral bending [range of motion] of cervical spine at 2 weeks and 3 months follow-up. The [miniscalpel-needle] release technique is more effective than acupuncture needling treatment or self neck-stretching exercise in the treatment of [myofascial pain syndrome] at 3 months follow-up."	Allocation non-concealed. No blinding. No control of co-interventions noted. Data suggest invasive groups (acupuncture, miniscapel) had more improvement than central of treatment end at 3 months. The miniscapel needle relative is not commonly used in the US.
Korthals-de Bos 2003 RCT Sponsored by Netherlands Organization for Scientific Research and Health Insurance Council's fund for investigative medicine. No COI.	5.0	N = 183 with non-specific neck pain >2 weeks duration, mean age (SD) 44.6 (12.4) for manual therapy group, 45.9 (11.9) for physiotherapy group and 45.9 (10.5) for general practioner care group	Manual therapy (6 weekly sessions, low velocity mobilization, exercises) (n = 60) vs. PT (12 sessions over 2 weeks of exercises, traction, stretching, massage) (n = 59) vs. General practice (education of favorable prognosis, ergonomics, analgesics) (n = 64). Outcome assessments at baseline, 3, 7, 13 and 52 weeks after treatment. Mailed questionnaire at 26 weeks.	Total costs (Direct Healthcare, Direct Non-healthcare, Indirect Costs): MT €403 vs. PT €1297 vs. GP €1379. ($p=,0.05$) for MT vs. PT or GP. No differences between GP and PT.	"Our economic evaluation alongside a pragmatic randomized controlled trial showed manual therapy to be more cost effective than physiotherapy and continued care provided by a general practitioner in the treatment of non-specific neck pain."	Follow-up report of Hoving 2002 focused on economic analysis. Study suggests manual therapy of low velocity manipulation more cost effective than physiotherapy or general care without physical methods. Applicability of results outside Netherlands unclear.
Hoving 2006 RCT Sponsored by Netherlands Organization for Scientific Research and Fund for Investigative Medicine of Health Insurance	5.0	N = 183 with non-specific neck pain or stiffness that agitated during active or passive ROM >2-weeks duration, age 18-70	Manual therapy (6 weekly sessions of low velocity mobilization, exercises) (n = 60) vs. Physical Therapy (12 sessions over 2 weeks of exercises, traction, stretching, massage) (n = 59) vs. General Practice (education of favorable prognosis, ergonomics, analgesics) (n = 64). Assessments at baseline, 3 7, 13, 26 and 52 weeks.	Perceived 100% Recovery: At 13 weeks, difference between MT and GP of 29.5 (95% CI 12.9, 46.1), At 52 Weeks 15.4 (-1.3, 3.21). No differences in Severity Physical Dysfunction, Pain Intensity, Neck Disability Index scores, Main functional limitation scores between any group at 13 or 52 weeks.	"[A]fter MT had speeded up recovery in the short term, GP and PT treatment caught up in the long term, and differences between the three treatment groups at 12 months of follow-up were small and no longer statistically significant."	Follow-up study to Hoving 2002. Co-interventions common in all groups (more of same or crossover therapy). Outcomes measures of Global Perceived Recovery of unknown reliability. Study results suggest all groups improve, with no significant differences between interventions at 3 months or 1-year.

Council. No mention of COI.						
Martel 2011 RCT Sponsored by National Board of Chiropractic Examiners (NBCE) and Foundation for Chiropractic Education and Research (FCER). No COI.	5.0	N = 98 with non-specific neck pain 12 weeks or longer, mean age (SD) 36.8 (10.5) for spinal manipulation group, 43.3 (10.5) for spinal manipulation and home exercise group, and 43.3 (10.9) for attention-control group.	Spinal manipulation group (n = 36) vs. Spinal manipulation with exercise group (n = 33) vs. Control group (n = 29).	When comparing before and after treatments, all improved in mean VAS pain (p = 0.0003), NDI (p = 0.0005), and BQ (p = 0.0001). No statistically significant differences between groups.	"This study hypothesised that participants in the combined intervention group would have less pain and disability and better function than participants from the 2 other groups during the preventive phase of the trial. This hypothesis was not supported by the study results. Lack of a treatment specific effect is discussed in relation to the placebo and patient provider interactions in manual therapies. Further research is needed to delineate the specific and non-specific effects of treatment modalities to prevent unnecessary disability and to minimise morbidity related to NCNP. Additional investigation is also required to identify the best strategies for secondary and tertiary prevention of NCNP."	All subjects had 10 manipulations prior to allocation. Average pain and disability index scores were low at trial onset (3.4 of10). Home exercise consisted of stretches and some strengthening, but did not include aerobic exercise. Data suggest no benefit of monthly manipulation for maintenance or prevention.
Andersen 2012 RCT Sponsored by Danish Working Environment Research Fund. No COI.	4.5	N = 449 office workers with and without neck and/or shoulder pain, the mean age (SD) 47 (10) for 1WS group, 46 (10) for 3WS group, 45 (10) for 9WS group, and 46 (10) for reference group.	Supervised high-intensity strength training 1 hour once a week group for 20 weeks (1WS) (n = 116) vs. 20 minutes 3x a week group (3WS) (n = 126) vs. 7 minutes 9x a week group (9WS) (n = 106) vs. Reference group (n = 101). Assessment at baseline, 2, 4, 6, 8, 10, 12, 14, 16, 18 and 20 weeks after randomization.	Neck pain significantly decreased in 1WS and 3WS ($p<0.05$). The 9WS group had no significant decrease in neck pain.	"One hour of specific strength training effectively reduced neck and shoulder pain in office workers. Although the three contrasting training groups showed no statistical differences in neck pain reduction, only 1WS and 3WS reduced DASH. This study suggests some flexibility regarding time-wise distribution when implementing specific strength training at the workplace."	Cluster randomization techniques rather than individuals. High drop-out rate. Poor compliance limits conclusions. Data suggest benefit from exercise in this population (computer users) to reduce existent neck pain. Fewer, longer sessions may provide more benefit (1 hr once per week, 20 min 3x/wk)
Helewa 2007 RCT No mention of sponsorship or COI.	4.5	N = 151 with regular or prolonged neck/shoulder or back pain in past 12 months, mean age36.6 for training group and mean 37.8 for control group.	Thermal Massage, a moist hot or cold pack according to their preference, for 20 minutes (n = 37) vs Neck Support, received a neck support pillow to be used during sleep (n = 38) vs. Active exercise, a program of active neck and postural	NPQ at 12 weeks, (p = 0.06); main effects of Exercise, (p = 0.146) and Pillow, (p = 0.443), not statistically significant; but interaction of Exercise plus Pillow, (p = 0.029).	"Treatment by physiotherapists trained to teach both exercises and the use of a neck support pillow achieved the most favorable benefit for participants with chronic neck pain; either strategy alone was not more effective than a control regimen."	Meaningful differences between groups at baseline.

			exercises (n = 38) vs. Combined exercise and sleeping neck support pillow and placebo (n = 38). Follow-up for 12 months.			
Ang 2009 RCT Sponsored by The Swedish Defense Research Agency. One or more authors received or will receive benefits from a commercial party related to subject of article.	4.5	N = 68 helicopter pilots with neck pain. Mean age for Exercise and Control groups: 37.3 and 37.7 years.	Exercise group (n = 34) received supervised neck/shoulder exercise vs. Control group (n = 34) encouraged to continue with ordinary exercise activity. Follow-up at 12 months.	Odds Ratio for Pain-free status of Exercise vs. Control – Past Week: 3.2 (1.3-7.8, p = 0.013); Past 3-months: 1.9 (1.2-3.2, p = 0.008).	"In this trial, a supervised neck/ shoulder exercise regimen was considered effective over a 12-month period for reducing the prevalence of neck pain in air force pilots."	Ambiguous COI statement. Study population not generalizable. Data suggest exercise is superior to control.

Medications……..

NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) AND ACETAMINOPHEN

Nonsteroidal anti-inflammatory drugs (NSAIDs) have been utilized to treat musculoskeletal pain, although the exact mechanism of efficacy remains unclear. While they inhibit prostaglandin synthesis and thus impair inflammation, many of the MSDs do not have significant inflammation, including cervicothoracic pain. NSAIDs also have potent analgesic capabilities. These medications, as well as medications to counter gastrointestinal effects, are reviewed in detail in the Hip and Groin Disorders guideline.

There are four commonly used cytoprotective classes of drugs: misoprostol, sucralfate, double-dose histamine Type 2 receptor blockers (famotidine, ranitidine, cimetadine, etc.), and proton pump inhibitors (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole). There probably are not substantial differences in efficacy for prevention of gastrointestinal bleeding,(665) although evidence suggests the histamine-2 blockers are less effective for protection of the gastric mucosa and evidence also suggests sucralfate is weaker than proton pump inhibitors. There also are combination products of NSAIDs/misoprostol that have documented reductions in risk of endoscopic lesions. Providers are cautioned that H2 blockers might not protect from gastric ulcers(666-668) (see Hip and Groin Disorders guideline).

1. *Recommendation: NSAIDs for Acute, Subacute, Chronic, or Post-operative Cervicothoracic Pain*
   NSAIDs are recommended for treatment of acute, subacute, chronic, or post-operative cervicothoracic pain.

   Indications – Acute, subacute, chronic, or post-operative cervicothoracic pain; over-the-counter (OTC) agents may suffice and be tried first.
   Frequency/Duration – Scheduled dosage rather than as-needed preferable; as-needed prescriptions may be reasonable for mild or moderate chronic cervicothoracic pain.
   Indications for Discontinuation – Resolution of cervicothoracic pain, lack of efficacy, or development of adverse effects that necessitate discontinuation.
   Benefits – Modest reduction in spine pain and earlier recovery.
   Harms – Gastrointestinal bleeding, other bleeding, and possible delayed fracture healing. Possible elevated cardiovascular risks including myocardial infarction, especially for high-dose COX-2 inhibitors. Renal failure may occur particularly in the elderly or those with otherwise compromised function.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – High

2. *Recommendation: NSAIDs for Acute, Subacute, or Chronic Cervicothoracic Radicular Pain Syndromes*
   NSAIDs are recommended for treatment of cervicothoracic radicular pain syndromes.

   Indications – Radicular pain syndromes.
   Frequency/Duration – In acute radicular pain syndromes, scheduled dosage rather than as needed is preferable; as-needed prescriptions may be reasonable for mild or moderate chronic radicular pain.
   Indications for Discontinuation – Resolution of symptoms, lack of efficacy, or development of adverse effects that necessitate discontinuation. It should be noted that resolution of radicular symptoms generally takes significantly longer than resolution of acute cervicothoracic pain.
   Benefits – Modest reduction in spine pain and earlier recovery.
   Harms – Gastrointestinal bleeding, other bleeding, and possible delayed fracture healing. Possible elevated cardiovascular risks including myocardial infarction, especially for high-dose COX-2 inhibitors. Renal failure may occur particularly in the elderly or those with otherwise compromised function.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – High

3. *Recommendation: NSAIDs for Patients at Risk for GI Adverse Effects*
   Concomitant prescriptions of cytoprotective medications are recommended for patients at substantially increased risk for gastrointestinal bleeding.

   Indications – Patients with a high-risk factor profile who also have indications for NSAIDs, cytoprotective medications should be considered, particularly if longer-term treatment is contemplated. Risk factors include prior gastrointestinal bleeding, increased age, diabetes mellitus, and smoking.

Frequency/Duration – Frequency as recommended by manufacturer.

Indications for Discontinuation – Intolerance, development of adverse effects, lack of efficacy, or discontinuation of NSAID.

Benefits – Reduced risk of gastrointestinal bleeding when used with an NSAID.

Harms – Misoprostol may cause diarrhea. Other medications typically well tolerated, although as with all medications, allergic intolerances have been reported.

Strength of Evidence – **Strongly Recommended, Evidence (A) –** Proton pump inhibitors, misoprostol
Moderately Recommended, Evidence (B) – Sucralfate
Recommended, Evidence (C) – H2 blockers

Level of Confidence – High

4. *Recommendation: NSAIDs for Patients at Risk for Cardiovascular Adverse Effects*
It is recommended that patients with known cardiovascular disease or multiple risk factors for cardiovascular disease should know the risks and benefits of NSAID therapy for pain discussed.
Benefit – Counter risk of adverse event.
Harms – None.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – High

Acetaminophen or aspirin is strongly recommended as the first-line therapy as these appear to be the safest to use for these patients.

Frequency/Duration – If needed, NSAIDs that are non-selective are preferred over COX-2 specific drugs. In patients receiving low-dose aspirin for primary or secondary cardiovascular disease prevention, to minimize the potential for the NSAID to counteract the beneficial effects of aspirin, the NSAID should be taken at least 30 minutes after or 8 hours before the daily aspirin.(669)
Benefits – Addresses spine pain without increased risk of cardiovascular event.
Harms – Less effective than NSAID. Aspirin also more prone towards gastrointestinal bleeding and other hemorrhage.

Strength of Evidence – **Strongly Recommended, Evidence (A)**
Level of Confidence – High

5. *Recommendation: Acetaminophen for Cervicothoracic Pain*
Acetaminophen is recommended for treatment of cervicothoracic pain with or without radicular symptoms, particularly for those with contraindications for NSAIDs.
Benefits – Addresses spine pain without increased risk of cardiovascular event.
Harms – Less effective than NSAID. Aspirin also more prone towards gastrointestinal bleeding and other hemorrhage.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – High

Rationale for Recommendations
There is less quality evidence for use of NSAIDs and acetaminophen in cervicothoracic pain compared to low back pain and arthroses (see Low Back Disorders and Hip and Groin Disorders guidelines). A review found only 5 RCTs with a total of 270 people.(670) There are no randomized placebo controlled trials evaluating NSAIDs and cervicothoracic pain. There is evidence that NSAIDs decrease pain in lumbosacral spine pain (see Low Back Disorders guideline) as well as other joint pain.

There is quality evidence that NSAIDs reduce pain and improve functional status among acute, subacute, and chronic cervicothoracic pain patients.(671-674) These RCTs compared NSAIDs to other interventions such as manipulation in acute and subacute cervicothoracic pain,(675, 676) acupuncture(675, 677) and documented improvement with NSAIDs, but did not find a statistically significant improvement compared to the other interventions. Less clear, primarily due to in part to diagnostic uncertainties, are the beneficial effects that appear to be present for the treatment of radicular pain syndromes.(678)

Results are positive whether considering COX-1 (non-selective) or COX-2 (selective) NSAIDs,(673, 675, 679) although the magnitude of benefit is not generally large for any given medication. There is a dearth of head-to-head comparative trials of NSAIDs. Evidence that one medication is superior to another is lacking for cervicothoracic pain. There also is no strong evidence that any specific dosing pattern is superior.

There are no quality studies of acetaminophen as a single agent in the adult working population. There is one moderate-quality RCT evaluating single dose acetaminophen compared to ibuprofen and codeine in ages 6 to 17 in acute musculoskeletal pain, showing ibuprofen to have more significant pain relief.(674) However, paracetamol, a close analog, has been studied more extensively in subacute/chronic cervicothoracic pain and has some evidence of efficacy.(673, 675) There has not been any evidence that paracetamol is superior or equivalent to NSAIDs.(673)

NSAIDs are not invasive, have low side effect profiles in a healthy working age patient population, and when generic medications are used are low cost. The potential for some NSAIDs to increase the risk of cardiovascular events should be considered and requires additional quality studies to fully address. A recent review should be consulted before prescribing for high cardiovascular risk individuals.(669)

Evidence for the Use of NSAIDs and Acetaminophen
There are 3 high-(674, 679, 680) and 13 moderate-quality(665-668, 671-673, 675, 676, 681-684) RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.(677)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: non-steroidal anti-inflammatory, NSAIDs, non-steroidal anti-inflammatory agents, Aspirin (acetylsalicylic acid), Celecoxib, Dexibuprofen, Dexketoprofen, Diclofenac, Diflunisal, Droxicam, Etodolac, Etodolac, Etoricoxib, Fenoprofen, Flurbiprofen, Ibuprofen, Indomethacin, Isoxicam, Ketoprofen, Ketorolac, Lornoxicam, Loxoprofen, Lumiracoxibm, Meclofenamic acid, Mefenamic acid, Meloxicam, Nabumetone, Naproxen, Nimesulide, Oxaprozin, Parecoxib, Piroxicam, Rofecoxib, Salsalate (salicylsalicylic acid), Sulindac, Tenoxicam, Tolfenamic acid, Tolmetin, Valdecoxib, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 349 articles, and considered 13 for inclusion. In Scopus, we found and reviewed 201 articles, and considered 2 for inclusion. In CINAHL, we found and reviewed 5 articles, and considered 1 for inclusion. In Cochrane Library, we found and reviewed 16 articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 16 articles considered for inclusion, 15 randomized trials and zero systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Clark 2007 RCT Sponsored by research grant from Children's Hospital of Eastern Ontario Research Institute. Conflict of interest: Dr. Plint supported in part by salary-support award from Children's Hospital of Easter Ontario Research Institute.	9.5	N = 300 children with pain from acute musculoskeletal injuries. Age 6-17.	Acetaminophen, 15mg/kg (n = 112) vs. Ibuprofen, 10mg/kg (N = 112) v.s Codeine as single dose, 1mg/kg (n = 112). Assessments at 30, 60, 90 and 120 minutes after treatment. Follow-up for 2 days.	Not until after 60 minutes that patients in ibuprofen group showed significantly greater improvement compared to codeine and acetaminophen groups for pain score, ($p < 0.001$). No difference between codeine and acetaminophen for changes in pain scores. No difference in patients requiring more analgesic, ($p = 0.32$).	"[A]mong children with pain from acute musculoskeletal injuries presenting to a pediatric ED, a single dose of ibuprofen provides greater pain relief than codeine or acetaminophen."	Single dose treatment evaluated 60 minutes after treatment. No good delineation of which injuries responded better to which medications. Fractures of the extremities were also included in analysis.
Khwaja 2010 RCT No mention of sponsorship. No COI	8.5	N = 61 with acute cervical strain, ages 18 years or older with a mean age of 34 (11) years.	Ibuprofen, 800mg and inactive placebo tablet, 3x a daily by mouth (n = 20) vs. Cyclobenzaprine, similarly appearing inactive placebo tablet, 5mg, 3x daily (n = 21) vs. Ibuprofen plus cyclobenzaprine, 800mg Ibuprofen and 5mg cyclobenzaprine 3x daily (n = 20). All treatments s needed for 7 days.	Pain intensity difference on day 6 different among 3 groups, ($p = 0.05$). Reduction in pain scores in 3 study groups, ($p = 0.001$).	"The addition of cyclobenzaprine to ibuprofen in the treatment of ED patients with acute cervical strains resulting from MVCs or falls does not appear to result in more effective pain relief or faster resumption of normal daily activities."	Short follow-up time, active interventions may be superior to ibuprofen.
Muller 2005 RCT No mention of sponsorship or COI.	8.0	N = 69 with chronic mechanical spinal pain syndromes, mean >2 years. Mean age was 39 years.	Acupuncture,50mm long; 0.25mm gauge, for 20-minute appointments (n = 36) vs. Manipulation, 2 20-minute office visits a week (n = 36) vs Medication, normally celecoxib, 200-400mg/d, next drug of choice refecoxib, followed with acetaminophen (n = 43). At least 1 year follow-up.	Neck pain scale (VAS) significant for both manipulation ($p = 0.04$) and acupuncture ($p = 0.006$) but not medication ($p = 0.70$); neck disability index significant for manipulation ($p = 0.045$) vs. acupuncture ($p = 0.005$) and medication ($p = 0.26$). Those who received any time after randomization a treatment other than allocated regimen "differed significantly ($p <0.05$) between the treatment groups." Respective percentages: manipulation 38.7%, acupuncture 53.3%, medication 81.2%.	"Overall, patients who have chronic mechanical spinal pain syndromes and received spinal manipulation gained significant broad-based beneficial short-term and long-term outcomes. For patients receiving acupuncture, consistent improvements were also observed, although without reaching statistical significance (with a single exception). For patients receiving medication, the finders were less favorable."	No differentiation between different areas of the spine. Initially acupuncture and manipulation groups had provider contact twice a week vs drug-only group with contact once every 2 weeks. Majority of patients (75.8%) responded at 12 months, but range of time to respond up to 36 months in some.

Lovell 2004 RCT No mention of sponsorship or COI.	7.5	N = 51 with acute musculoskeletal pain. Mean age 36 years.	Oral valdecoxib 40mg (n = 26) vs. Oxycodone 10mg in combination with acetaminophen 650mg (n = 25). Assessments at 30 and 60 minutes after treatment and 24 hours after.	Mean pain (95%CI) at baseline/60 minutes comparing valdecoxib vs oxycodone: 81(75, 86)/ 47 (37, 57) vs 75 (69, 82)/51 (42/60). Adverse events (%) sedation/dizziness: 15 vs 11, (p = 0.03). Nausea/dyspepsia: 3 vs 3, (p = 0.96).	"Valdecoxib is as effective as an oxycodone-acetaminophen combination in treating ED patients with acute musculoskeletal pain at 30 minutes and less likely to cause sedation or the need for rescue analgesia over the next day."	Blinding because of side effects.
Predel 2013 RCT Sponsored by Novartis Consumer Health SA, Nyon, Switzerland. No COI.	7.5	N = 72 with acute neck pain (NP), ages 18 and above, mean age of 33.8 years.	DDEA) 1.16% gel, dose of 2g gel applied topically by fingertips on affected area and massaged into skin for 1 minute (Topical diclofenac diethylamine (n = 36) vs. Placebo gel (n = 36). In all subjects, study medication applied for 5 days with study visits at day 1 (baseline and 1 hour after 1st application of study drug, day 2 (24 h±4 hour after 1st application of study drug), day 3 (48 h± 4h after first application of study drug) and day 5 (study end, 96 h + 24 h after first application of study drug).	Primary outcome, pain-on-movement (POM) at 48 hours, was statistically significantly lower in DDEA 1.16 % gel (19.5 mm) than placebo 56.9 mm, (p < 0.0001). POM showed a statistically significant greater reduction with DDEA 1.16% gel than placebo from the first assessment at 1 hour to the final visit at 96 hour, (p < 0.0001). PAR was significantly lower with DDEA 1.16% than placebo at all post-baseline visits (p < 0.0001). NDI score showed that patients improved significantly with DDEA 1.16% gel than compared to placebo from the first to last assessment, (p < 0.0001)	"DDEA 1.16% gel, which is available over-the-counter, was effective and well tolerated in the treatment of acute neck pain. The tools used to assess efficacy suggest that it quickly reduced neck pain and improved neck function".	Intervention appears superior to placebo. Short follow-up time.
Giles 2003 RCT Sponsored by state funds. No COI.	6.5	N = 115 with chronic spinal pain syndromes. Mean age 27 years.	Medication (n = 43) vs. Acupuncture (n = 36) vs. Spinal manipulation (n = 36). Follow-up for 9 weeks after beginning of treatment.	Manipulation achieved best overall results: improvements of 50% (p = 0.01) on Oswestry scale, 38% (p = 0.08) on NDI, 47% (p <0.001) on SF-36, and 50% (p <0.01) on VAS for back pain, 38% (p <0.001) lumbar standing flexion, 20% (p <0.001) lumbar sitting flexion, 25% (p = 0.1) cervical sitting flexion, 18% (p = 0.02) for cervical sitting extension. Acupuncture better result than manipulation on VAS for neck pain (50% and 42%).	Authors concluded that the manipulation arm performed better than acupuncture which was better than medication.	Individualization of treatments results in lack of standardization and substantially precludes drawing robust conclusions. Post-randomized individualized treatment in all 3 arms. Ill-defined mixture of diagnoses, combined with non-randomization of some treatments arguably relegates study to a non-RCT.
Yelland 2007 RCT	6.5	N = 59 with osteo-arthritis pain. Mean age 64 years.	SR paracetamol, 2x 665mg tablets vs. Celecoxib, 200mg daily	Celecoxib showed better scores than SR paracetamol (0.2 (0.1) for pain, 0.3 (0.1), stiffness, and	"N-of-1 trials may provide a rational and effective method to best choose drugs for	80% had similar results with both drugs.

Crossover Sponsored by GlaxoSmithKline Consumber Healthcare. COI: GlasxoSmithKline also supported salaries of J.N. and N.M.			(n = 32), or 200mg 2x a day (n = 9) vs. Placebo; 3 cycles, 2 weeks each. Follow-up for 12 weeks.	0.3 (0.1) functional limitation; 33/41 individual patients (80%) failed to identify differences between SR paracetamol and celecoxib in terms of overall symptom relief. Of 8 patients able to identify differences, 7 had better relief with Celecoxib and 1 with SR paracetamol.	individuals with osteoarthritis. SR paracetamol is more useful than celecoxib for most patients of whom management is uncertain."	
Ehsanullah 1988 RCT No mention of sponsorship or COI.	6.0	N = 297 with rheumatoid arthritis or osteoarthritis, age range for Ranitidine group was 25-85 and placebo 22-87.	Ranitidine 150mg twice daily (n = 137) vs. Placebo (n = 126). Follow-up for 8 weeks.	Cumulative incidence of peptic ulceration by 8 weeks: 10.3% (27/263); 2 out of 135 (1.5%) developed duodenal ulceration in ranitidine group, compared with 10 out of 126 (8%) taking placebo. Frequency of gastric ulceration same (6%) for 2 groups at 8 weeks.	"Ranitidine 150 mg twice daily significantly reduced the incidence of duodenal ulceration but not gastric ulceration when prescribed concomitantly with one of four commonly used non-steroidal anti-inflammatory drugs."	Different NSAIDs used in trial. Piroxicam caused significantly more duodenal ulceration than naproxen or diclofenac. Prior history of ulcer a large risk factor in developing a new ulcer. Ranitidine assisted in prevention of ulcers and data suggest may be helpful in high risk patients.
McReynolds 2005 RCT No mention of sponsorship or COI.	6.0	N = 58 with acute neck pain, mean age in Ketorolac group 30 years. Mean age in Osteopathic Manipulative group 29 years.	Single dose of IM ketorolac (n = 29) vs. Osteopathic manipulative treatment (n = 29). Follow-up or enrolled for over 3 and one half years.	Significantly greater decrease in pain intensity (p = 0.02; ± 0.2-1.9) in the OMT group.	"[O]MT is a reasonable alternative to parenteral nonsteroidal anti-inflammatory medication for patients with acute neck pain in the ED setting."	Excluded radicular signs and symptom patients, but included patients with neck pain from MVAs. Looked at pain before treatment and 1 hour after treatment without longer follow up. Manipulation group had individualized treatments based on presenting signs and symptoms.
Graham 2002 RCT Sponsored by grant from TAP Pharmaceutical Products Inc. No mention of COI.	6.0	N = 537 without H pylori and long-term users of NSAIDs and who had history of gastric ulcer.	Placebo plus misoprostol 200µg QID, 4x a day (n = 134/134) vs. Lansoprazole QD, 200µg once daily or 30mg of once daily until end of study (n = 136 /133). Follow-up for 12 weeks.	Patients on NSAIDs. Either dose lansoprazole remained free from gastric ulcer longer vs placebo (p < 0.001). Misoprostol group remained free of gastric ulcers longer than placebo (p <0.001), 15mg lansoprazole (p = 0.01), or 30mg lansoprazole (p = 0.04).	"Proton pump inhibitors such as lansoprazole are superior to placebo for the prevention of NSAID-induced gastric ulcers but not superior to misoprostol, 800 µg/d."	Not blinded to misoprostol. H pylori negative.
Robinson 1989 RCT Sponsored by a grant from Glaxo Inc., Research Triangle Park,	5.5	N = 144 with normal endoscopic findings requiring NSAIDs. Mean age Ranitidine group 50.1 and 45.9 in placebo group.	Ranitidine 150mg twice daily (n = 72) vs. Placebo, twice daily (n = 72). Follow-up for 8 weeks.	"There was no statistically significant different between the ranitidine and placebo groups in the overall distribution of the stomach grades. However, 51% (31/61) of the patients in the ranitidine group vs 40% (20/50) of the patients in the placebo	"[R]ranitidine therapy (150 mg twice daily) was effective in preventing duodenal, but not gastric, injury resulting from eight weeks of NSAID treatment."	8 weeks treatment also included with NSAID (ibuprofen, naproxen, sulindac, indomethacin, piroxicam).

North Carolina. No mention of COI.				group maintained a damage score of 0 by week 8."		
Childers 2005 RCT Sponsored by McNeil Consumer & Specialty Pharmaceuticals. No mention of COI.	5.0	N = 1000 with acute neck or back pain with muscle spasm, the mean age 41.2 ± 12.6.	Low dose cyclobenzaprine (n = 334) vs. Cyclobenzaprine and low dose ibuprofen (n = 330) vs. cyclobenzaprine and high dose (n = 336). Follow-up for 3 and 7 days after treatment.	All 3 treatment groups had significant improvements from baseline after 3 and 7 days of therapy in patient-rated spasm and pain (p <0.001) for all comparisons. Mean percent ODI scores improved from baseline to after 3 days and improved from baseline to after 7 days in all 3 treatment groups (p <0.001 for all comparisons. Within each treatment group, statistically significant improvement in ratings of medication helpfulness from Day 3to 7, (p <0.001).	"Combination therapy with low dose cyclobenzaprine (5mg TID) and ibuprofen (400mg TID or 800mg TID) is not superior to low dose cyclobenzaprine alone in adult patients with acute neck and back pain with muscle spasm, and combination therapy was well tolerated."	Weaknesses of an open-label trial balanced by a large study population and a major research question of different regimens that is not usually addressed in RCTs. Pain duration <14 days. No physician follow-up visits done after baseline. No discussion of some baseline characteristics, such as obesity or mechanism of injury.
Robinson 1991 RCT Sponsored by grant from Glaxo Inc. Research Triangle Park, IN. No mention of COI.	4.5	N = 673 patients receiving NSAIDs for arthritic or MSD conditions.	Ranitidine 150mg twice daily (n = 343) vs. Placebo for 4 weeks or 8 weeks (n = 330). Follow-up for 4 weeks in one study and 8 weeks for the second study.	Protective effect against duodenal mucosal lesions including duodenal ulcers (3 studies) and gastric mucosal lesions including gastric ulcers (1 study) observed vs placebo.	"[R]antidine is effective in preventing NSAID-associated duodenal ulcers and may be appropriate prophylaxis for certain high-risk patients."	4 RCTs for 4 or 8 weeks treatment. Data suggest protective for DU not GU.
Cho 2014 RCT Sponsored by program of Kyung Hee University for young medical research in 2009. No COI	4.5	N = 45 with chronic neck pain, ages between 25 and 55 years.	Acupuncture group (AC): 9 acupuncture sessions 3x a week (n = 15) vs. NSAIDs treatment group (NS): NSAIDs daily (n = 15) vs. NSAIDS (Zaltoprofen, 80mg daily) and 9 acupuncture sessions for 3 weeks. (acupuncture with NSAIDs treatment (AN), n = 15). Acupuncture groups had insertion of disposable stainless steel needles (0.25mm×40mm into muscle to depth of 20mm. Follow-up at baseline, 1, 3, 7 weeks.	VAS score was statistically significant between baseline and each point of assessment in the three groups: AC vs NS vs AN group; 6.7±0.7 vs 6.07±0.5 vs. 7.1±1.3 (p = 0.009). However, no significant difference between them.	"[T]his pilot study has provided the feasibility, safety and sample size for a full-scale trial of acupuncture with NSAIDs for chronic neck pain in comparison with acupuncture or NSAID treatment alone. Although preliminary, the finding that acupuncture with NSAIDs provides no greater benefit than acupuncture or NSAIDs alone raises questions about the mechanism of reciprocal action".	Data suggest combination Acupuncture and NSAID is superior.
Yamauchi 2008 RCT	4.5	N = 68 undergoing posterior cervical, ages 20-70 years.	Ket-1 group, bolus ketamine 1mg/kg followed by continuous ketamine 42μg. kg^{-1}. h^{-1} for 24 h (1mg/kg) (n	Pain scores in Ket-2 group lower than in Ket-1 and control group; Mean±SD *p<in ket-2 group 0.005 vs control group, + (p <0.05) vs. Ket-1 group. Fentanyl	"Small-dose ketamine improved the analgesic effects of fentanyl after cervical surgery."	Details sparse, 10 day follow-up.

No mention of sponsorship or COI.			= 22) vs. Ket-2 group, bolus ketamine 1mg/kg followed by continuous ketamine 83μg. kg⁻1. h⁻1 for 24 h (2mg/kg) (n = 23) vs. Control group, Isotonic saline determined. 0.5μg.kg⁻1. h⁻1 of fentanyl delivered on basal infusion and 0.5 μg/kg on demand with 6 minutes lockout for 48 hours (n = 23). In both groups, Nonsteroidal anti-inflammatory drugs (NSAIDs) (diclofenac suppository 50mg) administered after surgery.	consumption dose/NSAIDs requirement in Ket-2 group less than other 2 groups; Ket-2 vs. control group vs Ket-1 (Mean±SD *P < 0.05 vs control group, †P < 0.05 vs ket-1 group/ (0.6 ± 0.7*† vs 1.8 ± 0.4 vs 1.3 ± 0.8)		
Hsieh 2010 RCT Sponsored by GlaxoSmithKline Pharmaceuticals Ltd. No mention of COI.	4.5	N = 153 with myofascial pain syndrome (MPS) in the upper trapezius, ages 18 years or older. Mean age 38.4 ± 10.7 years.	Diclofenac sodium patches, 60mg diclofenac sodium in hydrophilic adhesive applied to nonwoven polyester. Patches 10×14cm (n = 97) vs. Control patches, menthol and hydrophilic adhesive only. Stretch exercises used (n = 56). In both groups, efficacy and safety parameters assessed before patch application (day 0, 4, 8). Patches applied on myofascial trigger points (MTrPs) area of upper trapezius 3x a day for 7 days. Rescue medication (acetaminophen) allowed.	By end of treatment, diclofenac sodium patch improved in VAS score by 51.3% (Day 8) vs baseline values (p <0.01). Diclofenac patch superior to baseline values for neck mobility and functional disability parameters: cervical active range of motion (18.4% vs 6.6%, p <0.01), neck disability index (32.4% vs -25.6%, p = 0.03), and patient global assessment, (p < 0.05). Diclofenac patch also superior to control patch at both Day 4 (18.6% change vs 10.0% change) and end of study (22.5% change vs. 10.0% change, (p <0.01). Treatment group showed less skin irritation and erythema than control group (16%-18% in control group and 3%-6% in treatment group, (p <0.05)	"[T]his study demonstrate that the diclofenac sodium patch was superior to the control patch in terms of reducing pain and improving functional outcomes, and did not result in significant adverse effects."	Short follow-up time. No meaningful difference between groups.

ANTI-DEPRESSANTS

For many years, anti-depressants have been utilized for the treatment of chronic pain.(685-687) This section addresses the use of anti-depressants specifically to treat cervicothoracic pain with or without depression.

There are two main classes of anti-depressant medication used in the management of pain.(688) The first class – tricyclic anti-depressants (TCAs) – are believed to primarily work through inhibiting the reuptake of norepinephrine and include the antidepressants amitriptyline, doxepin, imipramine, desipramine, nortriptyline, protriptyline, maprotiline, and clomipramine. The second class – the selective serotonin reuptake inhibitors (SSRIs) – includes fluoxetine, sertraline, paroxetine, fluvoxamine, citalopram, and escitalopram. Dual reuptake inhibitors are also available, known as serotonin and norepinephrine reuptake inhibitors or SNRIs, which include duloxetine and venlafaxine. Knowledge of the different classes of agents is critical for the successful treatment of chronic pain. These recommendations are segregated into whether the anti-depressant blocks norepinephrine or not (including dual serotonin-norepinephrine agents), as that appears to be the critical feature that produces efficacy for treatment of pain.

1. *Recommendation: TCAs and SNRIs for Chronic Cervicothoracic Pain*
   Norepinephrine reuptake inhibitor antidepressants (TCAs) and dual reuptake inhibitors (SNRIs) – e.g., amitriptyline, imipramine, nortriptyline, maprotiline, doxepin, duloxetine, and venlafaxine – are recommended for the treatment of chronic cervicothoracic pain.
   Indications – Chronic pain not adequately treated with NSAIDs and an active exercise program. This intervention may be particularly helpful if there is nocturnal sleep disruption and mild dysthymia.(689-691)

   Frequency/Duration – Generally a low dose at night, gradually increased (e.g., amitriptyline 25mg QHS, increased by 25mg each week or Doxepin 50mg up to 300mg (2.5mg/kg)(689, 692) until a sub-maximal or maximal dose is achieved, sufficient effects are achieved, or adverse effects occur. All quality trials utilized lower doses, (e.g., amitriptyline 25 to 75mg a day in part to avoid adverse effects and necessity of blood level monitoring). Imipramine is less sedating, thus if there is carryover daytime sedation, it may be a better option. If the patient cannot sleep at night, amitriptyline is the recommended initial medication to prescribe.

   Indications for Discontinuation – Resolution of pain, intolerance, lack of efficacy, or development of adverse effects.
   Benefits – Modest improvements in spine pain. May improve sleep quality.
   Harms – Daytime somnolence, interference with work, dry mouth, cardiac risks, and other adverse effects.

   Strength of Evidence – **Recommended, Evidence (C)**
   Level of Confidence – Moderate

2. *Recommendation: Serotonin-Norepinephrine Reuptake Inhibitors "SNRIs, aka "Dual Action Agents," and Tricyclic Antidepressants (TCAs) for Radicular Pain*
   There is no recommendation for or against use of norepinephrine reuptake inhibitor anti-depressants (e.g., tricyclic anti-depressants – amitriptyline, imipramine, nortriptyline, desipramine, maprotiline, doxepin) and mixed serotonin norepinephrine reuptake inhibitors (e.g., duloxetine) for treatment of post-operative or radicular cervicothoracic pain absent other indicators for treatment, as there is no quality evidence supporting their efficacy (See Low Back Disorders Guideline). They may be a reasonable option for select cases particularly with sleep disruption with concerns regarding habituating agents or inability to manage with NSAIDs or other agents. There is some evidence of efficacy for treatment of patients with proximal limb radiation.(899,906)

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
   Level of Confidence – Low

3. *Recommendation: SSRIs for Acute, Subacute, Chronic, Postoperative Cervicothoracic Pain*
   The selective serotonin reuptake inhibitors, (e.g., paroxetine, as well as bupropion and trazodone) are not recommended for treatment of chronic cervicothoracic pain. (They may be nevertheless recommended for treatment of depression as noted previously.) There is strong evidence that treatment with these medications is not of benefit in other pain syndromes including low back pain (see Low Back Disorders guideline), thus their use is not recommended for the management of chronic cervicothoracic pain. (Utilization of these medications may still be indicated for treatment of depression).

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

4. *Recommendation: Anti-depressants for Acute or Subacute Cervicothoracic Pain*
   Absent other indicators of a need for treatment with TCAs and SNRIs, anti-depressants are not recommended for managing acute or subacute cervicothoracic pain as there is no quality evidence supporting their efficacy and other treatment options have documented efficacy. Limited use in the late subacute phase may be reasonable.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendations
There is quality evidence TCA anti-depressants are effective for treating cervicothoracic pain and muscle tension pain compared with placebo when utilizing doxepin.(689, 690) TCA and SNRI antidepressants have quality evidence for treatment of other chronic spinal pain(693-695) (see Chronic Pain and Low Back Disorders guidelines). A moderate-quality study suggested that fluoxetine was similar to amitriptyline in treatment effect on chronic spinal pain.(692) However, while there is limited direct evidence for use of SSRIs for treatment of cervicothoracic pain, there is robust evidence that SSRIs are ineffective for treatment of LBP and thus are also not recommended for treatment of cervicothoracic pain (696, 697) (see Chronic Pain and Low Back Disorders guidelines). TCAs and SNRIs are not invasive, have low to moderate adverse effects when used in low doses for treatment of pain, and are low to moderate cost depending on length of treatment. They are recommended for treatment of patients with chronic cervicothoracic pain and cervical radiculopathy that are insufficiently treated with NSAID and an active exercise program.

Evidence for the Use of Anti-depressants
There are 4 moderate-quality RCTs or crossover trials incorporated into this analysis.(689-692)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Antidepressive agents, antidepressant drugs, antidepressants, norepinephrine reuptake inhibitors, TCA, TCAs, MAOIs, SMSs, SARIs, SSRI, SNRIs, Doxepin, Clomipramine, Nortriptyline, Vortioxetine, Citalopram, Duloxetine, Trazodone, Escitalopram, Paroxetine, Fluoxetine, Fluvoxamine, Sertraline, Desvenlafaxine, Levomilnacipran, Milnacipran, Tofenacin, Venlafaxine, Vilazodone, Etoperidone, Viloxazine, Amitriptyline, Butriptyline, Clomipramine, Desipramine, Dosulepin, Imipramine, Iprindole, Lofepramine, Melitracen, Nortriptyline, Trimipramine, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 30 articles, and considered 4 for inclusion. In Scopus, we found and reviewed 316 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 0 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 8 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 4 articles considered for inclusion, 4 randomized trials and 0 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Hameroff 1982 RCT No mention of sponsorship or COI.	7.0	N = 30 with chronic cervical or lumbar pain and clinical diagnosed depression (a score ≥ 18 on the Hamilton Depression Rating Scale), the mean age 46.6 ± 2.3.	Doxepin treatment (50mg h.s. increased to 300mg) group (n = 15) vs. Placebo group, 50mg a day for 3 days, plus 50mg BID for 3 days, plus 50mg TID (n = 15). Assessments at washout, baseline, 1, 2, 4 and 6 weeks.	Significant improvements in doxepin group for global assessment (p = 0.026), Hamilton Depression Scale Scores (p = 0.030), Profile of Mood States (p = 0.011), percent of time pain felt (p = 0.05), effect of pain on muscle tension (p = 0.030), Effect of pain on sleep (p = 0.005), and reduction in enkephalin-like activity, (p = 0.037).	”Combined plasma levels of doxepin and its metabolite desmethyldoxepin that corresponded with therapeutic effect were approximately 70 ng/ml (2.5 mg/kg oral dose), although some benefits occurred at approximately 35 ng/ml. However, depression in outpatients with chronic pain may respond differently.”	Measured plasma levels of Doxepin and opioids as well. Each patient had depression. Most participants had failed many other treatment modalities including other medications, biofeedback and injections. No delineating between low back pain patients and cervicothoracic pain patients. “Doxepin is an option for patients who have chronic spinal pain and have failed other treatments with concomitant signs of depression.”
Hameroff 1984 RCT No mention of sponsorship or COI.	5.5	N = 60 with chronic pain of low back or cervical spine concomitant with clinical depression, the mean age (± SD) 48.9 (± 2.4) for doxepin group and 48.4 (±2.0) for placebo group.	Doxepin group, dosage began at 50mg and increased gradually to 300mg h.s. (unless marked symptomatic improvement) (n = 30) vs. Placebo control group or Doxepin began at 50mg and increased gradually to 300mg QHS unless marked symptomatic improvement (n = 30). Assessments at washout, baseline, 1, 2, 4 and 6 weeks.	Doxepin began at 50mg and increased gradually to 300mg QHS unless marked symptomatic improvement or adverse effects occurred. No significant p-value statistics reported for the analyzed variables between groups.	“Documented benefit and lack of significant side effects in a group of patients for whom other modalities had been virtually exhausted indicate that doxepin is a valuable treatment for patients with chronic pain and concomitant clinical depression.”	Pain severity ratings also improved, leading the authors to conclude that doxepin is a valuable treatment for patients with chronic pain and depression.

Pilowsky 1982 RCT Crossover Sponsored by Australian National Health and Medical Research Council. No mention of COI.	5.5	N = 52 with chronic pain in various locations (neck, back, chest, etc.), the mean age not reported.	25mg Amitriptyline, 2 tablets at night first 2 days, then 3 tablets at night for 2 days, then 4 tablets at night for 10 days with an increase to 6 tablets at night thereafter for 6 weeks) (n = 26) vs. Placebo control receiving (lactose) 2 tablets at night for first 2 days, then 3 tablets at night for 2 days, then 4 tablets at night for 10 days with an increase to 6 tablets at night thereafter for 6 weeks (n = 26). Follow up assessments at 2, 4 and 6 weeks.	In Weeks 2 and 4, 8 vs 3 or 4 who had partial or complete relief, but at Week 6, was 4 vs. 3, suggesting no lasting benefit. Significant reduction in pain scores in the amitriptyline group over placebo group at 2 and 4 weeks ($p < 0.05$), but not at 6 weeks. Fortnightly side effects scores were significantly higher in the amitriptyline group at 2 weeks ($p < 0.05$), 4 weeks ($p < 0.01$) and 6 weeks ($p < 0.01$)	"Overall, these findings do not alter the clinical impression that in treating chronic 'benign' intractable pain with antidepressants, best results can probably be expected in patients who show substantial evidence of a depressive illness with a prominent 'endogenous' component."	Study does not contain a table describing basic statistics comparing subjects in 2 arms. Anatomic locations rather than diagnoses described and distributed throughout body (some multiple); lower back was most common (56%), then lower limb (43%) and upper limb (31%).
Schreiber 2001 RCT No mention of sponsorship or COI.	5.5	N = 40 with LBP and whiplash associated cervical pain, median age 49.5 for Amitriptyline group and 55.5 for Fluoxetine group.	Amitriptyline 25mgs a day to maximum of 75mgs a day (n = 20) vs. Fluoxetine 20mgs a day in morning for 6 weeks (n = 20). Assessments once a week for 6 weeks.	Steady decline in pain for both groups, but no significant differences between groups for pain scores. "The mean initial scores on the 21-item Hamilton scale on the amitriptyline group were 5.21 ± 2.86 and in the fluoxetine group 3.96 ± 2.35. Though far from the cut-off point for depression, the Hamilton scores improved during treatment with either drug and scores at end of week 6 were 1.5±1.22 ($p < 0.005$) in amitriptyline group and 1.8±1.35 ($p <. 005$) in fluoxetine group. CES-D scored followed same pattern: a decline from 14.28±2.84 at base line to 12.07±1.2 ($p = 0.025$) in amitriptyline group, and from 13.65±1.22 to 12.19±1.02 ($p <.005$) in fluoxetine group."	"[F]luoxetine relieved low back pain and whiplash associated cervical pain with efficacy similar to that of amitriptyline, offering an alternative for patients unable to tolerate the tricyclic antidepressants' side effects."	No placebo, which makes interpretation difficult. Patients not blinded to medications. Both WAD and low back pain patients included. No exact diagnoses given to patients.

ANTI-EPILEPTIC AGENTS

Anti-epileptic agents are believed to have analgesic properties and have been utilized off-label for some chronic pain syndromes since the 1960s.(698) These agents have been primarily used to treat neuropathic pain, such as chronic radicular syndromes.(699) Trigeminal neuralgia has also been treated with anti-epileptic agents; however, a Cochrane review reported that there was insufficient evidence of efficacy for that purpose.(700)

Gabapentin, a GABA analog, is an anticonvulsant originally approved by the U.S. Food and Drug Administration (FDA) for treating seizures, particularly in conjunction with other anticonvulsants. The FDA later approved its use as a treatment of post-therapeutic neuralgia. It is prescribed for various pain syndromes including acute or chronic pain, spinal cord injury, Guillain-Barre syndrome and other various neuropathic pain syndromes. (701, 702) The mechanism of action is unknown. It is believed to act directly on the central nervous system, although not at the GABA receptor. Gabapentin is not a controlled substance, but does have psychoactive properties and therefore does carry a slight risk of abuse.

1. *Recommendation: Topiramate for Chronic Cervicothoracic Pain*
   Topiramate is recommended for limited use in select patients with chronic cervicothoracic pain as a fourth- or fifth-line agent.

   Indications for Initiation – Failure of multiple other modalities including trials of different NSAIDs, aerobic exercise, stretching exercise, strengthening exercise, tricyclic anti-depressants, distractants, and manipulation.

   Frequency/Dose – Initiate by gradually increasing the dose – beginning dose of 50mg, increasing by 50mg a week.(703) The most appropriate steady dose is unclear, but appears to be 300mg. Patients should be carefully monitored for the development of adverse events.

   Indications for Discontinuation – Resolution, development of adverse effects, lack of efficacy, or failure to adhere to a functional restoration program. Careful monitoring of employed patients is indicated due in part to elevated risks for central nervous system (CNS) sedating adverse effects.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

2. *Recommendation: Carbamazepine for Chronic Radicular or Neuropathic Pain*
   Carbamazepine is recommended as a potential adjunct as a fourth- or fifth-line treatment for chronic radicular or neuropathic pain after attempting other treatments (e.g., different NSAIDs, aerobic exercise, other exercise, manipulation). While there is not quality evidence for treatment of chronic radicular cervicothoracic pain, a trial of carbamazepine may be considered if other medications have failed. Oxcarbazepine and lamotrigine may be useful agents if there is insufficient relief from carbamazepine.

   Indications for Initiation – Failure of multiple other modalities including trials of different NSAIDs, aerobic exercise, stretching exercise, strengthening exercise, tricyclic anti-depressants, distractants, and manipulation.

   Frequency/Duration – Frequency and dosing are based on the medication prescribed.

   Indications for Discontinuation – Resolution of cervicothoracic pain, lack of efficacy, or development of adverse effects that necessitate discontinuation. Careful monitoring of employed patients is indicated due to elevated risks for CNS-sedating adverse effects.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

3. *Recommendation: Topiramate for Neuropathic Pain*
   Topiramate is not recommended for neuropathic pain, including peripheral neuropathy.(704)

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

4. *Recommendation: Gabapentin for Peri-operative Pain*
   Gabapentin is recommended for peri-operative management of pain to reduce need for opioids, particularly in patients with adverse effects from opioids.

   Indications – Peri-operative pain management.

   Frequency/Duration – Dosing is begun at 300mg q8h, and slowly increased if sedation is not occurring.

Indications for Discontinuation – Resolution, lack of efficacy, or intolerance. Careful monitoring of employed patients is indicated due in part to elevated risks for CNS-sedating adverse effects.
Benefits –Reduced opioid use, which may potentially speed recovery and produce better outcomes.
Harms – Drowsiness, dizziness and other CNS sedating effects are the most common adverse effects. Increased fatalities associated with opioids (1537).

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – High

5. *Recommendation: Gabapentin for Chronic Non-neuropathic or Cervicothoracic Pain*
Gabapentin is not recommended for chronic non-neuropathic pain or cervicothoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

6. *Recommendation: Gabapentin for Chronic Radicular Pain Syndromes*
There is no recommendation for or against the use of gabapentin for chronic radicular pain syndromes as the low back pain evidence is conflicting. (705, 706)

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendations
There are no quality studies for cervicothoracic pain disorders. Overall, the quality of the available literature is low for the low back. A high-quality trial compared topiramate to placebo in chronic low back pain. They reported reduced pain and overall improvement in the topiramate group.(703) A moderate-quality trial evaluated topiramate compared to placebo in diabetic polyneuropathy and found no significant difference in pain control.(704) For treatment of low back pain, there is limited evidence of efficacy of carbamazepine. In a moderate-quality trial carbamazepine plus opioids was compared to placebo in peripheral neuropathy patients. Significant delay in pain increase in the carbamazepine group was observed compared to placebo(707) (see Low Back Disorders guideline).

There are no sham-controlled or quality trials evaluating the use of gabapentin or pregabalin for cervicothoracic pain disorders. Gabapentin and the closely related compound pregabalin have been evaluated in quality studies for treatment of multiple pain syndromes.(702) However, results are not uniformly positive for all conditions (see Chronic Pain guideline for other conditions). There are conflicting results for treatment of chronic low back pain.(705, 706) A meta-analysis failed to find statistical benefit of gabapentinoids for treatment of low back pain, thus raising concerns about efficacy for the cervical spine, and reported several adverse effects (705, 1538-1540). Gabapentin has been shown to reduce post-operative pain and the need for opioids in patients undergoing back surgery(708-711) (see Low Back Disorders guideline).

Evidence for the Use of Anti-Epileptic Agents
There is 1 other study in Appendix 1.(712)

Anti-Epileptic Agents – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Anti-Epileptic agents (Carbamazepine OR Topiramate), cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 783 articles, and considered 1 for inclusion. In Scopus, we found and reviewed 3 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 0 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 11 articles, and considered 0 for inclusion. We also considered for inclusion 15 articles from other sources. Of the 1 article considered for inclusion, 1 randomized trial and 0 systematic studies met the inclusion criteria.*

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

: gabapentin, pregabalin, cervicalgia, pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, postop, postoperative*, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies*
to find 262 articles. Of the 262 articles, we reviewed 79 articles and included 2 articles (2 randomized controlled trials and 0 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Cohen 2014 (Score=3.5)										Pharmacotherapy plus PT poorly defined and highly variable between patients. Large proportion of non-compliance in conservative and combined treatment.
Levendoglu 2004 (Score=6.0)	Gabapentin	RCT	The authors declared no sponsorship or COI.	N= 20 Paraplegic Patients with complete spinal cord injury (thoracic and lumbar regions)	Mean age: 35.9±9.8 years; 13 males, 7 females.	Group A (n=10): (GBP treated group) vs. Group B (n=10): (Placebo control group) Doses for both group Doses for both groups: week 1, 900 mg/day; week 2, 1800 mg/day; week 3, 2400 mg/day; and week 4, 3600 mg/day.	Follow-up at baseline, 4 weeks.	VAS scores show significant difference between the GBP-treated group and placebo group at all times ($P<0.001$). Baseline VAS scores show no changes at 8 weeks ($p<0.05$).	"Gabapentin can be added to the list of first-line medications for the treatment of chronic neuropathic pain in spinal cord injury patients. It is a promising new agent and offers advantages over currently available treatments."	Data suggest significant pain reduction over 8 weeks.

CAPSAICIN, "SPORTS CREAMS" AND OTHER CREAMS AND OINTMENTS

Capsaicin is the active ingredient in peppers which makes them "hot." Applied to the skin as a cream or ointment, it is thought to reduce pain by stimulating nerve endings, thus being effective through distraction. Rado-Salil Ointment is a proprietary formulation of 14 agents, the two most common of which are menthol (55.1%) and methylsalicylate (26.5%). There are many other commercial products that similarly cause either a warm or cool feeling in the skin. All of these agents are thought to work through a counter-irritant mechanism (i.e., feel the dermal sensation, rather than feeling cervicothoracic pain). There is evidence that capsaicin compounds should not be used chronically due to reported adverse effects on neurons.(713)

1. *Recommendation: Capsaicin for Acute, Subacute, and Chronic Cervicothoracic Pain*
   Capsaicin (capsicum) is recommended for treatment of acute and subacute cervicothoracic pain or temporary flare-ups of chronic cervicothoracic pain.

   Indications – For acute, subacute, and temporary flare-ups of chronic cervicothoracic pain, capsicum is recommended for treatment. Providers should be aware that there are other treatments that appear to likely have greater efficacy (e.g., NSAIDs, progressive exercise program, etc.). However, capsaicin may be a useful adjunct. These compounds may also be used in those patients who prefer topical treatments over oral treatments and other more efficacious treatments, especially if they have but have only mild cervicothoracic pain. Capsaicin appears superior to Spiroflor in low back pain trials.(714) Other creams and ointments may be useful, although there is no quality evidence to guide recommendations.
   Duration/Frequency – As directed on the product label. Long-term use is not recommended.
   Indications for Discontinuation – Resolution of cervicothoracic pain, lack of efficacy, or development of adverse effects that necessitate discontinuation. It is recommended not to be used for more than 1 month, as the costs become high and patients are recommended to be transitioning to an active treatment program.
   Benefits –Modest reductions in pain through distraction.
   Harms – Local irritation and theoretical neuronal death with longer-term use.(715)

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

2. *Recommendation: Spiroflor for Acute, Subacute, or Chronic Cervical and Thoracic Pain*
   Spiroflor is not recommended for treatment of acute, subacute, or chronic cervical and thoracic pain as it appears less efficacious then capsaicin and there are other treatments that are efficacious.
   Strength of Evidence **– Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

3. *Recommendation: Topical NSAIDs or Other Creams and Ointments for Acute, Subacute, or Chronic Cervical and Thoracic Pain*
   There is no recommendation for or against the use of topical NSAIDs or other creams and ointments for treatment of acute, subacute, or chronic cervical and thoracic pain.
   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**

4. *Recommendation: DMSO for Chronic Cervical and Thoracic Pain*
   DMSO is not recommended for treatment of chronic cervical and thoracic pain.
   Strength of Evidence –**Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

5. *Recommendation: N-Acetylcysteine for Chronic Cervical and Thoracic Pain*
   N-Acetylcysteine is not recommended for treatment of chronic cervical and thoracic pain.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

6. *Recommendation: EMLA Cream for Chronic Cervical and Thoracic Pain*
   EMLA cream is not recommended for treatment of chronic cervical and thoracic pain.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

7. *Recommendation: Wheatgrass Cream for Chronic Cervical and Thoracic Pain*
   Wheatgrass cream is not recommended for treatment of chronic cervical and thoracic pain.
   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

8. *Recommendation: Other Creams and Ointments for Acute, Subacute, and Chronic Cervicothoracic Pain*
   There is no recommendation for the use of other creams and ointments for treatment of acute, subacute, or chronic cervicothoracic pain as there is no evidence of efficacy.
   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendations
There are no quality trials of topical creams for cervicothoracic pain. Capsicum compounds have evidence of efficacy in quality studies in the low back, although they do not appear particularly potent. There are no studies of long-term chronic use, thus no information about long-term efficacy or dermal or other toxicity (see Low Back Disorders guideline).

Evidence for the Use of Capsaicin
There is 1 low-quality RCT in Appendix 1.(716)

Capsaicin (Capsicum) – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: capsicin, capsicum, sports creams, other creams and ointments neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed, we found and reviewed 58 articles, and considered 3 for inclusion. In Scopus, we found and reviewed 54 articles, and considered zero for inclusion. In CINAHL, we found and reviewed zero articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed zero articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 3 articles considered for inclusion, 1 randomized trials and 2 systematic studies met the inclusion criteria.*

LIDOCAINE PATCHES
Topical lidocaine patches have been increasingly used to treat numerous pain conditions ranging from to carpal tunnel syndrome (CTS) to postherpetic neuralgia.(717, 718)

Recommendation: Lidocaine Patches for Acute, Subacute, Chronic or Postoperative Cervical and Thoracic Pain
Lidocaine patches are not recommended for treatment of acute, subacute, chronic or postoperative cervical and thoracic pain.
Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There is one trial on treatment of trapezius pain suggesting possible modest short term benefits that did not last one month.(719) There is one trial failing to show benefit for treatment of low back pain.(720)

Evidence for the Use of Lidocaine Patches
There is 1 moderate-quality RCT incorporated into this analysis.(719)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Lidocaine patch/ Neck Pain, cervicalgia, cervical pain, cervical Radiculopathy, radicular pain, postoperative neck pain, postoperative cervical pain, herniated disk; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation,

random, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 8 articles in PubMed, 48 in Scopus, 0 in CINAHL, 8 in Cochrane Library. We considered for inclusion 8 from PubMed, 48 from Scopus, 0 from CINAHL, 8 from Cochrane Library and 0 from other sources. Of the 64 articles considered for inclusion, 1 randomized trial and 0 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Lin 2012 RCT No COI. Sponsorship, Ptus Pharmaceuticals Ltd provided placebo patches.	5.5	N = 60 with myofascial pain syndrome of the upper trapezius. Mean±SD age: 35.78±11.61 years.	5% Lidocaine patches (n = 31) vs. Placebo patches matched vehicle patch from Lotus Pharma) (n = 29). Follow-up 12 hours, 1 and 3 weeks after removal of final patch on day 7.	Verbal Rating Scale (VRS) on day 14: lidocaine vs. placebo: 1.06±0.79 vs. 1.50±0.76, p = 0.03. VRS not significantly different after 28 days (p = 0.22).	"The application of 5% lidocaine patch for 7 days provides at least 7 days of improvement in pain and in associated neck disability after termination of intervention in patients with MPS of the upper trapezius."	Some baseline differences in pain duration which could impact results. Study suggests lidocaine patches may reduce upper trapezius pain when compared to placebo for at least 14 days.

COLCHICINE

Colchicine is a drug that inhibits microtubule formation. Its primary use is in the treatment of acute attacks of gout. Because of its anti-inflammatory properties, it has been used for several decades to treat pain.(721, 722) Thiocolchicoside is a muscle relaxant derived from colchicoside.(723, 724)

1. *Recommendation: Oral and IV Colchicine for Acute, Subacute, or Chronic Cervicothoracic Pain*
   Oral and IV colchicine are not recommended for acute, subacute, or chronic cervicothoracic pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

2. *Recommendation: Thiocolchicoside for Acute, Subacute, or Chronic Cervicothoracic Pain*
   There is no recommendation for or against the use of thiocolchicoside for acute, subacute, or chronic cervicothoracic pain.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendation

There are no quality trials for cervicothoracic pain disorders. There are conflicting studies on the value of colchicine for treatment of low back pain and no studies suggesting prolonged benefits.(721, 722, 724-726) Colchicine and thiocolchicoside are not invasive or minimally invasive depending on formulation, have considerable adverse effects, and are low to moderate in cost. In the absence of quality evidence, suggested recommendations for the cervicothoracic spine reflect those for the lumbosacral spine (see Low Back Disorders guideline).

Evidence for the Use of Oral and IV Colchicines

There are no quality studies incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Neck Pain, cervicalgia, cervical Pain, cervical radiculopathy, radicular pain, postoperative neck pain, postoperative cervical pain, herniated disk, cervicalgia, neck pain, cervical pain, cervical radiculopathy, radicular pain, herniated disk, postoperative neck pain, postoperative cervical pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 714 articles, and considered 0 for inclusion. In Scopus, we found and reviewed 0 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 0*

articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 220 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 0 articles considered for inclusion, 0 randomized trials and 0 systematic studies met the inclusion criteria.

SYSTEMIC GLUCOCORTICOSTEROIDS (AKA "Steroids")

Glucocorticosteroids are used to treat herniated discs primarily through local injections (e.g., epidural glucocorticosteroid injections). It is theorized that these medications reduce localized inflammation and swelling, although they appear to have some capacity to reduce pain. As an alternative to the invasiveness of an injection, pulses of oral glucocorticosteroids or parenteral injections have been used to treat these patients. These medications have also been utilized for treatment of cervical pain, whiplash, and other spine pain (727) (see Low Back Disorders guideline).

1. *Recommendation: Systemic Glucocorticosteroids for Acute Severe Radicular Pain Syndromes*
   Systemic glucocorticosteroids are recommended for treatment of acute and subacute radicular pain.(728, 729) (Finckh 06; Goldberg 15)

   Indications – Acute, moderate to severe radicular pain thought to be due to a herniated intervertebral disc.

   Frequency/Dose – Dosing recommendation is from the highest quality study for lumbar radiculopathy and is Prednisone 60 mg for 5 days, then 40 mg for 5 days, and then 20 mg for 5 days for a combined cumulative dose of 600mg over 15 days.(729)
   Benefits – Modest short-term reduction in acute and subacute radicular pain compared with placebo and moderately improved long term function.
   Harms – Insomnia, Headache, joint pain, nervousness, indigestion, sweating.(729) Cumulative steroid doses over time associated with adverse effects including worse glucose control, hypertension, osteoporosis, fractures, osteonecrosis, gastrointestinal bleeding, and infections.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence - Moderate

2. Recommendation: Glucocorticosteroids for Acute, Subacute, Chronic or Postoperative Cervical or Thoracic Pain

Glucocorticosteroids are moderately not recommended for treatment of acute, subacute, chronic or postoperative cervical or thoracic.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence - Moderate

Rationale for Recommendation
Glucocorticosteroids to treat radicular pain syndromes have been particularly assessed in quality studies of the lumbar spine (see Low Back Disorders guideline). The highest quality studies have the best definitions of patients and provided better assurance the diagnosis was sciatica/radiculopathy. The highest quality study(729) showed benefits with functional improvement at one year. The next strongest study also showed treatment benefit. Two lower quality negative studies,(730, 731) have less clear case definitions, yet one study suggested a trend towards efficacy among patients with a positive straight-leg raising test.(730) One study that assessed this intervention for treatment of LBP without radicular pain was negative.(732)

Systemic glucocorticosteroids are either minimally invasive or not invasive depending on the route of administration. The highest quality study documents intermediate to long-term improvements in subjective function (ODI) when treating radiculopathy.(729) Adverse effects are mostly manageable for a single short course, yet adverse effects may include avascular necrosis and diabetic patients may have worsened glucose control while using glucocorticoids. It is low cost. By analogy to the lumbar spine, glucocorticosteroids are recommended for management of acute and subacute cervical radicular pain syndromes thought to be due to a herniated intervertebral disc. Glucocorticosteroids are not recommended for management of acute, subacute, chronic and postoperative spine pain.

Evidence for the Use of Glucocorticosteroids
There is 1 high-quality RCT incorporated into this analysis.(728)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: epidural injection, glucocorticoid, steroid injection, dexamethasone, betamethasone, methylprednisolone, triamcinolone, neck pain, cervicalgia, cervical pain, cervical radiculopathy, radicular pain, postoperative neck pain, postoperative cervical pain, herniated disk, controlled clinical trial, controlled trails, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 148 articles and considered 20 for inclusion. In Scopus, we found and reviewed 620 articles and considered 2 for inclusion. In CINAHL we found and reviewed 8 articles and considered 1 for inclusion. In Cochrane Library we found and reviewed 5 articles and considered 0 for inclusion. We also considered for inclusion 2 articles from other sources. Of the 25 articles considered for inclusion, 14 randomized trials and 8 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Finckh 2006 RCT No sponsorship and no mention of COI.	9.0	N = 60 with acute sciatica (6 week duration) of radiologically confirmed discogenic origin, mean age 49.0 in glucocorticoid group and 45.5 in placebo group.	Glucocorticoid or IV bolus of 500mg methylprednisolone group (n = 31) vs. Placebo (saline) as an adjuvant to standard care (including NSAIDs and physical therapy) (n = 29). Follow-up for 30 days.	Significantly less pain Days 1 to 2. At Day 30, statistics not presented, but appear to show significant benefit from glucocorticosteroid group. Single IV pulse of glucocorticoids found to provide small and transient improvement in sciatic leg pain and no effect on functioning or objective signs or radicular irritation.	"Although an IV bolus of glucocorticoids provides a short-term improvement in leg pain in patients with acute discogenic sciatica, its effects are transient and have small magnitude."	Patients had pain radiating below knee, positive straight leg raise or neurologic deficit, and a positive, corroborative MRI or CT. May be relevant that there was a trend towards more neurologic deficits in glucocorticosteroid group (52% vs 34%).

2. *Recommendation: Glucocorticosteroids for Acute Whiplash Associated Injury*
   Glucocorticosteroids are recommended for acute whiplash injury Grades II and III.

   Indications – Acute whiplash injury, within the first 8 hours after injury in whiplash Grades II and III. (Grade II includes cervical pain and musculoskeletal signs, Grade III includes neurologic signs such as decreased or absent deep tendon reflexes, weakness, numbness or sensory deficits).

   Frequency/Dose – Single intravenous dose methylprednisolone (30mg/kg over 15 minutes) followed by 45 minute pause, then 23-hour infusion (5.4mg/kg per hour). Patients whose weight was less than 75kg were given half as much methylprednisolone.(727)

   Benefits – Modestly faster resolution of the pain.

   Harms – Anxiety, lack of sleep, worse glycemic control, infection. Cumulatively over time with subsequent doses, many other adverse effects including hypertension, adrenal insufficiency via suppression, osteoporosis.

   Strength of Evidence – **Recommended, Evidence (C)**
   Level of Confidence – Low
3. *Recommendation: Glucocorticosteroids for Acute, Subacute, or Chronic Cervicothoracic Pain*
   Glucocorticosteroids are not recommended for acute, subacute, or chronic cervicothoracic pain without radicular pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendations

There are no quality trials comparing systemic steroids (oral or IV or IM) to placebo for treatment of cervical radiculopathy. By analogy to lumbar radiculopathy, it is expected there is limited ability of oral steroids to briefly improve cervical radiculopathy(728) (see Low Back Disorders guideline). Thus, by inference from lumbar

radiculopathy, oral steroids are recommended for limited use in the treatment of radiculopathy patients who have inadequate pain management with NSAIDs and who decline epidural injection.

There is one high-quality, double-blinded, placebo-controlled trial assessing utility of IV methylprednisolone in acute Grade II and III whiplash patients and reported significant improvements at 6 months.(727) Improvements included less pain at 6 months, disability and sick leave. The trial did not address adverse effects and had variable dosing by weight, while not reporting baseline weights by groups, thus potentially lowering the study quality somewhat. Nevertheless, an evidence-based recommendation in favor of use for this limited patient population is supportable.

There are no quality studies evaluating oral glucocorticosteroids for acute, subacute, or chronic cervicothoracic pain with or without radiculopathy. However, there is quality evidence that these medications are ineffective for treatment of low back pain. (732) Thus, by inference, they are believed to be ineffective for cervical pain and are not recommended.

Systemic glucocorticosteroids are either minimally invasive or not invasive depending on the chosen route of administration. One study evaluated a dexamethasone tapered dose over 7 days. The regimen was initiated with 64mg on day one, 32mg on Day 2, 16mg on Day 3, 12mg on Day 4, and 8mg Days 5 to 7(730) (see Low Back Disorders guideline). NSAIDs are believed to be more efficacious and are generally preferable. Adverse effects include osteonecrosis (avascular necrosis), particularly from long-term administration, and diabetics will have worsened glucose control; thus, the benefits must be carefully weighed against these risks. These medications are low cost for oral administration, but may be moderate cost for parenteral routes. Thus, based on evidence of efficacy, there are limited indications for these medications.

Evidence for the Use of Glucocorticosteroids for Whiplash Associated Injury
There is 1 high-quality RCT incorporated into this analysis.(727)

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Pettersson 1998 RCT Double-blind No mention of sponsorship or COI.	8.0	N = 40 with whiplash injury, age range 19-65.	Methylprednisolone,with 20 sets of active substance, 30 mg/kg in 15 minute bolus and 5.4mg/kg every hour infusion (n = 20) vs. Placebo, 20 sets of placebo substance (n = 20). Follow-up for 6 months after initial treatment.	Significant difference in disabling symptoms at 6 months follow-up between actively treated patients and placebo group (p = 0.047), total number of sick days (p = 0.01), and sick-leave profile (p = 0.003).	"[A]cute treatment with high dose corticosteroids in patients with whiplash injury may be beneficial in preventing extensive sick leave after whiplash injury. However, the number of patients studied was small, and therefore further prospective controlled studies are needed."	Looked at psychological profiles of patients at baseline. Unsure of co-morbidities for each group. No adverse effects noted. No cost analysis. Used soft collar 1-2 weeks after injury in each group. Had physiotherapy and took analgesics. Rate of co-interventions not noted. Dose of methylprednisolone varied based on patient weight. IV methyl-prednisolone an option in acute whiplash associated disorder patients in ER or hospital setting.

TUMOR NECROSIS FACTOR-ALPHA INHIBITORS

See Low Back Pain Guideline.

SKELETAL MUSCLE RELAXANTS

Skeletal muscle relaxants comprise a diverse set of pharmaceuticals designed to produce "muscle relaxation" through different mechanisms of action – generally considered to be effects on the central nervous system (CNS) and not on skeletal muscle.(733, 734) Thus, whether or not these drugs have an analgesic effect, their mechanism of action is unknown. In addition, almost every drug in this category produces symptoms of CNS sedation or depression, thus significantly limiting their utility. The consequent limitations imposed are particularly pertinent for patients who operate motor vehicles, machinery, or are otherwise engaged in safety-sensitive positions (crane operators, scaffolding climbers, roofing, air traffic controllers, operators of motorized vehicles, construction workers, law enforcement officers, etc.). The sedation induced by these drugs may improve sleep patterns.

As these drugs produce CNS depression,(735) it may be unsurprising that there is a low but definite risk of abuse. The risk of abuse appears to be substantially lower than with narcotics. However, there are patients in whom abuse has been reported involving some if not all of these agents.(736, 737) Carisoprodol is more commonly abused, since one of its active metabolites is meprobamate.(736) Regardless, caution is recommended in prescribing these agents particularly when a patient has a history of substance abuse or requests specific medications.(738)

Perhaps due to the combination of lack of clear understanding of mechanism(s) of action, significant adverse CNS effects, and abuse potential, clinical guidelines regarding muscle relaxants vary across countries. However, new evidence may lead to stronger conclusions, enabling future guidelines to become more concordant.(739)

1. *Recommendation: Muscle Relaxants for Moderate to Severe Acute Cervicothoracic Pain*
   Muscle relaxants are recommended as a second-line treatment in cases of moderate to severe acute cervicothoracic pain that has not been adequately controlled by NSAIDs.

   Indications – Moderate to severe acute cervicothoracic pain; best in patients with clinically palpable muscle spasm, limited ROM, limitation of activities of daily living, and tenderness on palpation with symptoms less than 14 days.(672, 740-743) Caution should be used in prescribing skeletal muscle relaxants for those with a history of depression, personality disorder, and/or substance addiction/abuse (including alcohol or tobacco) as most of RCTs exclude participants with these co-morbidities.(672, 742-744)

   Frequency/Dose – Initial dose recommended nocturnally and not during workdays or when patients plan to operate motor vehicles. Daytime use is acceptable in circumstances where there are minimal CNS-sedating effects and little concern about sedation compromising function or safety. If significant daytime somnolence results, the medication may need to be discontinued, particularly if it interferes with performance of work, aerobic exercises, or other components of the rehabilitation plan. It is not recommended that the first dose be taken prior to starting a work shift or operating a motor vehicle or machinery. No significant improvement reported in symptoms between the 5mg and 10mg doses of cyclobenzaprine, but found increased somnolence with 10mg dose; patients taking 10mg dose had the highest incidence of premature discontinuation due to adverse effects.(744) If a muscle relaxant is felt to be necessary in patients with psychological issues noted above, cyclobenzaprine is recommend, as its chemical structure resembles a tricyclic anti-depressant, and addiction and abuse are less likely.[v]

   Indications for Discontinuation – Resolution of pain, non-tolerance, significant sedating effects that carry over into the daytime, or other adverse effects.
   Benefits – Modest reduction in acute cervicothoracic pain compared with placebo.
   Harms – Sedation, daytime fatigue. Modest potential for abuse. Risk for safety including motor vehicle crash and other injuries.

   Strength of Evidence – **Recommended, Evidence (C)**
   Level of Confidence – Moderate

2. *Recommendation: Muscle Relaxants for Mild to Moderate Acute Cervicothoracic Pain*
   Muscle relaxants are not recommended for mild to moderate acute cervicothoracic pain due to problems with adverse effects.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

[v]Baclofen and Tizanidine are reviewed in studies in the Low Back Disorders guideline. There are no quality trials found for cervical or thoracic spine disorders.

3. **Carisoprodol is not recommended for moderate to severe acute cervicothoracic pain that has not been adequately controlled by NSAIDs or for acute exacerbations of chronic pain, or acute post-surgical situations.**

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

4. *Recommendation: Muscle Relaxants for Acute Radicular Pain or Post-surgical Use*
   Muscle relaxants are recommended as second- or third-line agents for cases of acute severe radicular pain syndromes or in acute post-surgical patients.

   Indications – Moderate to severe radicular pain syndromes or post-surgical pain. In radiculopathy pain relief from "muscle relaxants" would presumably be from an analgesic effect and not from a "muscle relaxant" effect, since radicular pain by definition is neuropathic pain and not muscular pain. Generally, muscle relaxants should be prescribed nocturnally initially and not during workdays or when patients plan on operating motor vehicles. However, other agents may be more efficacious for relieving radicular pain, e.g., NSAIDs.

   Frequency/Dose – Initial dose to be administered in evening. Daytime use is acceptable in circumstances where there are minimal CNS-sedating effects. If significant daytime somnolence interferes with patients work activities, aerobic exercises, or other rehabilitation activities, then the medication may need to be discontinued.

   Indications for Discontinuation – Resolution of pain, non-tolerance, lack of efficacy, significant sedating effects that carry over into the daytime, or other adverse effects.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

5. *Recommendation: Muscle Relaxants for Subacute or Chronic Cervicothoracic Pain*
   Muscle relaxants are not recommended for subacute or chronic cervicothoracic pain as there is no evidence to support their use. Additionally, there are relatively high adverse effect profiles and possible abuse potential.

   Strength of Evidence **– Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendations
Skeletal muscle relaxants have been evaluated in quality studies, although the quality of studies comparing these agents to placebo are likely overstated due to the unblinding that would be inherent in taking a drug with substantial CNS-sedating effects. Nevertheless, there is quality evidence that skeletal muscle relaxants improve acute cervicothoracic pain, particularly for the first 4 to 7 days.(672, 741, 743, 745, 746) However, a concerning adverse event is the significant potential for CNS sedation which has typically affected between 25 to 50% of patients.(744, 745) Thus, it is recommended that the prescription of skeletal muscle relaxants for daytime use be carefully weighed against the need to drive vehicles, operate machinery, or otherwise engage in occupations where mistakes in judgment may have serious consequences. Skeletal muscle relaxants also have a modest, but significant, potential for abuse(747) and caution should be used when prescribing them for patients with a history of substance abuse or dependence.

Although the mechanism of action is unclear, skeletal muscle relaxants have demonstrated efficacy in acute cervicothoracic pain,(672, 740, 743, 744) have significant adverse effects, and are low cost, especially if generic medications are prescribed. Thus, skeletal muscle relaxants are recommended for select management of moderate to severe acute cervicothoracic pain. There is little evidence of muscle relaxant efficacy for treatment of chronic cervicothoracic pain. They are not recommended for continuous management of subacute or chronic cervicothoracic pain, although they may be recommended for brief management of acute exacerbations in the setting of chronic cervicothoracic pain. (748)

Diazepam appears inferior to skeletal muscle relaxants, (740, 742) has a higher incidence rate of adverse effects, and is addictive. Diazepam is not recommended for use as a skeletal muscle relaxant. Cyclobenzaprine has advantages of lower abuse potential and some chemical analogy to tricyclic anti-depressants.(749)

Evidence for the Use of Skeletal Muscle Relaxants

There are 2 high-(680, 750) and 12 moderate-quality(672, 740-745, 748, 749, 751-753) RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.(754) There is fair evidence that cyclobenzaprine, carisoprodol, orphenadrine, and tizanidine are effective compared to placebo in patients with musculoskeletal conditions (primarily acute back or neck pain).

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: muscle relaxants, baclofen, carisoprodol, chlorzoxazone, cyclobenzaprine, dantrolene, diazepam, metaxalone, methocarbamol, orphenadrine, tizanidine, neuromuscular blocking agents, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 1,227 articles, and considered one for inclusion. In Scopus, we found and reviewed 149 articles, and considered two for inclusion. In CINAHL, we found and reviewed zero articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 4 articles, and considered zero for inclusion. We also considered for inclusion 2 articles from other sources. Of the 17 articles considered for inclusion, 15 randomized trials and 2 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Payne 1964 RCT No mention of sponsorship or COI.	9.0	N = 54 with musculoskeletal or MSD complaints referable to cervical, dorsal, and brachial regions, mean age males 49.0 (27-66), average age females 49.6 (19-77).	Phrase 1; placebo, meprobamate 40 mg, diazepam 5 mg, or 2 days on each (n = 47) vs. Phrase 2; placebo, meprobamate 40 mg, diazepam 5 mg, 5 days on each (n = 24). Follow-up for 6 days in Phase 1, and 15-day study for the Phase II.	Diazepam and meprobamate had better or improved sleep rates compared to placebo, ($p < 0.01$). In Phase 1 and Phase 2, no differences between 2 phases among 3 medications for alleviation of pain or morning stiffness.	"The present study indicates that patient response to meprobamate and diazepam in the treatment of these conditions on gross clinical observation is qualitatively similar."	All took all medications for 2 days in Phase I, and 5 days in Phase II. No differences in pain or morning stiffness. Sleep better on active drugs than placebo. Unsure how long they had pain or exact etiology. No mention of previous therapies.
Khwaja 2010 RCT No mention of sponsorship. No COI.	8.0	N = 61 admitted to ER within 24 hours of motor vehicle accident or fall, reporting neck pain; mean age 34	Ibuprofen 800mg and inactive placebo tablet, 3x a day (n = 20) vs. Inactive placebo tablet, Cyclobenzaprine 5mg, 3x a day (n = 21) vs. Ibuprofen 800mg and cyclobenzaprine 5mg, 3x a day (n = 20). Treatment for 7 days or until pain relief adequate.	No significant differences to report between groups, ($p = 0.17$).	"The addition of cyclobenzaprine to ibuprofen in the treatment of ED patients with acute cervical strains resulting from MVCs or falls does not appear to result in more effective pain relief or faster resumption of normal daily activities."	Pain scores improved in all groups but little is any difference between all groups with more side effects in combination treatment of ibuprofen and cyclobenzaprine.
Basmajian 1978 RCT Double-blind No mention of sponsorship or COI.	6.5	N = 105 in Study I and 50 in the Study II with spasms and pain in neck and low back for at least 30 days, age distribution was not described.	Study 1: Cyclobenzaprine 10mg, 1 tablet 3x daily, maximum 6 tablets per day (n = 34) vs. Diazepam, 5mg, 1 tablet 3x daily, maximum of 6 a day (n = 36) vs. placebo, inert tablets (n = unknown). Study 2: Cyclobenzaprine 10mg, 1 tablet 3x daily, maximum 5 tablets per day (n = 27) vs. Placebo same appearance as treatment tablet, 3x daily, maximum 5 tablets (n = 28). Follow-up 2 weeks.	Included 2 studies. End of Week 1 EMG mean values: Cyclobenzaprine % change 140%, ($p < 0.05$). Placebo -4.8% NS, Diazepam 45.5% NS. End of Week 2 EMG mean values: Cylcobenzaprine % change 178.4%, ($p < 0.01$), placebo -5.5% NS, diazepam 81.0% NS.	"[In] the study of chronic neck spasms where cyclobenzaprine was significantly more effective clinically. At an average dose of 30mg per day it was well-tolerated without clinically significant adverse reactions."	By combining 2 studies in 1 report, neither is well described.
Basmajian 1983 RCT	6.5	N = 40 with reflex cervical muscle spasms, age range 19-55 years.	Diazepam, 5mg (n = 14) vs. Sodium Phenobarbital, 30mg (n = 14) vs. Placebo (n = 12). All participants received	In all 3 treatment groups, no trend seen in pain or active motion and palpation. All 3 groups had similar mean outcomes.	"Although this controlled double-blind study failed to reveal clinically significant differences, diazepam compared to phenobarbital	Therapy done for 3 days. No good description of blinding of assessors in paper. No description of how long patients had

Sponsored by Department of Medical Research. No mention of COI.			initial intramuscular (IM) dose followed by oral drug: baseline evaluation, 1ml IM dose, 2 tablets by mouth at 10pm day 1; 1 tablet in morning and 1 in evening on days 2 and 3; 1 tablet in morning and final recordings. Sstudy completed after 4 days.		and a placebo was shown to have a statistically significant desirable effect on the neuromotor reflex cervical muscle spasms."	neck pain or any specific diagnosis or mechanism of injury. No functional significance found in study.
Malanga 2009 RCT Sponsored by ECR Pharmaceuticals, Richmond, VA, USA, and Cephalon, Inc. No mention of COI.	6.5	Study 1: n = 156,254; Study 2: n = 217,450; muscle spasm associated with acute, painful musculoskeletal conditions; mean age 42.7 (13.6) for placebo, 39.6 (13.8) for CER 15mg, 42.3 (13.1) for CER 30mg, 40.3 (12.2) for CER 10mg (study 1); mean age 40.6 (12.3) for placebo	Study 1: Placebo (n = 38) vs CER 15mg, 1x daily (n = 45) vs. CER 30mg, 1x daily (n = 42) vs. CIR 10mg, 3x daily (n = 31). Study 2: Placebo (n = 45) vs. CER 15mg, 1x daily (n = 44) vs. CER 30mg, 1x daily (n = 41) vs. CIR 10mg, 3 times daily (n = 44).	More patients reported good to excellent for medication helpfulness in both CER groups compared to placebo at Day 4. In Study 1 it was significant, (p = 0.007) for CER 30mg vs placebo. In Study 2, also significant, (p = 0.018) for CER 15mg vs placebo. In Study 1, improvements with CER 30mg vs placebo for relief of local pain on Day 8, (p = 0.010).	"After 4 days of treatment, once-daily CER 15 (study 2) and 30 mg (study 1) were effective for the treatment of muscle spasm associated with acute, painful musculoskeletal conditions."	Looked at both back and neck pain. Duration of pain at start of study was 7 days or less. Treatment for 14 days. Excluded acute trauma patients and patients with history of substance abuse and patients in workers' comp or litigation. CER dose given at night. There was a large placebo response, no effect seen on physician rated outcomes.
Borenstein 2003 RCT Sponsored by Merck & Co. Inc. No mention of COI.	6.0	Study 1: n = 737; Study 2: n = 668; with acute musculoskeletal spasm. Study 2: mean age 43.6 for Cyc 2.5mg, 42.6 for Cyc 5mg, and 41.5 for placebo; study 1: mean age 42.3 for cyc 5mg, 41.5 for cyc 10mg, 42.3 for placebo.	Study 1: Cyclobenzaprine, 5mg (n = 242) vs Cyclobenzaprine10mg (n = 249) (2.5/5mg TID) Vs. Placebo (n = 246) Study 2: Cyc 2.5mg (n = 223) vs Cyc 5mg (n = 222) vs. Placebo (n = 223). 7 day treatment period.	A moderate-quality report of 2 RCTs (score = 6.0/11) compared cyclobenzaprine hydrochloride (5mg/10mg TID) with a placebo in Study 1 (N = 737), and in Study 2, cyclobenzaprine (2.5/5mg TID) with placebo for 668 patients with LBP (1/3 having neck pain). 372 Dropouts in Study 1 were 27.3% placebo, 28.6% 5mg, and 44.2% 10mg. In Study 2, dropouts 37.5% placebo, 35.7% 5mg, and 26.8% 10mg.	"Cyclobenzaprine 2.5 mg TID was not statistically more effective than placebo."	While the authors conclude the 2.5mg dose is not efficacious, both data and graphs do not support that conclusion and suggest clinical results for that dosing regimen are likely intermediate between placebo and 5mg dosing regimens and they lacked power to detect differences.
Brown 1978 RCT No mention of sponsorship or COI.	5.5	N = 49 with long-term intractable pain of cervical and lumbar origin aggravated by skeletal muscle spasm and	Diazepam, 2 tables of 5mg TID, plust placebo (n = 16) vs. Cyclobenzaprine hydrochloride, one tablet of 10mg TID, plus placebo (n = 16) vs.	Compared diazepam (5mg TID) with cyclobenzaprine (10mg TID) with placebo for 49 patients with long-term intractable pain of cervical and lumbar origin. Global improvements (marked/moderate): 11/16 (68.8%) cyclobenzaprine vs 8/16	Authors found cyclobenzaprine to be an effective skeletal muscle relaxant that did not possess anti-depressant actions in animals and humans.	All study measures subjective. Patients were chronic pain patients referred to a pain clinic for treatment. Half of placebo group had at least slight improvement in pain. All participants had

		tenderness, age not given.	placebo, 10mg (n = 17). 2-week trial period.	(50%) diazepam vs 5/17 (29.4%) placebo.		2 weeks of physical therapy.
Tisdale 1975 RCT No mention of sponsorship or COI.	5.5	N = 180 with muscle spasm and pain associated with acute musculoskeletal disorders of traumatic or inflammatory etiology; mean 39.2 for Methocarbamol, and 35.9 for placebo.	Methocarbamol 500mg q.i.d. (n = 90) vs. placebo for 7-9 days (n = 90). Follow up 48 hours and after 7 to 9 days.	After 48 hours, methocarbamol had an advantage over placebo for all severity degrees of muscle spasm very severe, ($p < 0.005$). Methocarbamol superior for returning to normal daily activities and overcoming limitation of motion.	"Methocarbamol was shown to be highly effective in reducing muscle spasm and pain in acute musculoskeletal disorders secondary to trauma and inflammation."	Duration of pain <14 days, encompassed all MSK disorders from various types of injuries. Follow-up at 48 hours and 7-9 days, medication lasted 7-8 days. No mention of side effects. Difficult to assess which patients may truly benefit.
Bouchier-Hayes 1984 RCT No mention of sponsorship or COI.	5.0	N = 49 with LBP and wry neck; mean age 30.68 (12.49) for Chlormezanone, and 30.08 (9.31) for placebo.	Chlormezanone 3 times a day (20 tablets total 200 mg each) (n = unknown) vs. an identical appearing placebo (n = unknown) for 6 days. 6 day treatment period.	Throughout 6-day treatment course, chlormezanone group reported less pain (graphic form). Percent of soldiers returning to full duty within 4 days: placebo 0% vs chlormezanone 30.4%.	As study is among soldiers, it is not clear if this includes delayed onset muscle soreness which is believed to be a completely different diagnostic entity with a different clinical course.	Five days of treatment. Study group otherwise healthy soldiers with acute low back and neck pain. Chlormezanone widely discontinued in 1996 due to adverse effect of toxic epidermal necrolysis; not a viable treatment option today.
Childers 2005 RCT Sponsored by McNeil Consumer & Specialty Pharmaceuticals. No mention of COI.	5.0	N = 772 with acute neck or back pain with muscle spasm; mean age for CYC 5 42.7 (12.7), 41.3 (12.5) for CYC5/IBU400, and 40.1 (12.4) for CYC5/IBU800.	Low dose cyclobenzaprine (5mg TID) (n = 256) vs. cyclobenzaprine and low dose ibuprofen (5mg/400mg TID) (n = 257) vs. cyclobenzaprine and high dose ibuprofen (5mg/800mg TID) (n = 259). Follow up at baseline, days 3 and 7.	In patients with combined neck/back pain, no statistically significant differences in primary endpoint (7-day PGIC) among groups after 7 days of treatment; no differences detected in 3-day PGIC. No statistically significant difference among treatments in 7-day PGIC in patients with neck pain only (CYC5, 3.0±1.0; CYC5/ IBU400, 3.1±0.9; CYC5/IBU800, 3.0 ± 0.9) or back pain only (3.0 ± 1.0, 3.1 ± 0.9, 2.9 ± 1.0). Mean PGIC significantly different from "no change" after 3 and 7 days of therapy in all 3 treatment groups, ($p < 0.001$). All 3 groups had significant improvements from baseline after 3 and 7 days of therapy in patient-rated spasm and pain. Mean percent ODI scores improved from baseline to after 3 days and improved from baseline to after 7 days in all 3 groups, (p	Combination therapy with low dose cyclobenzaprine (5mg TID) and ibuprofen (400mg TID or 800mg TID) is not superior to low dose cyclobenzaprine alone in adult patients with acute neck and back pain with muscle spasm, and combination therapy was well tolerated.	Weaknesses of an open-label trial are balanced by a large study population and a major research question of different regimens that is not usually addressed in RCTs. Pain duration <14 days. No physician follow-up visits done after baseline. No discussion of some baseline characteristics, such as obesity or mechanism of injury.

				<0.001) for all comparisons. Within each treatment group, statistically significant improvement in ratings of medication helpfulness from Day 3to 7, (p <0.001).		
Bercel 1977 RCT No mention of sponsorship or COI.	4.5	N = 54 with signs and symptoms of moderate to severe chronic muscle spasm secondary to osteoarthritis of cervical or lumbar spine; age range of 21-69.	Cyclobenzaprin, 10mg TID (n = 27) vs. placebo, three-to-four-day placebo washout period (n = 27). Follow-up at weeks 1, 2, and 3.	More patients in the marked or moderate improvement categories taking cyclobenzaprine (13/27 vs 8/27). Also differences in muscle spasm and local pain.	"Cyclobenzaprine was superior to placebo in providing relief for the primary symptom of muscle spasm and the concomitant symptoms of pain, limitation of motion, and limitation of activities of daily living."	Lack of study details including no baseline characteristics of participants makes indications for treatment difficult. After 1 week of no medication, no differences between groups. For patients with spinal OA duration >30 days, cyclobenzaprine 30mg a day reported to improve clinical outcomes, but only while taking medication.
Miller 1976 RCT No mention of sponsorship or COI.	4.5	N = 50 with MSDs, of the neck and trunk; age range 13 to 64 years.	Parafon forte, 4x daily (n = 25) vs. Soma compound, 2 tablets, 4x daily (n = 25). Follow up at baseline, days 2 and 5.	Parafon Forte superior in terms of pain, spasm, limitation of motion, total symptomatology, (p <0.05). Global evaluations show Parafon Forte superior to Soma compound on Day 2 and final day, (p <0.05).	"The results of the comparative study proved on the basis of well-defined objective measurements and precisely characterized subjective rating, the superiority of Parafon Forte for the relief of painful musculoskeletal disorders."	All MSK pain included in study. Parafon Forte is Chlorzoxazone with acetaminophen. Differences between groups in types of pain. Monitored for side effects as a primary outcome measure. Treatment for 5 days.
Bose 1999 RCT Sponsored by Eisai Asia Regional Services, Singapore, and Eisai Co. Ltd., Tokyo, Japan. No mention of COI.	4.0	N = 215 with cervical spondylosis; mean age 45.3 (10.1) for Eperisone, and 44.7 (11.8) for placebo.	Eperisone 50 mg (n = 75) vs. placebo for 6 weeks (n = 82). Follow up at baseline, weeks 1, 3 and 6.	Nuchal region pain improvement significantly better with eperisone at Week 6, (p < 0.005). ROM improved with eperisone at end of 3 weeks of treatment.	"[T]his clinical trial in patients with cervical spondylosis confirms the usefulness of eperisone by primarily reducing pain and improving range of motion of the neck."	Patients diagnosed with cervical spondylosis. Treatment for 6 weeks. Unknown duration of symptoms. There was a large improvement in placebo group as well.
Weil 2010 RCT Sponsored by ECR Pharmaceuticals, Richmond, VA, Cephalon, Inc. Frazer, PA provided medication. Weil disclosed conflict of	4.0	N = 330 with muscle spasm of cervical/lumbar region ≤7 days duration, with local pain, tenderness; mean age for 15mg 38.6; mean age for 30mg 39.9, mean	Cyclobenzaprine extended-release (CER) 15mg: once daily (n = 127) vs. CER 30mg: once daily (n = 126) vs. Cyclobenzaprine immediate release (CIR) 10mg: 3 times daily (n = 123) vs. Placebo (n = 128). Patients required to	Primary Measures: N (%) for Medication helpfulness (5-point scale): CER 15mg vs. CER 30mg vs. placebo: day 4: good to excellent: 65 (51.2) vs. 68 (54.0) vs 46 (35.9), (p <0.025); Secondary Measures: relief of pain: CER 30mg vs. placebo: day 4: 74 (58.3) vs 60 (46.9), p <0.025; Medication helpfulness:	"[T]hese results suggest that the efficacy of cyclobenzaprine, traditionally dosed up to 3 times daily for the treatment of acute muscle spasm, can be achieved through once-daily dosing with an extended release formulation. Cyclobenzaprine extended release was	Short follow-up time (14 D), pooled analysis of 2 studies.

interest with Alpharma, Cephalon, Inc, Ferring Pharmaceuticals, King Pharmaceuticals and Xanodyne Pharmaceuticals; Ruoff disclosed conflict of interest with Abbot Laboratories, Cephalon, Inc., GlaxoSmithKline, Merck and CO., Inc., and Takeda Pharmaceuticals North America, Inc.; and Taylor disclosed conflict of interest with Cephalon, Inc.		age for 10mg 40.7; mean age for placebo 41.6.	take 1 capsule orally 3x a day for 14 days: 1 capsule between 6 AM and 7 AM, 1 between 12 PM and 1 PM, and 1 between 6 PM and 7 PM). Follow-up days 4, 8, and 14.	good to excellent: CER 30mg vs. placebo: day 8: 78 (61.9) vs 61 (47.7), p <0.025; day 14: CER 15mg vs. CER 30mg vs. placebo: 85 (66.9) vs. 88 (69.8) vs 66 (51.6), p <0.025; relief of pain: CER 15mg vs. CER 30mg vs. placebo: day 8: 95 (74.8 vs 93 (73.8) vs. 76 (59.4), (p <0.025).	generally well tolerated and patients receiving CER experienced a lower rate of reported somnolence than patients receiving CIR."	

OPIOIDS – Oral, Transdermal, and Parenteral (Includes Tramadol)
Opioids are addressed in a separate guideline. The treatment recommendations are summarized below. See the Opioids guideline for all supporting evidence.

Acute Pain (Up to 4 Weeks)

1. Recommendation: Routine Use of Opioids for Treatment of Non-Severe Acute Pain
Routine opioid use is strongly not recommended for treatment of non-severe acute pain (e.g., low back pain, sprains, or minor injury without signs of tissue damage).
Harms – May inadequately treat acute, severe pain.
Benefits – Faster recovery, less debility, reduced accidents risks, risks of dependency or addiction.
Strength of Evidence – **Strongly Not Recommended, Evidence (A)**
Level of Confidence – High

2. Recommendation: Opioids for Treatment of Acute, Severe Pain
Opioids are recommended for treatment of acute, severe pain (e.g., crush injuries, large burns, severe fractures, injury with significant tissue damage) uncontrolled by other agents and/or with functional deficits caused by pain. They also may be indicated at the initial visit for a brief course for anticipated pain accompanying severe injuries (i.e., failure of other treatment is not mandatory). A Schedule IV[vi] opioid may be indicated if there is true allergy to NSAIDs and acetaminophen, other contraindication to an alternative medication, or insufficient pain relief with an alternative. Recommend to taper off opioid use in 1 to 2 weeks.

Indications **–** Patients should meet all of the following:
1) Severe injury with a clear rationale for use (objective functional limitations due to pain resulting from the medical problem, e.g., extensive trauma such as forearm crush injury, large burns, severe radiculopathy).[vii]
2) Other more efficacious treatments should have been instituted,[viii] and either:
   2a) failed and/or
   2b) have reasonable expectations of the immediate need for an opioid to obtain sleep the evening after the injury.
3) Where available, prescription databases (usually referred to as Prescription Drug Monitoring Program (PDMP)) should be checked and not show evidence for conflicting opioid prescriptions from other providers or evidence of misreporting.[ix]
4) Non-opioid prescriptions (e.g., NSAIDs, acetaminophen) absent contraindication(s) should nearly always be the primary treatment and accompany an opioid prescription.
5) Low-dose opioids may be needed in the elderly who have greater susceptibility to the adverse risks of opioids. Those of lower body weight may also require lower opioid doses.
6) Dispensing quantities should be only what is needed to treat the pain. Short-acting opioids are recommended for treatment of acute pain. Long-acting opioids are not recommended.
7) Due to greater than 10-fold elevated risks of adverse effects and death, considerable caution is warranted among those using other sedating medications and substances including: i) benzodiazepines; ii) anti-histamines (H_1-blockers); and/or iii) illicit substances.(457, 755-757) Patients should not receive opioids if they use illicit substances unless there is objective evidence of significant trauma or moderate to severe injuries. Considerable caution is also warranted among those who are unemployed as the reported risks of death are also greater than 10-fold.(457, 756) Due to elevated risk of death and adverse effects, caution is also warranted when considering prescribing an opioid for patients with any of the following characteristics: depression, anxiety, personality disorder, untreated sleep disorders, substance abuse history, current alcohol use or current tobacco use, attention deficit hyperactivity disorder (ADHD), post-traumatic

[vi]USA classifies controlled substances that includes a classification system, ranging from Class 1 to Class V corresponding to lower risks of abuse and dependence. Class I includes substances with a high potential for abuse and without a recognized medical use (e.g., heroin, marijuana, LSD). Class II includes most opiates, amphetamines and cocaine. Class III includes buprenorphine, dihydrocodeine, hydrocodone/codeine when compounded with an NSAID, Marinol. Class IV includes tramadol (in some states), carisoprodol, benzodiazepines, and long-activing barbiturates. Class V includes small amounts of codeine (e.g, 30mg, 60mg).
[vii]Other indications beyond the scope of this guideline include acute myocardial infarction or agitation interfering with acute trauma management.
[viii]Treatments to have tried generally include NSAIDs and acetaminophen. For LBP patients, additional considerations include muscle relaxants, progressive aerobic exercise, and directional exercise.
[ix]Exceptions such as acute, severe trauma should be documented.

stress disorder (PTSD), suicidal risk, impulse control problems, thought disorders, psychotropic medication use, chronic obstructive pulmonary disease (COPD), asthma, or recurrent pneumonia.(756, 758-779) Considerable caution is also warranted among those with other comorbidities such as chronic hepatitis and/or cirrhosis,(780) as well as coronary artery disease, dysrhythmias, cerebrovascular disease, orthostatic hypotension, asthma, recurrent pneumonia, thermoregulatory problems, advanced age (especially with mentation issues, fall risk, debility), osteopenia, osteoporosis, water retention, renal failure, severe obesity, testosterone deficiency, erectile dysfunction, abdominal pain, gastroparesis, constipation, prostatic hypertrophy, oligomenorrhea, pregnancy, human immunodeficiency virus (HIV), ineffective birth control, herpes, allodynia, dementia, cognitive dysfunction and impairment, gait problems, tremor, concentration problems, insomnia, coordination problems, and slow reaction time. There are considerable drug-drug interactions that have been reported (see Appendices 2-3 of the Opioids guideline).

Frequency/Duration – Generally, opioids should be prescribed at night or while not working.(781) Lowest effective, short-acting opioid doses are preferable as they tend to have the better safety profiles, less risk of escalation,(782) less risk of lost time from work,(783) and faster return to work.(784) Short-acting opioids are recommended for treatment of acute pain and long-acting opioids are not recommended. Recommend opioid use as required by pain, rather than in regularly scheduled dosing. If parenteral administration is required, ketorolac has demonstrated superior efficacy compared with opioids for acute severe pain,(785, 786) although ketorolac's risk profile may limit use for some patients. Parenteral opioid administration outside of obvious acute trauma or surgical emergency conditions is almost never required, and requests for such treatment are clinically viewed as red flags for potential substance abuse.
Indications for Discontinuation – Resolution of pain, sufficient improvement in pain, intolerance or adverse effects, non-compliance, surreptitious medication use, consumption of medications or substances advised to not take concomitantly (e.g., sedating medications, alcohol, benzodiazepines), or use beyond 2 weeks.
Harms – Adverse effects are many (see section below on "Opioids Benefits and Harms").
Benefits – Improved short-term pain control.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – High

3. Recommendation: Screening Patients Prior to Initiation of Opioids
Initial screening of patients is recommended with more detailed screening for: i) requiring continuation of opioids beyond 2 weeks for those with an acute severe injury, and ii) at consideration of initiation for severe pain but no objective evidence. Screening should include history(ies) of depression, anxiety, personality disorder, other psychiatric disorder, substance abuse, sedating medication use (e.g., anti-histamine/anti-H_1 blocker(756)), benzodiazepine use, opioid dependence, alcohol abuse, current tobacco use, other substance use history, COPD, PTSD, other psychotropic medications, (severe) obesity, cognitive impairment, balance problems/fall risk, osteoporosis, and renal failure (see Appendix 1 of the Opioids guideline). Those who screen positive, especially to multiple criteria, are recommended to: i) undergo greater scrutiny for appropriateness of opioids (may include psychological evaluation); ii) consideration of consultation and examination(s) for complicating conditions and/or appropriateness of opioids; and iii) if opioids are prescribed, more frequent assessments for compliance, achievement of functional gains,(457, 459, 787) adverse effects, and symptoms and signs of aberrancy.
Harms – Negligible. If a consultation is needed, there are additional costs that are incurred.
Benefits – Improved identification of more appropriate candidates for opioids. Identification of patients at increased risk of adverse effects. In cases where someone has elevated, but potentially acceptable risk, may alert the provider to improve surveillance for complications and aberrant behaviors.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – High

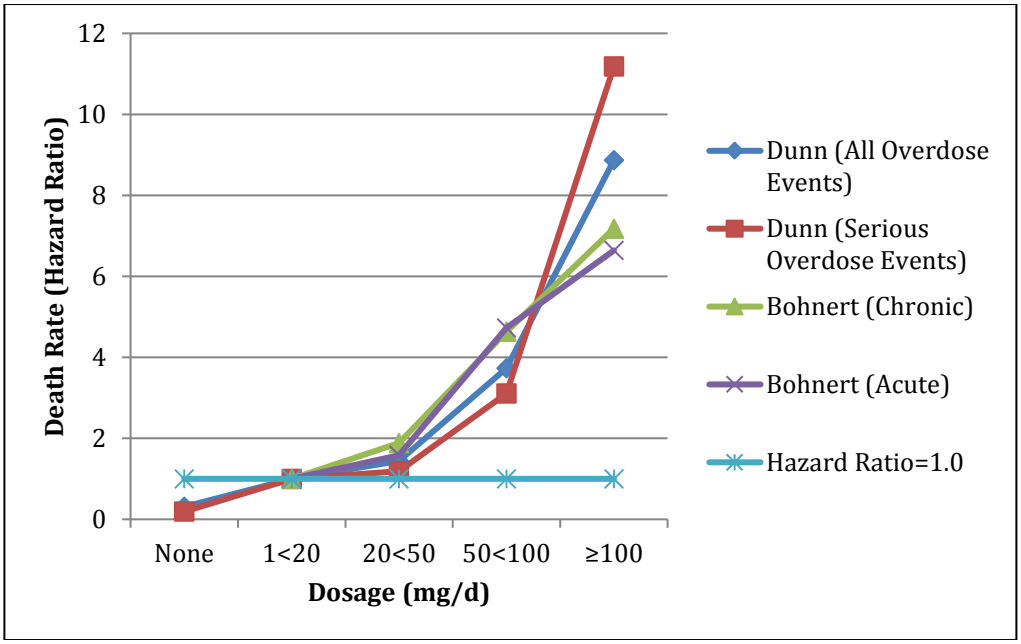
4. Recommendation: Opioid Dose Limits in Acute Pain
Dispense only that which is required. The maximum daily oral dose recommended for opioid-naïve, acute pain patients based on risk of overdose/death is 50mg morphine equivalent dose (MED)[x](788) (see Figure 2). In rare cases with documented functional improvement (see Appendix 1 of the Opioids guideline), higher doses may be considered, however, risks are substantially higher and greater monitoring is also recommended (see

[x]Statistical significance present for acute and chronic pain at and above 50mg per day of oral morphine equivalent dose.

Subacute/Chronic Opioid recommendations below). Lower doses should be used for patients at higher risk of dependency, addiction and other adverse effects. Monitoring is also recommended and consultation may be considered for those patients on higher doses.
Harms – Theoretical potential to undertreat pain in some patients with increased pain sensitivity.
Benefits – Reduced risk for adverse physical and cognitive effects, dependency, addiction and opioid-related overdoses and deaths.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – Moderate

Figure 2. Death Rate (Hazard Ratio) vs. Morphine Equivalent Dosage (mg/d)*



Adapted from Dunn 2010 and Bohnert 2011.
*Statistical significance present for acute and chronic pain at and above 50 mg per day of oral morphine equivalent dose.

Post-Operative Pain (Up to 4 Weeks) (After 4 weeks, see Subacute Pain)
Oral opioids are commonly prescribed after sinus surgery,(789) (Church 06) major noncardiac surgical procedures,(790) mastectomy and immediate breast reconstruction (IBR),(791, 792) coronary artery bypass graft surgery,(793) major abdominal surgery (abdominal laparoscopic, abdominal hysterectomy, bowel resection or radical hysterectomy),(794-797) orthopedic surgery,(798) and molar extraction.(799)

1. Recommendation: Limited Use of Opioids for Post-operative Pain
Limited use of opioids is recommended for post-operative pain management as adjunctive therapy to more effective treatments.
Indications – For post-operative pain management, a brief prescription of short-acting opioids as adjunct to more efficacious treatments (especially Cox-2 NSAIDs such as celecoxib, non-selective NSAIDs after risk of bleeding is no longer a concern).[xi] A brief course of opioids is often needed for minor surgical procedures. However, minor wound laceration repairs often require no opioids. Evidence suggests perioperative pregabalin for 14 days and/or continuous femoral nerve catheter analgesia instead of solely using oral opioids results in superior knee arthroplasty functional outcomes with less venous thromboses.(800) Additional considerations include:

1) Non-opioid prescriptions (e.g., NSAIDs, acetaminophen) should nearly always be the primary treatment and accompany an opioid prescription. Computerized programs may also assist in optimal management.(801)

[xi]More efficacious treatments also include therapeutic exercises, e.g., progressive ambulation especially for moderate to extensive procedures (e.g., arthroplasty, fusion).

2) The lowest effective dose of a short-acting opioid should be used,(782) as well as weaker opioids if possible.(783, 784)
3) Short-acting opioids are recommended for treatment of acute pain.
4) Dispensing should be only what is needed to treat the pain.[xii]
5) Long-acting opioids are not recommended.
6) Low-dose opioids may be needed in the elderly who have greater susceptibility to the adverse risks of opioids. Those of lower body weight may also require lower opioid doses.
7) Where available, prescription databases (usually referred to as Prescription Drug Monitoring Program (PDMP)) should be checked for other opioid prescriptions. Due to greater than 10-fold elevated risks of adverse effects and death, considerable caution is warranted among those using other sedating medications and substances including: i) benzodiazepines, ii) anti-histamines (H_1-blockers), and/or iii) illicit substances.(457, 755-757) Patients should not receive opioids if they use illicit substances unless there is objective evidence of significant trauma or moderate to severe injuries. Considerable caution is also warranted among those who are unemployed as the reported risks of death are also greater than 10-fold.(457, 756)

   Due to elevated risk of death and adverse effects, caution is also warranted when considering prescribing an opioid for patients with any of the following characteristics: depression, anxiety, personality disorder, ADHD, PTSD, suicidal risk, impulse control problems, thought disorders, psychotropic medication use, substance abuse history, current alcohol use or current tobacco use, untreated sleep disorders, COPD, asthma, or recurrent pneumonia.(756, 758-779) Considerable caution is also warranted among those with other comorbidities such as chronic hepatitis and/or cirrhosis,(780) as well as coronary artery disease, dysrhythmias, cerebrovascular disease, orthostatic hypotension, thermoregulatory problems, advanced age (especially with mentation issues, fall risk, debility), osteopenia, osteoporosis, water retention, renal failure, severe obesity, testosterone deficiency, erectile dysfunction, abdominal pain, gastroparesis, constipation, prostatic hypertrophy, oligomenorrhea, pregnancy, HIV, ineffective birth control, herpes, allodynia, dementia, cognitive dysfunction and impairment, gait problems, tremor, concentration problems, insomnia, coordination problems, and slow reaction time. There are considerable drug-drug interactions that have been reported (see Appendices 2-3 of the Opioids guideline).

   Inpatient management may moderate these recommendations provided there is careful monitoring, although these same management issues then apply post-discharge.
8) For patients taking opioids chronically prior to surgery, consultations with anesthesiology and/or pain management are generally needed as post-operative dosing may be very high and management is often quite challenging.
9) Ongoing prescriptions of opioids after the immediate post-operative period should generally be for patients who have undergone a major surgery or have other condition(s) necessitating opioids. Most patients should be making progress towards functional restoration, pain reduction and weaning off the opioids. Patients who have not progressed should be carefully evaluated for physical complications or psychiatric comorbidity, adherence to active treatments, and pending development of addiction or dependency.

Frequency/Duration – For moderate and major surgeries, opioids are generally needed on a scheduled basis in the immediate post-operative period. Other post-operative situations may be sufficiently managed with an as needed opioid prescription schedule. Provision of opioids sufficient to participate in therapeutic exercise (e.g., progressive ambulation) and allow sleep may be needed. However, high dose use at night is not recommended due to respiratory depression and disruption of sleep architecture. Weaning should begin as soon as function is recovering and pain is subsiding. Subsequent weaning to as needed opioid use is recommended.

Indications for Discontinuation – The physician should discontinue the use of opioids based on sufficient recovery, expected resolution of pain, lack of efficacy, intolerance or adverse effects, non-compliance, surreptitious medication use, self-escalation of dose, or use beyond 3 to 5 days for minor procedures, and 2 to 3 weeks for moderate/less extensive procedures. Use for up to 3 months may occasionally be necessary during recovery from more extensive surgical procedures (e.g., spine fusion surgery). However, with rare exceptions, only nocturnal use

[xii] Generally, this should be sufficient to cover two weeks of treatment. Prescriptions of 90-day supplies in the post-operative setting are not recommended.

is recommended in months 2 to 3 plus institution of management as discussed in the subacute/chronic guidelines below. For those requiring opioid use beyond 1 month, the subacute/chronic opioid use recommendations below apply.
Harms – Adverse effects are many (see section on "Opioids Benefits and Harms").
Benefits – Improved short-term, post-operative pain control. Some studies suggest this may modestly improve functional outcomes in the post-operative population.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – High

2. Recommendation: Screening Patients Prior to Continuation of Opioids
Screening of patients is recommended for patients requiring continuation of opioids beyond the second post-operative week. Screening should include history(ies) of: depression, anxiety, personality disorder, pain disorder, other psychiatric disorder, substance abuse history, sedating medication use (e.g., anti-histamine/anti-H_1 blocker), benzodiazepine use, opioid dependence, alcohol abuse, current tobacco use, and other substance use history, COPD, PTSD, other psychotropic medications, (severe) obesity, cognitive impairment, balance problems/fall risk, osteoporosis, and renal failure (see Appendix 1 of the Opioids guideline). Those who screen positive, especially to multiple criteria, are recommended to: i) undergo greater scrutiny for appropriateness of opioids (e.g., may include psychological and/or pain evaluation); ii) compliance with active therapies (e.g., ambulation and other exercise after arthroplasty); iii) consider consultation examination(s) for complicating conditions and/or appropriateness of opioids; and iv) if ongoing opioids are prescribed, ensure more frequent assessments for treatment compliance, achievement of functional gains,(457, 459, 787) and symptoms and signs of aberrancy.
Harms – Negligible. If a consultation is needed, there are additional costs that are incurred.
Benefits – Identification of patients at increased risk of adverse effects. Improved identification of more appropriate and safe candidates for opioids compared with attempting post-operative pain control with non-opioids. This should reduce adverse effects. In cases where someone has elevated, but potentially acceptable risk, this may alert the provider to improve surveillance for complications and aberrant behaviors.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – High

3. Recommendation: Opioid Dose Limits in Post-operative Pain
The maximum daily oral dose recommended for opioid-naïve, acute pain patients based on risk of overdose/death is 50mg morphine equivalent dose (MED)[xiii](788) (see Figure 2). Post-operative patients particularly require individualization due to factors such as the severity of the operative procedure, response to treatment(s) and variability in response. Higher doses beyond 50mg MED may be particularly needed for major surgeries in the first two post-operative weeks to achieve sufficient pain relief, however, greater caution and monitoring are warranted and reductions below 50mg MED at the earliest opportunity should be sought. Lower doses should be used for patients at higher risk of dependency, addiction and other adverse effects. In rare cases with documented functional improvement, ongoing use of higher doses may be considered, however, risks are substantially higher and greater monitoring is also recommended (see Subacute/Chronic Opioid recommendations).
Harms – Theoretical potential to undertreat pain, which could modestly delay functional recovery.
Benefits – Reduced risk for adverse effects, dependency, addiction and opioid-related deaths.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Subacute (1-3 Months) and Chronic Pain (>3 Months)

1. *Recommendation: Routine Use of Opioids for Subacute and Chronic Non-malignant Pain*
   Opioid use is moderately not recommended for treatment of subacute and chronic non-malignant pain. Opioid prescription should be patient specific and limited to cases in which other treatments are insufficient and criteria for opioid use are met (see below).
   Harms – May inadequately treat severe subacute or chronic pain.
   Benefits – Less debility, fewer adverse effects, reduced accident risks, lower risks of dependency, addiction, overdoses, and deaths.

[xiii]Statistical significance present for acute and chronic pain at and above 50 mg per day of morphine equivalent dose.

Strength of Evidence – **Moderately Not Recommended, Evidence (B)**
Level of Confidence – High

2. *Recommendation: Opioids for Treatment of Subacute or Chronic Severe Pain*
The use of an opioid trial is recommended if other evidence-based approaches for functional restorative pain therapy have been used with inadequate improvement in function.(802, 803) **Opioids are then recommended for treatment of function impaired by subacute or chronic severe pain (e.g., inability to work due to any of the following: chronic severe radiculopathy, chronic severe peripheral neuropathies, complex regional pain syndrome (CRPS), and severe arthroses)** (459) **(see Appendix 1 of the Opioids guideline).**

Indications – Patients should meet all of the following:
1) Reduced function is attributable to the pain. Pain or pain scales alone are insufficient reasons.(456-462, 804-810)
2) A severe disorder warranting potential opioid treatment is present [e.g., CRPS, severe radiculopathy, advanced degenerative joint disease (DJD)].(805)
3) Other more efficacious treatments have been documented to have failed.(805) Other approaches that should have been first utilized include physical restorative approaches, behavioral interventions, self-applied modalities, non-opioid medications (including NSAIDs, acetaminophen, topical agents, norepinephrine adrenergic reuptake blocking antidepressants or dual reuptake inhibitors; also antiepileptic medications particularly for neuropathic pain) and functional restoration. For LBP patients, this also includes[xiv] fear avoidant belief training and ongoing progressive aerobic exercise, and strengthening exercises. For CRPS patients, this includes progressive strengthening exercise. For DJD, this includes NSAIDs, weight loss, aerobic and strengthening exercises.
4) An ongoing active exercise program is prescribed and complied with.
5) Non-opioid prescriptions (e.g., NSAIDs, acetaminophen) absent a contraindication should nearly always be the primary pain medication and accompany an opioid prescription. Other medications to consider include topical agents, norepinephrine adrenergic reuptake blocking antidepressants or dual reuptake inhibitors; also antiepileptic medications particularly for neuropathic pain).
6) The lowest effective dose should be used.(782) Weaker opioids should be used whenever possible.(783, 784) Meperidine is not recommended for chronic pain due to bioaccumulation and adverse effects.
7) Low-dose opioids may be needed in the elderly who have greater susceptibility to the adverse risks of opioids. Those of lower body weight may also require lower opioid doses.
8) Dispensing should be only what is needed to treat the pain.[xv]
9) Extended-release/long-acting opioids are recommended to be used on a scheduled basis, rather than as needed.(805) As needed opioids should generally be avoided for treatment of chronic pain, although limited use for an acute painful event (e.g., fracture, sprain) is reasonable. Sublingual fentanyl is not recommended for treatment of subacute or chronic pain. Caution is warranted with fentanyl patches due to unpredictable absorption.
10) Where available, prescription databases (usually referred to as Prescription Drug Monitoring Program or PDMP) should be checked for conflicting opioid prescriptions from other providers or evidence of misreporting.
11) Due to greater than 10-fold elevated risks of adverse effects and death, considerable caution is warranted among those using other sedating medications and substances including: i) benzodiazepines; ii) anti-histamines (H_1-blockers); and/or iii) illicit substances.(457, 755-757) Patients should not receive opioids if they use illicit substances unless there is objective evidence of significant trauma or moderate to severe injuries. Considerable caution is also warranted among those who are unemployed as the reported risks of death are also greater than 10-fold.(457, 756)

[xiv]A previous trial of a muscle relaxant is generally recommended. However, if an opioid trial is contemplated, cessation of all depressant medications including muscle relaxants is advisable.
[xv]Generally, this should be sufficient to cover one week of treatment at a time during the trial phase. If a trial is successful at improving function, prescriptions for up to 90-day supplies are recommended.

Due to elevated risk of death and adverse effects, caution is also warranted when considering prescribing an opioid for patients with any of the following characteristics: depression, anxiety, personality disorder, untreated sleep disorders, substance abuse history, current alcohol use or current tobacco use, ADHD, PTSD, suicidal risk, impulse control problems, thought disorders, psychotropic medication use, COPD, asthma, recurrent pneumonia.(756, 758-779) Considerable caution is also warranted among those with other comorbidities such as chronic hepatitis and/or cirrhosis,(780) as well as coronary artery disease, dysrhythmias, cerebrovascular disease, orthostatic hypotension, asthma, recurrent pneumonia, thermoregulatory problems, advanced age (especially with mentation issues, fall risk, debility), osteopenia, osteoporosis, water retention, renal failure, severe obesity, testosterone deficiency, erectile dysfunction, abdominal pain, gastroparesis, constipation, prostatic hypertrophy, oligomenorrhea, pregnancy, HIV, ineffective birth control, herpes, allodynia, dementia, cognitive dysfunction and impairment, gait problems, tremor, concentration problems, insomnia, coordination problems, and slow reaction time. There are considerable drug-drug interactions that have been reported (see Appendices 2-3 of the Opioids guideline).

Frequency/Duration – Opioids use is generally initiated as a "trial" to ascertain whether the selected opioid produces functional improvement (see Appendix 1 of the Opioids guideline). Opioid use is generally prescribed on a regular basis,(811) at night or when not at work.(781) Only one opioid is recommended to be prescribed in a trial. More than one opioid should rarely be used. Lower opioid doses are preferable as they tend to have the better safety profiles, less risk of dose escalation,(782) less work loss,(783) and faster return to work.(784) Patients should have ongoing visits to monitor efficacy, adverse effects, compliance and surreptitious medication use. Opioid prescriptions should be shorter rather than longer duration.(812)
Indications for Discontinuation – Opioids should be discontinued based on lack of functional benefit(803) (see Appendix 1), resolution of pain, improvement to the point of not requiring opioids, intolerance or adverse effects, non-compliance, surreptitious medication use, medication misuse (including self-escalation and sharing medication), aberrant drug screening results, diversion, consumption of medications or substances advised to not take concomitantly (e.g., sedating medications, alcohol, benzodiazepines).
Harms – Adverse effects are many (see section on "Opioids Benefits and Harms"). May initiate path to opioid dependency.
Benefits – Improved short-term pain ratings. Theoretical potential to improve short-term function impaired by a painful condition.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

3. Recommendation: Screening Patients Prior to Initiation of Opioids

Screening of patients is recommended prior to consideration of initiating a trial of opioids for treatment of subacute or chronic pain. Screening should include history(ies) of depression, anxiety, personality disorder and personality profile,(784, 813, 814) other psychiatric disorder, substance abuse history, sedating medication use (e.g., anti-histamine/anti-H_1 blocker),(767) benzodiazepine use, opioid dependence, alcohol abuse, current tobacco use, and other substance use history, COPD, PTSD, other psychotropic medications, (severe) obesity, cognitive impairment, balance problems/fall risk, osteoporosis, and renal failure (see Appendix 1 of the Opioids guideline). Those who screen positive, especially to multiple criteria, are recommended to: i) undergo greater scrutiny for appropriateness of opioids (may include psychological and/or psychiatric evaluation(s) to help assure opioids are not being used instead of appropriate mental health care); ii) consideration of consultation and examination(s) for complicating conditions and/or appropriateness of opioids; and iii) if opioids are prescribed, more frequent assessments for compliance, achievement of functional gains and symptoms and signs of aberrant use.
Harms – Negligible. If a consultation is needed, there are additional costs that are incurred.
Benefits – Identification of patients at increased risk of adverse effects. Improved identification of more appropriate and safe candidates for treatment with opioids. This should reduce adverse effects. In cases where someone has elevated, but potentially acceptable risk, this may alert the provider to improve surveillance for complications and aberrant behaviors.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – High

4. Recommendation: Opioid Dose Limits in Subacute and Chronic Pain

The maximum daily oral dose recommended for subacute or chronic pain patients based on risk of overdose/death is 50 mg Morphine Equivalent Dose (MED).(760, 788) In rare cases with documented functional improvements occurring with use above 50mg MED, subsequent doses up to 100mg may be considered, however, risks of death are much greater and more intensive monitoring is then also recommended. Lower doses should be considered in high risk patients. Caution appears warranted in all patients as there is evidence the risk of dose escalation is present even among patients enrolled in a "hold the line (Stable Dose) prescribing strategy" treatment arm.(815) For those whose daily consumption is more than 50mg MED, greater monitoring is recommended to include: i) at least monthly to not more than quarterly appointments with greater frequencies during trial, dose adjustments and with greater co-morbid risk factors and conditions; ii) at least semiannual attempts to wean below 50 mg MED if not off the opioid; iii) at least semiannual documentation of persistence of functional benefit, iv) at least quarterly urine drug screening (see drug screening section); and v) at least semiannual review of medications, particularly to assure no sedating medication use (e.g., benzodiazepine, sedating anti-histamines).

Harms – None in a short-term trial. For chronic pain patients, theoretical potential to undertreat pain and thus impair function. However, there is no quality literature currently available to support that position.

Benefits – Reduced risk for adverse effects, dependency, addiction, and opioid-related deaths.

Strength of Evidence – **Recommended, Evidence (C)**

Level of Confidence – High

5. Recommendation: Use of an Opioid Treatment Agreement (Opioid Contract, Doctor/Patient Agreement, Informed Consent)

The use of an opioid treatment agreement (opioid contract, doctor/patient agreement, or informed consent) is recommended to document patient understanding, acknowledgement of potential adverse effects, and agreement with the expectations of opioid use (see Appendix 1 of the Opioids guideline). (802, 816-827) **If consent obtained, it is recommended appropriate family members be involved in this agreement.**

Harms – Negligible.

Benefits – Educates the patient and significant others that these medications are high risk, with numerous adverse effects. It allows for a more informed choice. It provides a framework for initiation of a trial, monitoring, treatment goals, compliance requirement, treatment expectations, and conditions for opioid cessation. It should reduce risk of adverse events and opioid-related deaths, although that remains unproven to date.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**

Level of Confidence – Moderate

6. Recommendation: Urine Drug Screening

Baseline and random urine drug screening, qualitative and quantitative, is recommended for patients prescribed opioids for the treatment of subacute or chronic pain to evaluate presence or absence of the drug, its metabolites, and other substance(s) use. In certain situations, other screenings (e.g., hair particularly for information regarding remote use(828-833) **or blood (for acute toxicity) may be appropriate.**

Indications – All patients on opioids for subacute or chronic pain.

Frequency – Screening is recommended at baseline, randomly at least twice and up to 4 times a year and at termination. More intensive screening is recommended for those consuming more than 50mg MED (see above). Federal guidelines recommend at least 8 tests a year among those utilizing opioid treatment programs.(834) Screening should also be performed "for cause" (e.g., provider suspicion of substance misuse including over-sedating, drug intoxication, motor vehicle crash, other accidents and injuries, driving while intoxicated, premature prescription renewals, self-directed dose changes, lost or stolen prescriptions, using more than one provider for prescriptions, non-pain use of medication, using alcohol for pain treatment or excessive alcohol use, missed appointments, hoarding of medications, and selling medications). Standard urine drug/toxicology screening processes should be followed (consult a qualified medical review officer).(835-837) If there is an aberrant drug screen result (either positive for unexpected drugs or unexpected metabolites or unexpectedly negative results), there should be a careful evaluation of whether there is a plausible explanation (e.g., drug not tested, drug metabolite not tested, laboratory cutpoint and dosing interval would not capture the drug/metabolite, laboratory error). In the absence of a plausible explanation, those patients with aberrant test results should have the opioid discontinued or weaned.(803)

Harms – No adverse clinical effects if properly interpreted.
Benefits – Identifies aberrant medication(s) and substance(s) use. Such uses are high-risk for opioid events including fatalities (see tables below). It provides objective evidence to cease an opioid trial or ongoing treatment. Identifies patients who may be diverting medication (those screening negative for prescribed medication).

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – High

Evidence for the Use of Opioids
There are 3 high-(674, 838, 839) and 2 moderate-quality RCTs(671, 840) incorporated into this analysis. There is 1 other study in Appendix 1.(841) See also the Opioids guideline.

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Lemming 2005 RCT No mention of industry sponsorship or COIs.	10.0	N = 33 whiplash associated disorder Grade II in chronic stage	Morphine (0.3mg/kg) vs. lidocaine (5mg/kg) vs. ketamine (0.3mg/kg) vs placebo (isotonic saline) for 30 minutes for each drug.	No significant differences among groups for VAS scores 5 days before and 5 days after testing. The 3 drugs showed significant decreases in pain intensities and unpleasantness after start of infusion, p values: 0.001-0.044.	"This study clearly indicates heterogeneity in responses to different pharmacological challenges among individuals with chronic whiplash-associated pain."	Chronic WAD II patients average 26 months of pain. Assessments up to 120 minutes with 30-minute infusion time of medication. No further evaluations done. Group of "global nonresponders" 33% of study group. Not a clinically viable option as no evidence of long-term benefit, high cost with short duration of pain relief.
Clark 2007 RCT Partially supported by Children's Hospital of E. Ontario Research Institute grant and salary support from same. No COIs disclosed.	9.5	N = 300 children with pain from acute musculoskeletal injuries	Acetaminophen vs ibuprofen vs codeine as a single dose.	Not until after 60 minutes that patients in ibuprofen group showed significantly greater improvement compared to codeine and acetaminophen groups for pain score, (p <0.001). No difference between codeine and acetaminophen for changes in pain scores. No difference in patients requiring more analgesic, (p = 0.32).	"[A]mong children with pain from acute musculoskeletal injuries presenting to a pediatric ED, a single dose of ibuprofen provides greater pain relief than codeine or acetaminophen."	Single dose treatment evaluated 60 minutes after treatment. No good delineation of which injuries responded better to which medications. Fractures of extremities also included in analysis.
Lemming 2007 Crossover trial No mention of industry sponsorship or COIs.	8.0	N = 20 chronic whiplash associated pain (WAD)	Placebo/placebo vs placebo/ remifentanil vs ketamine/ placebo vs ketamine/ remifentanil for 4 study sessions 1 week apart.	Pain intensity decreased over time with 3 groups that had active drugs. KET/REMI had most reduction of local pain, but KET/REMI and P/REMI reduced total pain equally.	"During these short-term infusions, adding ketamine to remifentanil enhanced the effects on chronic whiplash associated pain compared to the single drugs alone."	Excluded patients with history of drug abuse. Crossover design. Clinical feasibility is limited as these are both IV medications; no long-term follow up.
Ma 2008 RCT Supported by Shanghai Sixth People's Hospital Clinical Research grant. States no other COIs.	7.5	N = 116 chronic neck pain with acute pain episodes	Oxycodone (5-10mg and q12 hours a day) vs placebo (q12 hours a day) for 2-4 weeks.	Amount of acute pain flares, >3 times a day in Oxy-CR group decreased in Day 3 and 7 vs pre-treatment and placebo, (p <0.05); 20.7% had continued flare ups Day 7 and 21 followed by no complaints in Oxy-CR group, (p <0.01). VAS for OXY-CR lower than placebo, (p <0.05-0.01).	"Oxycodone controlled release could be an important optional drug for the management of refractory and frequent acute episodes of chronic neck pain in patients who failed to respond to non-opioid conservative treatment."	Chronic pain with acute flair. Diagnosed with spondylosis of neck. No clear diagnosis given for patients. Dosing for 2-4 weeks. Excluded any patients with alcohol or drug abuse. Assessment done up to 28 days. No long-term prescription or follow up.

Lovell 2004 RCT No mention of COI or sponsorship.	7.5	N = 51 acute musculoskeletal pain	Oral valdecoxib 40mg or oxycodone 10mg in combination with acetaminophen 650mg.	Mean pain (95%CI) at baseline/60 minutes comparing valdecoxib vs oxycodone: 81(75, 86)/47(37, 57) vs 75(69, 82)/51(42/60). Adverse events (%) sedation/dizziness: 15 vs 11, (p = 0.03). Nausea/dyspepsia: 3 vs 3, (p = 0.96).	"Valdecoxib is as effective as an oxycodone-acetaminophen combination in treating ED patients with acute musculoskeletal pain at 30 minutes and less likely to cause sedation or the need for rescue analgesia over the next day."	Blinding because of side effects. Idea of a rescue medication is knowing their medication status.

COMPLEMENTARY OR ALTERNATIVE METHODS OR DIETARY SUPPLEMENTS, ETC.
As cervicothoracic pain may last for extended periods of time, it is not surprising that many interventions have been attempted, including some that might be classified as herbal dietary supplements or as complementary or alternative treatments.(842-844) There are many other interventions shown to be efficacious for the treatment of acute, subacute, and chronic cervicothoracic pain, and it is strongly recommended that patients be treated with therapies proven to be efficacious for these conditions.

Recommendation: Complementary or Alternative Treatments or Dietary Supplements, etc., for Acute, Subacute, or Chronic Cervicothoracic Pain
There is no recommendation for or against use of willow bark (Salix), ginger extract, rose hips, camphora molmol, maleluca alternifolia, angelica sinensis, aloe vera, thymus officinalis, menthe peperita, arnica montana, curcuma longa, tancaetum parthenium, and zingiber officinicalis, avocado soybean unsaponifiables, oral enzymes, topical copper salicylate, S-Adenosylmethionine, and diacerein harpagoside for acute, subacute and chronic cervicothoracic pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There are no quality trials regarding complementary or alternative interventions or dietary supplements, etc. for cervicothoracic pain. Some have conflicting results – e.g., willow bark (Salix), rose hips, avocado soybean unsaponifiables, and ginger extract – for treatment of arthroses (see Hip and Groin Disorders guideline). These interventions are not proven efficacious for the treatment of acute, subacute, or chronic cervicothoracic pain or for radicular pain syndromes. There is strong evidence that harpagoside is effective in the treatment of low back pain (845, 846) (see Low Back Disorders guideline).

However, none of these agents has had a standardized dose, resulting in a lack of clarity of patient dosing. All of the studies comparing the agent to a standard NSAID dose for treatment of arthroses found the NSAID superior; only those with lower doses of NSAIDs sometimes found evidence suggesting equivalency (see Hip and Groin Disorders guideline). These agents are not invasive, have unclear adverse effect profiles and over time are moderate to high cost. There is no recommendation for or against use of these agents.

Evidence for the Use of Complementary or Alternative Medicine
There are no quality studies incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Complementary and alternative medicine, and (complementary or alternative methods or dietary supplements, Willow bark (Salix), ginger extract, rose hips, camphora, molmol, maleluca alternifolia, angelica sinensis, aloe vera, thymus officinalis, menthe, peperita, arnica montana, curcuma longa, tancaetum parthenium, and zingiber officinicalis, avocado, soybean unsaponifiables, oral enzymes, topical copper salicylate, S-Adenosylmethionine, and diacerein harpagoside), cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 1282 articles, and considered 1 for inclusion. In Scopus, we found and reviewed 302 articles, and considered 2 for inclusion. In CINAHL, we found and reviewed 4 articles, and considered 2 for inclusion. In Cochrane Library, we found and reviewed 0 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 5 articles considered for inclusion, 0 randomized trials and 5 systematic studies met the inclusion criteria.*

VITAMINS
Vitamins have been used to treat essentially all disorders. There has been particular interest in anti-oxidants; however, it should be noted that all anti-oxidants are simultaneously pro-oxidants,(847, 848) thus evidence of

potential harm from vitamins, particularly vitamins A, E, and most recently folate is accumulating.(849-853) There is poor evidence that vitamins or minerals have beneficial therapeutic effects in normal or over-nourished societies.

Recommendation: Vitamins for Acute, Subacute, Chronic, Post-Operative Cervicothoracic Pain or Radiculopathy
The use of vitamins for patients with acute, subacute, chronic, or post-operative cervicothoracic pain and for patients with radiculopathy is not recommended in the absence of documented deficiencies or other nutritional deficit states,

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There is no evidence of vitamin efficacy in cervicothoracic pain. There are also no quality RCTs published in English that provide evidence of vitamin efficacy for use in low back pain (see Low Back Disorders guideline).

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Vitamins, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 374 articles, and considered 0 for inclusion. In Scopus, we found and reviewed 241 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 40 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 0 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 0 articles considered for inclusion, 0 randomized trials and 0 systematic studies met the inclusion criteria.*

ALLIED HEALTH PROFESSIONALS, PHYSICAL AND OCCUPATIONAL THERAPY, CHIROPRACTIC, ETC.

As there is no single discipline that solely performs any specific treatment, there are generally no recommendations for or against treatment by or with particular discipline(s). Instead, there is detailed guidance for the interventions irrespective of the profession of the practitioner. However, a practitioner should be experienced in the specific treatment or test being administered.

Recommendation: Physical Therapy, Occupational Therapy or Other Professionals for Mild to Moderate Acute, Subacute, or Chronic Cervical and Thoracic Pain
One or two visits to physical therapy, occupational therapy, or other professionals to initiate and reinforce an exercise program are recommended for mild to moderate acute, subacute, or chronic cervical and thoracic pain.
Indications – Mild to moderate spine pain that is felt to be mostly manageable by self-care.
Frequency – One or two visits to initiate and then reinforce an exercise program especially for acute pain. A third appointment may be needed later for a final visit. More appointments may be indicated for establishment and engagement in an active exercise program (see Exercise Section). For subacute or chronic spine pain and/or more severely and/or debilitated patients may need 4 to 6 appointments to initiate and begin to reinforce an exercise program.
Benefits – Increased probability of engaging in an exercise program. Potential reinforcement with provider recommendations.
Harms – Medicalization, prolongation and increased risk of chronicity.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Evidence for the Use of Physical and Occupational Therapy
There are 13 moderate-quality RCTs incorporated into this analysis.(489, 499, 501, 565, 595, 854-861) There are 9 low-quality RCTs in Appendix 1.(495, 548, 579, 862-867)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: physical therapy, occupational therapy, physiotherapy, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed, we found and reviewed 1,030 articles, and considered 25 for inclusion. In Scopus, we found and reviewed 2,759 articles, and considered two for inclusion. In CINAHL, we found and reviewed 94 articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 21 articles, and considered zero for inclusion. We also considered for inclusion two articles from other sources. Of the 29 articles considered for inclusion, 22 randomized trials and 7 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Physiotherapy vs. Surgery						
Engquist 2013 RCT Sponsored by the Medical Research Council of Southeast Sweden. No mention of COI.	4.5	N = 68 age 18-65 years with cervical radiculopathy, pain in one or both arms, symptoms for 8 weeks to 5 years, and one or 3 symptomatic disc levels.	Physiotherapy alone – individualized 3 step program: step 1, neck-specific exercises and procedures for pain relief, step 2, general exercises, step 3, pain coping, self-efficacy training, and stress management; performed at home daily by patient and twice a week at the clinic for a minimum of 3 months (n = 32) vs. Anterior cervical decompression plus fusion (ACDF) combined with physiotherapy, which started 3 months after surgery and continued for a minimum of 3 months (surgery group, n = 31). Follow-up at 6, 12, and 24 months.	Neck disability index: NS between groups (p = 0.23) but both groups improved from baseline (p < 0.001). Pain intensity: significant difference between groups during study period (p = 0.039); both groups improved from baseline (p < 0.001). Arm pain intensity: NS between groups (p = 0.580) but both groups improved from baseline (p < 0.001).	"[I]t was shown that surgery with physiotherapy resulted in a more rapid improvement during the first postoperative year, with significantly greater improvement in neck pain and the patient's global assessment than physiotherapy alone, but the difference between the groups decreased after 2 years."	Five patients dropped out after randomization. Data results surgery plus PT trending toward superiority of PT alone.
Physical Therapy and Exercise vs. Minimal Intervention						
Walker 2008 RCT No COI or sponsorship.	6.5	N = 98 with primary complaints of neck pain with or without unilateral upper extremity symptoms, mean age 48.8(14.1) for MTE group, and 46.2(15.0) for MIN group.	Manual Physical Therapy and Exercise (MTE), 1 to 3 manual interventions; thrust and nonthrust joint mobilization muscle energy, stretching (n = 50) vs. Minimal Intervention (MIN), general practitioner care, posture advice, maintain neck motion (n = 48). Follow-up at 3 and 6 weeks, and 1 year.	Mean (95% CI) for NDI: MTE vs. MIN: baseline: 15.5 (13.9-17.1) vs. 17.0(15.5-18.6); 1 year: 5.5(3.4-7.7) vs. 10.6(8.5-12.7), (p = 0.01). Mean (95% CI) for VAS cervical pain score: MTE vs. MIN: baseline: 53.7(47.9-59.6) vs. 51.1(45.3-56.9); 1 year: 17.7(11.0-24.4) vs. 24.5(17.8-31.2), (p = 0.016). Mean (95% CI) for upper extremity VAS pain: MTE vs. MIN: baseline: 25.6(18.8-32.3) vs. 18.2(11.4-25.0); 1 year: 9.2(3.2-15.2) vs. 12.5(6.5-18.5), (p = 0.0371).	"An impairment-based MTE program resulted in clinically and statistically significant short- and long-term improvements in pain, disability, and patient perceived recovery in patients with mechanical neck pain when compared to a program comprising advice, a mobility exercise, and subtherapeutic ultrasound."	Data suggest manual therapy plus exercise is superior to manual therapy for treatment of crucial pain and disability.
Chiropractic vs. Physiotherapy						
Skargren 1997 RCT	4.0	N = 323 who attended a general practitioner for low back or neck	Chiropractic Group (n = 179) vs. Physiotherapy Group (n = 144). Follow-up at 6 months.	Number of participants (percentage of participants) for VAS pain scale: chiropractic vs.	"The effectiveness and total costs of chiropractic or physiotherapy as primary treatment were similar to	Primary outcome was costs. No difference between groups.

Sponsored by County Council of Östergötland and Federation of County Councils. No mention of COI.		problems, mean age 41.4±11.6 for chiropractic group, and 40.5±11.9 for physiotherapy group.		physiotherapy: 56(22) vs. 61(21), ($p \leq 0.05$).	reach the same result after treatment and after 6 months."	
Cream application plus physical therapy						
Sharan 2011 RCT COI, D. Sharan received a research grant and consulting fees from Cymbiotics, Inc.; J Bookout is employed as Vice President of Cymbiotics, Inc., and R Barathur is President of Cymbiotics. N mention of sponsorship.	5.5	N = 74 with myofascial pain syndrome (MPS) of the neck for at least 2 weeks duration with ≥ 2 trigger points (MTrPs) in any one or more of the following muscles: trapezius, sternocleidomastoid, anterior scalene, suboccipital or levator scapulae muscles, age range 19-51.	CFEC (8 cetylated fatty esters, 5.6% and 1.5% menthol), cream application plus physical therapy, (CF-PT) (n = 37) vs. Placebo cream application plus physical therapy, (PL-PT) (n = 35). Participants asked to apply medication liberally to affected area 2x a day. Physical Therapy: ischaemic compression (90-120 seconds), followed by deep pressure soft tissue massage to inactivate trigger points, myofascial release technique; 2 sessions per week, 45 minutes per session. Follow up at baseline, weeks 2 and 4.	Mean ± SD for Neck Disability (NDI): baseline vs. week 2: CF-PT: 38.4±11.7 vs. 27.4±6.3, p<0.001: baseline vs. week 4: 38.4±11.7 vs. 18.8±7.8, (p < 0.001). Mean ± SD for Neck Pain (NPD-VAS): CF-PT: baseline vs. week 2: 46.3±10.2 vs. 34.8±7.4, p = 0.003, baseline vs. week 4: 46.3±10.2 vs. 25.3±10.4, p<0.001; PL-PT: baseline vs. week 2: 47.3±7.3 vs. 43.2±5.5, p<0.001, baseline vs. week 4: 47.3±7.3 vs. 34.0±8.3, (p < 0.001).	"Our results indicate that cetylated derivatives of fatty acids can effectively reduce pain and symptoms associated with neck MPS, when combined with physical therapy."	Data suggest experimental treatment superior to placebo. Intervention of PT poorly described or tracked.
Surgery vs. Physiotherapy vs. Neck Collar						
Persson 2001 RCT Sponsored by Vårdal Foundation and Neurosurgery Institution Foundation. No mention of COI.	4.5	N = 81 with cervico-brachial pain of more than 3 months duration; age range 28-56 for surgery, 31-61 for physiotherapy, 36-64 for neck collar.	Surgery (n = 27) vs. Physiotherapy, extended over 3 months, 15 sessions, 1-2 sessions per week, 30-45 minutes N = 27) vs Neck Collar (n = 27). Follow up at before treatment (control 1), 14-16 weeks after treatment had begun (control 2), and after a further 12 months (control 3).	Mean ± SD for VAS pain intensity: before treatment: surgery vs. physiotherapy vs. neck collar: 27±23 vs. 41±26 vs. 48±23, p<0.01. Mean±SD for worst pain intensity last week VAS: before treatment: surgery vs. physiotherapy vs. neck collar: 43±36 vs. 51±29 vs. 64±22, p <0.001.	"We recommend a multidisciplinary rehabilitation with cognitive behavioural therapy and psychological interventions."	Minimal statistically significant differences between groups.
Exercise vs. Physiotherapy						
McLean 2013 RCT Supported by Arthritis Research UK and Hull and East Yorkshire Hospitals NHS Trust. No COI.	5.5	N = 151 with non-specific neck pain, mean age 54.2±13.8 for GET group and 53.5±15.1 for UP group.	Graded Exercise Treatment (GET), 12 sessions over 6 week period, 2 hour training sessions, range of movement exercises for neck and endurance training for upper limbs (n = 75) vs. Usual Physiotherapy, between 40 and 60 minutes, manual therapy, exercise, advice and education (UP) (n = 76).	Mean improvements seen in NPQ score between baseline,6 weeks, 6 months and 12 month follow up, no p-values to report.	"Both GET and UP are appropriate clinical interventions for patients with non-specific neck pain, however, preferences for treatment and targeted strategies to address barriers to adherence may need to be considered in order to maximize the	Unstructured intervention with wide variability in specific modalities used.

			Follow up at 6 weeks, 6 and 12 months.		effectiveness of these approaches."	
Usual Physiotherapy						
Klaber Moffett 2005 RCT Sponsored by Northern and Yorkshire R&D Executive and Trent Region NHS Executive. No COI.	4.5	N = 268 with subacute and chronic neck pain, mean age 48.8±16.56 for brief intervention and 47.8±16.62 for usual physical therapy.	Brief Intervention, physiotherapist guided role play, use of videotaped interviews, and discussion (n = 139) vs. Usual Physiotherapy (n = 129). Follow-up at 3 and 12 months.	Mean (95% Ci) for difference: Mental Health: 3 months: -4.677(-8.371 to 0.983), p = 0.0133; energy and fatigue: -4.548(-8.804 to -0.292, p = 0.0363; general health perception: -2.234(-3.729 to -0.739, p = 0.0036. 12 month follow up: role-physical: -6.701(-12.961 to -0.441), p = 0.0360; role-emotional: -11.715(-17.571 to -5.858), p = 0.0001; mental health: -9.362(-15.053 to 3.671), p = 0.0014; energy and fatigue: -9.241(-14.663 to -3.819), p = 0.0009; pain: -6.749(-13.18 to -0.380), p = 0.0379; general health perception: -8.146 (-12.347 to -3.946), (p = 0.0002).	"Usual physiotherapy may be only marginally better than a brief physiotherapy intervention for neck pain. Patients with a preference for the brief intervention may do at least as well with this approach. Additional training for the physiotherapists in cognitive behaviour techniques might improve this approach further."	Did not meet enrollment goals, however, statistically significant differences at 12 months.
Physical Therapy vs. Self-Management						
Jull 2007 RCT Sponsored by the Centre of National Research on Disability and Rehabilitation Medicine (CONROD). No mention of COI.	4.5	N = 71 with chronic whiplash disorders, mean age 40.9±11.9 for MPT and 38.4±10.4 for SMP.	Multimodal Physical Therapy Program (MTP), specific low load exercises, manipulative therapy, education and assurance (n = 36) vs. Self-Management Program (SMP), booklet on education on whiplash, assurance on recovery and stressed the need to stay active (n = 35). 10 week intervention.	Mean±SD for NPI: MPT vs. SMP: -10.4±14 vs. -4.6±8.8, (p = 0.04), in favor of MTP group.	"This study has shown that physical rehabilitation can produce clinically meaningful changes for patients with chronic whiplash associated disorders in at least the immediate post-treatment period. The effect in the long-term must now be examined."	Short follow up period (10 weeks). Variability in treatment modalities with each treatment arm.
Multimodal Rehabilitation vs. Usual Care						
Hoving 2006 Long term follow up of Hoving 2002 RCT Supported by the Netherlands Organization for Scientific Research	6.5	See Hoving 2002	See Hoving 2002	Mean (95% CI) for Difference MT-GP group: 13 weeks vs. 52 weeks: perceived recovery: 29.5 (12.9 to 46.1) vs. 15.4 (-1.3 to 32.1), p = 0.02; physical dysfunction: 1.6 (0.8 to 2.3 vs. 0.9(0.01 to 1.7), p = 0.000; pain intensity: 0.9(0.1 to 1.8 vs 0.5(-0.4 to 1.3), p = 0.01; NDI: 1.9 (-0.2 to 4.0) vs. -0.02 (-2.3 to 2.3), p = 0.06;	"In conclusion, this study shows that after MT had speeded up recovery in the short term, GP and PT treatment caught up in the long term, and differences between the three treatment groups at 12 months of follow-up were small and no longer statistically significant."	Short intervention period (6 weeks). Intervention includes mixed modalities that are not well described.

and from Fund for Investigative Medicine of the Health Insurance Council. No mention of COI.				PT-GP: perceived recovery: 17.1 (-.03 to 34.6) vs. 6.5 (-10.9 to 23.8), p = 0.02; physical dysfunction: 1.3 (0.5 to 2.1) vs. 0.3 (-0.6 to 1.1), p = 0.000; pain intensity: 0.6 (-0.3 to 1.5) vs. -0.6 (-1.4 to 0.3), p = 0.01; NDI: 0.9 (-1.2 to 3.0) vs. -1.1 (-3.4 to 1.2), p = 0.06; MT-PT: perceived recovery: 12.3 (-4.6 to 29.3) vs. 9.0 (-7.9 to 25.8), p = 0.02; physical dysfunction: 0.2 (-0.6 to 1.0) vs. 0.6 (-0.3 to 1.4), p = 0.000; pain intensity: 0.3 (-0.6 to 1.2) vs. 1.0(0.1 to 1.9) p = 0.01; NDI: 1.0(-1.1 to 3.2) vs. 1.1 (-1.3 to 3.4), p = 0.06.		
Manual Therapy vs. Physical Therapy vs. Continued Care						
Hoving 2002 RCT Supported by the Netherlands Organization for Scientific Research and from the Fund for Investigative Medicine of the Health Insurance Council. No mention of COI.	5.5	N = 183 suffering for at least 2 weeks from nonspecific neck pain, aged 18 to 70.	Manual Therapy (MT), mobilization or coordination or stabilization techniques, 6 treatment sessions (n = 58) vs. Physical Therapy (PT), individualized exercise therapy, including active, passive, postural, stretching, relaxation, and functional exercises, 12 treatment sessions (n = 59) vs. Continued Care by the General Practitioner (GP), counseling and advice, booklet containing advice, 2 10-minute follow up visits (n = 61). Follow up at baseline, 3, 7, 13, 26, 52 weeks.	Mean ± SD for improvement in pain severity: MT-GP: 1.4(0.4 to 2.4); PT-GP: 0.2(-0.9 to 1.2); MT-PT: 1.2(0.2 to 2.3), no p-values to report, but stated statistically significant in results in abstract.	In daily practice, manual therapy is a favorable treatment option for patients with neck pain compared with physical therapy or continued care by a general practitioner.	Multiple modes of therapy used, not well described or reproducible.
General Practitioner Care vs. Physiotherapy						
Scholten-Peeters 2006 RCT No sponsorship or COI.	7.0	N = 80 with acute WAD grade 1 or 2 result of road-traffic accident with symptoms like neck pain, headache, or dizziness within 48 hours after trauma, mean age 33.8±10.3 for GP care, and	General Practitioner Care (GP), education and advice, including advice on graded activity (n = 42) vs. Physiotherapy, education, advice, graded activity, and exercise therapy (n = 38). Follow-up at baseline, 8, 12, 26, and 52 weeks after trauma.	No statistically significant differences were found between the two groups in the primary outcomes.	"We found no significant differences for the primary outcome measures. Treatment by GPs and PTs were of similar effectiveness. The long-term effects of GP care seem to be better compared to physiotherapy for functional recovery, coping, and physical functioning."	Minimal difference between groups. Poorly described interventions. Mixed models of treatment.

		31.9±9.0 for physiotherapy.				
Gustavsson 2011 Two year follow up of Gustavsson 2010 RCT Supported by the Center for Clinical Research Dalarna, Landstinget Dalarna and Uppsala University, Sweden. No COI.	5.0	See Gustavsson 2010	See Gustavsson 2010	Mean ± SD for NDI: PASS vs. IAPT: baseline: 137.4±40 vs. 129.4±43.8, p = 0.001; 2-year follow up: 22.4±14.2 vs. 31.3±16.7, p = 0.001CSQ pain control: 3.3±1.1 vs. 3.1±1.2 vs. 3.9±1.2 vs. 3.6±1.2, p = 0.002; CSQ catastrophizing: baseline:11.3±7.4 vs. 11.8±7.1, p = 0.033; 2 year follow up: 7.2±7.3 vs. 10.3±8, p = 0.033 ability to reduce pain: baseline: 2.9±1 vs. 2.9±0.9, p = 0.015; 2 year follow up: 3.6±1 vs. 3.1±1, p = 0.015.	The initial treatment effects of a self-management group intervention were largely maintained over a 2-year follow-up period and with a tendency to have superior long-term effects as compared to individually-administered physical therapy, in the treatment of persistent tension–type neck pain with regard to coping with pain, in terms of pain control, self-efficacy, and catastrophizing.	Treatment not standardized. Interventions poorly described.
Self-Management Group vs. Physical Therapy						
Gustavsson 2010 RCT Supported by Center for Clinical Research Dalarna, Landstinget Dalarna and Uppsala University, Sweden. No mention of COI.	6.0	N = 156 with neck pain seeking physical therapy treatment, mean age 45.7±11.5 for PASS group, and 45.7±11.6 for IAPT group.	Multicomponent Pain and Stress Self-Management Group Intervention (PASS), 7 weekly group sessions of 1.5 hour each, relaxation training, body awareness exercises (n = 77) vs. Individually Administered Physical Therapy (IAPT) (n = 79). Follow-up at baseline, 10 and 20 weeks; 1 and 2 years.	Mean ± SD for NDI: PASS vs. IAPT: baseline: 30.8±10.7 vs. 35.4±14, p = 0.001; 20 weeks: 23.9±13.3 vs. 33.7±16.5, p = 0.001; CSQ ability to control pain: baseline: 3.3±1.1 vs. 3.1±1.2, p = 0.000; 20 weeks: 3.9±1.0 vs. 3.0±1.0, (p = 0.000).	PASS had a better effect than IAPT in the treatment of persistent musculoskeletal tension-type neck pain regarding coping with pain, in terms of patients' self-reported pain control, self-efficacy, disability and catastrophizing, over the 20-week follow-up.	Assessment by questionnaire only. Reasonably well described intervention. Minimal difference between groups for most outcomes.

Devices

MAGNETS AND MAGNETIC STIMULATION

Proponents believe that magnetic fields have therapeutic value in the treatment of musculoskeletal disorders. There are different levels of magnetic field therapies available with studies of 700 Gauss up to 4000 Gauss magnetic fields having been reported.

Recommendation: Magnets and Magnetic Stimulation for Acute, Subacute, or Chronic Cervicothoracic Pain
Magnets are not recommended for the treatment of acute, subacute, or chronic cervicothoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – High

Rationale for Recommendation
While there are no high-quality sham controlled trials or trials comparing magnets to no treatment of cervical pain patients from which to draw robust conclusions, negative trials have been reported in the lumbar spine.(868, 869) Trials in the neck have had methodological issues. There have been reports suggesting improvements attributed to higher magnetic fields in myofascial pain syndrome patients.(870, 871) However, these studies had differences in baseline characteristics that potentially result in difficulty drawing reliable conclusions. There are no reports of a therapeutic benefit of MRI testing, which exposes patients to very high magnetic fields. The use of magnetic therapy with lower Gauss measures has not been shown to provide any lasting improvement in cervical pain.(872, 873) A low-quality study reported some improvement in WAD (whiplash associated disorder) patients; however, there are considerable weaknesses in study design resulting in a low quality rating.(874) A moderate-quality crossover pilot study of low back pain also suggested no benefit,(868) (see Low Back Disorders and Chronic Pain guidelines) thus by analogy, it may be presumed that magnets are ineffective for treatment of cervical pain. Magnets are not invasive, have no adverse effects, and are low cost, but with negative results in the lumbar spine are not recommended.

Evidence for the Use of Magnets and Magnetic Stimulation
There are 4 moderate-quality RCTs incorporated in this analysis.(870-873) There are 2 low-quality RCTs in Appendix 1.(874, 875)

Magnets and magnetic stimulation – A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Magnets, magnetic stimulation, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 760 articles, and considered 4 for inclusion. In Scopus, we found and reviewed 424 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 50 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 18 articles, and considered 2 for inclusion. We also considered for inclusion 3 articles from other sources. Of the 9 articles considered for inclusion, 4 randomized trials and 5 systematic studies met the inclusion criteria.*

Author/ Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Smania 2005 RCT No mention of sponsorship or COI.	7.0	N = 53 with myofascial pain; mean age 36.47 (11.58) in rMS group, 36.56 (14.94) in TENS and 44.61 (16.62) in sham group.	Magnetic therapy or rMS group, different coils were alternated in each session, 20 minute sessions (n = 17) vs. TENS group, the negative electrode was placed on the most painful TP of upper trapezius muscle and the positive one was placed on the acromial tendon insertional site (n = 18) vs Sham group, gel was spread over the zone of the TP and the ultrasound therapy device was applied while turned off (n = 18). Follow-up before 1-month and 3-months.	Peripheral repetitive magnetic stimulation (rMS) group showed significant improvement in all pain testing Neck Pain and Disability VAS and algometry and in TP evaluation. TENS group showed significant changes in performance in both TP and range of contralateral rotation; X = 8.92, d.f. = 3, (p = 0.030); ROM-rotation: x = 21.81, d.f. = 3, (p < 0.001). No significant changes in placebo group using Friedman test and Wilcoxon nonparametric tests.	"[R]MS may be a novel, non-invasive, and reliable therapeutic approach for MPS that might possibly lead to more substantial and longer lasting therapeutic effects than TENS."	Three groups, patients unblinded to exact treatment, placebo a sham procedure; 10 daily 20 minute visits. Evaluations done before and after each treatment and at 1 and 3 months. Evaluation done on VAS, pain with palpation of TPs, ROM of cervical spine. Baseline comparison had differing demographic and clinical features. Specifically age, education and previous physical therapy, concerning for potential randomization failure. Unclear how patients chosen.
Smania 2003 RCT No mention of sponsorship or COI.	6.5	N = 18 with myofascial pain; mean age 42.2±14.3 years.	Group 1, received repetitive magnetic stimulation or rMS 10 sessions, 20 minutes each (n = 9) vs. Sham application of a non-functioning ultrasound therapy device to the TP (N = 9). Follow-up for 1 week and 1 month.	In comparison rMS showed greater effectiveness. Improvement in T1-T2 for contralateral (Z = -2.28; p = 0.046) and ipsilateral rotation (Z = -2.38; p = 0.034) tests. In any outcome measure placebo did not show a significant effect of treatment on pain.	"The results of this study show that peripheral rMS may have positive short- and medium-term therapeutic effects on myofascial pain."	Excluded patients with fibromyalgia syndrome. Assessed VAS, NPVAS, manual palpation, algometric test, and ROM before and after each treatment and at 1 week and 1 month. Baseline comparability close except for age (sham group 6 years older). Noted an improvement in all areas tested. No comment on compliance/ dropout rate. Unclear how participants recruited.
Hong 1982 RCT No mention of sponsorship or COI.	6.5	N = 101 with neck and shoulder pain; mean age not specified.	Magnetic wore the necklace 24 hours per day for 3 weeks (n = NA) vs. Placebo necklaces 24 hours per day for 3 weeks (n = NA). Follow-up for 3 weeks.	52% improvement after wearing magnetic necklaces, 44% improvement in non-magnetic necklace group. Pain frequency and intensity reduced in both groups indicating placebo effect.	"We were unable to demonstrate any significant therapeutic effect of the Japanese TDK magnetic necklace on chronic neck and shoulder pain and stiffness."	Randomization not well explained. No good description of baseline comparability. Blinding appeared acceptable by statement that most patients thought they had a magnetic necklace.
Lin 1985 RCT	5.5	N = 101 with chronic neck and shoulder pain, age not specified.	Magnetic nature with surface flux density 0.13 T for 24 hours/day (n = NA) vs. Placebo necklaces not	Reported improvement in 14 of 27 subjects wearing magnetic necklaces and 11 of 25 wearing non-magnetic	"Following treatment, pain subjects reported a statistically significant reduction in frequency and degree of	Psychological test before start of study (SCL-90 and Social Desirability Scales), repeated at 3rd week with Rotter I-E

2nd report of Hong 1982 Sponsored in part by the TDK Corp. No mention of COI.			magnetized or 24 hours/day (n = NA). Follow-up for 4 weeks.	necklaces. Pain significantly reduced, after treatment with both types of necklaces, ($p < 0.001$). Placebo effect strongly evident.	discomfort; however, the reduction was equally as great in subjects who wore the nonmagnetic necklace, which implicates a significant placebo effect."	Scale. Baseline characteristics explained in appendix. Second report of study (Hong 1982) with psychological evaluation added, as well as better description of baseline characteristics.

IONTOPHORESIS
Iontophoresis is a drug delivery system utilizing electrical current to transdermally deliver either glucocorticosteroids or NSAIDs and that has apparent efficacy in the extremities where the dermis and adipose tissue overlying the target tissue is thin and penetration of the medicine to the target tissue is possible, which does not describe the spine.(876)

Recommendation: Iontophoresis for Acute, Subacute, or Chronic Cervicothoracic Pain or Radicular Pain Syndromes or Other Back-related Conditions
Iontophoresis is not recommended for the treatment of acute, subacute, or chronic cervicothoracic pain or radicular pain syndromes or other back-related conditions.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There are no sham controlled or quality studies regarding the use of iontophoresis in cervicothoracic pain. Iontophoresis is not shown to be efficacious for the treatment of acute, subacute, or chronic cervicothoracic pain or radicular pain syndromes or other back-related problems. It is not invasive and is not low cost. There are other interventions shown to be efficacious.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Iontophoresis, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 751 articles, and considered 0 for inclusion. In Scopus, we found and reviewed 27 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 0 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 9 articles, and considered 0 for inclusion. We also considered for inclusion 1 article from other sources. Of the 1 article considered for inclusion, 0 randomized trials and 1 systematic study met the inclusion criteria.*

Physical Methods
There are many modalities that have been used to treat cervicothoracic pain. This section includes detailed reviews of massage, reflexology, manipulation, traction, etc.

ACUPUNCTURE
Acupuncture is based in part on the theory that many diseases are manifestations of an imbalance between yin and yang, as reflected by disruption of normal vital energy flow (qi) in specific locations, referred to as meridians. Needling along one of the 361 classical acupuncture points on these meridians is believed to restore balance. This stimulation is classically done with thin, solid, metallic needles, which are frequently manipulated (or turned) manually or stimulated electrically (electroacupuncture). In addition to needling, acupuncture frequently involves moxibustion and cupping. Besides traditional Chinese acupuncture, there are many other types of acupuncture that have arisen, including accessing non-traditional acupuncture points.(544, 554, 877-880)

1. *Recommendation: Acupuncture for Chronic Cervicothoracic Pain*
Acupuncture is recommended for select use in chronic cervicothoracic pain with or without radicular symptoms as an adjunct to facilitate more effective treatments.

Indications – As an adjunct treatment option for chronic cervicothoracic pain as a limited course during which time there are clear objective and functional goals that are to be achieved. Considerations include time-limited use in chronic cervicothoracic pain patients without underlying serious pathology as an adjunct to a conditioning program that has both graded aerobic exercise and strengthening exercises. Acupuncture is recommended to assist in increasing functional activity levels more rapidly, and, if it is recommended, the primary attention should remain on

the conditioning program. In those not involved in a conditioning program, or who are non-compliant with graded increases in activity levels, this intervention is not recommended.

Frequency/Duration – Different frequencies and numbers of treatments used in quality studies ranged from weekly for 1 month to 20 appointments over 3 months. Usual program is 10 sessions over 3 to 4 weeks.(881) An initial trial of 5 to 6 appointments is recommended in combination with a conditioning program of aerobic and strengthening exercises. Future appointments should be tied to improvements in objective measures to justify an additional 6 sessions, for a total of 12 sessions.

Indications for Discontinuation – Resolution, intolerance, or non-compliance including non-compliance with aerobic and strengthening exercises.
Harms – Rare needling of deep tissue, such as artery, lung, etc. and resultant complications. Use of acupuncture may theoretically increase reliance on passive modality(ies) for chronic pain.
Benefits – Modest reduction in pain.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – Low

2. Recommendation: Acupuncture for Acute or Subacute Cervicothoracic Pain
Routine use of acupuncture is not recommended for treatment of acute or subacute cervicothoracic pain or for acute radicular pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendations
There are quality studies evaluating the utility of acupuncture for treatment of chronic cervicothoracic pain, although they conflict to some extent regarding whether it is efficacious and which type of acupuncture to perform.(679, 882-884) One issue is the benefit of acupuncture versus electroacupuncture. A moderate-quality study showed that electroacupuncture was more effective than acupuncture alone.(885) Quality trials compared to sham demonstrated a short term improvement in range of motion and pain(882, 883, 886) and one of these moderate quality trials showed acupuncture was associated with improvements in pain-related activity, sleep, anxiety, depression, and satisfaction with life.(881) Trials comparing acupuncture with no treatment have shown a decrease in pain of up to 40% over baseline after 12 weeks.(887) The highest scored study (see evidence table) showed improvement in motion-related pain 1 hour after acupuncture above that seen for dry needling and sham acupuncture.(882) Benefits beyond the duration of treatment of up to 3 years have been suggested.(881) However, studies generally fail to control for attention bias, and also suggest that needling in locations other than traditional acupuncture points can provide equal benefit,(881, 888, 889) which leads to questions regarding whether it is the needling rather than the acupuncture that was beneficial. Other quality trials have compared acupuncture with physiotherapy and medications and other treatments, with some failing to find differences in outcomes. A moderate-quality study of acupoint electrical stimulation did not find improvement in patients with variable duration of pain ranging from acute to chronic.(890) Other studies found less of an effect or no effect, when compared to other treatments and placebo.(679, 886, 891) One moderate-quality study looked at acupuncture compared to sham acupuncture; both treatment groups improved without a significant difference between the two up to 16 weeks after intervention.(884)

There is no high quality evidence for treatment of acute cervicothoracic pain, radicular pain syndromes, or other cervical pain-related conditions. Acupuncture would not be expected to improve on the history of acute cervicothoracic pain treated with more effective treatments reviewed elsewhere.

Despite reservations regarding its true mechanism of action, the overall presence of quality trials demonstrating superiority of acupuncture to sham acupuncture provides quality evidence of efficacy, although the magnitude of benefits is modest and the treatment is passive. Acupuncture is minimally invasive, has relatively low adverse effects in experienced hands, and is moderate cost depending on numbers of treatments.

Evidence for the Use of Acupuncture
There are 5 high-(679, 882-885) and 42 moderate-quality (568, 585, 675, 681, 848, 862, 881, 886-920) RCTs or crossover trials incorporated into this analysis. There are 5 low-quality RCTs in Appendix 1.(677, 921-924)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: acupuncture, acupotomy, electroacupuncture, acupressure, acupuncture therapy, warm needling, dry needling, needling, de-qi, warm, dry, pressure, electric current, needle, pressure needling, cervicalgia, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular, pain, intervertebral disc displacement, herniated, herniat, displacement, displaced, disc, disk, discs, disks, neck pain, radicular pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review. In PubMed we found and reviewed 223 articles, and considered 49 for inclusion. In Scopus, we found and reviewed 42 articles, and considered 8 for inclusion. In CINAHL, we found and reviewed 8 articles, and considered 2 for inclusion. In Cochrane Library, we found and reviewed 14 articles, and considered 1 for inclusion. We also considered for inclusion 17 articles from other sources. Of the 77 articles considered for inclusion, 51 randomized trials and 21 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Acupuncture vs NSAIDs						
Muller 2005 RCT Sponsored by the Queensland State Government Health Department. No COI.	8.0	N = 69 with chronic mechanical spinal pain syndromes, mean >2 years, being at ≥17 years of age.	Acupuncture with 8-10 needles for 20 minutes (n = 22) vs. Manipulation with high-velocity low-amplitude spinal manipulative thrust (n = 25) vs. Celebrex 200 to 400mg/d or rofecoxib 12.5-25mg/d followed with acetaminophen (n = 22). At least 1 year follow-up.	Neck pain scale (VAS) was significant for both manipulation (p = 0.04) and acupuncture (p = 0.006) but not medication (p = 0.70); neck disability index was significant for manipulation (p = 0.045) vs. acupuncture (p = 0.005) and medication (p = 0.26). Those who received, at any time after randomization, a treatment other than allocated regimen. Differed significantly (p < 0.05) between the treatment groups." Respective percentages: manipulation 38.7%, acupuncture 53.3%, medication 81.2%.	"Overall, patients who have chronic mechanical spinal pain syndromes and received spinal manipulation gained significant broad-based beneficial short-term and long-term outcomes."	No differentiation between different areas of the spine. Initially acupuncture and manipulation groups had provider contact twice a week vs drug-only group with contact once every 2 weeks. Majority of patients (75.8%) responded at 12 months, but range of time to respond up to 36 months in some.
Giles 2003 RCT Sponsored by the Queensland State Government Health Department. No COI.	6.5	N = 115 with chronic spinal pain syndromes, and being at ≥17 years of age.	Celebrex 200-400mg/day or Vioxx 12.5mg/day (or 25mg/day) paracetamol 2-6 500mg tables / day (. = 43) vs. Acupuncture with 10-20 needles for 20 minutes (n = 36) vs. high-velocity low-amplitude spinal manipulative thrust (n = 36). Outcomes assessed at 2,5 and 9 weeks.	Manipulation achieved best overall results with improvements of 50%, (p = 0.01) on Oswestry scale, 38% (p = 0.08) on NDI, 47% (p <0.001) on the SF-36, and 50%, (p < 0.01) on VAS for back pain, 38%, (p < 0.001) for lumbar standing flexion, 20% (p < 0.001) for lumbar sitting flexion, 25% (p = 0.1) for cervical sitting flexion, and 18% (p = 0.02) for cervical sitting extension. Acupuncture showed better result than manipulation on VAS for neck pain (50% and 42%).	"[T]he consistency of the results provides, despite some discussed shortcomings of this study, evidence that in patients with chronic spinal pain, manipulation, if not contraindicated, results in greater short-term improvement than acupuncture or medication."	Individualization of treatments results in lack of standardization and substantially precludes drawing robust conclusions. Post-randomized individualized treatment in all 3 arms. Ill-defined mixture of diagnoses, combined with non-randomization of some treatments arguably relegates study to a non-RCT.
Aigner 2006 RCT No mention of sponsorship or COI.	4.0	N = 50 with whiplash injury within 4 days before first assessment. Mean age: 30 (17-59).	Adjuvant laser acupuncture plus cervical collar and a combination of paracetamol and chlormezanone (n = 25) vs. Same treatments but	No statistically significant advantage of the laser acupuncture treatment was found in the acute phase or the chronic phase.	"Adjuvant laser acupuncture with a 5 mW HeNe laser and an irradiation time of 15 s appears to be ineffective in the management of whiplash injuries."	Follow up was for 8-12 months after randomization. Reported no significant difference between active and placebo treatment.

			with use of placebo laser (n = 25). Follow-up for about 17 days.			
Birch 1998 RCT Sponsored by an intramural grant of Anesthesia Department of Brigham and Women's Hospital, Boston. No COI.	4.0	N = 46 with chronic myofascial neck pain. Age range 18-65 years	Relevant acupuncture using presterilized gauge 2 (0.18mm) Serin needles shallowly inserted in hands and feet and connected by IP cords, for 10 minutes, and then acupuncture points on neck, shoulder, and upper back for 10 minutes (n = 15) vs. irrelevant acupuncture place at different acupuncture points and connected by cords that look the same as IP cords, the needles were placed inserted in the same places as the relevant acupuncture, except for neck (n = 16) vs. NSAID (Trilisate) controls (n = 15). Follow up 3 months after completing study.	"The relevant acupuncture group had significantly greater pre/post-treatment differences in pain than the irrelevant acupuncture and control groups, ($p < 0.05$)."	"Relevant acupuncture with heat contribute to modest pain reduction in persons with myofascial neck pain. Previous experience with confidence in treatment help to predict benefit. Measurement of nonspecific effects of alternative treatment therapy is recommended in future clinical trials.	Significant baseline differences in prior acupuncture experience of uncertain impact (relevant acupuncture group far more experienced than other two groups).
Giles 1999 RCT Sponsored by Green Projects Donation Fund Limited via the Royal Melbourne Institute of Technology and by Townsville General Hospital and James Cook University. No mention of COI.	4.0	N = 77 with chronic spinal pain syndromes, duration at least 13 weeks. Age: ≥18 years.	Tenoxicam with ranitidine (n = 21) vs. High-velocity, low-amplitude spinal manipulation (n = 36) vs. Acupuncture 8-10 needles at trigger points and distally "near and far" technique, for 4 weeks. Acupuncture group 6 treatments, spinal manipulation 6 visits, medication 2 visits of 15-20 minute with clinician (n = 20). Outcomes assessed at 4 weeks.	"Spinal manipulation was the only intervention that achieved statistically significant improvements… with (1) a reduction of 30.7% on the Oswestry scale, (2) an improvement of 25% on the neck disability index, and (3) reduction of the visual analogue scale of 50% for low back pain, 46% for upper back pain, and 33% for neck pain (all $p < 0.001$)."	"[E]vidence that in patients with chronic spinal pain syndromes spinal manipulation, if not contraindicated, results in greater improvement than acupuncture and medicine."	Dropout rate 26% for manipulation, 52% acupuncture, 20% for medication ($p = .008$). Manipulation group 53% males vs 35% in acupuncture, 19% in medication group, suggesting potential randomization failure. Intervention periods significantly different between groups.
Acupuncture vs. sham						
Irnich 2002 Crossover Trial	9.0	N = 36 with chronic neck pain. Mean age 51.9 years old.	Non-local or NLA needles acupuncture (n = 12) vs. Dry or DN needling (n = 12) vs. Sham laser acupuncture (n = 12).	For motion-related pain, use of acupuncture at non-local points reduced pain scores by (11.2 mm; 95% CI 5.7 to16.7; $p = 0.00006$)	"Acupuncture at distant points improves ROM more than DN; DN was ineffective for motion-related pain."	Cross-over study design. Effects of treatment assessed within 1 hour after treatment with no long-term assessments. Used distant

Sponsored by the German Medical Acupuncture Association (DÄGfA). No mention of COI.			Wash out period at 1 week, follow-up not specified.	compared to DN and sham. DN had reduction of pain of 1.0 mm (95% CI -4.5, 6.5; p = 0.7). Use of DN slightly improved ROM by 1.7° (95% CI 0.2, 3.2; p =0.032) with use of non-local points improving ROM by an addition 1.9° (95% 0.3, 3.4, p = 0.016).		point acupuncture, dry needling and sham laser acupuncture.
Shen 2007 RCT Sponsored by the UCSF Osher Center for Alternative and Integrative Medicine. No mention of COI.	8.5	N = 15 with chronic myofascial pain. Age average±SD: 43.1±13.6 year old.	Acupuncture (n = 9) vs. Sham acupuncture for 15 minutes (n = 6). Follow-up for at least 12 weeks.	Acupuncture group pain scores 4.33±3.35 post-treatment change of -2.0. Sham acupuncture group 5.67±3.20 post treatment, change of -0.833. Perceived acupuncture treatment pain 3.73±2.83 post-treatment, change of -2.82. Perceived placebo acupuncture pain 8.0 ±2.16 post treatment, change of 2.0.	"In summary, this study found that acupuncture significantly increased the pain tolerance of the masseter muscle (p= 0.027)."	This was a study for TM, jaw pain. Pain for >/= 12 weeks, 1 male and 14 female participants. Pain assessment was immediate during visit without further assessment. It appeared to decreased masseter muscle pain, but difficult to assess clinical significance because of no long term follow-up or application.
Zhu 2002 Crossover trial No mention of sponsorship or COI.	8.5	N = 29 with chronic neck pain diagnoses chronic neck pain including neck pain, DJD, OA, cervical spondylitis, WAD, cervical sprain). Age range: 31-70 years old.	Acupuncture (n = 14) vs. Sham acupuncture 9 sessions (n = 15). Both local and distal points with electrical stimulation at distal points used. Acupuncture was individualized; 16 weeks follow-up.	Real acupuncture: 58% lower pain intensity, 53% fewer pain hours per day, 68% fewer analgesic pills per week, and 41% improvement in activity level, (p <0.005). Sham acupuncture: 37% lower pain intensity, 33% fewer pain hours per day, 70% fewer analgesic pills per week, and 31% improvement in activity level, (p <0.005).	"Results indicate that acupuncture may be a suitable intervention for those patients suffering from neck pain of duration more than six months."	Washout period between interventions was 3 weeks and may not have been long enough for the cross-over. Small numbers.
White 2004 RCT Sponsored by Henry Smiths Charity and Hospital Savings Association. No COI.	7.5	N = 135 chronic mechanical neck pain. Age range: 18-80 years	Acupuncture (n = 70) vs. Placebo for 8 treatments over 4 weeks (n = 65). 1-year follow up.	Both groups improved statistically from baseline. Primary outcome VAS pain scores (weeks 1-5) had statistically significant difference in favor of acupuncture (6.3mm [95% CI, 1.4 to 11.3mm]; p = 0.001). However, difference not clinically significant because it demonstrated only a 12% (CI, 3% to 21%) difference between acupuncture and placebo.	"Acupuncture reduced neck pain and produced a statistically, but not clinically, significant effect compared with placebo. The beneficial effects of acupuncture for pain may be due to both nonspecific and specific effects."	Both groups had symptom improvements. Individual acupuncture points according to pain and tender points. No fibromyalgia patients. Duration of illness longer in controls.

Chan 2009 RCT No mention of sponsorship or COI.	7.0	N = 60 with chronic neck pain. Age range 18-75 years old.	Wrist acustimulation for 30 min, twice a week for 4 consecutive weeks (n = 22) vs. Sham acustimulation (n = 27). Follow up at 4 weeks and 1 month post treatment.	Neck pain scores significantly reduced in acustimulation vs. control (p = 0.005) at 1 month follow-up (p = 0.01). Neck pain questionnaire scores decreased significantly after treatment (p <0.001) and 1-month follow-up (p < 0.001). Pain self-efficacy scores significantly improved in acustimulation vs. control immediately after treatment (p = 0.0016) and 1-month (p = 0.005).	"[W]rist acustimulation has an added value to standardized neck exercise used…Improvements occurred immediately after treatment and lasted for at least 1 month"	Blinding unclear despite use of sham arm. Data suggest clinical improvement of neck pain at 4 weeks of electric stimulation of wrist/ankle and at 1 month past treatment.
Sahin 2010 RCT No mention of sponsorship or COI.	7.0	N = 31 with chronic soft tissue neck pain lasting for more than 3 months. Age range 18-65 years old.	Electro-acupuncture (n = 15) vs. Sham acupuncture (n = 16). Follow up at post-treatment and 3 months.	3 sessions per week for 30 min/each for a total of 10 sessions. Group 1 VAS scores for motion pain improved significantly from pretreatment (p = 0.05), VAS scores at rest (p = 0.27), were not significant. Group 2 VAS scores for motion (p < 0.001) and at rest (p = 0.001).	"[B]oth genuine electroacupuncture and sham acupuncture were associated with reduction of neck pain as scored by VAS."	Study designed for n=80, only recruited 31. Power for detection of difference therefore may be inadequate. Data suggest no difference in analysis between sham and active electroaccupuncture.
Irnich 2001 RCT Sponsored by German Ministry for Education and Research and also by German Medical Acupuncture Association (DÄGfA). No COI.	6.5	N = 177 with chronic neck pain. Age range 18-85 years old.	Acupuncture (n = 56) vs. sham laser acupuncture (n = 61) vs. massage (n = 56). Follow-up at 3 months.	Acupuncture group had significantly greater improvement in motion related pain compared to massage (difference 24.22 (95% confidence interval 16.5-31.9), p = 0.0052) but not compared with sham laser (17.28(10.0 to 24.6), p = 0.327).	"[A]cupuncture is an effective short term treatment for patients with chronic neck pain, but there is only limited evidence for long term effects after five treatments."	No clear placebo arm control for acupuncture as sham was a placebo laser treatment. Short term results only.
Vas 2006 RCT No sponsorship. Partially funded by Consejeria de Salud de la Junta de Andalucia and by the IRYSS network. No COI.	6.5	N = 123 with chronic un-complicated neck pain. Age ≥17 years old.	Acupuncture: puncture bilateral with sterile, single-use needles, 25mm x 0.25mm or 40mm x 0.25mm, needles kept in place 30 minutes and manually stimulated every 10 minutes (n = 61) vs. Placebo-TENS for 30 minutes (n = 62). Follow-up at 6 months.	VAS pain score changes from baseline to 6-months follow-up were significantly different between acupuncture and control 14.4; 9% CI 2.9 to 25.8, (p = 0.014). Relative change in pain intensity of the neck was 62.2% (SD 28/2) for acupuncture vs 20.4% (SD 22.5) for control.	"Improvements in quality of life (physical aspect), active neck mobility and reduced rescue medication were clinically and statistically significant. In the treatment of the intensity of chronic neck pain, acupuncture is more effective than the placebo treatment and presents a safety profile making it suitable for routine use in clinical practice."	Dropouts more than 20% in both groups.

Thomas 1991 RCT Sponsored by Stiftelsen Groschinskys Minnesfond, King Gustav Vth 80-year anniversary fond, Torsten and Ragnar Söderbergs foundation and the Swedish Society Against Rheumatism. No COI.	6.5	N = 44 with chronic cervical osteoarthritis. Age range 42-77 years old.	Acupuncture for 40 minutes (n = NA) vs. Sham-acupuncture (n = NA) vs diazepam 5mg a day (n = NA) vs. Placebo diazepam (n = NA). All patients went through all the interventions. Follow-up not specified.	Reduction of pain of those treated with acupuncture not statistically significant from those treated with diazepam or placebo acupuncture, but was significant compared to placebo-diazepam. All groups showed a significant reduction in pain except placebo-diazepam group.	"When comparing the different modes of treatment, acupuncture induced the most significant alleviation of pain and unpleasant-ness. This indicates that benzodiazepines may be replaced by acupuncture in the treatment of pain and other conditions associated with unpleasantness."	Baseline descriptive statistics not included, although crossover trial design including all subjects substantially reduces concerns about between group differences. Generalizability unclear. Success of blinding of sham acupuncture questionable particularly if included those familiar with acupuncture.
Liang 2011 RCT Sponsored by research project Eleventh Five-year Scientific Project supported by State Ministry of Science and Technology and Scientific Project supported by Guangdong Provincial Administration of Science and Technology. No COI.	6.0	N = 178 with neck or shoulder pain for ≥6 months. Age range 18-60 years old.	Traditional acupuncture on classic acupuncture points to a depth of 20mm (n = 88) vs. Placebo acupuncture on sham points 1 cm lateral to standard points at a point of 3mm depth (n = 88). 3 week study including 6 treatments 3 times per week for 30 minutes. Follow up at 1 and 3 months.	VAS scores at 3-months follow-up in the acupuncture group 2.88 (1.72) compared to control 3.19 (1.31), between subjects, ($p = 0.045$). Physical functioning was not significantly different between groups 84.26 (15.24) vs 85.88 (14.01), ($p = 0.447$).	"[V]AS scores decreased in both groups after intervention and during follow-up ($p < 0.01$); and the VAS score of the study group was lower than the control group ($p < 0.05$) after the treatment and during follow-up."	Nonblinded assessor with use of physician perception as outcome measure. Objective measures suggests positive benefit for acupuncture vs sham, although differences are likely of small of no clinical significance (VAS 2.88 vs 3.19). Study conducted in China. Data suggest statistical differences between groups in NPQ, VAS, vitality, and social functioning scores from baseline, although differences are not likely clinically significant and thus do no support superiority in this population.

Witt 2006 RCT Sponsored by German social health insurance funds: (TK); BKK Aktiv; Betriebskrankenkasse der Allianz Gesellschaften; Bertelsmann BKK; Bosch BKK; BKK BMW; DaimlerChrysler BKK; BKK Deutsche Bank; Ford Betriebskrankenkasse; BKK Hoechst; HypoVereinsbank Betriebskrankenkasse; Siemens-Betriebskrankenkasse; Handelskrankenkasse; Innungskrankenkasse Hamburg. No COI.	5.5	N = 3766 with chronic neck pain with a duration of >6 months. Age ≥18 years.	Acupuncture group (n = 1880) vs. Control for 15 sessions (n = 1886). Follow-up at 3 and 6 months.	Acupuncture group had more pronounced improvement in neck pain and disability compared to control group. Neck pain and disability scores, 16.2 (SE: 0.4) to 38.3 (SE: 0.4); and by 3.9 (SE 0.4) to 50.5 (SE0.4), difference 12.3, 95% CI 11.3; 13.3, (p = 0.001).	"[S]tudy shows that treating patients with chronic neck pain in routine primary care in Germany with additional acupuncture resulted in a clinically relevant benefit. Acupuncture could be considered as a viable option in the medical care for patients with chronic neck pain."	Large multicentre study. Baseline variability in age and outcome measures. Compliance difficulties to assess due to individualized treatment protocol rather than standard protocol. Data suggest acupuncture may provide benefit in addition to usual care. No data on any differences in usual care utilization were discussed. The degree of clinical benefit is unseen.
Sun 2010 RCT Sponsored by Taiwan Department of Health Clinical Trial and Research Center of Excellence. No mention of COI.	5.5	N = 35 with chronic neck myofascial pain syndrome. Age range 31-66 years	Acupuncture group or AG (n = 18) vs. Sham acupuncture group or SG, for six treatments (n = 17). Follow-up post treatment, 4 weeks, and 12 weeks.	Neck ROM significantly improved in both acupuncture group ($p < 0.01$) and sham group ($p < 0.05$). VAS scores significantly improved in acupuncture group ($p < 0.05$). Both groups improved significantly in total scores from short-form McGill pain questionnaire outcomes at 12-weeks vs. baseline, ($p < 0.01$).	"[A]G has greater improvement in physical functioning and role emotional of Short Form-36 quality of life at F2, suggesting that acupuncture may be used to improve the quality of life in patients with chronic neck [myofascial pain syndrome]."	Allocation concealed compliance unclear. Author indicates single blinding of assessor, but makes case for patient blinding. Data suggest both groups improved. Differences between groups are of uncertain clinical significance.
Shen 2009 RCT Sponsored by UCSF Osher Center for Alternative and Integrative Medicine. No mention of COI.	5.0	N = 28 with confirmed diagnosis of chronic myofascial pain of the jam muscles. Age ≥18.	Acupuncture with Seirin 30-gauge (n = 16) vs. Sham acupuncture using same needles as intervention but shortened 10mm (n = 12). Outcome assessed post treatment.	No significant difference between groups.	"A single acupuncture session using one acupoint at Hegu large intestine 4 significantly reduced more myofascial pain endpoints when compared to sham acupuncture."	Pilot study. Hight drop out rate in placebo group makes results difficutl to interpret.

Petrie 1986 RCT No mention of sponsorship or COI.	5.0	N = 25 with chronic neck pain; mean age 52.9 in acupuncture and 48.1 in sham group.	Acupuncture using standard 28 g needles (n = 13) vs. Sham transcutaneous nerve stimulation or sTNS (n = 12). Both treatment were given twice weekly for 4 weeks. Follow up at 1 month.	"No significant difference occurred in any outcome measure over the treatment period in either group, although trends were present toward improvement, especially at follow-up."	"We conclude that, although an incremental analgesic effect of 15% cannot be excluded, acupuncture may not have any therapeutic effect greater than placebo in chronic cervical pain."	Attempted to assess placebo affect by telling patients TNS sham treatment a new valid treatment for pain. Some differences in baseline characteristics especially analgesic use and initial pain ratings before study where a statistically significant difference between groups.
Fu 2009 RCT Sponsored by Guangdong Administration of Science and Technology, and Eleventh Five-year Scientific Supported Project by State Ministry of Science and Technology. No mention of COI.	5.0	N= 117 with cervical spondylosis. Age range 21-54 years old.	Acupuncture with a 40mm in length and 0.3 in diameter needle, for 20 minutes, plus infrared radiation (n = 59) vs. Sham acupuncture with 40mm in length and 0.22 in diameter needle applied at different acupoints for 20 minutes, plus infrared radiation (n = 58). Follow-up at 3 month.	By 3 months after treatment both groups did not differ significantly in VAS scores, ($p > 0.05$).	"[A]cupuncture has good immediate and medium-term clinical efficacy in the treatment of neck pain in CS patients, and its pain alleviating effect is varied in patients of different syndrome types."	No observer blinding noted. Lack of details for controlling co-interventions, measuring compliance. All subjects received infrared. Sham acupuncture method was to perform needling in non traditional points. Data suggest benefit as measured by statistical differences, although clinical significance appears modest or uncertain.
Itoh 2007 RCT Sponsored by project research foundation of Japan Society of Acupuncture and Moxibustion (JSAM). No mention of COI.	4.5	N = 40 with non-radiating chronic neck pain for ≥ 6 months and normal neurological exam. Age range 47-80 years.	Acupuncture (n = 10) vs. Trigger point acupuncture (n = 10) vs. non-trigger point acupuncture (n = 10) vs. Sham acupuncture (n = 10). Outcomes assessed at 3, 6, 9 and 12 weeks.	Results most marked for trigger point acupuncture group, and there was little difference otherwise. Graphic data suggest some rebound in 3-week interim period without treatment.	"Trigger point acupuncture therapy may be more effective on chronic neck pain in aged patients than the standard acupuncture therapy."	Study claims blinding, but unless procedures identical, could be at least somewhat unblinded, although assessment of blinding scores appear to indicate that standard acupuncture group more likely to believe they had true insertion of needles into muscles. Also, attempt to find trigger points would inadvertently include massage that was potentially unequal between 4 small groups.
Nabeta 2002 RCT Sponsored by Japan Society for Promotion of Science, the Japan Society of Acupuncture and Moxibustion and	4.5	N = 34 with chronic neck and shoulder pain. Age range 20–63 years.	Acupuncture with needle inserted to muscle (n = 17) vs. Sham acupuncture (n = 17). Follow-up for 1 month.	After Week 3, both groups improved significantly for neck, ($p < 0.05$) and shoulder, ($p < 0.001$); only back pain improved for acupuncture group, ($p < 0.001$) after treatment.	"[T]here was no overall statistically significant difference between the real and sham acupuncture to the tender points, 9 days after the third treatment. However, real acupuncture produced statistically	Study details not well described. Data suggest that improvements in pain ratings were of short-term duration. No evidence of long-term efficacy.

Foundation for training and licenser examination in anma-massage-acupressure, acupuncture, and moxibustion. No mention of COI.					significant short-term improvements."	
Petrie 1983 RCT No mention of sponsorship or COI.	4.5	N = 13 with chronic cervical pain, ≥2 years duration. Age range 54-88 years old.	Acupuncture plus completed a simple pain scale (n = 7) vs. Placebo 2x weekly for 4 weeks TNS, plus completed simple pain scale (n = 6). Follow-up for 4 weeks.	"[A]cupuncture showed a significantly greater amount of pain relief than those treated with placebo TNS, ($p < 0.01$)."	"[A] significant improvement in longstanding cervical pain was shown using acupuncture."	Small sample size groups. No e-stim with acupuncture. Study in hospitalized patients, unclear why hospitalized. Baseline characteristics differed for gender and diagnoses. Two (33%) patients diagnosed with ankylosing spondylitis in placebo and none in acupuncture group.
Electroacupuncture						
Sator-Katzenschlager 2003 RCT No mention of sponsorship or COI.	8.0	N = 21with chronic cervical pain. Mean±SD age: 52 ±12 years for control vs. 52±9 years for electroacupunctur	Auricular electro-acupuncture with continuously stimulated (2-mA constant current, 1 Hz monophasic) (n = 10) vs. Conventional manual auricular acupuncture (n = 11). Follow-up after 4 weeks of treatment.	"[R]eduction in VAS pain scores was significantly larger, ($p < 0.005$) in the electrical acupuncture group than in the conventional manual acupuncture group."	"[W]e recommend electrical stimulator acupuncture as an adjunct therapy in chronic cervical pain patients. Cumulative analgetic effects may be achieved by longer electrical stimulation periods."	Each group stopped analgesic medications and started 8mg of lornoxicam BID with rescue medication up to 8-50mg tramadol QD. All received physiotherapy. Acupuncture needles inserted on dominant side of ear. No differentiation for diagnosis with neck pain or etiology of pain.
He 2005 RCT No sponsorship. He Dong has had a PhD scholarship from Norwegian Research Council.	7.0	N = 24 females with chronic neck and shoulder pain. Age range 20-50 years	Traditional Chinese acupuncture applied 10x during 3-4 weeks either at presumed acupuncture points for pain or test group (n = 14) vs. Acupuncture at sham points or control group (n = 10). Acupressure also given between treatments in both groups. Follow-up 6 months, 3 years after therapy.	Pain-related activity at work was significantly less in the test group than control by the end of treatment, ($p < 0.04$). There were significant differences between the groups for quality of sleep, anxiety, depression and satisfaction with life, ($p < 0.05$).	"Intensive acupuncture treatment may improve activity at work and several relevant social and psychological variables for women with chronic pain in the neck and shoulders."	Study evaluated psychological effects of acupuncture. Controls exercised less at 3 years.
Cameron 2011 RCT	6.5	N = 124 with whiplash injury more than 1 month	Real electro-acupuncture (n = 60) vs. Stimulated electro-acupuncture 2x weekly for 6 weeks (n =	VAS scores in acupuncture from baseline to follow-up were significant compared to sham -0.5 (95% CI -1.0 to -	"Real electro-acupuncture was associated with a significant reduction in pain intensity over at least 6	Data suggest no clinically significant differences between active and sham intervention.

Sponsored by New South Wales Motor Accidents Authority. No COI.		previously. Age range 18-65 years.	64). Follow-up 3 and 6 months.	0.1). Neck disability index was -0.4 (95% CI -1.7 to 1.1) compared to sham.	months. This reduction was probably not clinically significant. There was no improvement in disability or quality of life."	
Yip 2007 RCT Sponsored by School of Nursing Departmental Research Committee for this study. No mention of COI.	5.5	N = 46 with subacute non-specific spinal pain neither low back nor neck. Age ≥18 years	Transcutaneous acupoint electrical stimulation (TAES) and electromagnetic millimeter wave (EMMW) therapy 35-40 minutes for 8 treatments over 3 weeks and painkiller or intervention, (n = 23) vs, Painkiller only or control group (n = 24). Follow up at 1 week and 3 months.	Mean (95% CI) change of VAS score (for both low back and neck pain groups) on intervention group vs. control group: -2.16 (-3.27 to -1.05) vs 0.20 (-0.78 to 1.18), immediate post intervention, (p = 0.007). Not significant at 1 week and 3 month follow up. (p = 0.09 and (p = 0.27), respectively. Mean (95% CI) change of VAS score (for neck pain group only) on intervention group vs control group: -1.72 (-3.00 to -0.47) vs 0.67 (-2.12 to 0.78), (p = 0.41) immediate post intervention; 1.86 (-2.88 to -0.84) vs -0.84 (-1.86 to 0.18) p=0.24, at 1 week; and 1.10 (-2.22 to 0.39) vs -0.63 (-2.11 to 0.86), (p = 0.70) at 3 months. Mean (95% CI) change of VAS score for stress and stiffness levels post-intervention for intervention group vs control group: -3.58 (-4.64 to -2.52) vs -1.13 (-2.28 to 0.02), (p = 0.009) for stiffness levels; -2.92 (-3.84 to -2.01) vs -0.56 (-1.83 to 0.71), (p = 0.003) for stress levels.	"Our study shows that there was relief in pain intensity, stress and stiffness level immediately after eight sessions of combined TAES and EMM treatment, although, in general, the effect is not sustained over a week. Moreover, the effect in pain relief is not found for the neck pain subgroup."	Both groups given a "painkiller." No blinding attempted. Baseline characteristics significantly different in duration of pain and age, concerning for randomization failure.
Coan 1981 RCT No mention of sponsorship or COI.	5.5	N = 30 with cervical spine pain syndrome, ranging from neck pain and/or radicular arm and hand pain for at least 6 months. Age range 27-74 years old.	Acupuncture: individualized, depending on symptoms. Electroacupuncture and moxibustion on some (n = 15) vs. No treatment. Acupuncture was given after 8 weeks or control group (n = 15). 12 week follow-up.	"After 12 weeks, 12 of 15 (80%) of the treated group felt improved, some dramatically, with a mean 40% reduction of pain score, 54% reduction of pain pills, 68% reduction of pain hours per day and 32% less limitation of activity."	"We believe that an 80% remission rate (in treatment group) far outweighs the 33% placebo response rate expected in pain studies."	Pain score higher in acupuncture group, as was prior use of pain pills. Diagnoses varied. Delayed acupuncture controls biases in favor of active treatment. Individualization of treatment makes conclusions more difficult to draw.

Loy 1983 RCT No mention of sponsorship or COI.	5.0	N = 60 with cervical spondylosis. Age range 40-70 years old.	Standard physiotherapy 20 minutes 3x a week (n = 30) vs. Electroacupuncture with 0.32mm (30-gauge) needles in 2-6 acupuncture points for 30-40 minutes 3 sessions a week (n = 30). Outcomes assessed at 3- and 6-weeks.	At end of first 3 weeks treatment: PT group had 31.3% relief of symptoms, EAP group had 67.4% relief.	"[W]hile both methods were effective, electro-acupuncture produced an earlier symptomatic improvement with increased neck movement, especially in patients with mild degenerative changes of the cervical spine."	Acupuncture group appeared to have more contact with physician. Radiological classification done before treatment. Majority of patients had "grade 2" degeneration at C5-6, C6-7.
Acupuncture vs. others						
Salter 2006 RCT Supported by a Medical Research Council Studentship (Gemma Salter) and Department of Health postdoctoral fellowship in complementary and alternative medicine (Hugh MacPherson). No COI.	6.5	N = 24 with chronic neck pain of various diagnoses (cervicalgia, spondylosis, whiplash, wry neck torticollis, neck sprain and stiff neck). Age ≥18 years old.	Acupuncture for up to 10 sessions; both fixed and variable components (n = 10) vs. General practice (GP) care consisting in medication, massage, exercise chiropractic, surgery, physiotherapy, and hydrotherapy (n = 14). Outcomes assessed at 3 months.	Northwick Park Questionnaire scores at baseline and 3 months: GP care (38.4 decreased to 25.7) vs acupuncture (34.3 to 22.7). Medication use at baseline and 3 months among the GP group was unchanged (42.9% to 41.7%), but decreased from 40% to 11.1% in the acupuncture group.	"We found a trend towards higher levels of satisfaction among those patients referred to acupuncture, compared to those receiving usual GP care alone…The results of this pilot have provided useful data on key features of a full-scale trial of acupuncture for chronic neck pain."	Usual care group may have been equivalent to "more of the same" which is a recognized biased study design. It appears that a large trial was planned.
David 1998 RCT No mention of sponsorship or COI.	5.5	N = 70 with non-inflammatory chronic neck pain. Age range 18-75 years old.	Physiotherapy consisting on standard mobilization techniques (n = 35) vs. Acupuncture with 0.25x2.5 Acumedic needles for 15 minutes, and manipulated at 7 minutes (n = 35). 6 sessions at weekly interval. Outcomes assessed at 6 weeks and 6 months.	VAS score was major influence on score at week 6 (p <0.01). "The Wilcoxon test showed a marginally significant difference between the treatments at 6 weeks (p = 0.09) with physiotherapy appearing to be slightly more effective."	"Both acupuncture and physiotherapy are effective forms of treatment. Since an untreated control group was not part of the study design, the magnitude of this improvement cannot be quantified."	Good standardization in ROM measurement procedure. Acupuncture not done with electrical stimulation. No placebo group. No improvement in short-term pain and disability outcomes in patients with subacute or chronic neck pain comparing groups.
Ma 2010 RCT Sponsored by the Grant of Science and Technology of Guangdong Province, People's Republic of	5.5	N = 43 with myofascial pain syndrome from 1 to 5 years. Age range 18-80 years old.	Group 1 miniscalpel-needle release therapy in conjunction with self neck-stretching exercises (n = 15) vs. Group 2 received acupuncture needling treatment and performed self neck-stretching exercises (n = 15) vs. Group 3 control group	Miniscapel VAS scores significantly decreased at 2 weeks (p <0.01), 3 months (p <0.01) follow-up. Contralteral bending ROM of cervical spine was (p < 0.01) at 2 weeks and 3 months. Acupuncture group also had significant improvements in VAS scores	"[T]his study supports the hypothesis that [miniscalpel-needle] release and acupuncture needling treatment effectively reduced myofascial pain, increased the pain threshold at [trigger points] area, and increased contralateral bending [range of motion] of	Allocation non-concealed. No blinding. No control of co-interventions noted. Data suggest invasive groups (acupuncture, miniscapel) had more improvement than central of treatment end at 3 months. The miniscapel needle relative is not commonly used in the US.

China. No mention of COI.			with only self neck-stretching exercises (n = 13). Outcomes assessed at 2 weeks and 3 months.	($p < 0.05$) at both follow-ups and in contralateral ROM of cervical spine ($p < 0.05$) at both follow-ups. Neck stretching also improved at 3 months follow-up $p < 0.05$).	cervical spine at 2 weeks and 3 months follow-up. The [miniscalpel-needle] release technique is more effective than acupuncture needling treatment or self neck-stretching exercise in the treatment of [myofascial pain syndrome] at 3 months follow-up."	
Pfister 2010 RCT Sponsored by from National Institutes of Health (Bethesda, MD). No COI.	5.5	N = 70 who had undergone neck dissection for cancer and expressed pain and/or dysfunction in neck and/or shoulder.	Acupuncture once a week for 4 weeks (n = 34) vs. Usual care of no specific treatment (physical therapy, analgesia, and/or anti-inflammatory drugs) or physician recommendation (n = 36). Follow up at 42 days.	Final assessment after fourth treatment. Accupuncture compared to control in Constant-Murley score 11.2 (95% CI 3.0 to 19.3; p = 0.008). Numerical Rating Scale -1.7 (95% CI -0.8 to -2.7; p <0.001). Acupuncture was more effective for patients using medication at baseline, (p = 0.034).	"[S]ignificant reductions in pain, dysfunction, and xerostomia were observed in study patients receiving acupuncture versus usual care. Acupuncture treatment was well tolerated. Although further study is needed, these data support the potential role of acupuncture in addressing post-neck dissection pain and dysfunction, as well as xerostomia."	Partial randomization failure with difference in baseline primary outcomes. Lack of blinding. Data suggest acupuncture may provide clinical benefit after 4 weekly sessions for post-needle dissection pain.
Carlsson 1990 RCT Sponsored by Renee Eanders Hjälpfond and the Swedish Fund for Scientific Research without Animal Experiments. No mention of COI.	4.5	N = 92 females with chronic tension headache. Age range 18-60 years old.	Acupuncture or undefined, (n = 31) vs. Physiotherapy individualized 10-12 sessions, 30-45 minutes over 2-3 months (n = 31) vs. Control group (n = 33). Follow up at 4-9 weeks after treatment.	Mean (SD) difference of intensity of headache before and after treatment in physiotherapy group vs. acupuncture: -1.21 (0.90; p <0.001) vs -0.54 (1.01; p <0.05). Mean (SD) rotation only significant in neck mobility measures comparing patients (acupuncture and physiotherapy) vs. controls before treatment: 71° (15°) vs 79° (7°), (p <0.01).	"The headache was more improved in the physiotherapy group, and there was a marked reduction in the intake of analgesics. The tenderness was reduced in all muscles tested in the physiotherapy group but only in some of the muscles after acupuncture. The limitations of neck rotation was not influenced by either treatment."	Physiotherapy included a more intense interaction between participant and provider compared to acupuncture, biasing against acupuncture. Control group ill defined, uncertain if they had headaches to compare to interventional groups. Many different medications taken by participants; only ASA and acetaminophen recorded and analyzed. Baseline characteristics unclear.
Acupuncture vs other acupuncture applications						
Willich 2006 RCT Sponsored by German social health insurance funds. No COI.	6.5	N = 3,451 with chronic neck pain. Age ≥18 years.	Immediate acupuncture treatment (n = 1,753) vs. Delayed acupuncture treatment for 10-15 acupuncture sessions (n = 1,698). Follow-up at 3 months.	Acupuncture associated with significantly higher costs over 3 months study duration compared to routine care (€925.53 ± 1,551.06 vs €648.06 ± 1,459.13; mean difference: €277.47 [95% CI: €175.71 - €379.23].	"In conclusion, our study shows that treating patients with chronic neck pain with acupuncture in addition to routine resulted in a marked clinical relevant benefit and was relatively cost-effective. Acupuncture should be considered a viable option in	Cost-effectiveness analysis of a separately published study on effectiveness. Out-of-pocket (i.e., OTC medications not included). Controls a wait group receiving treatment after 3 months, thus biased in favor of intervention. Control

					the medical care of patients with chronic neck pain."	group older than intervention group. Visits from 10-15 for treatment group. No specific diagnoses made.
Witt 2006 RCT Sponsored by the German social health insurance funds. No COI.	6.5	N = 3,451 with chronic neck pain without specific diagnosis or etiology.	Acupuncture (n = 1,753) vs. Control for 15 acupuncture sessions more than 3 months (n = 1,698). Follow-up at 3 and 6 months.	"At three months, neck pain and disability improved by 16.2 (SE: 0.4) to 38.3 (SE: 0.4); and by 3.9 (SE: 0.4) to 50.5 (SE: 0.4), difference 12.3, ($p < 0.001$) in the acupuncture and control group."	"In conclusion, our study shows that treating patients with chronic neck pain in routine primary care in Germany with additional acupuncture resulted in a clinically relevant benefit. Acupuncture could be considered as a viable option in the medical care for patients with chronic neck pain."	Acupuncture and numbers of visits not standardized. Additional interventions allowed. Included non-randomized acupuncture group. Controls a wait group given acupuncture after 3-month follow- up, thus bias in favor of acupuncture.
Ceccherelli 2006 RCT Sponsored by Italian Association of Scientific Research and Development (A.I.R.A.S.) of Padova. No mention of COI.	6.0	N = 62 with cervical myofascial pain. Age range 25-55 years.	Somatic acupuncture for 20 minutes, once a week (n = 31) vs. Somatic acupuncture paired with auriculotherapy (n = 31). Follow-up at 1 and 3 months.	Results indicated that both somatic acupuncture and somatic plus ear acupuncture have a positive effect in reducing pain.	Authors concluded that somatic plus auriculotherapy was "not statistically significantly superior to somatic therapy alone in the treatment of cervical myofascial pain."	21% (13/62) male. Lack of baseline characteristics makes indications difficult. Auricular acupuncture had no significant improvement.
Fu 2007 RCT No mention of sponsorship or COI.	5.5	N = 47 with myofascial trigger points (MTrP) in neck. Age range 18-80 years.	Fu's subcutaneous needling (FSN) with insertion points along direction of muscle fibers 7-8cm away from MTrP (n = 22) vs. FSN with insertion across direction points 7-8cm away from MTrP (n = 25). Needles moved smooth and rhythmically from side to side horizontally 200 times in 2 minutes.	Motion related pain, pain under pressure, and range of motion improved significantly with FSN in both groups ($p < 0.01$) and ($p < 0.05$).	"FSN is superior to acupuncture in the following aspect. FSN is easy to learn and exercise in the clinic because of the optional insertion points. In acupuncture, the insertion points for certain disease are fixed and the distribution of the meridian points in the whole body must be learned first before the acupuncture clinic."	Single blinding mentioned, but who and how unclear. Leaving soft tube of needle under skin 8-24 hours after treatment likely impractical. This study and technique is described for completeness in this section, however it may not represent quality evidence for or against efficacy of acupuncture.
Hansson 2007 RCT Sponsored by grants from Jamtlands County Council and Crown Princess Margareta's	4.5	N = 144 with chronic nociceptive pain in neck or low back >3 months. Age range 18-70 years.	Intramuscular acupuncture (n = 59) vs. Periosteal acupuncture (n = 55) vs. An information control (n = 30). Follow-up at 1 month, and 1 week after first follow up.	"No significant differences between the acupuncture groups, nor between the acupuncture and control groups in the treatment period."	"No differences between periosteal and intramuscular acupuncture were found. One month after treatment both acupuncture interventions reduced anxiety in patients suffering from chronic nociceptive musculoskeletal pain in the	At each visit, instructed to be active. Allowed to maintain any exercise program and/or drug regimen. Acupoints in the periosteal group were chosen individually.

Working Group for the Visibly Disabled. No COI.					neck or low back when compared with a control intervention."	
Ceccherelli 2010 RCT Supported by A.I.R.A.S. (Italian Association for Research and Scientific Update), Padova, Italy. No mention of COI.	4.5	N = 44 with cervical myofascial syndrome with pain present within last 3 months. Age range 26-60 years.	Somatic acupuncture with 11 needles (n = 18) vs. Somatic acupuncture with 5 needles (n = 26). Outcomes assessed at 1 and 3 months.	Scores form the McGill Pain Questionnaire for both groups revealed significant improvements at end of therapy (p <0.05), at 1-month (p <0.05), and 3-months, (p <0.05). VAS scores significant for both groups at end of therapy (p <0.05), at 1-month and 3-months, (p <0.05). No significant difference between groups.	"For this pathology, the number of needles, 5 or 11, seems not to be an important variable in determining the therapeutic effect when the time of stimulation is the same in the two groups."	Data suggest no difference in using 11 needles vs 5 needles per treatment for cervical myofascial pain. Lack of control group limits conclusions.
Dry Needling						
Ga 2007 Acupunct Med RCT No mention of sponsorship or COI.	6.5	N = 39 with myofascial pain syndrome in elderly patients. Age range 63-91 years.	Acupuncture needling (n = 18) vs. 0.5% lidocaine injection (n = 21). Outcome assessment at 1 month.	No significant differences in reduction of VAS pain scores between groups up to 1 month, (p <0.001 for both). Cervical movement improved. "Changes in depression showed only trends."	"Both acupuncture needling and 0.5% lidocaine injection into the trigger points were associated with reduced subjective pain intensity and improved cervical ROM among the elderly participants with myofascial pain syndrome of the upper trapezius muscle."	All >60 years of age. Few demographic data. Dry needling with acupuncture needles versus hollow hypodermic needles. Improvements in both groups at 1 month.
Ga J Altern Complement Med 2007 RCT Supported by INHA University Research Grants. No mention of COI.	5.0	N = 40 with myofascial pain in elderly patients. Age range 63-90 years.	DRY group: dry needling of all trigger points (TrP) with acupuncture needles of stainless steel fixed by a plunger needle holder (n = 18) vs. Intramuscular Stimulation (IMS group) consisting on dry needling of all the TrPs with additional paraspinal needling at 0, 7, and 14 days (n = 22). Follow up at 4-weeks.	Mean±SD for VAS comparing Dry group vs. IMS group: 6.98±1.32 vs 6.71 ± 1.84 at pre-treatment, and 3.82 ± 2.47 vs 3.11 ± 2.01 at day 28, (p <0.001). Mean ± SD for FACES comparing Dry group vs IMS group: 3.50 ± 0.71 vs 3.59 ± 0.73 at pre-treatment, and 2.11 ± 1.13 vs 1.68±0.84 at day 28, (p <0.001). Mean±SD for PTS comparing Dry group vs IMS group: 2.44 ± 0.70 vs 2.36±0.66 at pre-treatment, and 1.33 ± 0.69 vs 1.27 ± 0.88 at day 28, (p < 0.001).	"TrP and paraspinal dry needling is suggested to be a better method than TrP dry needling only for treating myofascial pain syndrome in elderly patients."	Average age of participants 78. Did not describe randomization. Only had 3 baseline demographic variables age, gender, BMI. No mention of duration of symptoms or etiology other than exclusion criteria.
Acupressure						
He 2004 RCT	7.5	N = 24 females chronic neck and shoulder pain. Age	Acupressure or treatment group or TG and ear acupressure; 3 treatments	Intensity of Pain: Immediately following treatment: TG-15 units +/- 5,	"Adequate acupuncture treatment may reduce chronic pain in the neck and	Used combination of body acupuncture, body acupressure, and ear

No mention of sponsorship or COI.		range 20-50 years old.	a week for 10 treatments (n = 14) vs. Sham or control group or CG acupuncture, 3 treatments a week for 10 treatments (n = 10). 3 years follow-up.	CG-36 units +/- 8 (p = 0.02), 6 months following therapy: TG- 24 +/- 7, CG- 36 +/-8 (p = 0.15), 3 years following treatment: TG 19 +/-6, CG 44 +/-11, (p < 0.04).	shoulder as well as related headaches. The effect may last for at least 3 years."	acupressure. Control group similar procedures in different locations. Same acupoints used for each group regardless of pain. Long-term follow-up.
Yip 2006 RCT Supported by School of Nursing Departmental Research Committee. No mention of COI.	6.0	N = 32 subacute non-specific neck pain. Age: ≥18 years.	8 sessions of acupressure massage with natural aromatic lavender oil and conventional treatment for 35-40 minutes over a 3-week period or MAG group (n = 14) vs. Conventional treatment or CG group (n = 18). Follow-up at 1 week and 1 month post intervention.	Baseline to post- 1 month mean±SD for pain level comparing MAG vs CG: 0.77±0.51 vs 0.98 ± 0.48, (p = 0.43). Baseline to post- 1 month mean±SD for stiffness level comparing MAG vs CG: 0.77±0.63 vs 1.13±0.99, (p = 0.42). Baseline to post- 1 month mean±SD for Neck Disability Score comparing MAG vs CG: 0.61±0.71 vs 0.80 ± 0.44 (p = 0.33).	"This study shows that the combined effect of eight sessions of acupressure with aromatic lavender oil reduces short-term neck pain, stiffness, and stress reduction for a month period. Moreover, the intervention also improves the range of motion of the neck. All intervention group members reported their acceptance of acupressure with aromatic lavender oil. As an add-on treatment for neck pain."	Neck pain for 2 weeks. Acupressure group had 8 treatments over 3 weeks. Follow-up 1 month post treatment. 81% of female. Allowed "conventional treatment" in both arms, but this treatment not recorded except for number of pain killers taken.
Acupuncture vs. NSAIDs						
Cho 2014 RCT Sponsored by program of Kyung Hee University for young medical researcher in 2009. No COI.	4.5	N = 45 with chronic neck pain. Age range 25-55 years.	Acupuncture (AC) for 3 weeks (N = 15) vs. NSAID (NS): 80mg 3 times daily of zaltoprofen (n = 15) vs. Acupuncture and NSAID (AN): receiving 80mg 3 times daily of zaltoprofen while receiving 9 acupuncture sessions for 3 weeks (n = 15). Follow-up at 1, 3, and 7 weeks.	Mean ± SD for neck disability index (NDI) comparing AC vs NS vs AN: 22.2 ± 5.9 vs 22.3 ± 4.0 vs 26.3 ± 5.0 at baseline; 17.5 ± 4.9 vs 17.3 ± 5.7 vs 17.7 ± 5.4 (p <0.01). Mean ± SD for Beck's depression index (BDI) comparing AC vs NS vs AN: 28.7 ± 4.8 vs 30.7 ± 5.6 vs 33.1 ± 7.8 at baseline; 25.7 ± 4.4 vs 28.5 ± 7.3 vs 27.2 ± 6.3 (p < 0.05).	"In conclusion, this pilot study has provided the feasibility, safety and sample size for a full-scale trial of acupuncture with NSAIDs for chronic neck pain in comparison with acupuncture or NSAID treatment alone. Although preliminary, the finding that acupuncture with NSAIDs provides no greater benefit than acupuncture or NSAIDs alone raises questions about the mechanism of reciprocal action."	No difference between groups.
Dry needling vs. Placebo						
Mejuto-Vázquez 2014 RCT No mention of sponsorship. No COI.	6.5	N = 17 with acute mechanical, idiopathic, unilateral neck pain. Mean±SD age 25±4 years.	Trigger point dry needling (TrPDN) for a single session (n = 9) vs. Control did not receive any intervention (n = 8). Follow-up 1 week.	Mean ± SD of neck pain intensity in TrPDN group compared to control: 5.7 ± 1.8 vs 5.3 ± 2.0 at pretreatment; 2.0 ± 1.7 vs 4.6 ± 2.1 at 1 week. 95%CI difference between groups at	"The results of this randomized clinical trial suggest that a single treatment session with TrPDN decreases pain intensity and widespread pressure pain sensitivity and	Small sample size (N=17). Short follow-up (1 week). Data suggest dry needling superior to wait list controls.

				posttreatment: 2.1 (1.0, 3.2); and at 1 week post treatment: 3.0 (2.1, 3.9), (p <0.01).	increases cervical range of motion in the short term (1 week posttreatment) in individuals with acute mechanical neck pain."	
Interactive Neurostimulation						
Schabrun 2012 Sponsored by a Clinical Research Fellowship from the National Health and Medical Research Council of Australia. Study received one free-of-cost INS device from the Neuro Resource Group, Inc. No COI.	6.5	N = 23 with pain of neck or shoulder for >2 weeks. Mean age 23.15 (18-29) years.	Interactive Neurostimulation (INS) using InterX®5002 for 10 minutes (n = 12) vs. Sham or unpowered device was used (n = 11). Follow-up at 5 days.	Mean±SD VAS score immediately at post intervention and at 5-day follow up for INS group vs sham group: 2.6 ±2.0 and 1.5±1.6 (57%, respectively) vs 2.7 ± 1.7 and 1.3 ± 1.1 (48%, respectively). Effect of group, (p = 0.9); group x time interaction, (p = 0.18). Mean ± SD neck disability index score from pre-treatment to 5 day follow up for INS group vs sham group: 7.2 ±8.7 to 8.3 ±5 .0 (48%) vs 18.1 ±13.1 to 9.8 ±8.5 (54%). Effect of group (p = 0.60); group x time interaction, (p = 0.37).	"INS is a new and emerging therapy that may be efficacious for managing musculoskeletal conditions such as myofascial pain syndrome. Although there was no significant change in pain levels or NDI scores, this trial demonstrates improvements in function in individuals with MTPs following INS therapy, which may be of clinical significance for certain patients with neck or shoulder pain."	Small sample size (N=23). Short follow up TX at 5 days. Data suggest no difference between Active and Sham.

CRYOTHERAPIES

Cold or cryotherapies involve applications of cold or cooling devices to the skin, such as towels moistened with cold water, ice wrapped in a blanket, ice massage, cold water and/or ice placed in a "water bottle," gel packs, cooling sprays, or single-use chemical packets that produce cooling on breaking one pouch inside the other to start a chemical reaction.

Cryotherapy is theorized to result in a delay or reduction of inflammation.(925) Application of cold will result in vasoconstriction, though a subsequent vasodilatory response to reassert homeostasis is also likely. Similar to heat therapies, most researchers believe that cryotherapies do not directly result in healing. Rather, the general beliefs are that these thermal treatments affect only the skin and subcutaneous fat and yet skin stimulation may distract the patient from other painful stimuli, thus allowing faster resumption of normal activities or increased tolerance of therapeutic exercises. Despite lacking evidence of direct healing benefits, the potential for increased function and earlier recovery may still be worth utilizing cryotherapies for the patient's benefit, particularly as the cost for some of these methods is minimal.

1. *Recommendation: Cryotherapies for Management of Acute Cervicothoracic Pain*
   Self applications of low-tech cryotherapies are recommended for management of acute cervicothoracic pain. Cryotherapies may be tried for other forms of cervicothoracic pain, though they may be less beneficial.

   Indications – Moderate to severe acute cervicothoracic pain patients with sufficient symptoms that an NSAID/acetaminophen and progressive graded activity are believed to be insufficient. May be tried as well for subacute or chronic pain, but suggested threshold for discontinuation is lower, particularly as active modalities are generally far preferable to passive modalities for rehabilitation of non-acute cervicothoracic pain.

   Frequency/Duration – It is recommended that the therapy be for 15 minutes or less to avoid damage to tissue. It may be repeated as often as every 30 minutes.

   Indications for Discontinuation – Non-tolerance, including exacerbation of cervicothoracic pain.

   Benefits – Potential modest reduction in spine pain. Self-efficacy, although relying on a passive modality.
   Harms – Cold injuries. Time may be devoted to passive modality instead of active exercises.
   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

2. *Recommendation: Routine Use of Cryotherapies in Health Care Provider Offices or Home Use of High-tech Devices*
   Routine use of cryotherapies in health care provider offices or home use of a high-tech device for the treatment of cervicothoracic pain is not recommended. However, single use of low-tech cryotherapy (ice in a plastic bag) for severe exacerbations is reasonable.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Moderate

Rationale for Recommendations

Self-application of cryotherapies using towels or reusable devices is not invasive, is without complications, and does not have any appreciable costs. These are recommended as potential distractants or counter-irritants. Other forms of cryotherapy can be considerably more expensive, including chemicals or cryotherapeutic applications in clinical settings, and are not recommended.

Evidence for the Use of Cryotherapies

There is 1 moderate-quality RCT incorporated into this analysis.(926) There is 1 low-quality RCT in Appendix 1.(927)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: cryotherapy, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In*

PubMed we found and reviewed 18 articles, and considered two for inclusion. In Scopus, we found and reviewed 40 articles, and considered one for inclusion. In CINAHL, we found and reviewed two articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 2 articles, and considered one for inclusion. We also considered for inclusion one article from other sources. Of the 5 articles considered for inclusion, 2 randomized trials and 3 systematic studies met the inclusion criteria.

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Heat vs Cold						
Garra 2010 RCT No mention of sponsorship or COI.	6.0	N = 60 with neck of back pain <24 hours duration resulting from minor injury, mean age 38±5 for heat, and 36±11 for cold.	Heat Therapy, electric heating pad, 30 minutes, set on high to average skin temperature of 132°F, varying between 130 and 136°F (n = 31) vs. Cold Therapy, Instant Cold Pack, 30 minutes, average skin temperature of 28.7°F varying between 19.9 and 34.1°F (n = 29). Follow-up before and after treatment.	No statistically significant differences were found between the two groups in the VAS pain score; 75 mm [95% CI = 66 to 83] vs 72 mm [95% CI = 65 to 78], (p = 0.56) or after (66 mm [95% CI = 57 to 75] vs 64 mm [95% CI = 56 to 73], (p = 0.75) therapy.	"The addition of a 30-minute topical application of a heating pad or cold pack to ibuprofen therapy for the treatment of acute neck or back strain results in a mild yet similar improvement in the pain severity. However, it is possible that pain relief is mainly the result of ibuprofen therapy."	Short follow up. No meaningful differences between groups.

HEAT THERAPIES

There are many forms of heat therapy for treatment of cervicothoracic pain. These include hot packs, moist hot packs, sauna, warm baths, infrared, diathermy, and ultrasound.(928) The depth of penetration of heat is minimal for local convective means, but the other modalities have deeper penetration.(929) Unlike in the lower spine, there are few studies that look specifically at using heat therapy. They include heat therapies often as a part of a treatment protocol.

Hot Packs, Heat Wraps, and Moist Heat

The application of warmth or heat is frequently divided into dry or moist heat. Moist heat involves the application of a wet towel or other device that brings the warmed water into direct contact with the skin. Dry heat does not involve direct application of water on the skin surface. In the simplest form, a heated towel is used. Heat wraps include devices that produce heat at greater depth than typical convective heat.(930, 931) Moist heat most commonly involves heating wet towels, soaking a towel in warm water, or using commercial products that are soaked in a warm bath prior to application on the skin surface.(928, 932)

Recommendation: Heat Therapy for Acute, Subacute, or Chronic Cervicothoracic Pain

Heat therapy, including a heat wrap, is recommended for treatment of acute, subacute, or chronic cervicothoracic pain. However, use in chronic cervicothoracic pain is recommended to be minimized to flare-ups with the primary emphasis in chronic cervicothoracic pain patients being placed on functional restoration elements including aerobic and strengthening exercises. **Self-application of heat is recommended.**

Indications – Self-applications may be periodic or continuous. These applications should be home-based as there is no evidence for particular efficacy of provider based heat treatments.

Frequency/Duration – Self-applications may be periodic and include different regimens – e.g., 15 to 20 minutes, 3 to 5 times a day.(932)

Indications for Discontinuation – Intolerance, increased pain, or development of a burn or other adverse event.

Benefits – Potential modest reduction in spine pain. Self-efficacy, although relying on a passive modality.
Harms – Heat injuries. Time may be devoted to passive modality instead of active exercises.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – Low

2. *Recommendation: Application of Heat Therapy by a Health Care Provider for Chronic Spine Pain*
Application of heat (such as infrared, moist heat, whirlpool) by a health care provider is not recommended for chronic spine pain as the patient can perform this application independently.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation
A moderate-quality trial compared manipulation and mobilization with and without moist heat therapy. The authors reported that a clinically meaningful reduction in most severe pain was 60% more likely among participants assigned to heat therapy vs no heat at the 2 week follow-up assessment.(932) Heat therapy in the form of a commercial heat wrap has not been studied as well in cervical pain as in lumbar pain. While there is a lack of direct RCTs evaluating heat, with the evidence that is available in cervicothoracic pain, it is reasonable to prescribe. It is most beneficial to use heat in conjunction with a treatment program that is active.(932)

Evidence for the Use of Heat Therapy
There are 3 moderate-quality RCTs incorporated into this analysis.(926, 928, 932)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Heat therapy (including heat wrap), Hot Packs, Heat Wraps, and Moist Heat, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 718 articles, and considered 2 for inclusion. In Scopus, we found and reviewed 944 articles, and considered 1 for inclusion. In CINAHL, we found and reviewed 40 articles, and considered 1 for inclusion. In Cochrane Library, we found and reviewed 22 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 3 articles considered for inclusion, 3 randomized trials and 0 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Hurwitz 2002 Am J Public Health RCT Sponsored by grant from Health Resources and Services Administration, Dr Hurwitz also supported by grant from National Center for Complementary and Alternative Medicine.	6.5	N = 336 with neck pain patients excluded 3rd party liability claims or workers' comp	Manipulation with or without heat, manipulation with or without electrical muscle stimulation, mobilization with or without heat (n = 171) vs. Mobilization with or without electrical muscle stimulation (n = 165). 6 months follow-up.	Mean reductions in pain and disability were similar in the manipulation and mobilization groups through 6 months. See also Hurwitz et al, Spine 2002.	"Cervical spine mobilization is as effective as manipulation in reducing neck pain and related disability among chiropractic patients. In addition, they show that neither heat nor EMS, alone or in combination with manipulation or mobilization, appreciably improves clinical outcomes, although heat may be of short-term benefit for some patients."	No mention of blinding. Treatment protocols not well defined for quantity or exact technique. No placebo group. Heat alone did not show clinical benefits.
Garra 2010 RCT No mention of sponsorship or COI.	6.0	N = 60 with acute back or neck strains; mean (±SD) age 37 (±13) years	Heat therapy, application of heat packs) (n = 31) vs. Cold therapy, application of old packs (n = 29). Secondary outcome measures included percentage of patients requiring rescue analgesia, degree of pain relief, and future desire for similar packs.	Mean decrease in pain scores also similar in heat and cold groups (9 [±16] mm vs 8 [±10] mm, respectively) (Difference 1, 95% CI -5.7 to 7.9, (p = 0.75) Secondary: Requested rescue medication, administered rescue medication, patient satisfaction are not significant.	"The addition of a 30-minute topical application of a heating pad or cold pack to ibuprofen therapy for the treatment of acute neck or back strain results in a mild yet similar improvement in the pain severity. However, it is possible that pain relief is mainly the result of ibuprofen therapy."	Short follow up. No meaningful differences between groups.
Hurwitz 2002 Spine RCT Sponsored by grants from the Agency for Healthcare Research and Quality and the Southern California University of Health Sciences. Dr. Hurwitz was supported by a grant from the National Center for Complementary and Alternative Medicine. Conflict of interest:	5.0	N = 681 with acute, subacute, and chronic LBP patients. workers' comp patients excluded	Chiropractic care with physical modalities: spinal mobilization or manipulation, strengthening and flexibility exercises, instruction in proper back care or DC group (n = 169) vs. Chiropractic care without physical modalities: DC group plus heat/cold therapy, ultrasound, electrical muscle stimulation or DCPm group (n = 172) vs. Medical care with PT: medical therapy and instruction on proper back care, heat/cold therapy, ultrasound, EMS, soft tissue and joint mobilization, traction, supervised therapeutic exercise, and strengthening and	"The mean changes in low back pain intensity and disability of participants in the medical and chiropractic care-only groups were similar at each follow-up assessment (adjusted mean differences at 6 months for most severe pain, 0.27, 95% confidence interval, -0.32-0.86; average pain, 0.22, -0.25-0.69; and disability, 0.75, -0.29-1.79). Physical therapy yielded somewhat better 6-month disability outcomes than did medical care alone (1.26, 0.20-2.32)."	"Differences in outcomes between medical and chiropractic care without physical therapy or modalities are not clinically meaningful, although chiropractic may result in a greater likelihood of perceived improvement, perhaps reflecting satisfaction or lack of blinding. Physical therapy may be more effective than medical care alone for some patients, while physical modalities appear to have no benefit in chiropractic care."	Trial's primary weakness was complete lack of controlling for numerous interventions, which limits the conclusions about any one intervention.

Federal and foundation funds were received to support this work.			flexibility exercises or MD Pt group (n = 170) vs. Medical care without PT: instruction in proper back care and strengthening and flexibility exercises, prescription for analgesics, muscle relaxants, anti-inflammatories, lifestyle recommendation or MD group (n = 170). Follow-up at 2, 6, 26, 52, and 78 weeks.			

DIATHERMY

Diathermy is a type of heat treatment that has been used clinically to heat tissue.(558, 933) There are two forms of diathermy – short wave and microwave. High-dose diathermy is also used to coagulate tissue. Proponents of diathermy utilize it to treat a wide range of conditions; they believe it penetrates deeper than hot packs or heating pads and stimulates healing.(933, 934)

Recommendation: Diathermy for Cervicothoracic Pain

Diathermy is not recommended for treatment of any cervicothoracic pain-related condition.

Strength of Evidence – **Not Recommended, Evidence (C)**
Level of Confidence – Moderate

Rationale for Recommendation

There are no sham-controlled studies evaluating diathermy in cervicothoracic pain. A moderate-quality trial evaluated diathermy with advice and exercise, compared to advice and exercise alone and did not find any benefit at 6 month follow up.(558) Diathermy is moderate cost, not invasive, and has low potential for adverse effects as typically utilized. It is more expensive than other alternatives such as heat and moderate quality evidence suggests it is ineffective.

Evidence for the Use of Diathermy

There is 1 high-(935) and 2 moderate-quality RCTs (one with two reports)(558, 578, 579) incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: diathermy, diathermies, dielectric heating, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 51 articles, and considered 3 for inclusion. In Scopus, we found and reviewed 53 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 1 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 1 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 3 articles considered for inclusion, 3 randomized trials and 0 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Andrade Ortega 2014 RCT Double-blind Sponsored by the Instituto de Salud Carlos III. No COI.	9.5	N = 149 with nonspecific chronic cervical pain for 3 months or longer, the mean age (SD) 43.6 (11.2) for group C, 45.5 (7.9) for group P, and 43.6 (10.9) for group U.	Group C receiving continuos microwaves, 80 W for 20 minutes, plus TENS and exercise home plan (N = 50) vs Group P receiving pulsed microwaves, mean of 5 W for 20 minutes, plus TENS and exercise home plan (n = 48) vs. Group U receiving sham treatment, plus TENS and exercise home plan (n = 51). Follow-up assessment after treatment (session 15) and at 6 months.	Role Physical (RP) at 6 month follow up approaching significance, mean (SD): Group C- 38.4 (38.9), Group P- 50.1 (44.0), Group U- 52.6 (44.8), (p = 0.070). All other measurements of the treatments' efficacy resulted in insignificant values.	"Our study suggests that microwave diathermy provides no additional benefit to a treatment regimen of chronic neck pain that already involves other treatment approaches (eg, exercise, TENS), in terms of pain, disability, patient satisfaction, perceived outcome, quality of life, adherence to exercise, and use of therapeutic co-interventions."	No stastically significant differences between groups after treatment.
Koes 1992 a,b 3 reports of 1 RCT No mention of sponsorship or COI.	5.0	N = 256 with chronic back and neck pain mean duration 1 year. Mean age 43.	Manual therapy, manipulation and mobilization of spine (n = 65) vs. Physiotherapy exercises, massage and/or PT modalities such as heat, electrotherapy, ultrasound, shortwave diathermy (n = 66) vs. Placebo therapy treatment twice a week for 6 weeks; maximum 3 months (n = 64) vs General practicioner (n = 61). Number of treatments varied markedly from 1 for GP and placebo to 14.7 for physiotherapy. Follow-up at 6 and 12 months.	At 12 months, manipulative therapy marginally superior to physiotherapy in "improvement," but not for all other measures and time intervals. Difference in improvement scores between both groups was 0.9 (CI 95%, 0.1 to 1.7).	"[M]anipulative therapy and physiotherapy are better than general practitioner and placebo treatment. Furthermore, manipulative therapy is slightly better than physiotherapy after 12 months."	Updated in Brenden's Massage search. This article is also relevant to Diathermy
Dziedzic 2005 RCT Sponsored by Arthritis Research Campaign and the West Midlands R & D NHS. No COI.	4.0	N = 350 with non-specific neck disorders (primary care patients), 78% duration >3months; excluded WC and litigation	Advice and exercise plus manual therapy (n = 115) vs. Advice and exercise plus pulsed shortwave (n = 114) vs. Advice and exercise alone (n = 121). Maximum 8 therapy visits over 6 weeks. Assessments at 6 weeks and 6 months.	Mean Northwick Park SD reduction score 10.1+/-12.6 at 6 weeks for advice and exercise. Advice with manual therapy 8.7+/-12.1 and advice, exercise, and PSWD 7.7+/-10.8. No significant difference between groups.	"[N]either manual therapy nor PSWD conferred any additional clinical benefit over a short course of active physical treatment incorporating an advice and exercise package delivered by experienced musculoskeletal physical therapists."	Advice and Exercise only group had significantly lower number of visits and duration of treatment, and also had less medication use and fewer doctor visits likely biasing against that group.

INFRARED THERAPY
Infrared is a heat treatment created by various devices producing electromagnetic radiation in the infrared spectrum.(575, 936)

Recommendation: Infrared Therapy for Acute, Subacute, Chronic, or Radicular Cervicothoracic Pain
There is no recommendation for or against the use of infrared therapy for treatment of acute, subacute, chronic, or radicular cervicothoracic pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendations
There are no quality sham-controlled trials of infrared therapy in cervicothoracic pain patients. A moderate-quality trial compared TENS plus infrared therapy, exercise plus infrared therapy, and infrared therapy in patients with >3 months of intermittent cervicothoracic pain.(575) Since infrared therapy was used in all treatment groups, no conclusion about its effectiveness is possible. The authors reported improvement in muscle strength, improvement in the Northwick Park Neck Pain Questionnaire, but no improvement in verbal numerical pain scale, medication use, or number of subjects taking sick leave because of neck pain at 6 weeks in the infrared therapy only group. The improvement in the Northwick Park Neck Pain Questionnaire was maintained in the infrared therapy only group at 6 months.(575) Infrared is moderate cost, not invasive, and has little potential for adverse effects. It is more expensive than other alternatives such as heat and has not been shown to be superior to less expensive forms of heat therapy. There is no evidence to suggest it is effective and thus there is no recommendation.

Evidence for the Use of Infrared Therapy
There are 2 moderate-quality RCTs incorporated into this analysis.(575, 598)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: infrared therapy, infrared rays, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 33 articles, and considered 1 for inclusion. In Scopus, we found and reviewed 49 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 2 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 1 articles, and considered 1 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 3 articles considered for inclusion, 2 randomized trials and 1 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Chiu 2005 RCT Sponsored by Area of Strategic Development Fund of the Hong Kong Polytechnic University and Health Services Research Fund. No mention of COI.	7.0	N = 218 with neck pain lasting longer than 3 months, ages 20-70 years	TENS group with TENS applied to acupuncture sites (Ex21, GB21 and LI11) for 30 minutes plus infrared (IR) for 20 minutes and neck care advice (n = 73) vs. Exercise group with IR plus intensive neck exercise program, twice a week for 6 weeks, active exercises, resistance (n = 67) vs. Control group receiving IR plus neck care advice, twice a week for 6 weeks (n = 78). Follow up assessments at 6 weeks and 6 months.	At 6 weeks assessment, Lowest Northwick Park Neck Pain Questionnaire scores showed significant results of improvement over the control for TENS, ($p = 0.034$) and Exercise Group, ($p = 0.02$); significant improvements in isometric neck muscle strength after six months in exercise group, ($p < 0.001$) and in TENS group, ($p = 0.009$) over control group. Number of patients taking sick leave at 6 months: 5.5% TENS ($p = 0.03$) vs 3% exercise ($p = 0.01$) vs 9% for controls.	"After the 6-week treatment, patients in the TENS and exercise group had better and clinically relevant improvement in disability, isometric neck muscle, strength, and pain."	Study's main results suggest exercise superior to TENS or infrared for chronic neck pain. TENS placed over acupuncture sites for neck pain.
Diab 2012 RCT No sponsorship or COI.	4.0	N = 96 with unilateral lower cervical spondylotic radiculopathy for greater than 3 months, spondylotic changes of C5-C6 and C6-C7 that exceeded 50% or more in side to side amplitude differences for dermatomal somatosensory-evoked potentials measurements, mean age (SD) 46.3 (±2.05) for study group and 45.9 (±2.1) for control group	Infrared (10 minutes), Ultrasound (10 minutes with 1.5 w/cm2 intensity) and Exercise (strengthening and stretching) study group (n = 48) vs Infrared (10 minutes) and ultrasound (10 minutes with 1.5 w/cm2 intensity) only control group (n = 48). Assessments at 10 weeks and 6 months following treatment.	At 10 weeks after treatment, study group showed significant improvement over control: Craviovertebral angle- Study: 41.07 ± 2.9 vs Control: 34.8 ± 3.3, ($p = 0.000$). Pain- Study: 3.2 ± 1.3 vs Control: 3.9 ± 1.4, ($p = 0.01$). Dermatomal evoked potentials (C6)- Study: 0.82 ± 0.13 vs Control: 0.56 ± 0.19,($p = 0.000$). Dermatomal evoked potentials (C7)- Study: 0.6 ± 0.16 vs Control: 0.43 ± 0.19, ($p = 0.001$). After 6 months: Craviovertebral angle- Study: 39.5 ± 3.3 vs Control: 34.5 ± 3.4,($p = 0.000$). Pain- Study: 2.7 ± 1.3 vs Control: 4.6 ± 1.5, ($p = 0.000$). Dermatomal evoked potentials (C6) - Study: 0.79 ± 0.12 vs Control: 0.41 ± 0.17, ($p = 0.000$). Dermatomal evoked potentials (C7) - Study: 0.59 ± 0.12 vs. Control: 0.28 ± 0.18; ($p = 0.000$).	"Forward head posture correction using a posture corrective exercise programme in addition to ultrasound and infrared radiation decreased pain and craniovertebral angle and increased the peak-to-peak amplitude of dermatomal somatosensory evoked potentials for C6 and C7 in cases of lower cervical spondylotic radiculopathy."	Participants also participated in an exercise program. Study with co-interventions that precludes ability to use for guideline of an intervention.

ULTRASOUND (Therapeutic)
Ultrasound consists of sound waves that are absorbed differently based on the protein content of the tissue. Proponents states this allows heating of deep tissues such as joints, muscle and bone and this leads to repair of soft tissue injuries and is a way to relive pain.(937) The head of the ultrasound instrument should be kept in constant motion to minimize discomfort and prevent tissue damage. Therapeutic ultrasound has more than 60 years of clinical history.(937) It has been frequently used for the treatment of pain, soft-tissue lesions, and a host of musculoskeletal disorders.

Recommendation: Ultrasound for Acute, Subacute, or Chronic Cervicothoracic Pain
There is no recommendation for or against the use of ultrasound for treatment of acute, subacute, or chronic cervicothoracic pain. In situations where deeper heating is desirable, a limited trial of ultrasound is reasonable for treatment of acute cervicothoracic pain, but only if performed as an adjunct with exercise.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There are no quality trials of ultrasound for the treatment of cervicothoracic pain. There is a low-quality trial comparing manipulation to ultrasound therapy in conjunction with NSAIDs and neck collar that was conducted in acute whiplash patients. Improvements in both groups in range of motion, pain, and disability rankings were reported.(938) Ultrasound is not invasive, has few adverse effects, but is moderately costly. There is no recommendation for or against its use in treatment of cervicothoracic pain.

Evidence for the Use of Ultrasound
There are no quality trials of ultrasound for the treatment of cervicothoracic pain. There is 1 moderate-quality RCT for myofascial trigger points incorporated into this analysis.(939) There are 2 low-quality RCTs in Appendix 1.(938, 940)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: ultrasound, ultrasound therapy, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 718 articles, and considered 53 for inclusion. In Scopus, we found and reviewed 4 articles, and considered 6 for inclusion. In CINAHL, we found and reviewed 40 articles, and considered 1 for inclusion. In Cochrane Library, we found and reviewed 22 articles, and considered 0 for inclusion. We also considered for inclusion 15 articles from other sources. Of the 2 articles considered for inclusion, 1 randomized trials and 1 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Aguilera 2009 RCT No COI or sponsorship.	4.0	N = 66 with myofascial trigger points (MTrPs) in trapezius muscle.	Group 1(G1): ischemic compression (IC) (n = 22) vs. Group 2(G2): Ultrasound (US) (n = 22) vs. Group 3 (G3): sham US (n = 22).	G1, G2 and G3 paired with active range of motion (AROM) in degrees, basal electrical activity (BEA) in mV, and pressure tolerance (PT) in mm. Significant differences for G1, in the parameters AROM, BEA, and PT. The mean (SD), p-values for AROM/BEA and PT: 4.54 (8.43), p = 0.020/0.001 27 (0.001	"Both modalities had a treatment effect of latent MTrPs in healthy subjects. The results showed a relation among AROM of cervical rachis, BEA of the trapezius muscle, and MTrP sensitivity of the trapezius muscle gaining short-term positive effects with use of IC."	Lack of details for allocation, baseline comparability. No true blinding described. Study outcome measured after 1 treatment was no specifically defined. Data suggest similar outcomes of IC and US. Clinical significance ill defined.

				56), p = 0.002, and 8.23 (14.78), p = 0.035. Also, significant differences for G2, in parameters BEA and PT. Mean (SD), p- values 0.000 89 (0.000 91), p = 0.000 in BEA and 7.50 (7.86), p= 0.000 in PT. No significant differences found for G3.		

LOW-LEVEL LASER THERAPY

Low-level laser treatment usually involves laser energy that does not induce significant heating (see Myofascial Pain Syndrome in Shoulder Disorders guideline for additional recommendation).(941-945)

Recommendation: Low-level Laser Therapy for Acute, Subacute, or Chronic Cervicothoracic Pain
There is no recommendation for or against the use of low-level laser therapy for the treatment of acute, subacute, or chronic cervicothoracic pain.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There are trials of LLLT for the treatment of cervicothoracic pain, however, there are methodological issues with nearly all available studies and the studies somewhat conflict. More sham-controlled trials suggest benefit than those that do not. Quality trials, including assessing adequacy of blinding, are needed prior to a recommendation.

Evidence for the Use of Low-Level Laser Therapy
There are 2 high-(944, 946) and 4 moderate-quality RCTs(939, 942, 945, 947) incorporated into this analysis.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

Neck Pain, Cervicalgia, Cervical Pain, Cervical Radiculopathy, Radicular Pain, Postoperative neck Pain, Postoperative cervical Pain, Herniated Disk, neck pain, cervical pain, cervical radiculopathy, radicular pain, herniated disk, postoperative neck pain, postoperative cervical pain, laser therapy, low-level, Low level laser therapy, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies; to find 408 articles. Of the 408 articles, we reviewed 14 articles and included 12 articles (6 randomized controlled trials and 6 systematic reviews).*

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Konstantinovic 2010 (9.0)	Low level laser therapy (LLLT)	RCT	No mention of sponsorship. The authors declared no COI.	N=60 with acute neck pain with unilateral radiculopathy	Mean age: 40.13 years; 25 males, 35 females.	Group A: local active LLLT (wavelength 905 nm, frequency 5,000 Hz, power density of 12 mW/cm2, and dose of 2 J/cm2, treatment time 120 seconds, at whole doses 12 J/cm2) (n = 30) vs. Group B: treated with local placebo LLLT. Measurements were taken at baseline and 3 weeks (n = 30).	Follow-up at baseline, 4 weeks, 4 and 16 months.	A statistically significant difference between the groups was only verified for duration of symptoms (t = –2.016, P = 0.048). In comparision with baseline both groups showed statistical significance P < 0.001. Between the groups Group A showed a higher statistical significance that of Group B in all fields except neck pain.	"LLLT gave more effective short-term relief of arm pain and increased range of neck extension in patients with acute neck pain with radiculopathy in comparison to the placebo procedure."	Author conclusions that LLLT is more effective than sham LLLT are misleading, as there is little clinical significance in the primary outcome measure of VAS pain scores (reduction VAS- arm 29.77 vs 20.68, VAS neck 23.35 vs. 19.01). Thus, no clinically significant difference is demonstrated.
Chow 2006 (8.0)	Low level laser therapy (LLLT)	RCT	No mention of sponsorship or COI.	N = 90 with unilateral or bilateral chronic neck pain (for at least 3 months), were able to attend a full course of 14 treatments given twice a week, and were naïve to treatment with low-level laser therapy (LLLT).	Mean age: 56.1 years; 31 males, 59 females.	All patients had 14 treatments over 7 weeks. Group A: low-level laser therapy (300 mW, 830 nm) (n = 45) vs. Group B: sham laser (n = 45).	Follow-up at baseline, 1 month.	(Author reported results mean [95% CI]) There was a significant difference in improvement in raw VAS (Group A: -2.7 [-3.3, -2.1] vs. Group B: 0.3 [-1.4, 0.9], P < 0.001), the physical component score of SF-36 (Group A: 3.2 [-0.3, -5.1] vs. Group B: -1.3 [-3.9, -1.4], P < 0.022, please see comments), Northwick Park Neck Pain	"Laser therapy with a wavelength of 830 nm and an output power of 300 mW provides clinically relevant benefit in the management of chronic neck pain as a monotherapy."	Author was contacted about result for physical component score of SF-36 for accurate result.3 month follow-up. Baseline changes – VAS laser 5.1 v 4.0, worse severly 53 v 20%. As 2 lasers used, unblinding of provider may have occurred.

								Questionnaire (Group A: -3.5 [-5.1, -1.9] vs. Group B: -0.6 [-1.8, 0.6], P < 0.005), Neck Pain and Disability Score (Group A: -15.2 [-20.4, -9.9] vs. Group B: -3.1 [-7.6, 1.4], P < 0.001), VAS on McGill Pain Questionnaire (Group A: -2.1 [-3.0, -1.1] vs. Group B: 0.1 [-0.9, 0.7], P < 0.001), and Percentage of Self-Assessed Improvement (Group A: 2.1% [-7.4, 11.6] vs. Group B: 41.7% [27.7, 55.8], P < 0.001).		
Saayman 2011 (6.5)	Low level laser therapy (LLLT)	RCT	Sponsored by the Chiropractic Day Clinic of the University of Johannesburg, The department of Chiropractic, and the Laser Research Center. The authors declared no COI.	N=60 with CFD (Cervical Facet Dysfunction) 60 ambulatory women between the ages of 18 and 40 years with CFD for more than 30 days.	Mean age: 29 years; 0 males, 60 females.	Group 1: patients received chiropractic joint manipulation therapy (CMT) (n=20) vs. Group 2: patients received low level laser therapy (LLLT (n=20) vs. Group 3: patients received both CMT and LLLT (n=20).	Follow-up at baseline, 4 weeks.	No differences existed between the 3 groups at baseline. A significant difference was seen between groups 1 (CMT) and 2 (LLLT) for cervical flexion, between groups 1 (CMT) and 3 (CMT + LLLT) for cervical flexion and rotation, and between groups 2 (LLLT) and 3 (CMT + LLLT) for pain disability in everyday life, lateral flexion, and rotation.	"All 3 groups showed improvement in the primary and secondary outcomes. A combination of CMT and LLLT was more effective than either of the 2 on their own. Both therapies are indicated as potentially beneficial treatments for cervical facet dysfunction. Further studies are needed to explore optimal treatment	Study included only females with diagnosis of "cervical facet dysfunction" . No control group included. Data suggest similar effect of CMT and LLLT. Data suggest potential additive effect in consideration. Lack of blinding may have resulted in bias as group with intervention

									procedures for CMT and LLLT and the possible mechanism of interaction between therapies."	may have expected more relief.
Aguilera 2009 (4.0)	Low level laser therapy (LLLT)	RCT	The authors declared no sponsorship or COI.	N= 66 healthy individuals diagnosed with latent myofascial trigger points.	Mean age: 37.2 years; 29 males, 37 females.	Group 1: patients received ischemic compression (IC) treatment (n=22) vs. Group 2: patients received ultrasound (US) (n=22) vs. Group 3: patients received sham ultrasound (n=22).	No mention of follow-up.	Significant changes were found both in G1 and G2, but not in G3. Active range of motion (AROM), basal electrical activity (BEA)-dominant side, and Pressure pain threshold (PT) of myofascial trigger points (MTrPs)-dominant side were improvement significantly in G1 (p=0.02, 0.002, and 0.035 respectively). BEA-dominant side and PT-dominant side in G2 were improved significantly (p=0.00, 0.00 respectively).	"In this group of participants, both treatments were shown to have an immediate effect on latent MTrPs. The results show a relation among AROM of cervical rachis, BEA of the trapezius muscle, and MTrP sensitivity of the trapezius muscle gaining short-term positive effects with use of IC."	Lack of details for allocation, baseline comparability. No true blinding described. Study outcome measured after 1 treatment but not specifically defined. Data suggest similar outcomes with IC and US. Clinical significance is ill defined.

MANIPULATION AND MOBILIZATION

Manipulation and mobilization are two types of manual therapy. These include wide arrays of different techniques and schools of thought. Some consider these two interventions to be on a spectrum of velocity and applied force. In general, mobilization involves assisted, low-force, low-velocity movement within or at the limit of joint range of motion. Manipulation involves higher-force, higher-velocity, and low-amplitude action with a focus on moving a target joint.

From the standpoint of evidence-based practice guidelines development, there are numerous types of manipulation utilized in many different studies.(562, 675, 897, 948-953) These issues result in difficulties comparing methods, techniques, or results across the available literature. Differences between techniques appear to be largely unstated in the available systematic reviews, which have aggregated all studies together. Adjustment is generally a synonym for manipulation in the chiropractic profession. There are studies evaluating thoracic manipulation for cervical pain without cervical manipulation.(954)

Many practitioners begin with lower force manipulation or mobilization techniques, and reserve higher force manipulation techniques for those who do not respond to lower force techniques to limit adverse effects and complications. Manipulation is generally considered a safe procedure, but like all other treatments is not without risks. For example, reported fatal outcomes have occurred and are particularly attributed to cervical manipulation.(932) Reports of more severe but rare adverse effects include vertebrobasilar dissection, carotid artery injury, and disc herniation or spinal cord compression myelopathy, although these reports need to be considered in the context of natural progressions of cervical pain without any intervention.(955) The mean age of patients experiencing vertebrobasilar dissection in the case reports is 38 and the risk has been reportedly due to cervical manipulation with a rotary component.(932) However, more recent population based studies have questioned the incidence of vascular injury from manipulation, suggesting instead that this may more often be an acceleration or natural progression of an event in progress.(956) Mobilization is less likely to lead to side effects than is manipulation.

The most common adverse response to neck manipulation is local discomfort that resolves within 24 to 48 hours.(932) (Hurwitz AJPH 02)There have been reports of vertebral artery dissection that result in posterior circulation stroke purportedly following cervical manipulation.(948) There has been much debate on the frequency of these events and multiple reports suggest low risk.(957) Population-based case control study of all patients who seek chiropractic care in Ontario revealed a frequency of 8 cases occurred within 7 days of receiving chiropractic care in 109 million person years of observation in Ontario.(956) Of particular interest was the observation that the odds ratio of a stroke occurring after a primary physician visit for cervical pain was the same as that noted following a chiropractic office visits, raising doubt as to whether there is any relationship between the manipulation and stroke. Vertebral artery dissections are heralded by cervical pain and frequently headache that can bring a patient to either a chiropractor or general physician's office, and if not recognized can progress to stroke that can be fatal. This should be considered in the differential diagnosis of cervical pain.

1. Recommendation: Manipulation/Mobilization for Acute, Subacute, or Chronic Cervicothoracic Pain

Manipulation/mobilization of the cervical and/or thoracic spine is recommended for short-term relief of cervical pain or as a component of an active treatment program focusing on active exercises for acute cervicothoracic pain. However, high amplitude, high velocity manipulation is not recommended.

Frequency/Duration – Dependent on severity. Most patients with more severe spine conditions may receive up to 12 visits over 6 to 8 weeks, typically one to 3 times a week;(958-960) total treatments dependent on response to therapy. Substantial progression (e.g., return to work or activities, increasing ability to tolerate exercise, reduced medication use) should be documented at each follow-up visit. Treatment plan should be reassessed after each 2-week interval. Most guidelines suggest that if there is significant response in the above outcomes, it is worth considering another 2 weeks of treatment. If no response to 2 weeks of application of a particular manipulation treatment, it should be discontinued and 2 weeks of a different method of manipulation/mobilization or other treatment should be considered. If there is no response after 4 weeks and two 2-week trials of different manipulation/mobilization techniques, it is unlikely that further manipulation/mobilization will be helpful.

Indications for Discontinuation – Lack of demonstrated continued functional response after 6 manipulation/mobilization sessions (2 trials of 2 or more different methods), resolution of symptoms, or failure to participate in an active rehabilitation program.
Benefits – Potential for faster resolution of pain and improved function.
Harms – Worsening of neck pain, especially immediately after manipulation.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
Multiple studies evaluate thoracic and cervical spine manipulation, (537, 932) whereas other studies evaluated one or the other.(949, 959, 961-964) Other studies do not delineate between the two different types of therapies.(578, 579, 675, 679, 965, 966)

There are no quality trials comparing mobilization to sham or placebo for treatment of acute cervical pain. The closest study appears to be that of Cleland et al (2007), but it was impaired by methodological limitations. Most studies compare mobilization to manipulation, or use mobilization as a component of other interventions, significantly weakening the ability to infer efficacy of manipulation.(581) Most studies had small samples sizes with most <70.(959, 960, 967, 968) A moderate-quality trial evaluating mobilization suggested greater benefit compared with directed exercise and continued care by a general practitioner. However, this study included acute, subacute, and chronic pain without delineation between duration in the results, and the general practitioner care appeared to fail to include treatments thought to be efficacious.(565) A moderate-quality trial comparing cervical manipulation to mobilization suggested improvement in pain and range of motion in both groups after a single treatment, but manipulation was reportedly associated with overall better pain improvement on the NRS-101 and larger gains in range of motion.(6) Thus, the available quality evidence conflicts on treatment of cervicothoracic pain.(969) Hoving suggested mobilization is a favorable treatment option for patients with cervical pain compared with directed exercise or continued care by a general practitioner, although the general medical care may have been suboptimal.(565)

There are no sham-controlled trials of manipulation. Only a few RCTs evaluated subacute cervicothoracic pain and did so in combination with chronic cervicothoracic pain without reporting findings based on duration of symptoms.(960) A moderate-quality study comparing a single episode of cervical manipulation versus mobilization in subacute and chronic patients reported manipulation to have greater improvement in cervicothoracic pain at rest and active range of motion.(961) A moderate-quality study that did not describe well the duration of symptoms found an increase in range of motion after a single thoracic spine manipulation compared to no intervention.(970) (Krauss 08) Where another study compared manipulation and exercises alone and in combination and reported no significant clinical differences at 12-month follow up in chronic pain patients.(537)

A moderate-quality study of patients with chronic pain examined manipulation, manipulation and exercise and an exercise only group. They found that the manipulation alone group had less improvement compared to manipulation with exercise and exercises alone at 16 months after 11 weeks of treatment.(537) One study of 119 patients with cervicothoracic pain greater than 3 months duration reported improvement in all groups, but did not find any difference in the manipulation group when compared to physiotherapy and intensive training of cervical musculature for 6 weeks.(548) A moderate-quality study suggested acupuncture was more effective than manipulation or medications in treating chronic cervical pain.(675) Another moderate-quality study compared manipulation with sham ultrasound to sham ultrasound alone and suggested an improvement in pain in the manipulation group at 12 weeks.(971) While the RCTs show that other interventions are equally beneficial, the manipulation groups also experienced significant improvement in pain control and range of motion. Manipulation in subacute and chronic cervicothoracic pain is recommended and is best utilized in combination with an active exercise program.(537, 972) It was not possible to determine which technique was beneficial for which patient populations. There was also insufficient evidence for cervicothoracic pain with radicular findings.

A study evaluated a Clinical Prediction Rule for cervicothoracic pain using thoracic manipulation that is somewhat analogous to those for the lumbar spine (see Low Back Disorders guideline). They reported predictors for increasing the likelihood of a positive outcome with thoracic manipulation.(973, 974) These 6 variables were symptoms <30 days, no symptoms distal to the shoulder, neck extension does not aggravate pain, FABQPA score

<12, diminished upper thoracic spine kyphosis, and cervical extension ROM <30 degrees. Once this information has been reproduced and validated there may be a group of patients identified where thoracic manipulation may be recommended with greater specificity. However, a recent RCT reported that the above CPR was not able to be validated.(975) Another group assessed a clinical prediction rule and noted better response to treatment if: initial Neck Disability Index <11.5, bilateral involvement pattern, no sedentary work >5 hours a day, feeling better while moving the neck, not worse while extending the neck, and a diagnosis of spondylosis without radiculopathy.(976)

2. Recommendation: Manipulation for Chronic Cervicogenic Headache Pain
Spinal manipulation of the cervical and/or thoracic spine is recommended for treatment of chronic cervicogenic headache pain.

Frequency/Duration – Once or twice a week for 4 to 5 appointments, up to 8 total appointments recommended if there is benefit after 4 to 5 appointments.(599, 977)

Indications for Discontinuation – Resolution of symptoms, adverse effects from treatment, lack of demonstrated positive effect on headache intensity and/or frequency, or non-participation in an active rehabilitation therapy program.(978)

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence – Low

3. Recommendation: Manipulation for Chronic Cervicogenic Headache Pain
High-amplitude, high-velocity spinal manipulation of the cervical and/or thoracic spine is not recommended for treatment of cervical spine conditions.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
A moderate-quality study evaluated 80 patients with chronic cervicogenic headache randomized to either 8 or 16 spinal manipulation sessions in 8 weeks as the intervention group, and 8 or 16 sessions of "light massage" as the control group. The authors reported both clinical and statistical benefit of manipulation lasting up to 24 weeks with decreased reported pain and decreased reported analgesic use. There was no clear benefit of 16 versus 8 visits.(977) A moderate-quality study evaluated cervical manipulation with sham manipulation in a modified crossover study design suggested improvement with cervical range of motion, but did not find improvement in headache pain.(979) Another moderate-quality study in headache patients evaluated cervical manipulation compared to low level laser treatment and massage and failed to find a difference in cervical range of motion, analgesic use per day, headache intensity per episode and number of headaches per day.(978, 980) A moderate-quality study that was a continuation of an earlier study evaluated high velocity low amplitude manipulation with laser and massage as placebo. They reported significant improvement in cervicogenic headache.(981) A moderate-quality study evaluated manipulation versus exercise and found that exercise groups produced better long term outcomes than placebo or manipulation alone.(599) High-amplitude, high-velocity manipulation is not recommended due to concerns it may increase risk of adverse effects such as arterial dissection.

4. Recommendation: Cervical Manipulation for Tension Headaches
Cervical manipulation is not recommended for tension headaches.(982-984)

Strength of Evidence – **Not Recommended, Evidence (C)**
Level of Confidence – Low

Rationale for Recommendation
There is a moderate-quality study of 75 patients evaluating cervical manipulation versus laser light therapy and soft tissue massage as placebo. The authors did not find any benefit of manipulation after 19 weeks of follow up.(983) Another moderate-quality study evaluated manipulation compared to amitriptyline for tension headaches. They found after discontinuation of treatment, manipulation had positive outcomes over amitriptyline; however, they did not address possible withdrawal headaches from amitriptyline.(984)

5. Recommendation: Regular or Routine Manipulation or Mobilization

Regular or routine manipulation or mobilization, prolonged treatment (manipulation several times a month for years), and prophylactic treatment is not recommended.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – High

Rationale for Recommendation
There is no quality evidence of efficacy for prolonged treatment (manipulation several times a month for years). There is no quality evidence that prophylactic treatment is effective for primary prevention (before first episode of pain) or for secondary prevention (after recovery from an episode of cervicothoracic pain), and prophylactic treatment is not recommended. There is also no evidence that manipulation on a regular or routine basis is beneficial.

6 *Recommendation: Manipulation for Radicular Pain Syndromes with Acute Neurological Deficits*
Manipulation is not recommended for the treatment of radicular pain syndromes with acute neurological deficits, especially with progressive neurological loss.

Strength of Evidence **– Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

7 *Recommendation: Manipulation for Radicular Pain Syndromes without Neurologic Deficits*
There is no recommendation for or against manipulation for the treatment of radicular pain syndromes without neurologic deficits.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendations
There is no quality evidence to address manipulation with neurological deficits; however, there are concerns about the use of manipulation in the presence of acute or progressive neurological deficits. Young et al. conducted an RCT evaluating cervical traction for radicular pain. Each group received manual therapy consisting of HLVA of the cervical and thoracic spine in addition to exercise. They reported improvement in both groups; however the study was not designed to evaluate the effects of manipulation of cervical radiculopathy.(562) Another study compared cervical lateral glide mobilization to ultrasound and reported benefits for manipulation. The evaluations were taken immediately following the single intervention without long-term follow up.(985)

Evidence for the Use of Manipulation and Mobilization
There are 4 high-(562, 679, 986, 987) and 76 moderate-quality RCTs or crossover trials (one with two reports) incorporated into this analysis.(6, 222, 497, 536, 537, 544, 548, 565, 567, 573, 574, 576, 578, 579, 581, 584, 675, 676, 897, 932, 949, 950, 958, 959, 961-963, 965-971, 977-979, 981-985, 988-1021) There are 25 low-quality (617, 867, 1022-1046) RCTs and 5 other studies (964, 1044, 1046-1048) in Appendix 1.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: manipulation and mobilization, disorder terms-cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Non-experimental Studies. In PubMed we found and reviewed 756 articles, and considered 130 for inclusion. In Scopus, we found and reviewed 1,436 articles, and considered 5 for inclusion. In CINAHL, we found and reviewed 134 articles, and considered 8 for inclusion. In Cochrane Library, we found and reviewed 32 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 143 articles considered for inclusion, 104 randomized trials and 13 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Acute Neck Pain						
Gonzalez-Iglesias 2009 Man Ther RCT No mention of sponsorship or COI.	7.5	N = 45 with acute mechanical neck pain; mean age of 34±4 years.	Experimental group, electrotherapy/thermal, thoracic manipulation once per week, for 3 weeks (n = 23) vs. Control group, no manipulation procedure (n = 22). Follow-up at baseline, pre-treatment and 1 week after discharge of last session. Three week intervention.	Thoracic spine manipulation group showed greater increases in all cervical motions studied (95% CI); flexion 10.6° (8.8-12.5°); extension 9.9° (8.1-11.7°); right lateral flexion 9.5° (97.6-11.4°); left lateral flexion 8° (6.2-9.8°); right rotation 9.6° (7.7-11.6°); and left rotation 8.4° (6.5-10.3°).	"[T]he inclusion of thoracic manipulation combined with a standard electrotherapy/thermal program results in significantly greater reductions in neck pain and disability as well as increases in neck mobility in the short-term in patients with acute mechanical neck pain."	Repeat report, see comments on Gonzalez-Iglesias 2009.
Bove 1998 RCT Sponsored by Nordisk Insitut for Kiropraktik og Klinisk Biomekanik, Fonden til fremme af kiropraktisk forskning og postgraduate uddannelse, and Foundation for Chiropractic Education and Research. No mention of COI.	7.0	N = 75 with tension-type headaches; mean age of 38 years.	Experimental group received cervical joint manipulation (n = 38) vs. Control group received low-power, placebo laser therapy (n = 37). Follow-up at weeks 7, 11, 15, and 19.	Primary outcomes: the number of headache hours per day / mean headache intensity per headache episode/consumption of analgesics per day: reduced approximately by 1.5 hours by week 7, 95% CI, -2.4 to -0.6 / intensity was unchanged, 95% CI, -12 to 11/analgesics consumption lessened in both groups by week 7, 95% CI, -0.5 to -0.1.	"As an isolated intervention, spinal manipulation does not seem to have a positive effect on tension-type headache."	As control group also showed apparent benefits (e.g., headache hours/day decreasing an average 3.4 to 1.9 hours a day), it is suggested that these headaches have a high placebo response rate.

Puentedura 2011 RCT No mention of sponsorship or COI.	7.0	N = 24 with neck pain baseline Neck Disability Index (NDI) of 10/50 points; mean age 33.7±6.4 years.	Thoracic spine thrust joint manipulation or TJM, 5 sessions, first two included thoracic TJM and cervical ROM exercise, and rest 3 sessions, were standardized therapeutic exercise program (n = 10) vs. Exercise program or cervical group, first 2 sessions included 3-finger ROM exercise as thoracic group, plus standardized exercise as thoracic group (n = 14). Follow-up at 1 and 4 weeks, and 6 months.	There was no difference between the cervical and thoracic manipulation groups, at baseline, (p = 0.482), 1 week, (p = 0.28), and 4 weeks, (p = 0.021), and there was significant difference at 6 months, (p = 0.004). Overall, patients who received cervical TJM demonstrated greater improvements in Neck Disability Index, ($p \leq 0.001$) and pain rating scale, ($p \leq 0.003$), at all follow-ups.	"[P]atients with mechanical neck pain who fit the CPR for thoracic spine thrust manipulation may demonstrate better overall outcomes with TJM directed to the cervical spine as opposed to the thoracic spine."	Highly select population (25% of screened patients were eligible). Baseline difference in duration of pain. Both groups received only 2 active manipulations of 5 sessions of PT. Data suggest benefits of cervical spine thrust manipulation over thoracic lack of central group and small sample size limit conclusions of overall effectiveness.
Fernandez de las Penas 2009 RCT No mention of sponsorship or COI.	6.5	N = 45 acute mechanical neck pain; mean age of 34±5 years.	Experimental group received thoracic thrust manipulation along with electro- and thermotherapy (n = 23) vs. Control group received electro- and thermotherapy alone (n = 22). Assessments performed after 1, 3, and 5 visits. No long-term follow-up.	Differences for pain ($F = 181.4$; $p < 0.001$), flexion ($F = 113.2$; $p < 0.001$), extension ($F = 68.5$; $p < 0.001$) right ($F = 60.5$;$p < 0.001$) and left ($F = 84.3$; $p < 0.001$) rotations, and right ($F = 52.8$; $p < 0.001$) and left ($F = 64.1$; $p < 0.001$) lateral-flexions for the experimental.	"The results suggest that patients receiving thoracic manipulation do not exhibit tolerance to repeated applications with regard to pain and mobility measures in acute mechanical neck pain. Further studies should investigate the dose-response relationship of thoracic thrust manipulation in this population."	No sham treatment. Small numbers.
Nilsson 1996 RCT Sponsored by European Chiropractors Union. No mention of COI.	6.0	N = 39 headache sufferers with decreased passive cervical ROM; mean age of 39 years.	Manipulation group received HVLA cervical manipulation (n = 19) vs. Soft-tissue group received low-level laser in upper cervical and deep friction massage in lower cervical/upper thoracic (n = 19). Diary entry follow-up 1 week post treatment.	Passive ROM increased significantly Week 1 to 5 both groups. Total pROM 330°±26° soft tissue vs 323°±24° (p = 0.35). Mean total pROM 313°±28° Week 1 soft tissue vs 329°± 26° Week 5 (p = 0.001). Mean total pROM 307° ±28° Week 1 manipulation vs 323° ±24° Week 5, (p = 0.02).	"It seems that any changes in passive range of motion after spinal manipulation are of a temporary nature. The question of immediate and long term changes to active and passive ROM is essential to our understanding of the physiological changes induced by spinal manipulation."	Passive cervical range of motion was the main outcome measure in headache patients. Observer of ROM pre and post blinded to treatment allocation. No baseline characteristics included. Unclear duration of symptoms in participants.

Cleland 2007 RCT Sponsored by American Academy of Orthopaedic Manual Physical Therapists and Steens Physical USA. No mention of COI.	6.0	N = 60 primary complaint of neck pain; mean age 43.3±12.7 years.	Non-thrust group received nonthrust mobilization/manipulations (n = 30) vs. Thrust group received thrust mobilization/manipulations (n = 30). Follow-up between 2 and 4 days post-treatment.	Baseline differences appear to favor non-thrust group (10% vs 30% workers' comp). Thrust group showed significant reduction in disability compared to non-thrust at follow-up, 18.0 vs. 24.0, (p <0.001). Thrust group also showed significant reduction in the numeric pain rating scale, 2.7 vs 3.9, (p < 0.001).	"[T]horacic spine thrust mobilization/ manipulation results in significantly greater short-term reductions in pain and disability than does thoracic nonthrust mobilization/ manipulation in people with neck pain."	Evaluation of patients after 2 to 4 days after treatment, combined with the apparently variable duration of follow-up time ranging from 2 to 4 days after treatment, result in this article being largely unusable for purposes of development of treatment guidance despite its grading as moderate-quality for other criteria. Appears other co-interventions such as medication use also present and uncontrolled.
McReynolds 2005 RCT No mention of sponsorship or COI.	6.0	N = 58 with acute neck pain; excluded radicular signs and symptoms, but included neck pain from MVAs; mean age ketorolac and manipulative groups: 30±9 and 29±8 years.	Manipulative group received HVLA thrust, muscle energy, and soft tissue techniques (n = 29) vs. Ketorolac group received 30mg Ketorolac tromethamine injected intramuscularly (n = 29). 1 hour post-treatment assessment. No long-term follow-up.	Osteopathic manipulative group showed a significant change in pain intensity from pre-treatment to post-treatment compared to the ketorolac group, 2.8 vs 1.7, (p = 0.02).	"[O]MT is a reasonable alternative to parenteral nonsteroidal anti-inflammatory medication for patients with acute neck pain in the ED setting."	Recorded pain before treatment and 1hr post, without any longer follow up. Manipulation group had individualized treatments based on presenting signs and symptoms.
Cleland 2010 RCT Sponsored by Foundation for Physical Therapy and the Orthopaedic Section of the American Physical Therapy Association. No mention of COI.	5.5	N = 140 patients with a primary report of neck pain; mean age 39.9±11.3 years.	Exercise-only group received a stretching and strengthening program (n = 70) vs. Manipulation plus exercise group received thoracic spine thrust manipulations and range of motion exercises (n = 70). Follow-up at weeks 1 and 4; and 6 months.	There was a significant difference at 1 week in favor of the manipulation group vs exercise only for disability (3.6 difference between groups, p = 0.003) and for pain score (0.7 difference between groups, p < 0.001). Outcomes measured by NDI scores (p = 0.79) and NPRS score, (p = 0.22) did not show significant differences over time between groups.	"The results of the current study did not support the validity of the previously developed CPR. However, the 2-way interaction between group and time suggests that patients with mechanical neck pain who do not exhibit any contraindications to manipulation exhibit statistically significant improvements in disability in both the short- and long-term follow-up periods."	Larger dropout rate in exercise only group. Baseline differences present and impacts are unclear. Data suggest clinical prediction rule did not work; but manipulation groups modestly better than non-manipulation groups.

Pikula 1999 RCT No mention of sponsorship or COI.	4.0	N = 50 acute <2 weeks unilateral neck pain without history of trauma, neurological signs; mean ages for SMT group 1, 2 and Placebo: 39.5, 42.6, and 44.2 years.	SMT group 1 received short lever, high velocity and low amplitude thrust ipsilateral to neck pain (n = 12) vs SMT group 2 received same manipulation contralateral to neck pain (n = 12) vs. Placebo group received detuned ultrasound (n = 12). Pre- and Post- intervention assessment. No long-term follow-up.	Between 3 study groups, no significant differences between flexion and contralateral rotation. Between ipsilateral spinal manipulation and placebo, manipulation showed a significant improvement in extension (57.3 vs 46.0, (p = 0.05)) and ipsilateral flexion; 34.4 vs 32.1, (p = 0.0005).	"This pilot study demonstrates that VAS shows greater improvement when ipsilateral spinal manipulative therapy is used versus contralateral spinal manipulative therapy or a placebo when used on patients with mechanical neck pain. This is an immediate effect and it is statistically significant (p<.05)."	Each received one therapy and then immediately evaluated. No blinding. No short to longer term results reported.
Subacute Neck Pain						
Pool 2010 RCT Sponsored by Netherlands Organization for Health Research and Development. No COI.	7.0	N = 146 with subacute (4-12 weeks) non-specific neck pain; mean ages for BGA and manual therapy groups: 44.5±12.0 and 45.6±11.1 years.	BGA group participated in behavioral graded activity program (n = 71) vs. Manual Therapy group received specific spinal mobilization techniques and exercises (n = 75). Follow-up at weeks 13 and 52.	BGA vs manual therapy at 0, 13, 52 weeks. Global Perceived Effect (0-7): no differences pain VAS (0-10): No differences Neck Disability Index: Total change at 1 year, 14.68 to 4.28 vs 13.4 to 5.42, (p = 0.05). No differences at each individual measurement between groups.	"It can be concluded that there are only marginal, but not clinically relevant, differences between a behavioral graded activity program and manual therapy."	Compliance implied by reported visits. No report of co-interventions. Study suggests no differences in behavioral graded activity compared with manual therapy. Both groups of non-specific subacute neck pain had significant improvement. Natural history not included in study.
Bosmans 2011 RCT Sponsored by Netherlands Organization for Health Research and Development. No mention of COI.	7.0	N = 146 with subacute nonspecific neck pain; mean±SD age; 44.5±12.0, 45.6 (11.1).	BGA group participated in a behavioral graded activity program (n = 71) vs. MT group received manipulation and specific mobilization techniques (n = 75). Long-term follow-up only for cost effectiveness.	The improvement in disability and pain in BGA group were statistically larger than in the MT group; group difference for Continuous improvement -2.4 (-4.5 to -0.22, 95% CI); improvement NDI scores ≥ 4, 0.13 (0.00 to 0.26); pain continuous improvement -0.88 (-1.7 to -0.02); improvement ≥ 3, 0.19 (0.05 to 0.33); and QALYs gained, -0.02 (-0.06 to 0.02).	"In conclusion, significant improvements in pain and disability were found in primary care patients with nontraumatic neck pain, although substantial investments should be made to reach a 0.95 probability that BGA is cost effective in comparison with MT for these outcome measures."	Data suggest cost effectiveness greater for manipulation although there was no statistical difference in the primary outcome measured of "global perceived effect," limiting conclusion of economic efficacy.

Coppieters 2003 RCT No mention of sponsorship or COI.	6.5	N = 20 subacute cervico-brachial pain; mean ages for mobilization and ultrasound groups: 49.1±14.1 and 46.6±12.1 years.	Mobilization group received cervical segmental contralateral lateral glide treatment (n = 10) vs. Ultrasound group received therapeutic ultrasound (n = 10). No long-term follow-up.	Results immediately post-treatment; manipulation vs. ultrasound. Elbow extension (degrees) 137.3-156.7 vs. 127.5 to 128.5 (p <0.0306), Pain intensity: 7.3-5.8 vs 7.7-7.3 (p <0.0306). Symptom provocation: 22.3%-12.6% vs. 26.7%-22.9%. Reported significance intragroup improvement in manipulation group.	"A cervical lateral glide mobilization has positive immediate effects in patients with subacute peripheral neurogenic cervicobrachial pain if a cervical segmental motion restriction is present which can be regarded as a plausible cause of the neurogenic disorder or as a contributing factor that impedes natural recovery."	Comparison statistics between groups is unclear. No placebo group. Small sample size. No clear conclusions can be drawn from study.
Chronic Neck Pain						
Young 2009 RCT Sponsored in part by Saunders Group. No mention of COI.	8.5	N = 81 with cervical radiculopathy; mean ages for treatment and control: 47.8±9.9 and 46.2±9.4 years.	Treatment group received manual therapy, exercise, and intermittent cervical traction (n = 45) vs. Control group received manual therapy, exercise, and SHAM intermittent cervical traction (n = 36). Follow-up at weeks 2 and 4.	Adjusted mean differences for primary outcomes of NDI / NPRS at weeks 2 and 4; p = 0.34 or 14.0 (12.3) and 11.1 (12.3) for MTEX Traction group compared to p = 0.42, or 1.8(-7.0 to 3.5) and 1.5 (-6.8) MTEX group.	"The results suggest that the addition of mechanical cervical traction to a multimodal treatment program of manual therapy and exercise yields no significant additional benefit to pain, function, or disability with cervical radiculopathy."	Data suggest cervical traction does not change outcomes in patients with cervical radiculopathy undergoing a multimodal program.
Muller 2005 RCT Sponsored by the Queensland State Government Health Department. No mention of COI.	8.0	N = 115 with chronic mechanical spinal pain syndromes, mean >2 years; mean age 39 years.	Acupuncture 8 to 10 needles placed in local paraspinal intramuscular maximum pain areas with 5 needles placed in distal acupuncture points (n = 36) vs. Manipulation high-velocity low-amplitude spinal manipulative thrust to a joint (n = 36) vs. Medication Celebrex 200 to 400mg a day or rofecoxib 12.5 to 25mg a day followed with acetaminophen (n = 43). Follow-up at 9 weeks and 12 months.	ITT analysis, for neck pain frequency was significant for manipulation (p = 0.03), but not for acupuncture (p = 0.09) or medication (p = 0.36); VAS was significant for both manipulation (p = 0.04) and acupuncture (p = 0.006) but not for medication (p = 0.70); NDI was significant for manipulation (p = 0.045) compared to acupuncture (p = 0.005) and medication (p = 0.26). With compilers only analysis neck pain frequency was significant for manipulation (p = 0.006) but not acupuncture (p = 0.24) or medication (p = 0.75); neck pain scale (VAS was significant for manipulation (p = 0.004) but not acupuncture (p = 0.1) or medication (p = 0.44); neck disability index as significant for manipulation (p	"Overall, patients who have chronic mechanical spinal pain syndromes and received spinal manipulation gained significant broad-based beneficial short-term and long-term outcomes. For patients receiving acupuncture, consistent improvements were also observed, although without reaching statistical significance (with a single exception). For patients receiving medication, the finders were less favorable."	No differentiation between different areas of the spine. Initially acupuncture and manipulation groups had contact with providers 2 times a week where drug only group had contact once every 2 weeks.

				= 0.02) compared to acupuncture (p = 0.06) and medication (p = 0.31). Similar results were obtained for back variables as well. The respective percentages were manipulation 38.7%, acupuncture 53.3% and medication 81.2% respectively."		
Bronfort 2001 RCT Sponsored by the Consortium for Chiropractic Research. Spine Journal COI category 14.	7.5	N = 191 with chronic non-specific neck pain; mean age 44.3±10.6 years.	SMT/Exercise group received spinal manipulation and low-technology exercise (n = 63) vs. MedX group received resistance exercises on the MedX cervical extension and rotation machines (n = 60) vs. SMT group received spinal manipulation and SHAM micro-current therapy (n = 64). Follow-up at 5 and 11 weeks, and 3, 6, and 12 months.	Weeks 5 and 11; pain F (2, 173) = 2.2, (p = 0.12), neck disability F (2, 172) = 0.8, (p = 0.45), and general health F (2, 173) = 0.79, (p = 0.18). The differential number of side effects across treatments was not statistically significant, x22 = 1.44, (p = 0.49).	"With the exception of patient satisfaction, for which SMT with exercise was superior to SMT alone, no clinically important group differences were observed after 11 weeks of treatment. During the follow-up year, there was a cumulative advantage for both SMT with exercise and MedX exercise as compared with SMT alone. Overall, the use of strengthening exercise, whether in combination with SMT or in the form of a high technology MedX program, appears to be more beneficial to patients with chronic neck pain than the use of SMT alone."	Baseline differences in pain frequency. Study suggests no clinically significant differences for chronic neck pain. Lack of placebo arm precludes conclusion on effectiveness on any treatment arm compared with natural history. All groups improved significantly from baseline.
Haas 2010 RCT No mention of sponsorship. COI: Drs. Haas, Spegman, and Peterson received investigator salary from NCCAM/NIH.	7.5	N = 80 with chronic cervicogenic headache (CGH); mean age 36±11 years.	8 SMT group received 8 visits high-velocity low amplitude cervical and upper thoracic spinal manipulation (n = 20) vs. 16 SMT group received 16 visits vs. 8 LM group (n = 20) received 8 visits 5min light massage (n = 20) vs. 16 LM group received 16 visits (n = 20). Follow-up at weeks 12 and 24.	There was no a significant difference between dose effect (16 vs 8 sessions), however, a greater dose effect was seen in the 16 sessions, but it did not reach significance. CGH pain scale scores were significantly reduced in SMT compared to LM at 24 weeks -9.8 (95% CI -18.7 to -1.0).	"Clinically important differences between SMT and a control intervention were observed favoring SMT. Dose effects tended to be small."	Data suggest CSMT to cervical and thoracic spine resulted in greater improvement in pain vs light dosage. Pilot study intervention to determine optimal number of manipulation sessions. Data suggest no differences in 8 vs 16 sessions over 6 week period. Fewer headaches at follow-up in spinal manipulation group then light massage.

Kanlayanaphotporn 2009 RCT Sponsored by the Thailand Research Fund and the Commission on Higher Education. No mention of COI.	7.0	N = 60 with mechanical neck pain >1 week (all subjects reported chronic pain); mean ages for preferred mobilization and random mobilization groups: 39.7±10.0 and 44.8±13.6 years.	Preferred Mobilization group received unilateral posteroanterior (PA) mobilization (n = 30) vs. Random Mobilization group received 1 of 3 mobilization techniques applied as placebo: Central PA, Unilateral PA, or Contralateral PA (n = 30). Follow-up 5 minutes post treatment.	No significant difference between groups in demographic details, (p >0.05). Significant decreases in neck pain at rest and pain on most painful movement, (p < 0.001), with significant increase in active cervical ROM after mobilization on most painful movement, (p = 0.002).	"The present study provides evidence that the use of unilateral PA mobilization on the painful side in subacute or chronic unilateral neck pain patients seems unimportant."	Multiple study flaws including author stating study triple blinded, although patients and provider could not reasonably be blinded. Intervention of unilateral PA mobilization appears included as a treatment in comparison group. Study suggests no difference in techniques as measured immediately after 1 treatment.
Lau 2011 RCT No mention of sponsorship or COI.	7.0	N = 120 with chronic mechanical neck pain.	Group A or thoracic manipulation or TM including 8 sessions 2 weeks infrared radiation therapy or IRR for 15 minutes over painful site (n = 60) vs. Group B or control group without the manipulative procedure received 8 sessions 2 weeks same IRR therapy together with same educational materials (n = 60). Outcome measures:; Numeric Pain Rating Scale or NPRS, 2 sets of questionnaires (Northwick Park Questionnaire or NPQ), neck mobility, and SF36 or health-related quality of life.	TM showed significantly greater decrease in NPQ, compared to control at 6-months, p = 0.018 and 0.007, respectively. MT group showed greater reduction in pain compared to control from immediate post treatment, p = 0.001, to the 6-month follow-up, p = 0.002 and 0.001.	"The effect of TM was shown to be positive in reducing neck pain, improving dysfunction and neck posture, and neck ROM up to half a year post-treatment."	Data suggest statistical difference favoring TM group, but clinical significance appears marginal in pain VAS and range of motion scores.
Giles 2003 RCT Sponsored by the Queensland State Government Health Department and The Townsville Hospital. NO mention of COI.	6.5	N = 115 with chronic spinal pain syndromes; mean age 39 years.	Medication group received 1 of 3 medications: Celebrex, Vioxx, or paracetamol, with preference to Celebrex (n = 40) vs. Acupuncture group received HWATO Chinese needles (n = 34) vs. Manipulation group received high-velocity, low-amplitude thrust spinal manipulation (n = 35). No long-term follow-up.	Manipulation achieved best overall results with improvements of 50% (p = 0.01) on Oswestry scale, 38% (p = 0.08) on NDI, 47% (p <0.001) on SF-36, and 50% (p <0.01) on VAS for back pain, 38% (p <0.001) for lumbar standing flexion, 20%, (p <0.001) for lumbar sitting flexion, 25% (p = 0.1) for cervical sitting flexion, and 18%, (p = 0.02) for cervical sitting extension. Acupuncture better than manipulation on	"The consistency of the results provides, despite some discussed shortcomings of this study, evidence that in patients with chronic spinal pain, manipulation, if not contraindicated, results in greater short-term improvement than acupuncture or medication. However, the data do not strongly support the use of only manipulation, only acupuncture, or only nonsteroidal	Individualization of treatments results in lack of standardization and substantially precludes drawing robust conclusions. Post-randomized individualized treatment in all 3 arms. Ill-defined mixture of diagnoses, combined with non-randomization arguably relegates study to a non-RCT.

				VAS for neck pain (50% vs 42%).	antiinflammatory drugs for the treatment of chronic spinal pain."	
Whittingham 2001 Crossover RCT Sponsored by the Australian Spinal Research Foundation, the Chiropractic Centennial Foundation, and the Royal Melbourne Institute of Technology Alumni Fund. No mention of COI.	6.5	N = 105 with cervicogenic headache; mean age for group 1 and 2: 39.4±11.6 and 41.9±12.5 years.	Group 1 received sham manipulation for 3weeks; cervical spinal manipulation for 3weeks; then no treatment for 3 weeks (n = 49) vs. Group 2: cervical spinal manipulation for 3weeks; no treatment for 3weeks; than sham manipulation for 3weeks (n = 55). Outcome assessment at 0, 3, 6, 9, and 12 weeks.	Active ROM in cervical spine increased significantly during first 6 weeks of treatment in manipulation group, (p <0.006). Right ROM at 12 weeks: 70°±1.1° Group 2 vs. 73°±1.3° Group 1. Left ROM 12 weeks: 69°±1.1° Group 2 vs 72°±1.6° Group 1. Right lateral flexion 12 weeks: 47°±1.1° Group 2 vs 40°±1.6° Group 1. Left lateral flexion 12 weeks: 45°±1.1° Group 2 vs 47°±1.6° Group 1Results at 12 weeks were approaching significance for right ROM (p = 0.14), right lateral flexion (p = 0.13) and left ROM (p = 0.12) if favor of the manipulation group.	"Spinal manipulation of the cervical spine increases active range of motion."	Attempted to blind participants by using sham manipulation. Included a semi-cross over study design. No clinical outcomes other than active ROM studied. No functionality or pain ratings reported.
Nilsson 1997 RCT Sponsored by grants from European Chiropractors Union, Foundation for Chinese Research and Postgraduate Education, and from Research Committee the Danish Chiropractors Association. No mention of COI.	6.5	N = 54 with cervicogenic headache; mean age 37 years.	Manipulation group received HVLA cervical manipulation (n = 28) vs. Soft-tissue group received low-level laser in upper cervical and deep friction massage in lower cervical/upper thoracic (n = 25). Diary entry follow-up 1week post treatment.	Headache hours decreased 69% in manipulation vs 37% in controls, (p = 0.03). Use of analgesics decreased 36% in manipulation group vs. no change in control group. Result not significant but approached significance at, (p = 0.14).	"[S]pinal manipulation has a significant positive effect in cases of cervicogenic headache."	Continuation of 1995 study adding additional participants. Conducted protocol slightly differently in 15 additional patients. Data suggest manipulation may be helpful for treatment of cervicogenic headaches.
Jordan 1998 RCT Sponsored by the Danish Medical Research Council,	6.5	N = 119 with chronic neck pain >3 months duration. Calculated, weighted mean age of 36 years.	Physiotherapy group received hot packs, massage, continuous ultrasound, and manual traction (n = 35) vs. Training group performed intensive exercise including stationary bike and	Participants filled out questionnaire that addressed pain, disability and endurance. Pain ratings decreased (baseline/completion/12 month): intensive training (12/6/6) vs physiotherapy	"There was no clinical difference between the three treatments. All three treatment interventions demonstrated meaningful improvement in all primary effect parameters."	Intensive training at 5 to 6 minutes did not include substantial aerobic exercise and included bicycling which may result in a postural issue and

Danish Arthritic Association, Medical Research Fund for Copenhagen, Faroe Islands and Greenland, Foundation for Chiropractic Research and Education, and The Fund to Promote Chiropractic Research and Postgraduate Education. No mention of COI.			strengthening programs (n = 34) vs. Chiropractic group received HVLA manipulation to the cervical spine (n = 33). Follow-up assessments conducted at 4 and 12 months.	(12/6/8) vs chiropractic (13/6/6). Disability ratings similar: (8/5/5) vs (9/4/6) vs (8/4/5). Endurance in groups (baseline/completion): intensive (60/120s) vs physiotherapy (70/110s) vs. chiropractic (60/90s). No significant differences between groups, (p >0.05).		program appears to have primarily consisted of strengthening exercises. Study is of a heterogeneous group of interventions. Endurance lowest in chiropractic group. No significant differences among groups.
Hakkinen 2007 RCT/Crossover Sponsored by Jyvaskyla Central Hospital. No mention of COI.	6.0	N = 125 females with chronic neck pain, mean 3 years duration; mean ages for experimental and treatment groups: 43±8 and 42±9 years.	Experimental group performed neck stretching exercises (n = 63) vs. Treatment group received manual therapy (n = 62). Follow-up at 12 weeks.	Both groups had neck muscle strength improvement of 11-14% after 4 weeks, no further improvement Weeks 4 to 12 for both groups. Pain decreased 64% in manual therapy group and 53% in stretching group during first 4 weeks, (p < 0.001).	"Both manual therapy and stretching were effective short-term treatments for reducing both spontaneous and stain-evoked pain in patients with chronic neck pain."	Did not clearly document what intervention group did after 4 weeks of therapy (e.g., continued exercises), but did in stretching only group. No mention of washout period between interventions.
Martínez-Segura 2012 RCT No mention of sponsorship or COI.	6.0	N = 90 with bilateral chronic mechanical neck pain; mean±SD age 37±8 years.	Right Cervical group received cervical thrust manipulation on the right side (n = 29) vs. Left Cervical group received cervical thrust manipulation on left side (n = 28) vs. Thoracic group received thoracic thrust manipulation (n = 33). Assessments performed pre and post treatment. No long-term follow-up.	There was significant main effect of time for all tested sites compared to baseline for all 3 groups experiencing bilateral increase in PPT, and significant effects for all time cervical spine movements, indicating all groups experiencing similar increase in CROM, (p <0.001). 2-by-2, by-3, 2-by-3, and 2-by-2-by-2 mixed model ANCOVA did not reveal a significant interaction for the remaining effects such as group by time (p = 0.210), side by time (p = 0.287) and group by time and by side, (p = 0.637)	"The results of the current randomized clinical trial suggest that cervical and thoracic thrust manipulation induce similar changes in PPT, neck pain intensity, and CROM in individuals with bilateral chronic mechanical neck pain."	Data suggest no differences in thrust techniques included for bilateral neck pain. Lack of control group limits conclusions on efficacy of thrust manipulation. Gender did not influence the main effects of PPTs, neck pain, and for CROM.

Koes 1992 a,b 3 reports of 1 RCT Sponsored by the Dutch Ministry of Welfare, Health and Cultural Affairs and the Dutch National Health Insurance Council. No mention of COI.	5.0	N = 256 with chronic back and neck pain (not well described), mean duration; 1 year; mean age for; manual therapy / physiotherapy / placebo / and general practitioner: 49 (75) / 42 (64) / 44 (69), and / 38 (62).	Manual therapy, manipulation and mobilization of spine (n = 65) vs. Physiotherapy, exercises, massage and/or physical therapy (n = 66) vs Placebo therapy twice a week for six weeks (n = 64). Follow-up at baseline and 3, 6 and 12 weeks.	At 12 months, manipulative therapy marginally superior to physiotherapy in "improvement," but not for all other measures and time intervals. Difference in improvement scores between both groups 0.9 (95% CI 0.1 – 1.7).	"[M]anipulative therapy and physiotherapy are better than general practitioner and placebo treatment. Furthermore, manipulative therapy is slightly better than physiotherapy after 12 months." In a second report, "a substantial part of the effect of manual therapy and physiotherapy appeared to be due to nonspecific (placebo) effects." The third report concluded "the subgroup analysis suggests better results of manual therapy compared to physiotherapy in chronic patients (duration of present complaints of 1 year or longer) and in patients younger than 40 years old)."	Value of this type of trial diminished today as therapies may have been heavily relied upon that have been subsequently shown ineffective. Lack of treatment visits in GP group both appear to have provided major bias against it and suggest GPs unfamiliar with spine pain management and may not have been standardized. Other interventions varied and not well defined. Placebo unblinded for provider, potentially influencing advice on how to treat ongoing symptoms, thus influencing outcomes. Heterogeneous nature of these largely unstructured interventions prevents strong conclusions regarding efficacy.
Boline 1995 RCT No mention of sponsorship or COI.	5.0	N = 150 with chronic tension-type headaches; mean ages for manipulation and amitriptyline groups: 40.9 and 42.7 years.	Manipulation group received short-lever, low-amplitude, high-velocity thrust techniques (n = 70) vs. Amitriptyline group received 10mg/day amitriptyline the 1st week, 20mg/day the 2nd week, and 30mg/day onward (n = 56). Follow-up at 1, 2, 3, and 4 weeks post-treatment.	Four weeks after treatment, headache intensity and frequency lower in manipulation group than amitriptyline. At end of 6 week treatment period amitriptyline group showed significant difference in mean headache intensity compared to spinal manipulation 3.2 vs 4.3, (p = 0.01)	Authors concluded "spinal manipulative therapy is an effective treatment for tension headaches. Amitriptyline therapy was slightly more effective in reducing pain at the end of the treatment period but was associated with more side effects."	Dropouts were high in amitriptyline group (27.1%). As amitriptyline is not a particularly successful treatment strategy for a comparison group.
Schwerla 2008 RCT No sponsorship or COI.	4.5	N = 41 with chronic non-specific neck pain for >3 months excluded any neurological symptoms or current physical therapy; mean age for osteopathic and control groups: 41.5±6.1 and 44.8±9.4 years.	Osteopathic group received both sham/inert ultrasound and osteopathic treatment (n = 23) vs. Control group only received inert/sham ultrasound therapy (n = 18). Follow-up 12 weeks post-treatment.	Compared to beginning of study "actual pain" decreased by 2.7 points for osteopathic and 1.1 points in control group (p = 0.031, CI -2.99 to -0.15). Osteopathic group showed a significant reduction for pain compared to the ultrasound	"The results of this first rigorous randomised controlled trial seem to confirm previous empirical findings, and are in favor of an osteopathic treatment of CNP as a method with long-term effects on this	Did not mention exercise status of participants. No sham manipulation done.

				only (control group) group, 61.1 vs 46.5, (p = 0.019).	frequently encountered condition."	
Hoyt 1979 RCT Sponsored by the Rehabilitation Services Administration. No mention of COI.	4.5	N = 22 with chronic muscle contraction headache; mean age not reported.	Group 1 received both palpatory exam for restricted axial skeleton movement and osteopathic manipulation (n = 10) vs. Group 2 received palpatory exam for restricted axial skeleton movement (n = 6) vs. Group 3 received instruction to rest in supine position for 10 minutes (n = 6). Assessments performed immediately post-treatment. No long-term follow-up.	The manipulation group showed significant reduction in rated headache pain compared to the examination and instruction groups, (p < 0.0003)	"[O]steopathic manipulation can reduce the severity of muscle-contraction headache."	This was an extremely short-term trial allowing for limited conclusions. It also does not describe the patients or methodological procedures well.
Non-Specific Neck Pain						
Ylinen 2007 RCT Sponsored by Jyvaskyla Central Hospital. No mention of COI.	7.5	N = 125 females with non-specific neck pain; mean ages for group 1 and 2: 42±9 and 44±8 years.	Group 1 received manual therapy for 4wks followed by 4wks stretching exercises (n = 62) vs. Group 2 received same treatments in reverse order (n = 63). Follow-up at 12 weeks.	Group 1 (manual therapy) at 4 weeks had average neck pain decreased by -26 (-33 to -20) on VAS, Neck stiffness -27 (-33 to -21), Headache -22 (-29 to -14). Group 2 (stretching only) at 4 weeks had neck pain decrease -19 (-27 to -12), neck stiffness -19 (-26 to -13), Headache -17 (-23 to -12) (SEE TABLE 2). Only measures statistically different between group 1 and 2 at 4 weeks were neck and shoulder pain and disability index (p = 0.013), and neck stiffness p = 0.01. No statistical difference between groups at 12 weeks after crossing over of treatment protocols between groups but still decreases in each area studied compared to baseline.	"Both stretching exercise and manual therapy considerably decreased neck pain and disability in women with non-specific pain. The difference in effectiveness between the 2 treatments was minor. Low-cost stretching exercises can be recommended in the first instance as an appropriate therapy intervention to relieve pain, at least in the short-term"	As stretching exercises are thought to have little if any benefit for chronic spine pain, this may be a placebo control group. Alternately, most patients would presumably have been treated with stretching exercises previously, which would produce a bias in favor of manual therapy.
Cleland 2005 RCT No mention of sponsorship or COI.	7.5	N = 36 with mechanical non-specific neck pain; mean ages for treatment and placebo groups: 36±8.5 and 35±11.3 years.	Treatment group received thoracic spine manipulation high velocity, low amplitude (n = 19) vs. Placebo group received sham manipulation; 1 treatment. Average 12 weeks of duration prior to study entry (n = 17). Assessment performed 5 minutes post-treatment.	Manipulation compared to sham pain was VAS 0-100): 41.6 to 26.1 compared to47.7 to 43.5, difference between groups, (p <0.01).	"Thoracic spine manipulation results in immediate improvements in perceived levels of cervical pain in patients with mechanical neck pain. Given the concerns regarding the risks of cervical spine manipulation, perhaps thoracic spine manipulation is a reasonable alternative or	Study limited to immediate post-treatment period. Study suggests benefit over sham manipulation. Blinding of sham group uncertain, as general population may have knowledge or expectations regarding manipulation technique

					supplement to cervical manipulation..."	(i.e., expect to feel or hear popping sound). Long-term efficacy unknown. Lack of power.
González-Iglesias 2009 J Orthop Sports Phys Ther RCT No mention of sponsorship or COI.	7.5	N = 45 with mechanical neck pain <1 month duration; mean age 34±5 years.	Experimental group received thoracic thrust manipulation, plus electro /Thermal therapy (n = 23) vs. Control group plus, electro /Thermal therapy (n = 22). Follow-up at weeks 2 and 4.	Elect/therm vs thrust pain (100mm VAS): 55.2±5.5 vs 54.7±8.2, 44.7±5.5 vs 20.2±7.8 ($p < 0.01$).	"Patients with mechanical neck pain who received thoracic spine thrust manipulation experienced greater improvements in pain, cervical range of motion, and disability at the fifth treatment session and at the 2-week follow-up, compared to those who received a program of electro/thermal therapy interventions."	Compliance inferred but not stated. Control for co-interventions not stated. Blinding of patients stated but methods indicate not true blinding. Study suggests spinal manipulation plus electrothermal therapy more effective than electrothermal therapy alone for acute cervical pain. No control group for natural history.
Martinez-Segura 2006 RCT No mention of sponsorship or COI.	7.5	N = 71 with mechanical neck pain; mean age 37±10 years.	Experimental group received high-velocity low-amplitude (HVLA) manipulation (n = 34) vs. Control group received manual mobilization procedure (n = 37). Assessments immediately pre and post treatment.	Experimental group with improved mobilization in all outcome measures ($p <0.001$). Pre-post scores for neck pain at rest in experimental group were 3.5(3.9-3.1) vs. 0.4(0.5-0.2) in control group, ($p < 0.001$).	"A single cervical high velocity-low amplitude manipulation was more effective in reducing neck pain at rest and in increasing active cervical range of motion than a control mobilization procedure in subjects suffering from mechanical neck pain"	Baseline characteristics sparse. Evaluation immediately after one procedure No long-term follow-up to see if increased active ROM and decreased pain had any functional improvement outcome.
Fernandez-de las Penas 2007 RCT Crossover No mention of sponsorship or COI.	7.0	N = 15 asymptomatic volunteers recruited from a student population; mean age 21±2 years.	Treatment HVLA thrust cervical manipulation (n = 15) vs. Placebo simulated HVLA thrust manipulation (n = 15) vs. Control held their head in ipsilateral side-flexion and contralateral rotation for 20sec without manual contact from therapist (n = 15). Follow-up assessment 5 minutes after each treatment.	Analysis of variance detected a significant effect for intervention, $F = 31.46$, ($p < 0.001$) and time, $F = 33.81$, ($p < 0.001$), but not side, $F = 0.303$, ($p >0.5$). A significant interaction between intervention and time, $F = 15.74$, ($p <.001$) also found. Gender did not influence comparative analysis, $F = 0.252$, ($p >0.6$).	"The application of a manipulative intervention directed at the posterior joint of the C5-6 vertebral level produced an immediate increase in PPT over the lateral epicondyle of both elbows in healthy subjects. Effect sizes for the HVLA thrust manipulation were large, suggesting a strong effect of unknown clinical importance at this stage, whereas effect sizes for both placebo and control procedures were small, suggesting no significant effect."	Very small numbers of asymptomatic chiropractic students. No long-term follow up.

Krauss 2008 RCT No mention of sponsorship or COI.	7.0	N = 32 with cervical pain, duration unclear; patients with radicular pain excluded; mean ages for experiment and control groups: 35±10.51 and 34.2±9.56 years.	Experimental group received translatoric spinal manipulation (n = 22) vs. Control group received no intervention (n = 10). No long-term follow-up.	Analysis revealed no significant within-group changes in control group in regards to left and right rotation (p = 0.62 and 0.90). Experimental group showed a significant change in left and right rotation (p < 0.01 and < 0.01). Thoracic spine manipulation group better ROM with an average increase (SD) of 8.23° (7.41°) in right rotation and left rotation 7.09° (5.83°).	"Cervical rotation range of motion improved in all subjects following the application of this form of manipulation to the UT segments. No patient reported any increase in cervical symptoms."	Lack of baseline characteristics. Assessment immediately after one manipulation vs no intervention without any follow up. Unable to draw clinical conclusions based on included information.
Hoving 2002 RCT Sponsored by Netherlands Organization for Scientific Research and Investigative Medicine of the Health Insurance Council. No mention of COI.	7.0	N = 183 with non-specific neck pain ≥2 weeks; mean age 45 years.	Manual therapy received joint mobilization therapy (n = 60) vs. Physical therapy group received active exercise therapies (n = 59) vs. Continued care group received standardized care from general practitioner (n = 64). Follow-up at weeks 3 and 7.	Success rates at 7 weeks: 68.3% for manual therapy, 50.8% for physical therapy, and 35.9% for continued care. Disability scores modestly favored manual therapy. Manual therapy scored better on most outcome measures.	"Although differences were not particularly large for all outcome measures, manual therapy seems to be a favorable treatment option for patients with neck pain."	All 3 groups had substantially different numbers of visits to providers, providing bias against continued care. Perceived recovery most statistically significant outcome measure in favor of manual therapy. Large differences in baseline duration of symptoms between groups. Also, difference in previous neck pain episodes noted between groups with continued care with 72%, MT group 63%, and PT group with 60%.
Dunning 2012 RCT Sponsored by the American Academy of Orthopedic Manual Physical Therapists. No mention of COI.	7.0	N = 107 with mechanical neck pain from 1 of 7 outpatient physical therapy clinics, including varied geographical locations (Arizona, Hawaii, Massachusetts, South Carolina, Texas, Virginia), over 20-month period (August 2009 to March 2011); mean±SD age; 42.0±12.8 years.	Thrust group received a single HVLA thrust manipulation (n = 56) vs. Non-Thrust group received upper cervical, nonthrust mobilization (n = 51). No long-term follow-up.	Mean percentage change in disability from baseline to 48-hour follow-up statistically significant, (p <0.001), or HVLA group experienced greater percentage in disability reduction of 50.5% ± 22.7% and nonthrust mobilization group 12.8% ± 25.2%. 2-by-2 model showed HVLA group to experience mean reduction in pain levels or 2.3 vs 4.4 in nonthrust mobilization group. HVLA experienced significantly greater improvements in passive C1-2	"The combination of upper cervical and upper thoracic HVLA thrust manipulation is appreciably more effective in the short term than nonthrust mobilization in patients with mechanical neck pain."	Participants included acute, subacute, and chronic pain durations. Single intervention only. Outcomes data reported in percentage change. Clinical significance of improvement not clear. No long term results reported.

				right rotation ROM/motor performance/global rotation; 8.4º vs. 3.5º/3.4mmHg vs. 1.2 mmHg / (p <0.001).		
Hurwitz 2002 RCT Sponsored by the Health Resources and Services Administration and the National Center for Complementary and Alternative Medicine.	6.5	N = 336 with neck pain excluded 3rd party liability claims or workers' comp; mean age 35±10.4 years.	Manipulation group received HVLA controlled dynamic thrust to upper thoracic or cervical spine (n = 171) vs. Mobilization group received low velocity, variable amplitude movements to the upper thoracic or cervical spine (n = 165). Follow-up at 6 months.	Mean reductions in pain and disability were similar in the manipulation and mobilization groups through 6 months. Participants in manipulation group more likely to experience minor discomfort during the 4 week treatment period compared to those in the mobilization group (16% vs 8.7%, (p = 0.05)) See also Hurwitz et al, Spine 2002.	"Cervical spine mobilization is as effective as manipulation in reducing neck pain and related disability among chiropractic patients. In addition, they show that neither heat nor EMS, alone or in combination with manipulation or mobilization, appreciably improves clinical outcomes, although heat may be of short-term benefit for some patients."	No mention of blinding. Treatment protocols not well defined for quantity or exact technique. No placebo group. Heat alone did not show clinical benefits.
Leaver 2010 RCT Sponsored by the Australian National Health and Medical Research Council. No COI.	6.5	N = 182 with nonspecific neck pain less than 3 months in duration; mean age 38.9±10.7 years.	Manipulation group received HVLA cervical thrust techniques (n = 91) vs. Mobilization group low-velocity, oscillating passive movement to the cervical spine (n = 91). Follow-up 10 weeks post treatment.	Patients treated with manipulation did not have a significant recovery compared to mobilization (HR=1.02; 95% CI 0.72 to 1.47; p = 0.897). Median time of recovery in manipulation group 47 days vs. 43 days in mobilization group. Difference not significant, (p = 0.909).	"Nearly half of the participants in this study, irrespective of treatment allocation, did not fully recover from the episode of neck pain with which they presented."	Data suggest no differences in outcomes for acute and subacute neck pain over 2-week treatment period. Lack of non-intervention. Control group.
Skillgate 2010 RCT Sponsored by Ekhagastiftelsen, Swedish Research Council, Stockholm County Council, Uppsala County Council, Capio, Swedish Maprapathic Association, Health Care Science Post-graduate School and the Centre for Health Care	6.5	N = 409 with non-specific neck and back pain; mean age 47 years.	Index group received naprapathic manual therapy (n = 206) vs. Control group received support and advice on staying active and pain coping strategies (n = 203). Follow-up at 52 weeks.	At 26 and 52 weeks pain was significantly better in the index group compared to control (p < 0.001 and p = 0.002). Index group had statistically significantly better disability scores on Chronic Pain Questionnaire (CPQ) at 26 and 52 weeks compared to control 1.2 (95% CI 1.0 to 1.4), (p = 0.043) and 1.3 (95% CI 1.1 to 1.5), (p = 0.005).	"[T]he clinically and statistically significant difference in pain intensity and disability between the groups remained at 26 and 52 weeks, and that the differences between groups considered over one year were statistically significant (p<0.01) also when consideration was taken to the covariance between the repeated measures."	Chronic pain mixed in study. Data suggest improved scores as long term follow-up. However, clinical significance uncertain as scales used were created by author. Thus, conclusions are limited.

Science at Karolinska Institutet. No mention of COI.						
Cassidy 1992 RCT Sponsored by the Canadian Memorial Chiropractic College and the Chiropractors' Association of Saskatchewan. No mention of COI.	6.0	N = 100 outpatients with unilateral neck pain with referral into trapezius muscle; duration varied from <1 week to >6 months; mean ages for manipulation and mobilization group: 34.5±13.0 and 37.7±12.5 years.	Manipulation group received cervical HVLA thrust manipulation (n = 52) vs. Mobilization group performed isometric contractions of hypertonic muscles (n = 48). Assessments performed pre and post treatment. No long-term follow-up.	Mean NRS-101 score decreased 17.3(±19.5) points in manipulated group and 10.5(±14.8) points in mobilized group (p = 0.05). Range of motion variables such as flexion and extension showed no significant differences between groups (p = 0.50 and p = 0.25 respectively)	"This study demonstrates that a single manipulation is more effective than mobilization in decreasing pain in patients with mechanical neck pain. Both treatments increase range of motion in the neck to a similar degree."	Baseline characteristics not well described. No adjustments made for pre-treatment differences. Results immediately post-treatment by questionnaire and cervical goniometer measurement. No clinical relevance over short or longer term. Exact diagnoses not known.
Bronfort 2012 RCT Sponsored by National Center for Complementary and Alternative Medicine and the National Institutes of Health. No mention of COI.	6.0	N = 272 with nonspecific neck pain of 2 to 12 weeks duration; mean ages for SMT, medication and HEA groups: 48.3, 46.8, and 48.6 years.	SMT received HVLA manipulation and low-velocity mobilization group (n = 91) vs. Medication group received nonsteroidal anti-inflammatory drugs, acetaminophen, or both. Narcotics for unresponsive participants (n = 90) vs. HEA group received a home exercise program (n = 91). Follow-up at weeks 26 and 52.	At 12 weeks, pain scores improved in both the SMT and HEA groups, but difference between 2 groups not significant (p = 0.087). Difference between HEA and medication group not significant. SMT group used far less medications long-term compared to the medication group, (p <0.001).	"[S]MT seemed more effective than medication according to various measures of neck pain and function. However, SMT demonstrated no apparent benefits over HEA."	Baseline use of NSAIDs not noted, likely and could be fatal flaw for medication arm of trial. Other 2 arms not precluded from using NSAIDs and use not reported. High loss to follow-up at 52 weeks limits long-term conclusions. Data suggest in short-term, no clinically significant differences between groups all of which improved. 90% medication group taking NSAID, opioid, acetaminophen, and muscle relaxants. Data suggest home exercise program least costly intervention and comparable outcomes to manipulation.
Sloop 1982 RCT	5.5	N = 39 with symptomatic cervical spondylosis or nonspecific neck pain; mean age 49 years.	Manipulation group received 20mg diazepam and cervical manipulation (n = 21) vs. Control group received only	No differences found regarding mean VAS scores for pain and activity between manipulation and control	"[T]he value of a single manipulation of the cervical spine has not been established and that further	Mean symptom duration 6 years. Follow-up 3, 12 weeks. Non-responders at 3

No mention of sponsorship or COI.			20mg diazepam (n = 18). Follow-up at 3 and 12 weeks.	groups, though both tests favored manipulation, (p = 0.20). At 3 weeks, 57% of patients receiving manipulation responded positively compared to 28 % of control. This was not significant however was approaching significance, (p = 0.13).	exploration of indications is needed. The use of intravenous diazepam should be considered because it allows a double-blind experimental design."	weeks underwent cross-over treatment. Each given 20mg IV valium before randomization. One treatment evaluated for 10 patients who received placebo who underwent a treatment, none had improvement with manipulation either.
Koes 1993 RCT Sponsored by Dutch Ministry of Welfare, Public Health, and Cultural Affairs and the Dutch National Health Insurance Council. No mention of COI.	5.0	N = 256 with non-specific back and neck complaints ≥6wks; mean age 43 years.	Manual therapy group received manipulation and mobilization techniques (n = 65) vs. Physiotherapy group received exercises, massage and/or physical therapy modalities (n = 66) vs. Placebo group received physical exam, detuned shortwave diathermy, and detuned ultrasound (n = 64) vs. GP group continued treatment with general practitioner (n = 61). Follow-up at 6 weeks.	Improvement in main complaint larger with manual therapy (4.3) than physiotherapy (2.5) for patients with chronic conditions (duration complaint of 1 year or longer). Improvement in main complaint larger with manual therapy (5.5) than physiotherapy (4.0) for patients younger than 40 (both measured after 12-month follow-up).	Concluded that manipulative therapy and physiotherapy better than general practitioner and placebo – "manipulative therapy is slightly better than physiotherapy after 12 months."	Study details not well described. General practice arm in particular may include suboptimal management. This seems to be an analysis of Koes 1992.
Martel 2011 RCT Sponsored by National Board of Chiropractic Examiners and the Chaire de rescherche en chiropratique FRCQ-Systeme Platinum. No COI.	5.0	N = 108 with non-specific neck pain 12 weeks or longer; mean ages for SMT, SMT plus exercise, and control groups: 36.8, 43.3, and 43.3 years.	Spinal Manipulative Therapy (SMT) group received spinal manipulation (n = 36) vs. SMT plus exercise group received spinal manipulation and exercise (n = 33) vs. Control group visited a clinic (n = 29). Pre- and Post-treatment assessment. No long-term follow-up.	When comparing before and after treatments, all patients improved in mean VAS pain (p = 0.0003), NDI (p = 0.0005), and BQ (p = 0.0001) compared to baseline. 55% of the control group, 56% of the Manipulation group and 73% of the SMT + exercise group stayed below a level of clinically acceptable pain.	"No significant change in HRQOL was associated with the preventive phase, but the 3 groups demonstrated statistically significant improvement in their fear avoidance behavior scores over time. Overall spinal manipulation or spinal manipulation combined with exercises did not yield significant advantages when compared to the no treatment strategy."	All subjects had 10 manipulations prior to allocation. Average pain and disability index scores were low at trial onset (3.4 of10). Home exercise consisted of stretches and some strengthening, but did not include aerobic exercise. Data suggest no benefit of monthly manipulation for maintenance or prevention.
Other						
Buchmann 2005 RCT	5.5	N = 26 inpatients at surgical or orthopedic department; mean ages for manipulation, mobilization, and placebo	Manipulation group received traction manipulation (n = 10) vs. Mobilization group received post isometric relaxation treatment (n = 8)	Effects found for spinal manipulation, (p < 0.01) and post-isometric relaxation, (p < 0.01) compared to the baseline values. Both treatments were	"Both treatments are superior to placebo. Postisometric relaxation seems to affect mainly the muscular parts of the treated	Small numbers. Excluded patients with acute neck pain making the population not applicable for neck

No mention of sponsorship or COI.		groups: 44±22, 46±14, and 49±7 years.	vs. Placebo group was done by laying the palms on the sides of the neck without any side-different pressure (n = 8). Follow–up at pre and post treatment, and within 24 hours of completing anesthesia.	shown to be superior to placebo post-therapeutically for the Cochran's test outcome measure, ($p < 0.01$).	segments and less so the other parts, such as the joint capsule or the segmental affiliated ligaments and fascia. Spinal manipulation seems to influence all other segmental parts more effectively, and the treatment effect persists longer."	pain treatment in the clinical setting.
Nansel 1992 RCT Sponsored by Consortium for Chiropractic Research and the National Institute for Chiropractic Research. No mention of COI.	5.5	N = 34 with goniometrically verified cervical lateral-flexion and/ or rotational left vs right passive end-range differences of 10° or greater on day of experiment; mean age not reported.	Upper group received upper cervical adjustments (n = 39) vs. Lower group received lower cervical adjustments (n = 35) vs. No treatment group (n = 24). Assessment 30 minutes post-treatment. No long-term follow-up.	Upper cervical adjustments marginally effective in ameliorating magnitudes of asymmetry when compared to no treatment controls, ($p < 0.05$), this effect not nearly as great as that seen in subjects who received lower cervical adjustments, upper vs lower, ($p < 0.001$).	"[K]knowledge gained by means of investigations such as the one reported here may play an important role in the development of more comprehensive biomechanical and physiological models which, in turn, will serve to provide for a better understanding of the cervical spine, in general.	Small numbers, healthy chiropractic students. No neck pain patients. Decreased rotation and lateral flexions seen in this asymptomatic young healthy population
Wood 2001 RCT No mention of sponsorship or COI.	5.0	N = 30 with neck pain and restricted cervical spine ROM without complicating pathosis for at least 1 month; mean age not reported.	MFMA group received mechanical force, manually assisted manipulation (n = 15) vs. HVLA group received specific contact high-velocity, low-amplitude manipulation (n = 15). Follow-up at 1 month.	There were no significant differences between groups for any outcome measures between groups, flexion was approaching significance, ($p = 0.100$) as well as the NRS 101 score on the questionnaire, ($p = 0.095$).	"The results of this clinical trial indicate that both instrumental (MFMA) manipulation and manual (HVLA) manipulation have beneficial effects associated with reducing pain and disability and improving cervical range of motion in this patient population."	Small numbers. No mention of dropout rate. No placebo or sham control cannot delineate natural history recovery from improvement with interventions. Both groups improved over an average of 8 visits.
Giles 1999 RCT Sponsored by Green Projects Donation Fund. No mention of COI.	4.0	N = 77 with chronic spinal pain syndromes, duration at least 13 weeks; mean age 42.0 years.	Manipulation group received HVLA spinal manipulation (n = 36) vs. Acupuncture group received Chinese needle acupuncture (n = 20) vs. Medication group received nonsteroidal, anti-inflammatory medication (n = 21). Pre- and Post-intervention assessment. No long-term follow-up.	Spinal manipulation was the only intervention that achieved statistically significant improvements… with (1) a reduction of 30.7% on the Oswestry scale, (2) an improvement of 25% on the neck disability index, and (3) reduction of the visual analogue scale of 50% for low back pain, 46% for upper back	"[E]vidence that in patients with chronic spinal pain syndromes spinal manipulation, if not contraindicated, results in greater improvement than acupuncture and medicine."	Dropout rate 26% for manipulation, 52% acupuncture, 20% medication ($p = .008$). Manipulation group 53% males vs 35% in acupuncture, 19% medication, suggesting potential randomization failure. Intervention periods significantly different

				pain, and 33% for neck pain (all p < 0.001).		between groups. Medication arm not defined, thus article not of quality for evaluating medication.
Acute Neck Pain						
Kanlayanaphotporn 2010 RCT Sponsored by Thailand Research Fund and the Commission on Higher Education. No mention of COI.	7.0	N = 60 with mechanical neck pain (acute, subacute or chronic); between the ages of 20-70 years.	Central posteroanterior (PA) mobilization, PA pressure over spinous process of cervical vertebra (n = 30) vs. Random mobilization, one of following – central PA, right unilateral PA, or left unilateral PA pressure (n = 30). Follow-up 5 minutes after treatment.	Both groups saw a reduction in neck pain at rest, p<0.001. there were no statistically significant differences between groups for pain at rest, pain on most painful movement, and active cervical range of motion, (p = 0.377-1.000).	"[B]oth the central PA mobilization and the random mobilization techniques have immediate effects in relieving neck pain both at rest and on the most painful movement in patients with mechanical neck pain"	Article contains acute, subacute and chronic neck pain. Both techniques showed immediate decrease in pain, but neither increased ROM. A longer sample size may substantiate more results.
Klein 2013 RCT No mention of sponsorship. No COI.	6.5	N = 61 with acute episode of non-specific neck pain and blocking of cervical joints; age 18-65 years.	Strain-counterstrain, activation of neurophysiologic reflex mechanisms with a 90 s hold and finger monitoring of tender points (n = 30) vs. Sham, position hold for 90 seconds (n = 31). No follow-up time mentioned.	There were no significant differences between groups for mobility restriction and patient assessment, (p = 0.33-0.94.)	"[I]n this trial strain-counterstain as a single intervention did not have immediate effects on mobility and pain over a sham treatment."	Intervention did not show immediate effects compared to sham for mobility improvement or pain reduction.
Antolinos-Campillo 2014 RCT Single-blind No mention of sponsorship or COI.	5.5	N = 40 with medical diagnosis of Grade I or II cervical whiplash; age 18 to 55 years.	IG or intervention group underwent the SMI technique for 4 minutes (n = 20) vs. CG or control group received a sham or placebo intervention (n = 20). Follow-up unclear.	Secondary outcome, self-perceived neck pain VAS 95% CI; -2.2 for control compared to -7.5 to 3.0 for intervention group, (p = 0.39). No significant between-group differences were found for neck pain and/or discomfort (p = 0.38).	"The SMI technique has an immediate positive effect on elbow extension in the ULNT-1. No immediate effects on self-perceived cervical pain or grip strength were observed."	ROM (elbow extension immediately improved in SMI group (p=0.01), but grip strength and neck pain did not.
Subacute Neck Pain						
Haas 2003 RCT Sponsored by the Consortial Center for Chiropractic Research, NCCAM/ NIH. No COI.	9.0	N = 104 with subacute neck pain; mean age 42.2±12.9, and 42.9±14.4 for control group.	Study group, manipulation targeted to individual cervical vertebrae according to whether cervical endplay was noted (n = 52) vs. Control group, manipulation according to sham endplay findings (n = 52). Follow-up: immediate and evening.	Mean ± SD for pain improvement: study vs control: change: immediate follow-up: -15.7±18.0 vs -15.7±20.4, p = 0.000; evening follow-up: -10.4±19.2 vs -11.7±19.0, p = 0.000	"Endplay assessment in and of itself did not contribute to the same-day pain and stiffness relief observed in neck pain patients receiving spinal manipulation. The impact on a longer course of treatment remains to be investigated. The data suggest that pain modulation may not be limited to mechanisms	Endplay assessment did not affect spinal pain or stiffness from a single event.

					associated with manipulation of putative motion restrictions."	
Gemmell 2010 RCT Study Supported by the National Institute of Chiropractic Research, USA, a subsidiary of Activator Methods. No COI.	6.0	N = 41 with subacute non-specific neck pain more than 4 weeks, but not longer than 12; mean age 46.8±11.8 for activator, 46.9±9.1 for manipulation, and 43.8±13.0 for mobilization	Manipulation, one to dynamic thrusts at one of the upper thoracic or cervical spine segments, 10 to 15 minutes (N = 15) vs Mobilization, low velocity low amplitude movements to the upper thoracic or cervical spine segments (N = 13) vs. Activator Instrument, patient in prone position, Activator IV on setting 1 for the Atlas and 2 for the cervical and upper thoracic segments (N = 13). Follow-up: baseline, 3, 6 and 12 months.	Mean ± SD (95% CI) for Numerical rating scale for pain (NRS): baseline to 12 month follow up: activator: 3±2.3 (1.93 to 4.69), $p < 0.05$; manipulation: 4±2.7 (1.79 to 5.20), $p < 0.05$; mobilization: 3±2.4 (1.60 to 4.27), ($p < 0.05$).	"Although the small sample size must be taken into consideration, it appears that all three methods of treating mechanical neck pain had a long-term benefit for subacute neck pain, without moderate or serious adverse events associated with any of the treatment methods."	Pragmatic RCT study. Underpowered so the possibility of type II error. More adverse events reported in activator group.
Picelli 2011 RCT No sponsorship or COI.	5.5	N = 18 with subacute whiplash associated disorders. Mean age 40.5 ± 12.8 years.	Treatment group received Fascial Manipulation (n = 9) vs. Control group received neck exercises plus mobilization (n = 9). Assessments performed before, immediately after, and 2wks after treatment.	Treatment group significantly better than Control only in Flexion and only immediately after treatment ($p = 0.03$), not at 2 week follow-up. Flexion Treatment vs Control: Before – 40.1 vs 35.1 Reid. After – 60.2 vs 46.3; 2 weeks – 53.8 vs 47.7.	"Patients with subacute WAD who underwent three sessions of Fascial Manipulation showed a greater improvement in neck flexion than those who performed ten sessions of conventional rehabilitation (exercises plus mobilization)."	A pilot study, small sample size (N=18). Study group (FMT) showed improved neck flexion immediately after treatment.
Escortell-Mayor 2011 RCT Sponsored by Instituto de Salud Carlos III, Fondo de Investgacion Santaria/ Fondos Europeos de Desarrollo Regional. No COI.	5.0	N = 90 with subacute or chronic mechanical neck disorders without neurological damage; aged between 18 and 60; mean 40.1±10.7	Manual Therapy (MT), neuromuscular technique, post-isometric stretching, spray and stretching, and Jones technique (n = 47) vs. ENS, portable, 80Hz (n = 43). Both groups: 10 treatment session of 30 minutes on alternate days; provided information on postural skills, isometric exercises and neck exercises. Follow-up before intervention, when intervention finished and 6 months.	No statistically significant p-values to report.	"Both analyzed physiotherapy techniques produce a short-term pain reduction that is clinically relevant."	Article contains both subacute and chronic neck pain Both intervention produced short term pain reduction, but at 6 months, only one-third of the patients reported benefits.
Masaracchio 2013 RCT	5.0	N = 66 with neck pain without symptoms distal to shoulder, pain <3-months, and baseline	Experimental groups received the same intervention as comparison group plus 4 thoracic spine thrust	Between-group change score: Numeric pain rating scale (NPRS) – 1.3 (95%CI 0.7-2.0); Neck disability index (NDI) –	"This study demonstrated that individuals with mechanical neck pain who received both thoracic	Possible attention bias due to more time spent with experimental group. Short follow-up

Sponsored in part by Long Island University's Intramural Grant Programs. No COI.		Neck Disability Index (NDI) score ≥20%, mean age 32.5±11.4 years.	manipulations; 2 targeting the upper thoracic spine and 2 the middle thoracic spine (n = 34) vs. Comparison group received posterior-to-anterior cervical spine nonthrust manipulations to the spinous processes of C2-C7 (n = 32). Assessments taken at baseline and 1wk follow-up.	8.8% (95%CI 5.4-12.2); Global rating of change (GROC) – 2 (p < 0.001; 95%CI 1-3).	spine thrust manipulation and cervical spine nonthrust manipulation plus exercise demonstrated better overall short-term outcomes on the NPRS, NDI, and GROC compared to individuals receiving only cervical spine nonthrust manipulation plus exercise."	time (1 week post treatment) suggests experimental group experienced better outcomes.
Chronic Neck Pain						
Suvarnnato 2013 RCT Sponsored by grant from the back, neck and other joint pain research group, Khon Kaen University. No mention of COI.	9.0	N = 39 with chronic mechanical pain lasting at least 3 months; mean age: 37.41 years.	Control group (n = 13) vs. Single thoracic manipulation group (n = 13) vs. Single thoracic mobilization group (n = 13). Assessments took place immediately after treatment and 24 hours after treatment.	Manipulation and mobilization both showed significant decrease in VAS pain score compared to baseline (p = 0.05), however differences not significant compared to each other or to control (p >0.05). Manipulation showed significant difference for cervical flexion (62.87 vs 56.57, p <0.01) and for cervical extension (59.31 vs 53.79, p <0.05) vs. control. Manipulation showed significant difference compared to mobilization for cervical extension (59.31 vs 54.45, p <0.05) and cervical left rotation (64.26 vs 58.89, p <0.05). Differences only significant at immediate follow-up and not at 24 hour follow-up. Mobilization showed significant difference vs. control for cervical flexion only, 62.57 vs. 56.57, p < 0.01)	"In summary, the subjects in this study reported reductions in pain at rest and increases in CROM in all movements of the cervical spine after single level thoracic manipulation at T6-T7 in patients with chronic mechanical neck pain. Single-level thoracic mobilization at T6-T7 for patients with chronic neck pain led to significantly reduced pain levels at rest and increased CROM (in some directions) by comparison with a control group."	Both experimental groups experienced pain and increased CROM post intervention and 24 afterwards.
Snodgrass 2014 RCT No mention of sponsorship or COI.	7.5	N = 64 with chronic nonspecific neck pain; mean age for Low force group 32.1 years, 34.4 years for the high force group and 33.7 for the placebo group.	High force (90N) Mobilization Technique group (n = 21) vs. Low force (30N) Mobilization Technique group (n = 22) vs. Placebo group consisting of a detuned laser. Assessments measured at baseline, immediately after treatment and 4 days after treatment.	Immediately after treatment significant difference between High force vs Placebo and High force vs Low force for VAS pain scores measured on a 100-mm scale (38.9 vs 20.9, 38.9 vs 27.1, p <0.05). At 4 day follow-up, High force group showed significantly lower VAS results compared to low force (15.2 vs 26.5, p <0.05). No significant	"This study demonstrates that a higher applied force (90 N) during a single application of cervical spine mobilization significantly reduces spinal stiffness in patients with chronic, nonspecific neck pain at a short-term follow-up (approximately 4 days)."	These results are limited to patients with chronic, nonspecific neck pain and relatively low disability.

				difference between groups for cervical range of motion between the three groups. Also no significant results for pain pressure threshold.		A higher applied force (90N) induced short term benefits (4 days after intervention) as measured by a decrease in spinal stiffness.
Reid 2008 RCT No mention of sponsorship or COI.	7.5	N = 34 with cervicogenic dizziness; mean ages for SNAG and Placebo groups: 63.4 ± 13.1 and 63.6 ± 13.7 years.	SNAG group described in Mulligan, 2004 (n = 17) vs. Placebo group received deactivated laser placebo treatments (n = 17). Assessments taken pre-treatment, after final treatment, and 6wks and 12 weeks post-treatment.	Dizziness severity in SNAG vs Placebo: Post-treatment (p = 0.03); 6 weeks (p = 0.03); 12 weeks (p = 0.09). Pain severity in SNAG vs Placebo: Post-treatment, (p < 0.001); 6 weeks (p = 0.001); 12weeks, (p = 0.01).	"The present study found that SNAGs are a safe and effective manual therapy technique for the treatment of cervicogenic dizziness and pain."	Pilot study only. Needs further study to demonstrate efficacy.
Izquierdo Pérez 2104 RCT No mention of sponsorship or COI.	7.0	N = 61 with mechanical neck pain for more than 12 weeks; between the ages of 20-65 years.	High velocity, low amplitude manual therapy technique or HVAL with a maximum of 2 thrusts (n = 19) vs. Mobilization (Mob) with oscillatory pressure applied at a frequency of 2 Hz for 2 min and repeated 3 times with 1 minute rest in between (n = 21) vs. Sustained natural apophyseal glide (SNAG) 3 sets of 10 repetitions. All patients received 4 treatment sessions over 2 weeks (n = 21). Follow-up immediately after treatment and 1, 2 and 3 months after treatment.	VAS-rest improved for all groups but trending toward significance for group/time interaction, (p = 0.06).	"This study revealed no superiority of HVLA, Mob or SNAG in outcomes, namely neck pain, disability, motion and global perception of change in the short term (3 months)."	There are no meaningful differences between groups.
Haas 2004 RCT Supported by Oregon Craniofacial Complementary and Alternative Medicine Center, National Center for Complementary and Alternative Medicine/National	7.0	N = 24 with chronic cervicogenic headache; mean age 38.9±11.9 for group 1, 46.6±6.9 for group 2, and 35.4±9.9 for group 3.	Group 1: 3 Spinal manipulation therapy visits (N = 8) vs. Group 2: 9 visits (N = 8) vs. Group 3: 12 visits (N = 8). Follow-up: baseline, 4 and 12 weeks.	Mean for Headache (HA) pain at 4 weeks; 4 visits per week: 18.7, (p = 0.04); 12 weeks: 3 visits per week: 19.4, (p = 0.035); 4 visits per week: 18.1, p = 0.048.	"A large clinical trial on the relationship between pain relief and the number of chiropractic treatments is feasible. Findings give preliminary support for the benefit of larger doses, 9 to 12 treatments, of chiropractic care for the treatment of cervicogenic headache."	3 treatment groups. Relatively small sample size, low dropout rate. Pilot showed that increasing the number of chiropractic visits per week decreased pain giving preliminary support.

Institutes of Health. No mention of COI.						
Reid 2014 RCT Sponsored by the Mulligan Concept Teachers Association Research Award and The University of Newcastle. No mention of COI.	7.0	N = 86 with cervicogenic dizziness; mean age 62.0 ± 12.7 years.	SNAG group as described in Mulligan, 2004 (n = 29) vs. MM group received Maitland mobilizations plus range-of-motion exercises (n = 29) vs. Placebo group received deactivated laser placebo treatments (n = 29). Assessments performed at baseline, following final treatment, and 12 weeks post-treatment.	VAS Dizziness mean difference: Post-treatment – SNAG vs Placebo -20.7 ($p < 0.001$), MM vs Placebo -15.5 ($p = 0.02$); 12wks – SNAG vs Placebo -18.4 ($p = 0.01$), MM vs Placebo -14.4 ($p = 0.03$).	"Both SNAGS and Maitland mobilizations provide comparable immediate and sustained (12 weeks) reductions in intensity and frequency of chronic cervicogenic dizziness."	Follow-up to pilot study in 2008. Placebo is sham laser not sham for treatments. Not significant for pain. No treater blinding.
Saavedra-Hernandez 2013 RCT No mention of sponsorship. No COI.	6.0	N = 82 with a primary complaint of bilateral chronic mechanical neck pain; mean age: 45 years.	Cervical Manipulative Group- received only cervical thrust joint manipulation (n = 41) vs. Full Manipulative Group- received several manipulative interventions (n = 41). Follow-up assessments 1 week after intervention took place.	There were no significant differences between groups at follow-up for cervical range of motion (rotation, flexion and extension) nor for neck pain. There was a significant difference in favor of the full manipulative group compared to the cervical manipulative group for neck disability index score11.6 vs 16.8, $p = 0.022$).	"In conclusion, in patients with chronic mechanical neck pain, manipulation of the cervical and thoracic spine leads to a greater reduction in disability at one week than manipulation of the cervical spine alone, whereas changes in pain and range of movement are not affected differently"	Both groups improved over time, notation was higher
Hall 2007 RCT No mention of sponsorship. Two authors are members of the Milligan Concept Teachers Association and receive a teaching fee.	6.0	N = 32 mean age 36±3 years with unilateral headache without side shift, headache with neck stiffness and/or pain for past 30 months at least once per week.	C1-C2 self-sustained natural apophyseal glide (SNAG) mobilization (n = 16) vs. Placebo, sham mobilization at C1-C2 using cervical self-SNAP strap (n = 16). 2 repetitions twice daily for 12 months. Assessments at 4 weeks and 12 months from baseline.	Rotation improvement: greater for C1-C2 Self-SNAG vs placebo, ($p < 0.001$). Headache severity index 4 weeks/ 12 months (mean ± SD): C1-C2 Self-SNAG 31±9 vs placebo 51±15, $p < 0.001$/ 24±9 vs 44±13, ($p < 0.001$).	"[H]eadache symptoms, when measures by a headache index, improved significantly more in subjects treated with a C1-C2 self-SNAG than in subjects treated with a placebo."	Data suggest that intervention is superior to placebo cointervention of physical activity was partially addressed.
Sterling 2010 RCT Sponsored by the National Health and Medical Research Council	5.5	N = 39 with reported neck pain resulting from a motor vehicle crash of greater than 3 months duration; mean age: 40.5 years.	SMT (lateral glide) group (N = 22) vs. Manual contact intervention group (N = 17). Assessments took place immediately after treatment.	There was no significant difference between groups for PPT at C6 after treatment ($p = 0.78$). PPT at the median nerve was approaching significance in favor of the SMT group ($p = 0.068$). Measurement of TPT (thermal pain thresholds)	"The results of this study show that cervical SMT (lateral glide technique) has the capacity to modulate spinal cord hyperexcitability in participants with chronic	27/39 participants were female. Pilot study has small sample size and short follow-up. SMT vs. manual contact showed no differences between groups, but study

of Australia. No mention of COI.				showed no significant difference between groups, (p = 0.55).	whiplash, at least in the short term."	suggest NFR threshold increased with SMT lateral glide.
Vernon 2012 RCT Sponsored by National Institutes of Health-Center for Complementary and Alternative Medicine and Canadian Institutes of Health Research. No COI.	5.5	N = 67 with chronic pain of at least 8 weeks in duration. NRS-101 pain scale range of 30-65 was also necessary for inclusion; mean age 38.8 for the SM group and 38.3 for the RM group.	Real cervical manipulation group (RM) (N = 33) vs. Sham cervical manipulation group (N = 34). Assessments took place immediately after treatment, 5 minutes after treatment and 15 minutes after.	Pain scores improved significantly over time for both groups compared to baseline (p = 0.049). No significant difference between groups (p > 0.05). Cervical ROM remained unchanged and there was no significant difference between groups, (p = 0.96).	"The double-treatment method of pairing real-sham and sham-sham procedures using carefully selected physical components that systematically account for patient experience during manipulation provides an effective and inert sham/placebo for manual manipulation of the cervical spine."	Sham validation study showing no difference between groups. Sham was effective in masking subjects.
Casanova-Méndez 2014 RCT No mention of sponsorship or COI.	5.5	N = 64 with chronic non-specific neck pain (NSNP) with or without pain radiating to the head, trunk and/or limbs; mean age 37.53±9.39 for dog technique, and 37.73±11.25 for toggle recoil.	Dog Technique Group (DTG), subject in supine position with arms across the chest, therapist guided manipulation (n = 30) vs. Toggle Recoil Group (TRG), subject lying prone, therapist guided manipulation (n = 34). Follow-up: baseline, immediately after, 20 minutes after.	Mean (95% CI): score changes immediately after intervention (TRG – DTG): ROM extension: 4.60 (7.97/1.21), p = 0.009; ROM right lateral flexion: score changes in 20 minutes after intervention: 4.26 (7.10/1.42), p = 0.004; ROM left rotation: immediately after intervention: 4.60 (8.22/0.97), (p = 0.014); 20 minutes after intervention: 5.26 (8.19/2.33), (p = 0.001).	"After a single intervention, no major or clinical differences were observed between the toggle recoil and the dog techniques for neck pain, mobility and mechanical sensitivity in subjects with NSNP."	Short study follow up (20 minutes Toggle Recoil technology appears superior to Dog technology.
Evans 2003 RCT Study sponsored by the Consortial Center for Chiropractic Research through National Center for Complementary and Alternative Medicine and the National Institute of Arthritis, Musculoskeletal and Skin Diseases of the National Institutes of	5.5	N = 28 with neck pain, stiffness, or tenderness; and with or without musculoskeletal or neurological signs5 that lasted less than 12 weeks; mean age 39.13±9.2.	Chiropractic Care, spinal manipulation with light soft tissue massage, activity modification (n = 10) vs. Medical Care, prescription acetaminophen, NSAIDs, and/or mild narcotic medication, activity modification (n = 9) vs. Self-Care Education, physical therapist guided, two 45 minute session, booklet regarding self-care (n = 9). Follow-up: baseline, 3 and 12 weeks.	No between groups comparisons were planned or performed due to the small sample size.	"Recruitment of patients appears feasible for a full-scale randomized clinical trial evaluating chiropractic spinal manipulation, medical care, and self-care education for acute and sub-acute neck pain."	Small sample size (N=28). Pilot Study to evaluate feasibility.

Health. No mention of COI.						
Lin 2013 RCT No mention of sponsorship or COI.	5.5	N = 63 with a diagnosis of mechanical neck pain and >3 month history of neck pain; mean ages for LM and TCM groups: 38.94yrs and 40.90yrs.	LM group received Long's Manipulation (n = 33) vs. TCM group received traditional Chinese massage (n = 30). Each group received 8 20 minute sessions every 3 days. Follow-up for both groups was performed immediate and 3mths post-treatment.	Immediate post-treatment LM vs TCM: Northwick Park Neck Disability Questionnaire (NPQ) – 12.08 vs 21.43 ($p < 0.001$); Numerical pain rating scale (NPRS) – 2.06 vs 4.04 ($p < 0.001$); Patient perceived satisfaction (PPS) – 8.81 vs 7.65, ($p < 0.001$). 3-month post-treatment LM vs TCM : NPQ – 15.07 vs 25.88 ($p = 0.001$); NPRS: 2.07 vs 4.54 ($p < 0.001$); PPS – 8.45 vs 7.31 ($p < 0.001$).	"The Long's manipulation was showed to produce greater effects than traditional Chinese massage in relieving pain and improving disability in the management of patients with chronic mechanical neck pain."	High number of patients lost to follow-up. Minimal differences between interventions were found. Both treatment areas improved over the study period.
Lluch 2014 RCT No mention of sponsorship or COI.	5.5	N = 18 with chronic idiopathic neck pain, neck pain $\geq$3months during past year, and pain intensity $\geq$3/10 on an NRS; mean ages for exercise and mobilization groups: 44.3yrs and 39.7yrs.	Exercise group received active assisted plus active cranio-cervical flexion (n = 9) vs. Mobilization group received passive mobilization plus assisted cranio-cervical flexion (n = 9). Assessment performed before and immediately after intervention.	Exercise vs Mobilization: % reduction in resting pain – -67.9 $\pm$ 27.5% vs -20.3 $\pm$ 41.2% ($p = 0.01$); % increase in pressure pain threshold – 17.2 $\pm$ 18.8% vs 0.7 $\pm$ 17.7%, ($p = 0.02$).	"Although both active and passive interventions offered pain relief, only the exercise group improved on a task of motor function highlighting the importance of specific active treatment for improved motor control of the cervical spine."	Relatively small sample size (n=18) and both active and passive interventions decreased pain with only the exercise group increasing motor function
Sterling 2001 RCT Sponsored by Dorothy Hopkins Award and Manual Therapy Special Interest Group (Australian Physiotherapy Association, Queensland Branch). No mention of COI.	5.0	N = 30 with history of mid to lower cervical spine pain greater than 3 months in duration; mean age: 35.77.	SMT treatment passive mobilization group (n = 10) vs. placebo group-manual contact applied over the C5/6 area (n = 10) vs. Control Group- no physical contact applied (n =10). Assessments took place immediately after treatment.	SMT group showed a significant difference for VAS pain scores compared to control ($F_{2,58}$=3.56, $p = 0.044$) and a significant difference compared to control and placebo for PPT scores. ($p<0.001$). There was a significant difference in favor of SMT compared to both placebo and control for SC AUC score ($F_{2,58} = 8.54$, $p < 0.01$), SC MAX score ($F_{2,58} = 9.79$, $p < 0.01$), and ST MIN ($F_{2,58} = 4.64$, $p < 0.05$). SMT also showed significant difference in EMG activity of superficial neck muscles at pressure levels of 22mm ($F_{2,58} = 26.28$, $p = 0.0001$), 24mm ($F_{2,58} = 47.5$, $p = 0.0001$), and 26mm ($F_{2,58} = 22.38$, $p = 0.0001$)	"SMT using a unilateral grade III PA mobilization technique applied to the symptomatic side of the C5/6 motion segment produced a hypoalgesic effect to mechanical but not thermal nociception and an excitatory effect on sympathetic nervous system activity."	Small sample size. Sparse baseline comparability. SMT produced a hypoalgesic effect to mechanical nociception short term.
La Touche 2013 RCT	5.0	N = 32 with chronic craniofacial pain or CCFP of myofascial	Anterior posterior upper cervical mobilization (APUCM) at a rate of 1	Mean ± SD VAS Session 1 – pre/post; Session 2 – pre/post; Session 3 – pre/post: treatment –	"[A]PUCM reduces pain intensity and increases	Data shows intervention improves pain ratios.

No mention of sponsorship. No COI.		origin (pain and dysfunction at the cervical and masticatory muscles); mean age treatment 33.19±9.49, sham 34.56±7.84.	oscillation per 2 seconds (0.5 Hz) for 7 minutes total, 3 sets of 2 minutes with 30 second rest in between (N = 16) vs Sham no mobilization applied, contract held for 3 sets of 2 minutes with 30 second rests in between (N = 16). Each patient received 3 sessions over 2 weeks. Study lasted 8 months. Follow-up immediately after session and 5 minutes after session.	43.88±7.3/29.66±8.97; 31.06±8.83/18.31±9.18; 29.31±11.8/14.75±11.8 vs sham – 42.38±9.41/41.5±7.9; 45.13±7.9/42.56±6.88; 44.31±8.51/42±9.05, ($p < 0.001$).	PPT in the cervical and craniofacial regions."	
Von Piekartz 2013 RCT No mention of sponsorship or COI.	4.5	N = 43 with some features of CGH as well as having the headache for more than 3-months; mean age: 36 years.	Orofacial care group (n = 22) vs. Usual Care Group (n = 21). Assessments took place at baseline after 6 treatment sessions (3 months) and at a final 6 month follow-up.	No significant difference between groups for mean cervical ROM change scores ($p > 0.05$). The Orofacial group showed significant improvement for cervical flexion (59.0 vs 45.1, $p < 0.05$) and cervical extension,76.0 vs 60.9, ($p < 0.05$) compared with the usual care group.	"Orofacial treatment in addition to usual manual therapy care focused on the cervical spine was more effective than usual care alone, in improving cervical movement impairment in people suffering from headache with cervical impairment and signs of TMD. These results, when viewed with previous evidence, suggests that people who suffer from headache who have signs of cervical impairment and TMD should receive additional orofacial treatment."	27/43 participants were female. Potential for patent selection bias due to PT failure. Combination treatment showed improvement both short-term and at 6 month follow-up.
Sillevis 2011 RCT Sponsored by Integrated Therapy Practice PC. COI-Integrated Therapy Practice PC is the employer of the principle researcher.	4.5	N = 101 with chronic cervical pain lasting for at least 3 months; mean age in the manipulation group was 42.7 years and in the mobilization group was 46.8 years.	Chronic Cervical Manipulation Group (N = 50) (Broken up into 3 groups: No pop (N = 18), Multiple pop (N = 18), One pop (N = 14) vs. Chronic Cervical Mobilization Group (N = 51). Assessments were taken 3 times immediately following treatment.	In manipulation group 32 of 50 had an audible pop detected. 18 of these had multiple pops detected. No significant effect of joint sounds on pupil diameter at any of the 60 second follow-up periods ($p = 0.34$, .54 and .84 respectively). Mean VAS pain score for no pop group showed significant decrease vs. multiple pop and 1 pop groups, 27.9 vs. 38.8 vs 36.4, ($p = 0.031$).	"The results of this study provide evidence that the presence of joint sounds as perceived by the practitioner did not influence the overall functioning of the sympathetic nervous system nor did it have an immediate clinically significant effect on the change in pain perception."	Statistics were not clear with regards to comparison with the mobilization group. Study methods limited joint sounds does not affect ANS following a T3_T4 spinal thrust manipulation as there was no significant differences between groups.
Quesnele 2014 RCT	4.5	N = 10 who received cervical spinal manipulation or CSM within 3 months prior to	Neutral (0°) neck position vs. Passive rotation (45°) vs. Maximum voluntary passive rotation within a comfortable	Combined contralateral and ipsilateral vertebral artery (VA) mean velocity (cm/s): Neutral – 16.1	"Phase-contrast MRI measure of blood velocity and flow through the V3 segment of the VA	Cervical spine manipulation and position did not change vertebral artery blood

Sponsored in part by Canadian Chriopractic Protective Association (CCPA) and NCMIC Research Foundation and Canadian Memorial Chiropractic College. COI: Dr. Triano lectures on behalf of NCMIC and CCPA and Dr. Noseworthy received honorarium for lecture from Bayer .		study; mean age 26.8 years.	range vs. C1-C2 cervical rotatory manipulation. Each participant received each treatment. Each participant received all 4 maneuvers and MRI sequencing following each one. Maneuvers were performed in consecutive, random order over 120 minutes.	Passive – 15.4 Maximum – 15.6 Cervical manipulation – 15.1 Combined contralateral and ipsilateral vertebral artery (VA) flow (mL/s): Neutral – 1.7 Passive – 1.7 Maximum – 1.7 Cervical manipulation – 1.6 No significant differences were observed in either blood flow or velocity.	showed no significant changes in association with either head rotations or chiropractic CSM procedure."	flow or velocity. Small sample size (n=10) and pilot study only.
Non-specific Neck Pain						
Aquino 2009 No mention of sponsorship or COI.	7.5	N = 48 with non-specific neck pain of at least 3 months in duration; mean age in control group 32.6 years and 35.6 years in the experimental group.	Mobilization over randomly selected level (Experimental Group) (N = 24) vs. Mobilization over symptomatic vertebral level (Control Group) (N = 24). Assessments were taken immediately post-treatment.	During post-treatment measurements no significant differences found between groups. Pain at a resting position not significant between groups, (p = 0.44) or within groups. Both control and experimental groups showed significant improvements within groups for pain during most painful movement and pain during vertebral palpation however, no significant differences between groups (p = 0.87 and p = 0.78, respectively).	" Cervical joint mobilizations produce immediate pain reduction during movement and palpation in patients with chronic neck pain. However, these effects are not influenced by the cervical segment being mobilized."	Pain reduction not specific to vertebral level of mobilization.
Saavedra-Hernández 2012 RCT No mention of sponsorship or COI.	5.5	N = 82 with chronic mechanical neck pain; mean±SD age 45±9; 50% females.	Manipulation group received cervical thrust manipulation (N = 40) vs. Kinesio-Tape group received Kinesio Tape application (N = 40). Follow-up at 1 week post-treatment.	Pain scores and neck disability index scores were not significant between groups ((p >0.)01). Manipulation group showed significant increase compared to kinesio taping in cervical right rotation (78.1 vs 72.0, p < 0.01) and cervical left rotation (78.8 vs 76.8, p < 0.01) at the 1 week follow-up. Other measures such as cervical flexion and extension showed no significant difference between the two groups.	"In patients with chronic mechanical neck pain, manipulation of the cervical and thoracic spine leads to a greater reduction in disability at one week than after manipulation of the cervical spine alone, whereas changes in pain and range of motion are not affected differently."	Author states single blinded but is not well described. Data suggest no increase in benefit of one technique over another. No statement of efficacy regarding manipulation due to lack of control group. Both groups improved overtime. Rotation was higher among manipulation

Paanalahti 2014 RCT Sponsored in part by the Swedish Naprapathic Association (SNA) and the Scandinavian College of Naprapathic Manual Medicine (SCNMM). COI: Holm and Lyander do consultancy for SCNMM. Asker has a part time position at SCNMM.	5.5	N = 791 seeking care for neck and/or back pain; mean age 35.0 years.	MT group received all manual therapy treatment techniques i.e. spinal manipulation, spinal mobilization, muscle stretching and massage (N = 249) vs. MT excluding spinal manipulation (N = 258) vs. MT excluding muscle stretching (N = 260). Follow-up performed weekly for six weeks.	Adverse events Odds Ratio for MT excluding spinal manipulation vs MT excluding stretching with MT as a reference: Short minor – 1.09 (95%CI 0.83-1.43) vs 1.09 (95%CI 0.84-1.43); Long minor – 1.37 (95%CI 0.91-2.08) vs 1.24 (95%CI 0.82-1.89); Short moderate – 0.82 (95%CI 0.58-1.16) vs 0.97 (95%CI 0.70-1.37); Long moderate – 1.09 (95%CI 0.79-1.52) vs 1.11 (95%CI 0.81-1.53).	"Adverse events after manual therapy are common and transient. Excluding spinal manipulation or stretching do not affect the occurrence of adverse events."	Three treatment arms, and manual therapy (spinal manipulation group) showed increased numbers of adverse events, especially muscle soreness.1.5
Schomacher 2009 RCT No mention of sponsorship or COI.	4.0	N = 128 with neck pain with or without irradiation into the arms; mean age for group A was 45.9 years. Mean age for group B was 53.2 years. NON	Group A (Mobilization treatment in the located segment) (N = 60) vs. Group B (Mobilization treatment in an area 3 segments away from the located one) (N = 68). Assessments took place immediately after treatment.	There were no significant differences between groups for NRS values for pain intensity, ($p = 0.12$) or for NRS values for sensation of movement, ($p = 0.15$). However, the differences within groups were significantly different when compared to baseline for both pain intensity and sensation of movement NRS scores, ($p < 0.01$)	"This study suggests that therapeutic movement has pain-alleviating effects even when applied at a distance from the concordant segment and provides similar immediate effects of reduction in pain intensity and improve-ment in sensation of movement."	Short term single time trial without follow up. No difference between groups for pain. Of limited utility for guidance.
Other						
Oliveira-Campelo 2013 RCT No sponsorship or COI.	5.0	N = 164 participants with latent myofascial trigger points (MTrP) in upper trapezius muscle, and an average $\geq$2 hours/day computer work; mean ages for WS, Pl, IC, PS, and MET groups: 20.44 $\pm$ 2.08, 20.23 $\pm$ 1.57, 20.08 $\pm$ 1.21, 20.6 $\pm$ 1.93, and 20.35 $\pm$ 2.14 years.	WS group waited in supine position for 30-secs (N = 25) vs. Pl group received the same contact points as those described in PS group, without execution of any movement, for 30-secs (N = 22) vs IC group received ischemic compression of upper trapezius muscle latent MTrP (N = 24) vs. PS group (n = 23) received passive stretching of the upper trapezius (N = 23) vs. MET group received muscle energy technique of upper trapezius	Contralateral flexion Pre and 10min post: MET – 39.8$\pm$4.6, 48.1$\pm$4.0 ($p < 0.01$); PS – 37.6$\pm$5.1, 46.8$\pm$4.9 ($p<0.01$); IC – 39.8$\pm$5.1, 46.0$\pm$5.8 ($p < 0.01$). Ipsilateral rotation Pre and 10min post: MET – 70.4$\pm$5.7, 74.3$\pm$5.4 ($p < 0.01$); PS – 70.6$\pm$6.4, 75.0$\pm$5.5 ($p < 0.01$); IC – 71.2$\pm$5.7, 76.3$\pm$4.5 ($p < 0.01$). Ipsilateral rotation Pre and 10min post: Pressure pain threshold Pre and 10min post: MET – 1.8$\pm$0.4, 2.6$\pm$0.5 ($p < 0.01$); PS – 1.9$\pm$0.4, 2.5$\pm$0.4 ($p < 0.01$); IC – 1.7$\pm$0.3, 2.8$\pm$0.4, (p	"Ischemic compression, passive stretching, and muscle energy techniques' single application on upper trapezius with latent MTrP leads to an increase on contralateral flexion and ipsilateral rotation range of motion as well as on the pain threshold immediately after session. All 3 techniques maintained improvements after 1 week; however, ischemic compression	5 arms to study. Follow up to 2010 pilot study. Latent trigger point of upper trapezius decreased pressure pain sensitivity and cervical range of motion to one week post manipulation.

			(N = 23). Assessments performed pre-intervention and 10mins, 24hrs, and 1week post-intervention.	<0.01). No between group significant differences for any assessments.	resulted in the most stable improvement."	

MANIPULATION UNDER ANESTHESIA (MUA) AND MEDICATION-ASSISTED SPINAL MANIPULATION (MASM)

Manipulation under anesthesia (MUA) and medication-assisted spinal manipulation (MASM) involves the administration of anesthesia or medication followed by manipulation of the spine with the intended effect of relieving cervicothoracic pain. Proponents believe this method of manipulation is superior to manipulation without anesthesia due to factors including the reduction in resistance to movement that occurs after the administration of the anesthetic. However, such reductions in resistance may increase the likelihood of injuries to the patient.

Recommendation: MUA and MASM for Acute, Subacute, or Chronic Cervicothoracic Pain

MUA and MASM are not recommended for the treatment of acute, subacute, or chronic cervicothoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

MUA and MASM have not been evaluated in chronic cervicothoracic pain patients, except in one study that used diazepam for its amnestic properties in blinding. However, that study concluded that after a single manipulation there was no benefit compared to no manipulation.(966) MUA/MASM is high cost, is invasive, and has increased potential for significant adverse effects. There are no specific contraindications to MUA beyond those of its individual components (e.g. anesthesia and SMT).(1049) These contraindications include spinal malignancy, hypermobility, instability, acute inflammation, infection, fracture, progressive neurological deficits, large aortic aneurysms, bleeding disorders, severe osteoporosis, acute gout, spinal cord compression, several canal stenosis, sequestered nucleus pulposus, or cardiopulmonary conditions precluding anesthesia.(1050) It has also been suggested that procedures such as MUA are not appropriate for patients who could improve with a simpler, more cost effective therapy that does not involve anesthesia.(1051) Judging from participant exclusion criteria used in previous studies on MAM, it would appear that patients with non-mechanical CLBP, active rheumatoid disease, tobacco use, severe coexisting disease, severe obesity, and involvement in workers' compensation or litigation are less likely to respond favorably to MUA, MUJA, or MUESI.(1049) Older forms of MUA as practiced many decades ago using more forceful long-lever techniques were associated with adverse events such as cauda equina syndrome, paralysis, and fracture.(1049) However, more recent studies evaluating newer, gentler techniques of MUA have not reported any serious adverse events.(1049) Temporary flare-ups in lumbosacral pain have been reported and are attributed to the stretching of adhesions and mobilization of inflamed joints achieved by MUA; such flare-ups are easily treated with postoperative care.(1052) A review of the MAM literature reported a total of 11 adverse events in 17 studies with a total of 1,525 participants (prevalence <1%).(1049) These adverse events included 8 cases of increased lumbosacral pain, one case of myelographic evidence of herniated intervertebral disc, and 2 cases of respiratory distress that resolved with Valium.(1049) An additional review of MUA reported no adverse events in any of the published studies, indicating they are likely rare.(1050) Most observational studies have reported no adverse events from MUA.(1049, 1053-1056)

Evidence for the Use of MUA and MASM

There is 1 moderate-quality RCTs incorporated into this analysis.(966)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Manipulation under anesthesia, MUA, medication-assisted spinal manipulation, MASM, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 626 articles, and considered zero for inclusion. In Scopus, we found and reviewed 76 articles, and considered zero for inclusion. In CINAHL, we found and reviewed zero articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed zero articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the one article considered for inclusion, zero randomized trials and zero systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Sloop 1982 RCT No mention of sponsorship or COI.	5.5	N = 39 symptomatic cervical spondylosis or nonspecific neck pain; mean age 49 years, range of 19-68.	Manipulation performed by 1 therapist, rheumatologist experienced in techniques (n = 21) vs. No manipulation performed with diazepam, 20mg intravenously (n = 18). Follow-ups at baseline and after three weeks and twelve weeks.	At 3 weeks, 57% of manipulation patients vs 28% of controls felt treatment had helped. Crossover attempted at 3 weeks; however, results not well described.	"[T]he value of a single manipulation of the cervical spine has not been established and that further exploration or indications is needed."	Diazepam dose "amnestic," thus likely equivalent to manipulation under anesthesia. Several study details missing.

MASSAGE

Massage is a commonly used treatment for cervicothoracic pain and is administered by multiple health care providers, as well as family or friends. Massage is theorized to aid muscle and mental relaxation and to result in increased pain tolerance through endorphin release.(1057) Other theories are that massage may enhance local blood flow and could increase clearance of chemical pain mediators or stimulate large diameter nerve fibers that have an inhibitory input on T-cells in the spinal cord, resulting in decreased pain.(1058) A complicating factor in this review is the varying methods of massage that are employed.(1059, 1060)

1. *Recommendation: Massage for Chronic Cervicothoracic Pain*
   Massage is recommended for select use in chronic cervicothoracic pain as an adjunct to more efficacious treatments consisting primarily of a graded aerobic and strengthening exercise program.

   Indications – For time-limited use in chronic cervicothoracic pain patients without underlying serious pathology as an adjunct to a conditioning program that has both graded aerobic exercise and strengthening exercises. The intervention is only recommended to assist in increasing functional activity levels more rapidly and the primary attention should remain on the conditioning program. In patients not involved in a conditioning program or who are non-compliant with graded increases in activity levels, this intervention is not recommended.

   Frequency/Duration – Six to 10 sessions of 30 to 35 minutes each, 1 or 2 times a week for 4 to 6 weeks.(1061) Objective improvements should be shown approximately half way through the regimen to continue this treatment course.

   Indications for Discontinuation – Resolution, intolerance, lack of benefit, or non-compliance with aerobic and strengthening exercises.
   Benefits – Modest reduction in pain.
   Harms – Short term discomfort during massage, and potentially longer term afterwards with more vigorous massage.

   Strength of Evidence – **Recommended, Evidence (C)**
   Level of Confidence – Low

2. *Recommendation: Massage for Acute and Subacute Cervicothoracic Pain and Chronic Radicular Syndromes*
   Massage is recommended as a treatment for acute and subacute cervicothoracic pain and chronic radicular syndromes in which cervicothoracic pain is a substantial symptom component.

   Indications – Patients with subacute and chronic cervicothoracic pain without underlying serious pathology, such as fracture, tumor, or infection.

   Frequency/Duration – Objective benefit (functional improvement along with symptom reduction) may be demonstrated after a trial of 2 sessions in order for further treatment to continue, for up to 10 sessions during which a transition to a conditioning program is accomplished.

   Indications for Discontinuation – Resolution, intolerance, or lack of benefit.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

3. *Recommendation: Mechanical Devices for Administering Massage for Cervicothoracic Pain*
   Mechanical devices for administering massage are not recommended for cervicothoracic pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendations
There are no sham trials of massage therapy for cervicothoracic pain. Massage is a commonly used to treat cervicothoracic pain. However, relatively few quality studies have been reported. Many studies have included massage as a component of a physical rehabilitation program, but not as the primary study focus.(497, 558, 577-579, 894, 908, 978, 980, 981, 1062) One moderate-quality trial evaluated therapeutic massage with self care instruction in chronic cervicothoracic pain patients. The exact massage protocol was individualized and included Swedish and therapeutic massage techniques. They reported significant improvement in Neck Disability Index, bothersomeness score, and Global Rating of Improvement at 4 and 10 weeks. However, at 26 weeks there was no statistical improvement in massage over self-care book. The benefit of massage was only present during the treatment period of 10 weeks.(1061) A moderate-quality trial comparing acupuncture, sham laser acupuncture, and conventional massage in chronic cervicothoracic pain, reported no significant improvement in the massage only group. Massage was 5 times over 3 weeks and the assessments were done at 1 week and 3 months after treatment.(898) A moderate-quality study comparing traditional Chinese therapeutic massage vs stretching and moist heat vs control in chronic cervicothoracic pain reported significant improvement in the massage group. This improvement was maintained 6 weeks after the massage therapy stopped.(569) Two high-quality trials involving manual massage reported a benefit of massage compared to other modalities for treatment of subacute and chronic low back pain(1063, 1064) (see Low Back Disorders guideline). Massage is not invasive, has low risk of adverse effects aside from short-term pain, and is moderately costly.

Evidence for the Use of Massage
There is 1 high-(583) and 18 moderate-quality RCTs (one with two reports)(497, 558, 569, 577-579, 894, 898Gam, 1998 #305, 978, 980, 981, 1004, 1061, 1062, 1065-1069) incorporated into this analysis. There are 2 low-quality RCTs in Appendix 1.(1043, 1070)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: massage, instrumentation, devices, equipment and supplies, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 208 articles, and considered 9 for inclusion. In Scopus, we found and reviewed 36 articles, and considered 1 for inclusion. In CINAHL, we found and reviewed 19 articles, and considered 1 for inclusion. In Cochrane Library, we found and reviewed 1 articles, and considered 0 for inclusion. We also considered for inclusion 13 articles from other sources. Of the 281 articles considered for inclusion, 20 randomized trials and 5 systematic studies met the inclusion criteria.*

Author/Year StudyType Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Vavrek 2010 RCT Funded by the National Center for Complementary and Alternative Medicine, Department and Human Services grant. No COI.	7.5	N = 80 with CGH pain. Mean age 38 for the SMT group and 37 for LM group.	8 spinal manipulation and 8 attention control physical examination sessions (n = 20) vs. 8 light massage and 8 attention control PE (n = 20) vs. Attention control PE only (n = 40). Follow-up was at 4, 8, 12 and 24 weeks.	Pain on right rotation and pain on cervical extension (p = 0.023 and p = 0.035) was the only statistically significant difference between treatment groups.	"At 12 weeks, a lower pain pressure threshold was indicative of those that still had the most intense subjective experience with headache pain vs cervical active ROM and pain with movement."	Secondary analysis of Haas 2010. Data presented in paper are not relevant to evidence-based recommendation on treatment.
Madson 2010 RCT No mention of industry sponsorship or COI.	6.5	N = 23 with nonspecific neck pain longer than 3 months duration. Age range 20-80 years	Sedative massage (SM) (n = 11) vs. joint mobilization (JM) (n = 12). Subjects received maximum 12 treatments (3x a week for 4 weeks). Measurements taken pre- and post-intervention at each visit.	NDI score effect size was 1.47 for JM group and 0.80 for SM. VAS score effect size was 0.96 for JM and 0.73 for SM.	"There were several limitations to our study…A design flaw resulted in subjects completing the NDI and VAS immediately after their final treatment session…outcomes observed may be attributable to regression to the mean."	Pilot study- no specific statistical comparison measures on intervention are provided. Thus, no recommendation for argument is made from this report.
Irnich 2001 RCT No sponsorship. Funded by the German Ministry for Education and Research. No mention of COI.	6.5	N = 177 with chronic neck pain. Mean age for the Acupuncture Group was 52.3, for Massage Group 52.7 and Sham group was 52.2	Traditional Chinese acupuncture (n = 56) vs Massage (n = 60) vs Sham laser acupuncture (n = 61). Treated 5x over 3 weeks, duration 30 minutes. Acupuncture sites included SI3, UB10, UB60, Liv3, GB20, GB34, TE5 Massage techniques included effleurage, petrissage, friction, tapotement, and vibration. Sham laser performed with inactivated laser pen. Assessments taken	One week after treatment, improvement in VAS scores best for acupuncture, followed by sham acupuncture laser, then massage. Acupuncture not statistically superior to sham laser. Stratified results for those diagnosed with myofascial pain syndrome similar. Results among those with pain >5 years, showed mean improvements in VAS scores, thus tending to show better results for massage than in overall analyses. Pain related to	"Acupuncture is an effective short term treatment for patients with chronic neck pain, but there is only limited evidence for long term effects after five treatments."	No clear placebo arm control for acupuncture because sham was a placebo laser treatment. Only short-term results.

			immediately after treatment, 3 days and 1 week. Final follow-up at 3 months.	motion improved by more than 50% compared with baseline in 57% who received acupuncture, 32% who received sham laser, 25% who received massage.		
Nilsson 1997 RCT No mention of sponsorship or COI.	6.5	N = 53 with cervicogenic headache. Age range 20-65 years.	Spinal manipulation (high-velocity, low-amplitude, 2x a week for 3 weeks, (n = 28) vs. low-level laser, deep friction massage to trigger points (2x a week for 3 weeks) (n = 25). Follow-up at 5 weeks.	Headache hours decreased 69% in the manipulation vs. 37% in the controls. Use of analgesics decreased 36% in the manipulation group vs. no change in the control group.	"Spinal manipulation has a significant positive effect in cases of cervicogenic headache."	Continuation of 1995 study adding additional participants. Conducted protocol slightly differently in 15 additional patients. Data suggest manipulation may be helpful for treatment of cervicogenic headaches.
Sherman 2009 RCT No sponsorship. Funded by: Grant Number R21 AT 001584 from the National Center for Complementary and Alternative Medicine. No COI.	6.5	N = 64 chronic neck pain. Mean age 46.9 years.	Massage (10 treatments over 10 weeks, Swedish and clinical massage techniques) (n = 32) vs Self-care group sent book (information on potential causes of neck pain, neck-related headaches, whiplash, strengthening exercises, body mechanics and posture) (n = 32). 26 week follow-up. Outcomes assessed at 0, 4, 10, and 26 weeks.	13% of massage and 21% of self-care participants reported visiting other health care providers for neck pain (p = 0.49). Using Copenhagen Neck Functional Disability Scale, there was a small change in pain and only modest differences between study groups, 4 week: mean score difference -1.6 (95% CI -3.4, 0.24) (p = 0.089); 10 week: mean score difference -0.7 (95% CI -2.8, 0.15) (p = 0.55).	"[O]ur data suggest that therapeutic massage is helpful in relieving neck pain and dysfunction for a substantial fraction of individuals, at least in the short term."	Massage protocol individualized by each therapist. Several different therapists in different locations. Control group mailed a book on neck pain and no additional provider contact; massage group could have up to 10 visits, providing bias in favor of massage. Baseline NSAID use different between groups with controls using more NSAIDs than massage. At 26 weeks, slight improvement in massage group disappeared.
Skillgate 2007 RCT No sponsorship. Funded by the Swedish Research Council. No mention of COI.	6.5	N = 409 non-specific back or neck pain for at least 2 weeks. Mean age index group 46 years. Mean age in control group 48 years.	Naprapathy (maximum 6 visits over 6 weeks, spinal manipulation/ mobilization, massage and stretching) Index Group (N = 206) vs. support and advice with evidence-based care. Control Group (N = 203). HEP participation rates unclear. Outcomes assessed at 0, 3, 7, and 12 weeks.	Higher percentage in intervention group stated that they were very much improved compared to control at 12 weeks for mean pain change 2.9 vs 2.3 CI = 0.9-1.7, for mean CPQ Disability change 1.5 vs. 0.8 CI=0.2-1.2 and for mean change for WDQ disability 1.5 vs. 0.8 CI=0.3-1.0.	"[N]aprapathic manual therapy implied greater improvement in pain and disability and also a higher success rate of recovery."	Different number of visits between 2 groups may bias. Both groups improved. No mention of HEP participation.

Gam 1998 RCT No mention of sponsorship. No mention of COI.	6.0	N = 67 with, myofascial trigger points (MTrP) in neck and shoulder	Ultrasound plus exercise plus massage (N = 18) vs Sham ultrasound plus exercise plus massage (N = 22) vs Control group (N = 18). Ultrasound at frequency of 100 Hz, pulse = 2 :8, intensity was 3 W/cm^2; massage was transverse friction on MTrP followed by myofascial technique for 10 minutes; 6 exercise addressed strenthening. neck/shoulder region. Follow-up for 6 weeks.	Active treatment groups superior to no treatment group at 6 weeks and controls offered active treatment at that time. There was so significant difference between groups for VAS pain score or analgesic usage at all follow-up times, ($p > 0.05$). Exercise compliance 68% at 6 months.	"The over-all conclusion of the present study is that US give no pain reduction, but apparently massage and exercise reduces the number and intensity of MtrP, but this reduction had little impact on the patients neck and shoulder complains."	Control group's worse ratings week after randomization and treatment initiation, as well as higher medication tablets consumed, suggests wait-list control group bias. Considerable baseline differences and controls had substantially longer duration of symptoms (12 vs. 7.5 months for placebo ultrasound vs. 4 months active ultrasound), concerning for potential randomization failure. Utilization of massage in 1st 2 groups a co-intervention and limits conclusions regarding utility of ultrasound or massage.
Nilsson 1996 RCT No mention of sponsorship. No mention of COI.	6.0	N = 39 headache sufferers with decreased passive cervical ROM. Mean age 39 years.	High-velocity, low amplitude cervical manipulation 6 sessions over 3 weeks with an addition mean of 12 toggle recoil manipulation (n = 20) vs. Low-level-laser therapy plus deep friction massage (trigger-point treatment of posterior shoulder girdle muscles plus laser light treatment) (n = 20). Total 6 sessions over 3 weeks.	Passive ROM increased significantly from Week 1 to 5 in both groups. Total pROM $330^0 \pm 26^0$ for soft tissue group vs. $323^0 \pm 24^0$ ($p = 0.35$). Mean total pROM $313^0 \pm 28^0$ Week 1 for soft tissue group vs. $329^0 \pm 26^0$ Week 5 ($p = 0.001$). Mean total pROM $307^0 \pm 28^0$ Week 1 for manipulation group vs. $323^0 \pm 24^0$ Week 5, ($p = 0.02$).	"It seems that any changes in passive range of motion after spinal manipulation are of a temporary nature."	Passive cervical ROM main outcome measure in headache patients. Observer of ROM pre and post blinded to treatment allocation. No baseline characteristics included. Unclear duration of symptoms in participants.
Hakkinen 2007 Crossover trial No mention of sponsorship. Funded by a grant from Jyväskylä Central Hospital. No mention of COI	6.0	N = 125 females with chronic neck pain, mean 3 years duration. Age range 25-53 years.	Manual therapy (10-minutes high-velocity thrusts with low-amplitude, 15 minutes of traditional massage, 5 minutes of passive stretching) twice a week for 4 weeks (N = 62) vs Neck stretching exercises 5 times a week for 4 weeks (N = 63). Follow-up at 4 and 12 weeks.	Both groups had neck muscle strength improvement of 11-14% after 4 weeks, and no further improvement from weeks 4 to 12 for both groups. Pain decreased 64% in the manual therapy group and 53% in stretching group during first 4 weeks, ($p < 0.001$).	"Both manual therapy and stretching were effective short-term treatments for reducing both spontaneous and stain-evoked pain in patients with chronic neck pain. It is possible that the decrease in pain reduced inhibition of the motor system and in part improved neck function."	Did not clearly document what the intervention group did after 4 weeks of therapy (e.g., continued exercises), but did in stretching only group. No mention of washout period between interventions.

Cramer 2011 RCT Funded by Pneumed GmbH, Idar-Oberstein, Germany. No mention of COI.	6.0	N = 50 with chronic non-specific neck pain. Ages 46.17 +12.21 years.	Treatment Group (TG) received 5 pneumatic pulsation treatments over 2 weeks utilizing a mechanical device (n = 25) vs. Control Group (CG) Continued with self-directed standard medical care (n = 25). Patients assessed after each visit.	TG reported significant decrease in pain intensity (p = 0.001), pain at motion (p = 0.004), and pressure pain threshold (p = 0.002) compared to CG.	"Upon completion of the trial, patients in the TG, who had received 5 pneumatic pulsation tratments over a period of 2 weeks, reportd a significant decrease in the intensity of their neck pain at rest and at motion and significantly less functional disability than patients in the CG, who had received standard medical care alone."	No blinding. No control for cointerventions, no compliance data reported. Increased contact time likely in study group. Data suggest mechanical suction device may provide additional benefit to usual care (physiotherapy, exercise, NSAIDs). No long term follow-up.
Lin 2013 RCT No mention of sponsorship or COI.	6.0	N = 63 with chronic non-specific neck pain.	Long's Manipulation Group (LM) (N = 33) vs Traditional Chinese Massage (TCM) (N = 30). Both groups received treatment every 3 days, totaling eight 20min sessions of therapy.	At 3-month follow-up, LM achieved greater improvement in pain intensity (p<0.001), neck disability (p=0.049), and satisfaction (p<0.001) than TCM.	"The Long's manipulation was showed to produce greater effects than traditional chinese massage in relieving pain and improving disability in the management of paitents with chronic mechanical neck pain."	High dropout rate of massage group. Data suggest increased benefit as measured by VAS plus Northwick Park Neck Pain Questionnaire for Chinese manipulation over Chinese massage for chronic neck pain, although both groups had improvments. .
Nilsson 1995 RCT No sponsorship. Funded by a grant from the European Chiropractors Union. No mention of COI.	5.0	N = 39 with frequent headaches who fulfilled IHS criteria for cervicogenic headache (excluding radiological criteria) Age range 20-60 years.	Spinal manipulation (n = 20) vs. low-level laser in upper cervical region and deep friction massage in lower cervical/upper thoracic region (n = 19). Both groups received treatment twice a week for 3 weeks. Follow-up for 6 weeks.	There were no significant differences between groups for any measure (p > 0.05) although mean change of NSAID consumption was approaching significance in favor of manipulation group compared to soft tissue group, -0.8 vs. -0.4 (p = 0.14).	“Results suggest a possible effect of manipulation on cervicogenic headache, but because of methodological problems, such an effect could not be unequivocally demonstrated.”	No blinding of assessors. Each group had equal exposure to providers. Data suggest massage had no beneficial effect vs. manipulation.
Koes 1992 a,b 3 reports of 1 RCT No mention of sponsorship. No mention of COI.	5.0	N = 256 with chronic back and neck pain mean duration 1 year. Mean age 43.	Manual therapy (manipulation and mobilization of spine) (n = 65) vs Physiotherapy (exercises, massage and/or PT modalities such as heat, electrotherapy, ultrasound, shortwave diathermy) (n = 66) vs Placebo therapy (N = 64) vs. General Practitioner group	At 12 months, manipulative therapy marginally superior to physiotherapy in improvement of main complaint 4.5 vs 3.8 (no p value reported). It was slightly more improved for mean global perceived threat at 12 months 3.5 vs. 3.2 as well as improvement in physical functioning 4.2 vs. 3.7. Results are not shown to	“[M]anipulative therapy and physiotherapy are better than general practitioner and placebo treatment. Furthermore, manipulative therapy is slightly better than physiotherapy after 12 months.” In a second report, “a substantial part of the effect of manual therapy and physiotherapy appeared to be due to nonspecific (placebo) effects.” The	Value of this type of trial diminished today as therapies relied on have been subsequently shown ineffective. Lack of treatment visits in GP group both appear to have provided major bias against it and suggest GPs unfamiliar with spine pain management and may not have been standardized. Other interventions varied and not well defined. Placebo

			(GP) (n = 61). Number of treatments varied markedly from 1 for GP and placebo to 14.7 for physiotherapy. Placebo received treatment twice a week for 6 weeks; maximum 3 months. Follow-up at 3 and 6 weeks and 6 and 12 months.	be significantly different because there is no P-value reported.	third report concluded "the subgroup analysis suggests better results of manual therapy compared to physiotherapy in chronic patients (duration of present complaints of 1 year or longer) and in patients younger than 40 years old)."	unblinded for provider, potentially influencing advice on how to treat ongoing symptoms, thus influencing outcomes. Heterogeneous nature of these largely unstructured interventions prevents strong conclusions regarding efficacy. Among 64 patients with chronic neck problems, no differences in severity of neck pain 3 and 12 weeks. At 12 weeks, no differences in ITT between any groups.
Cen 2003 RCT No mention of sponsorship. No mention of COI.	4.5	N = 31 with neck pain. Group A average age was 47, Group B was 48, Group C was 51	Traditional Chinese therapeutic massage (TCTM) (n = 10) vs. A home based, self-administered exercise program (n = 10) vs. Control group without treatment, head tilt, trapezius stretch, neck flexion, shoulder rolls and neck rolls (N = 11). Follow up at 6 weeks with a questionnaire.	TCTM group had significant reduction in scoring of pain questionnaire ($p < 0.05$) and significant improvement in ROM ($p < 0.05$), after 6 week's treatment, and after 6 week's follow-up. The exercise plus TCTM appeared to be equally effective as TCTM alone.	"Using the special mechanical characteristics of one-finger meditation massage and rolling massage- high frequency rubbing with soft but strong and penetrating force, these techniques provide significant benefit to those suffering from neck pain."	Pain for >1 year. Exercise group included 10 minutes of moist heat and stretching exercises. Massage group had 3 30-minute sessions for 6 weeks of study. Exercise group contacted by phone once a week during study; no contact with control. By comparing to an exercise program that is not been shown effective, in essence there are 2 controls. Massage may be helpful as a component of therapy, but study does not support it over exercise.
Carlsson 1990 RCT No mention of sponsorship. No mention of COI.	4.5	N = 62 females with chronic tension headache. Age range 18-60 years.	Acupuncture (undefined) (n = 31) vs Physiotherapy (individualized 10-12 sessions, 30-45 minutes over 2-3 months) (n = 31). Assessments done after each visit.	Headache intensity had become significantly lower in physiotherapy group vs. acupuncture group ($p < 0.05$). Significant correlation found between intensity of headache and tenderness of temporal, masseter ($p <0.05$) and trapezius muscles ($p <0.01$). Physiotherapy group significantly better than acupuncture group after treatment with respect to tenderness of corrugator, orbicularis occuli and	"The headache was more improved in the physiotherapy group, and there was a marked reduction in the intake of analgesics. The tenderness was reduced in all muscles tested in the physiotherapy group but only in some of the muscles after acupuncture. The limitations of neck rotation was not influenced by either treatment."	Physiotherapy included a more intense interaction between participant and provider (potential contact bias) compared to acupuncture, biasing against acupuncture. Control group ill defined, uncertain if they had headaches to compare to interventional groups. Many different medications taken by participants; only ASA and acetaminophen recorded and analyzed. Baseline characteristics are unclear.

				masseter muscles, ($p < 0.005$).		
Dziedzic 2005 RCT No sponsorship. Funded by grants from The Arthritis Research Campaign and the West Midlands R & D NHS. No COI.	4.0	N = 350 primary care patients with non-specific neck disorders, 78% duration >3monthsexcluded WC and litigation. Average age for Advice and exercise was 50.5 years. For Manual therapy was 52.8 years and PSWD was 50.3 years.	Advice and exercise plus manual therapy (N = 114) vs. Advice and exercise plus pulsed shortwave (N = 121) vs. advice and exercise alone (N = 115). Maximum 8 therapy visits over 6 weeks. Assessments at 6 weeks and 6 months.	Mean Northwick Park SD reduction score 10.1 +/- 12.6 at 6 weeks for advice and exercise. Advice with manual therapy 8.7 +/- 12.1 and advice, exercise, and PSWD 7.7 /- 10.8. No significant difference between groups.	"[N]either manual therapy nor PSWD conferred any additional clinical benefit over a short course of active physical treatment incorporating an advice and exercise package delivered by experienced musculoskeletal physical therapists. Advice and exercise alone reduced subsequent primary care consultation, although patient satisfaction levels were lower than those recorded when manual therapy was added."	Advice and Exercise only group had significantly lower number of visits and duration of treatment, and also had less medication use and fewer doctor visits
Buttagat 2011 RCT No sponsorship. No mention of COI.	4.0	N = 20 with scapulocostal syndrome and scapular pain lasting at least 12 weeks. Mean age for the massage group was 25.0 and 24.7 for physical therapy group.	Traditional Thai Massage group (TTM): 9 30 minute sessions over a period of three weeks (n = 10) vs. Physical Therapy Group: 9 30-minute sessions of hot pack and ultrasound therapy for 3 weeks (n = 10). Patients assessed immediately before and after 1st treatment, 1 day after last treatment and 2 weeks after last treatment.	Both groups showed significant improvements in pain intensity immediately following treatment ($p < 0.05$). TTM group showed significant improvement in pain intensity (VAS) vs. physical therapy group immediately after treatment 2.2 vs. 3.7 ($p < 0.05$), 1 day after last treatment 0.5 vs. 3.0 ($p < 0.05$) and 2 weeks after last treatment 0.48 vs. 3.58 ($p < 0.05$). TTM also showed significant improvement in pressure pain threshold vs. PT immediately following treatment 2.8 vs. 2.2 ($p < 0.05$), 1 day after final treatment 3.7 vs. 2.4 ($p < 0.05$) and 2 weeks after final treatment 3.48 vs. 2.07 ($p < 0.05$).	"The results of the present study reveal that a 30-min session of TTM or PT for 9 sessions around the scapular region is effective in reducing pain, feeling of muscle tension and anxiety and increasing PPT in patients with SCS. This treatment method is a non-pharmacological management with no side effects. We suggest that TTM should be considered as one of the alternative treatments for SCS."	Small sample size (N=20). Intervention poorly described. Two weeks called "long-term" effects.
Non-specific Neck Pain						
Lauche 2013	8.5	N = 61 with non-specific neck pain	Cupping Massage (CM) group (n = 30)	Patients in the CM group were treated on average	"In conclusion, cupping massage is no more	Both groups improved at 12 weeks, but cupping massage

RCT No mention of sponsorships. No COI.		lasting for at least 3 months for a minimum of 5 days/week. Average age 54.1 years old.	Vs Progressive Muscle Relaxation (PMR) group (n = 31). Patients followed up each week for 12 weeks.	1.4 times per week. PMR used 1.5 times per week. No significant difference between groups at 12 weeks for VAS pain score (p = 0.98) and NDI disability score (p = 0.07), although NDI score trending towards significance in favor of CM group. Inner peace and Vitality (Psychological outcomes) both significant for CM group (11.7, 11.5) compared to PMR group (9.0, 8.5 respectively) (p = 0.049 and p = 0.02).	effective than progressive muscle in reducing chronic non-specific neck pain. Both therapies can be easily used at home and can reduce pain to a minimal clinically relevant extent."	group reported increased well being and pressure pain sensitivity compared with PMR.
Sherman 2014 RCT No sponsorship or COI.	6.0	N = 228 with non-specific neck pain lasting 3 months or longer. Average age 46.7.	Control Group (N = 37) vs. Group 1: 1 Massage x 60 minutes a week (N = 38) vs. Group 2 2 Massages x 30 minutes a week (N = 38) vs. Group 3 2 Massages x 60 minutes a week (N = 39) vs. Group 4 3 Massages x 60 minutes a week (N = 37) vs. Group 5 3 massages x 60 minutes a week (N = 39). Followed-up for 5 weeks.	At 5 week follow up Neck Disability Index (NDI) and neck pain intensity measured. For NDI improvement, control group had mean of 8.6% with improvement, Group 3 showed a significant difference with 31.6% showing improvement (p = 0.03). Group 5 also showed significant improvement vs. control (47.4% p = 0.003). For neck pain intensity improvement, 25.7% in control group showed improvement. Group 3 showed significant improvement of 63.2% (p = 0.004) as did Group 5 at 76.3% (p <0.001). Groups 2 and 4 trending towards significance with p values of 0.15 and 0.12.	"Our findings also suggest that future trials evaluating massage for chronic neck pain, which we think would be important, should include multiple 60-minute treatments each week for the first 4 weeks of treatment, self-care recommendations, and longer-term follow-up."	Intervention is poorly defined

MYOFASCIAL RELEASE

Myofascial release is a soft tissue treatment technique that is most commonly used in the periscapular area to treat non-specific muscle soreness.(1071)

Recommendation: Myofascial Release for Acute, Subacute, or Chronic Cervicothoracic Pain or Radicular Pain Syndromes or Other Back-related Conditions

There is no recommendation regarding myofascial release for the treatment of acute, subacute, or chronic cervicothoracic pain or radicular pain syndromes or other back-related conditions.

Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**

Rationale for Recommendation

While there are several RCTs, there are no sham or other quality trials on myofascial release in cervicothoracic pain to address its utility. Myofascial release is not invasive, has mild adverse effects, but is moderate to high cost depending on numbers of treatments. There is no recommendation for treatment of cervicothoracic pain or radicular pain syndromes.

Evidence for the Use of Myofascial Release.

There are 4 moderate-quality RCTs incorporated into this analysis.(917, 997, 1072, 1073) There are 2 low-quality RCT in Appendix 1.(1074, 1075)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: myofascial release, myofascial therapy, myofascial trigger point therapy, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 118 articles, and considered 5 for inclusion. In Scopus, we found and reviewed 34 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 2 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 3 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 5 articles considered for inclusion, 5 randomized trials and 0 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Schabrun 2012 Sponsored by a Clinical Research Fellowship from the National Health and Medical Research Council of Australia. Study received one free-of-cost INS device from the Neuro Resource Group, Inc. No COI.	6.0	N = 23 with pain of neck or shoulder for >2 weeks. Mean age: 23.15 (18-29) years.	Interactive Neurostimulation (INS) using InterX®5002 for 10 minutes (N = 12) vs Sham group received the same treatment protocol using the same device but without any power in the device (N = 11). Follow-up at 5 days.	Mean±SD VAS score immediately at post intervention and at 5-day follow up for INS group vs sham group: 2.6 ±2.0 and 1.5±1.6 (57%, respectively) vs 2.7 ± 1.7 and 1.3 ± 1.1 (48%, respectively). Effect of group (p = 0.9); group x time interaction, (p = 0.18). Mean±SD neck disability index score from pre-treatment to 5 day follow up for INS group vs sham group: 7.2 ±8.7 to 8.3 ±5 .0 (48%) vs 18.1 ±13.1 to 9.8 ±8.5 (54%). Effect of group p = 0.60; group x time interaction, (p = 0.37).	"INS is a new and emerging therapy that may be efficacious for managing musculoskeletal conditions such as myofascial pain syndrome. Although there was no significant change in pain levels or NDI scores, this trial demonstrates improvements in function in individuals with MTPs following INS therapy, which may be of clinical significance for certain patients with neck or shoulder pain."	Preliminary study with small sample size and sparse baseline data. INS group had improvements in function in patients with MTP's.
Oliveira-Campelo 2013 RCT No sponsorship or COI.	5.0	N = 164 with latent myofascial trigger points (MTrP) in upper trapezius muscle, and an average >2 hours/day computer work. Mean ages for WS, Pl, IC, PS, and MET groups: 20.44 + 2.08, 20.23 + 1.57, 20.08 + 1.21, 20.6 + 1.93, and 20.35 + 2.14 years.	WS group waited in the supine position for 30-secs (N = 25) vs Pl group received the same contact points as those described in the PS group, without execution of any movement, for 30-secs (N = 22) vs IC group received ischemic compression of upper trapezius muscle latent MTrP (N = 24) vs PS group received passive stretching of the upper trapezius (N = 23) vs MET group received muscle energy technique of the upper trapezius (N = 23). Assessments performed pre-intervention and 10mins, 24hrs, and 1wk post-intervention.	Contralateral flexion Pre and 10min post: MET – 39.8+4.6, 48.1+4.0 (p<0.01); PS – 37.6+5.1, 46.8+4.9 (p < 0.01); IC – 39.8+5.1, 46.0+5.8 (p < 0.01). Ipsilateral rotation Pre and 10min post: MET – 70.4+5.7, 74.3+5.4 (p<0.01); PS – 70.6+6.4, 75.0+5.5 (p < 0.01); IC – 71.2+5.7, 76.3+4.5 (p < 0.01). Ipsilateral rotation Pre and 10min post: Pressure pain threshold Pre and 10min post: MET – 1.8+0.4, 2.6+0.5 (p < 0.01); PS – 1.9+0.4, 2.5+0.4 (p < 0.01); IC – 1.7+0.3, 2.8+0.4 (p < 0.01).No between group significant differences for any assessments.	"Ischemic compression, passive stretching, and muscle energy techniques' single application on upper trapezius with latent MTrP leads to an increase on contralateral flexion and ipsilateral rotation range of motion as well as on the pain threshold immediately after session. All 3 techniques maintained improvements after 1 week; however, ischemic compression resulted in the most stable improvement."	5 arms to study. Follow up to 2010 pilot study. Latent trigger point of upper trapezius decreased pressure pain sensitivity and cervical range of motion to one week post manipulation.
Gemmell 2008 RCT Single-blind	4.5	N = 45 with mechanical or non-specific neck pain for <3	Ischemic compression deep pressure with the thumb to the upper trapezius or TrP for 30 s - 1 min until TrP was no longer tender	VAS means (post-treatment), pressure pain threshold, cervical lateral flexion show no significant difference between groups or (p =	"Ischaemic compression is superior to sham ultrasound in	"Lack of details for compliance loss to follow-up. Study measured effect immediately post treatment

No mention of sponsorship. No COI.		months, pain at least 30mm on VAS, decreased cervical lateral flexion to opposite side, mean age (SD) 24 (3.3) for IC group, 24 (4.6) for TrPPR group, and 23 (1.5) for sham group.	or one minute had passed or IC group (N = 15) vs Trigger point pressure release of pressure (from TrP) when tissue resistance was felt or TrPPR group (N = 15) vs Sham ultrasound lotion was applied over TrP and ultrasound head moved slowly over the upper trapeziums muscle for 2 min or SUS group (N = 15). Assessment within 5 minutes of treatment.	0.5721), (p = 0.2171), and (p = 0.8805) for outcome of cervical flexion.	immediately reducing pain in patients with non-specific neck pain and upper trapezius trigger points. Further research is needed to determine if there is a difference between ischaemic compression and trigger point pressure release."	(single treatment). Data suggest trigger point ischemic compression provides greater immediate relief than sham ultrasound. No data on how long effects lasted. Subjects had mild pain to begin with (VAS ~ 4 of 10).
Blikstad 2008 RCT No mention of sponsorship. No COI.	4.0	N = 45 with non-specific cervical pain lasting longer than 4 weeks, but no longer than 12 weeks, rating at least a 4 on the NRS, ages 18-55.	Myofascial band therapy or MBT firm thumb pressure in slow stroking motion along upper trapezius muscle and active TrP for 1 minute (N = 15) vs Activator trigger point therapy placing the Activator IV perpendicular over the trigger point (N = 15) vs Sham - control using ultrasound lotion was applied over TrP and ultrasound head moved slowly over the upper trapeziums muscle for 2 minutes (N = 15). Assessment 5 minutes after treatment.	Primary outcome of pain reduction by 53.3% Activator Group vs 13.3% Myofascial band Group vs 13.3% Sham group Secondary outcome: left and right lateral cervical flexion / increased pain pressure threshold; (40% Activator vs 33.3% Myofascial band vs 40% Sham and 66.7% Activator vs 40% Myofascial Band vs 33.3% Sham) / 46.7% Activator vs 33.3% Myofascial band vs 20% Sham.	"The results suggest that activator TrPT to an upper trapezius TrP has an immediate effect in reducing pain in patients with sub-acute non-specific neck pain."	Short follow up (5 min). Details sparse. Small number of subjects in each treatment arm.

NEUROREFLEXOTHERAPY

Neuroreflexotherapy is an alternative treatment that was developed in Spain and involves implantation of numerous epidermal staples in trigger points in the back (or neck) as well as burins (small metallic punches) in "referred tender points in the ear" (1076) at depths up to 2mm.(1077) In contrast with acupuncture, the sites are chosen by dermatomal innervation. Implantation does not require anesthesia and staples remain in place for up to 90 days. Significant reductions in LBP have been reported at 1 year in uncontrolled studies.(1078)

Recommendation: Neuroreflexotherapy for Acute, Subacute, or Chronic Cervicothoracic Pain with or without Radiculopathy

Neuroreflexotherapy is not recommended for acute, subacute, or chronic cervicothoracic pain with or without radiculopathy.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

There are no sham controlled or quality trials evaluating neuroreflexotherapy in cervicothoracic pain patients. There are observational studies that reported improvement in both cervical and thoracic pain patients with neuroreflexotherapy.(1078, 1079) Skin scarring on "exposed skin" results from this treatment, and without quality studies proving efficacy, this should be carefully considered.

Evidence for the Use of Neuroreflexotherapy

There are no quality studies incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Neck pain, cervicalgia, cervical pain, cervical radiculopathy, radicular Pain, postoperative neck pain postoperative cervical pain, herniated disk, neck pain, cervicalgia, cervical pain, cervical radiculopathy, radicular pain, postoperative neck pain, postoperative cervical pain, herniated disk, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 680 articles, and considered 2 for inclusion. In Scopus, we found and reviewed 6 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 1 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 0 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 2 articles considered for inclusion, 0 randomized trials and 0 systematic studies met the inclusion criteria.*

SUBCUTANEOUS CARBON-DIOXIDE INSUFFLATIONS

Subcutaneous carbon-dioxide insufflations were used as a modality in naturopathy. Sources were often medical carbon-dioxide or gas from natural springs. The gas from natural springs contained more than just carbon-dioxide like nitrogen, argon, helium, and methane.(1080)

Recommendation: Subcutaneous Carbon-dioxide Insufflation for Acute, Subacute, or Chronic Cervicothoracic Pain with or without Radiculopathy

Subcutaneous carbon-dioxide insufflation is moderately not recommended for treatment of acute, subacute, or chronic cervicothoracic pain with or without radiculopathy.

Strength of Evidence **– Moderately Not Recommended, Evidence (B)**
Level of Confidence – Moderate

Rationale for Recommendation

There are alternative sham controlled trials of subcutaneous carbon-dioxide insufflations for cervicothoracic pain. One moderate-quality study evaluated subcutaneous carbon-dioxide insufflation vs sham ultrasound in acute cervicothoracic pain. They reported no difference in time to pain resolution between the groups.(1081) One moderate-quality trial evaluated subcutaneous carbon-dioxide insufflation with physical therapy vs physical therapy alone in subacute/chronic cervicothoracic pain patients. They reported no significant findings between the groups

when comparing pain perception or pain intensity.(1080) These treatments are invasive, have adverse effects, are moderately costly to high cost depending on numbers of treatments, and are ineffective. Thus, they are not recommended.

Evidence for the Use of Subcutaneous Carbon-dioxide Insufflation
There is 1 high-(1081) and 1 moderate-quality RCT incorporated into this analysis.(1080) There is 1 low-quality RCT in Appendix 1.(1082)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: subcutaneous carbon-dioxide insufflation, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed, we found and reviewed 2 articles, and considered both for inclusion. In Scopus, we found and reviewed 8 articles, and considered zero for inclusion. In CINAHL, we found and reviewed zero articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed zero articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 23 articles considered for inclusion, 3 randomized trials and 0 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Brockow 2008 RCT No mention of sponsorship or COI.	8.0	N = 126 acute non-specific neck pain; mean age 45±12.9 for SCI, and 45±14.0 for sham ultrasound.	Subcutaneous carbon-dioxide insufflation, 3 times a week, MedServ, 100ml (N = 63) vs Sham ultrasound plus infrared light, in acute cervico-thoracic pain, 9 interventions, three times a week, Sonostim, 1 intervention lasted 5 minutes (N = 63). Patients in both groups were given local infrared light (1 session = 10 minutes) and were instructed to not take more than one diclofenac sustained-released 75mg tablet each morning. Follow up at baseline and 28 days.	SCI group - 43% neck pain free. Sham ultrasound group - 46% neck pain free. No difference between groups in any outcome variable.	"The study indicates that subcutaneous carbon dioxide insufflations are not superior to sham ultrasound for treating patients with acute non specific neck pain. Because course of pain did not differ from the one expected from self limitation..."	Unable to blind due to different interventions. Subcutaneous carbon-dioxide insufflation not likely an effective treatment for acute cervicothoracic pain.
Brockow 2001 RCT No mention of sponsorship or COI.	6.5	N = 140 with non-specific neck or low back pain; mean age 65.5±5.5 for index group, and 64.2±8.7 for control group.	Standard physical treatment, combination of physical interventions (4 X exercise therapy, 30 min per session, 4 hot packs, 15 min per session; 4 X therapeutic continuous ultrasound, 10 min per session; 4 X TENS, 15 min per session; and 2 X health education on pain control, 60 min per session) (N = 64) vs Subcutaneous carbon-dioxide insufflations, 10 injections intravenously once a day, except for Saturday and Sunday, MedServ, 25 ml per injection (N = 69). Follow up at baseline and after 5 and 10 injections.	Injections 5 days a week. Pain ratings trended towards improvements more in intervention than control group, but both groups improved.	"[S]ubcutaneous carbon-dioxide insufflations do not seem to be a worthwhile adjunct in the given setting of inpatient rehabilitation. Trials in a monotherapeutic setting, which aim more at the efficacy of subcutaneous carbon-dioxide insufflations, might help to solve this issue."	No control group. No specific diagnoses given for pain.

TRACTION

Traction purportedly relieves "muscle spasm," stretches muscles, reduces intradiscal pressure, and thus has been theorized to reduce disc herniation, and enlarge the intervertebral foramen removing pressure on the nerve root. (15, 562, 1083) However, traction has not been reported as successful in several trials.(15, 562, 1083, 1084) Duration and magnitude of force is adjustable and sometimes varied. Types of traction include motorized, manual, bed rest, pulley-weight, gravitational, suspension, and gravity inversion, (540, 562, 1083, 1085, 1086) with manual and motorized being most commonly used. When traction is used in combination with other treatment modalities, it is often difficult if not impossible to determine the benefit of traction alone as compared to the entire rehabilitation program.(974, 1087, 1088) A review by Graham et al. noted that there was no evidence supporting continuous traction, and inconclusive evidence for intermittent traction.(1087)

Recommendation: Traction for Acute, Subacute, or Chronic Cervicothoracic Pain or Radicular Pain Syndromes
Traction is not recommended for treatment of acute, subacute, or chronic cervicothoracic pain or radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation

There are sham trials evaluating traction in cervicothoracic pain. A high-quality study evaluated cervical traction in patients receiving a multimodal approach consisting of manual therapy and exercise. They reported no significant difference between the active and sham groups after 4 weeks of treatment.(562) A moderate-quality trial evaluated chronic cervicothoracic pain with radiculopathy, and compared 6 to 15 pounds of mechanical traction based on the patient's weight to a sham 2 pounds of traction. They did not find any difference in outcomes at 3 months follow-up.(1083) Yet, a moderate quality trial found traction of additive benefit for radiculopathy.(564) A moderate-quality trial evaluated traction versus positioning versus collar versus two different types of placebo (heat and tablets) in chronic cervicothoracic pain with radiculopathy. The authors reported no significant difference in pain, ability to work, sleep, or range of motion.(15) A moderate-quality trial in patients with cervicothoracic pain with radiculopathy compared cervical traction, isometric exercises, postural advice and thiamin, to sham cervical traction (no weight added), NSAIDs, thiamine and advice. The authors reported a significant improvement in the cervical traction plus exercise group in pain score, tenderness index, pain frequency score, and VAS. However, it is difficult to assess if the improvement was a result of the traction or exercise.(540) A moderate-quality trial compared static cervical traction, intermittent cervical traction, manual traction and instruction for 6 weeks. They reported one statistically significant finding when comparing intermittent traction to instruction, increased right-sided cervical rotation. No other significant differences were reported.(1086) A moderate-quality study evaluated 6 to 12 pounds of cervical traction to sham traction and reported no significant difference in EMG activity after traction, pain, sleep or range of motion.(1084) In sum, there is no quality evidence that traction is efficacious. There are studies of mixed interventions (traction combined with manual therapy and exercises) that suggest efficacy of a combined approach; however, as there is quality evidence that exercise is effective, this suggests the other treatments and not traction may be responsible for providing the efficacy. Unfortunately, clinical trials have often not established that adequate application of weight/traction force was applied. Thus, traction is not recommended.

Home traction units may be self-administered and thus not high cost. Some may consider attempting using these devices to treat select patients, particularly if manual distraction or traction testing of the cervical spine during examination obliterates or markedly centralizes neck and upper extremity symptoms, and is used in combinations with other treatments such as exercise. However, efficacy is not demonstrated and other treatments with evidence of efficacy are recommended to be utilized first.

Evidence for the Use of Traction

There is 1 high- (562) and 12 moderate-quality (15, 540, 564, 571, 572, 900, 1083, 1084, 1086, 1089-1091) RCTs incorporated into this analysis. There are 5 low-quality RCTs in Appendix 1.(593, 1092-1095)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: traction, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled*

clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 100 articles, and considered 10 for inclusion. In Scopus, we found and reviewed 585 articles, and considered 2 for inclusion. In CINAHL, we found and reviewed 21 articles, and considered 1 for inclusion. In Cochrane Library, we found and reviewed 8 articles, and considered zero for inclusion. We also considered for inclusion 1 article from other sources. Of the 17 articles considered for inclusion, 16 randomized trials and 1 systematic studies met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Young 2009 Phys Ther RCT Sponsored by Saunders Group. No mention of COI.	8.5	N = 81 with cervical radiculopathy; mean age 47.8 (9.9) for MTEXtraction group, and mean age 46.2 (9.4) for MTEX group.	Manual therapy, exercise, intermittent cervical traction (N = 45) vs Manual therapy, exercise, and sham traction (N = 36). All received HEP and posture education. All groups had 2 visits a week for 4 weeks. Manual therapy was HVLA both cervical and thoracic. Follow up at baseline and weeks 2 and 4.	Improvements seen in both groups in pain and neck disability index. No significant difference between groups	"The results suggest that the addition of mechanical cervical traction to a multimodal treatment program of manual therapy and exercise yields no significant additional benefit to pain, function, or disability with cervical radiculopathy."	Data suggest cervical traction does not change outcomes in patients with cervical radiculopathy undergoing a multimodal program.
Klaber-Moffett Clin Rehabil 1990;4:205-11 RCT No mention of sponsorship COI.	7.0	N = 94 with neck and arm pain; mean age 49.32 (10.23) for weighted traction, and mean age 49.50 for (9.56) for placebo traction.	Weighted traction EMG recordings over the upper trapezius muscle (N = 44) vs placebo traction, not well described (N = 50). Follow up at baseline, after, and before treatment, follow-up generally, not well described.	According to independent t-tests no significant differences between 2 groups, except chronicity. For group effect results not significant (f = 0.23; df = 4, 70; NS).	"An association between lower levels of anxiety and a better chance of pain reduction were found in this study."	Randomization, allocation unclear. Some baseline difference in chronicity (5.7 years vs 2.9 years) that presumably favor placebo. Study showed trend, but no statistical differences in clinical outcomes for traction over sham traction. Both groups had a single session of neck education for 1 hour.
Klaber-Moffett Clin Rehabil 1990;4:287 RCT No mention of sponsorship or COI.	7.0	N = 52 with chronic neck pain with arm pain	Weighted traction, EMG recordings over the upper trapezius muscle (N = 43) vs placebo traction and EMG readings of trapezius muscle (N = 44), Follow-up for 2-3 days, approximated, not well described.	EMG readings showed a significant effect on time with patient supine (f = 5.81, df = 1, 42, p < 0.02) and in upright position (f = 2.89, df = 1, 42, NS).	"There was no significant correlation between EMG readings and pain reports...The results of this study do not support the hypothesis that tension in the neck musculature is reduced by cervical traction."	Sub-study of Moffett 1990. No difference in EMG activity between groups, no lasting differences. Unsure if reduction in EMG due to traction or recumbent position. Traction does not appear to reduce muscular tension after treatment completed.
Chiu 2011 RCT No mention of sponsorship or COI.	6.0	N = 95 with history of neck pain for > three months, mean 46.8 (10.4) for control group, and mean 50.9 (10.5) for traction group.	Traction group received intermittent cervical traction 20 minutes 2x a week for 6 weeks, traction poundage ranging from 10% to 20% of the patient's body weight + 20-40% of holding + 20-40% resting traction poundage (N = 40) vs Control group received only infrared irradiation as a placebo heat treatment for 20 minute, 2x a week for 6 weeks (N = 39).	No statistical difference between the groups in the Neck Pain Questionnaire / Verbal Numeric Pain Scale / cervical range of motion; (p > 0.05).	"[After] six weeks of intermittent neck traction, there were no statistically significant difference in neck pain, range of emotion and disability scores between the traction group and the control group."	No data on compliance, high drop-out rate (50%). Data suggest no difference in outcomes of traction and infrared heat (placebo heat treatment), but conclusions limited. High drop out in traction group suggest inefficacy.

			Follow-up at baseline, 6 and 12 weeks.			
Fritz 2014 RCT Sponsored by Intermountain Healthcare, the University of Utah, and Wilford Hall Medical Center. No mention of COI.	5.5	N = 86 with neck pain; mean age 46.9 (10.7)	Exercise Group, active exercise program (scapula, 3 sets of 10 reps, and cervical strengthening, 30 reps for 10 seconds), supine cervical flexion, 3 sets of 15 reps (N = 27) vs exercise and mechanical traction, same interventions as the exercise group, mechanical cervical traction added, Saunders 3D ActiveTrac or Chattanooga Triton table, intermittent traction with 60 seconds of pull force, 20 seconds of relaxation; 15 minutes per traction treatment, remained supine for 2 minutes before standing up (N = 31) vs. Exercise and over-door traction, same exercise interventions and using a Chattanooga Overdoor traction Device, traction treatment for 15 minutes, then remained sitting for two minutes (N = 27). Follow-up 4 weeks, 6 and 12 months.	Mean (95% CI) for Neck Disability index (NDI): exercise vs mechanical traction: 6 months: 13.3 (5.5, 21.2), p = 0.001; Mean (95% CI) for Neck Pain Intensity: exercise vs mechanical traction: 4 weeks: 1.6 (0.7, 2.6), p = 0.020; 6 months: 1.9 (0.7, 3.2), p = 0.004	"We found that adding mechanical traction to a standard exercise program, particularly with an in-clinic, motorized device, for patients with cervical radiculopathy led to greater improvements in disability and neck and arm pain. These improvements were particularly notable at the longer-term follow-ups."	Reasonably well defined exercise intervention. Data suggest traction of additive benefit.
Loy 1983 RCT No mention of sponsorship or COI	5.0	N = 60 with cervical spondylosis; mean age 53 for PT group, and 53.5 for the EAP group.	Physiotherapy, for 20 minutes, 3 times a week(N = 30) vs. Electroacupuncture, 2 to 6 hours, acupuncture points in each session, lasting from 40 to 40 minutes, three sessions a week (N = 30). Follow up at 3 and 6 weeks.	At end of first 3 weeks treatment: PT group had 31.3% relief of symptoms, EAP group had 67.4% relief.	"[W]hile both methods were effective, electro-acupuncture produced an earlier symptomatic improvement with increased neck movement, especially in patients with mild degenerative changes of the cervical spine."	Study not solely of traction. Acupuncture group appeared to have more contact with physician. Radiological classification done before treatment. Majority had "grade 2" degeneration at C5-6, C6-7.
Korthals-de Bos 2003 RCT	5.0	N = 183 with non-specific neck pain >2 weeks duration, mean age 44.6±12.4 for manual therapy, 45.9±11.9 for physiotherapy, and 45.9±10.5 for general practitioner care.	Manual therapy (6 weekly sessions, low velocity mobilization, exercises) (N = 60) vs PT (12 sessions over 2 weeks of exercises, traction, stretching, massage) (N= 59) vs General practice (education of favorable prognosis, ergonomics, analgesics) (N = 64). Follow ups at baseline, 3, 7, 13, and	Total costs (Direct Healthcare, Direct Non-healthcare, Indirect Costs): MT €403 vs PT €1297 vs GP €1379. (p = 0.05) for MT vs PT or GP. No differences between GP and PT.	"Our economic evaluation alongside a pragmatic randomised controlled trial showed manual therapy to be more cost effective than physiotherapy and continued care provided by a general practitioner in the treatment of non-specific neck pain."	Follow-up report of Hoving 2002 focused on economic analysis. Study suggests manual therapy of low velocity manipulation more cost effective than physiotherapy or general care without physical methods. Applicability of results outside Netherlands unclear.

Study sponsored by Netherlands Organization for Scientific Research. No COI.			52 weeks after randomization.			
Nordemar 1981 RCT No mention of sponsorship or COI.	5.0	N = 30 with acute cervical pain, mean age 43±16 for neck collar, 34±9 for TNS, and 42±17 for manual therapy.	Neck collar of semi-soft material vs neck collar plus transcutaneous nerve stimulation (15 minute treatments) (N = NA) vs. Neck collar plus analgesics plus manual therapy (soft tissue treatment, gentle traction and mobilization for 30 minutes 3x a week). (N = NA) vs. Neck collar plus analgesics and were told to rest, manual treatment by a physiotherapist, 30 min, 3x a week (N = NA). Follow up: neck collar group seen at 1, 2, 6, 12 week. TNS and mobilization seen at 2 weeks.	Age: NC 43+/-16, TNS 34+/-9, MT 42+/-17. Total mobility range after 1 week: NC 243+/-115, TNS 323+/-47, MT 316+/-84. Pain index after 1 week: NC 35+/-45, TNS 17+/-19, MT 18+/-25. Differences in mobility and pain after 1 week showed no significant changes between groups. At 6 weeks, 3 months all pain free. Pain <3 days.	"[T]ranscutaneous nerve stimulation is a valuable pain reducer and gives a more rapid restoration of cervical mobility in acute cervical pain."	Variable follow-up duration. Used cervical mobility as measurement for improvement. Only used data from 1 week of treatment because of rapid improvement seen in all groups. At one week saw increase in mobility in TENS group, but no difference in pain. Only 10 participants in each group.
Borman 2008 RCT No mention of sponsorship. No COI.	4.5	N = 42 with chronic cervical pain, neck pain (for > 6 months) with out radiation to arm for > 6 weeks, whiplash traumatic injuries, serious somatic diseases, manipulative or physiotherapeutic treatment in the past 3 months, evidence of affected nerve root,; mean age 50.4 (9.4) for Group I, and 48.2 (11.5) for Group II.	Group I, intermittent cervical traction therapy + traditional physical therapy modalities (N = 21) vs. Group II, traditional physical therapy including hot pack + ultrasound + exercise program (N = 21). All patients had received ergonomic principles in activities in daily living + description of recommended therapeutic exercises. Follow-up times before and after.	VAS pain / Nottingham Health Profile (NHP) pain & physical activity & sleep & emotional reaction; (6.05 ± 1.8 vs 4.81 ± 0.69) / (58.9 ± 28.3 vs 55.6 ± 27.9, & 32 ± 19.5 vs 35.7 ± 22.4, & 67.3 ± 35.7 vs 64 ± 45.9, & 45.6 ± 35.8 vs 48.6 ± 41.2), (p > 0.05). No statistically significant difference between the groups.	"In conclusion, no specific effect of traction over standard physical therapy was observed in our study group."	Onset of pain > 6 weeks (subacute and chronic). Lack of study details for randomization, allocation, compliance, and dropouts. Data suggest no significant differences between the groups. Lack of control group limits conclusions of efficacy of either treatment versus natural history.
Shakoor 2002 RCT	4.5	N = 199 with chronic cervical spondylosis, over 30 years old with chronic neck pain	Group A: CT, exercises, postural advice and thiamin (N = 100) vs Group B: NSAID plus ranitidine coverage, placebo CT,	In treatment group, flexion, extension, lateral bending significantly improved in ROM of cervical spine. Cervical traction effective in	"[A] significant improvement was observed in response to CT and exercise... We compared between CT and non-steroidal anti-	Many details sparse. Intervention included both cervical traction and isometric exercises. Placebo traction group had NSAIDs

Sponsored by Bangladesh Medical Research Council. No mention of COI.		and radicular symptoms; mean age 46.66 (12.08) for Group A, and 47.66 (10.99 for Group B.	instruction in posture and thiamin (N = 99). Follow up at pre and post treatment.	reducing symptoms. In placebo, improvement in flexion, extension, and lateral bending. NSAID effective in improving symptoms in placebo.	inflammatory drugs and found nearly significant improvement in CT plus exercise group than NSAID group (p=0.06)."	while traction group did not. Differences did not reach statistical significance.
Joghataei 2004 RCT Sponsored by University of Social Welfare and Rehabilitation Sciences. No mention of COI.	4.5	N = 30 with MRI confirmed unilateral C7 radiculopathy; mean age 46.93 (5.32) for control group, and 47.53 (5.6) for the experimental group.	Cervical traction, electrotherapy and exercise, 10 physical therapy sessions (N = 15) vs Electrotherapy and exercise only (N = 15). Follow up at baseline, and after 5 and 10 sessions.	No differences in grip strength after 10 sessions, (p = 0.65)	"The application of cervical traction combined with electrotherapy and exercise produced an immediate improvement in hand grip function in patients with cervical radiculopathy."	Claims double blind, but manipulation group could not be. Follow-up timing unclear as timed with treatments not time. Baseline differences in strength make primary outcome not interpretable.
Brewerton 1966 RCT Sponsored by National Fund for Research into Poliomyelitis and other Crippling Diseases. No mention of COI.	4.0	N = 493 with neck and arm pain, with radiculopathy, age range 40-60 years.	Traction; gentle active movements, 20 minutes, supine position and aspirin as needed (N = 114) vs. Positioning; participants treated as if they were having traction , but no traction was applied and aspirin as needed (N = 114) vs Collar only; wear collar throughout the day and night and aspirin as needed (N = 120) vs Placebo tablets; phenylbutazone, 3 times a day and aspirin as needed (N = 52) vs Placebo, untuned short-wave diathermy and aspirin as needed comparable positioning with no traction (N = 66). Interventions 3 times a week for 4 weeks.	No significant improvement between treatment groups, p statistics not provided. Pain at 4 weeks, reported to be getting worse; traction / positioning / collar / placebo (heat) / placebo (tablets); 10% / 5% / 7% / 9% / 6%, respectively.	"The rate of improvement was approximately the same in the five treatment groups, as judged by clinical assessment two weeks and four weeks after the beginning of treatment and by follow-up questionnaire at six weeks and six months."	Many details sparse. Accounted for number and duration of previous episodes. No information on duration of current pain. No specific diagnoses given. No mention of compliance.
Zylbergold 1985 RCT No mention of sponsorship or COI.	4.0	N = 100 with cervical spine disorders; mean 55.88 (10.92) for Static traction, 52.84 (11.91 for intermittent traction, 51.24 (14.62 for manual traction, and 52.32 (12.79) for neck care instruction.	Static Traction (25 lb, 15 min, 25° flexion), instruction in neck care, heat for 15 minutes, exercise program for range of motion and isometric exercises (N = 25) vs Intermittent traction (25 lb, 15 min, 10 sec on, 10 sec off), same care as above (N = 25) vs Manual Traction (25° flexion, 20 pulls), therapist guided, same care as above	For pain (p +0.03), forward flexion (p = 0.01), right rotation (p = 0.004), left rotation (p = 0.05) intermittent group did significantly better than no traction. No traction subjects more likely to need more treatment, medication after 6 week trial.	"[T]raction should be considered as an efficacious component in the treatment of cervical disorders. And when traction is indicated, intermittent traction deserves serious consideration."	All patients improved significantly over the 6 week period.

			(N = 25) vs. Neck Care instruction, same care as the first group, however, no traction (N = 25). Six week intervention with follow ups at the time of discharge from treatment or at the end of a 6-week period of treatment.			

DECOMPRESSIVE DEVICES
See Low Back Disorders Guideline.

ELECTRICAL THERAPIES

INTERFERENTIAL THERAPY

Interferential therapy is a form of electrical stimulation using amplitude modification of two out-of-phase medium-frequency currents to produce a low-frequency current.(1096, 1097) This procedure is similar to TENS and differs by having less impedance in the tissues and is reportedly more comfortable than traditional TENS treatment.

1. *Recommendation: Interferential Therapy for Subacute or Chronic Cervicothoracic Pain with or without Radicular Pain*
   Interferential therapy is not recommended for treatment of subacute or chronic cervicothoracic pain with or without radicular pain.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

2. *Recommendation: Interferential Therapy for Acute Cervicothoracic Pain with or without Radiculopathy*
   Interferential therapy is not recommended for treatment of acute cervicothoracic pain with or without radiculopathy.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendations
There are no sham controlled or quality trials in cervicothoracic pain patients. In low back pain, there are two RCTs that included interferential therapy. They did not report any difference with outcome measures when compared to manipulation in acute LBP (1097) or traction and massage in chronic low back pain (1096) (see Low Back Disorders guideline).

Evidence for the Use of Interferential Therapy
There are no quality studies incorporated into this analysis.

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: interferential therapy, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 753 articles, and considered 0 for inclusion. In Scopus, we found and reviewed 28 articles, and considered 6 for inclusion. In CINAHL, we found and reviewed 0 article, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 1 article, and considered 1 for inclusion. We also considered for inclusion 15 articles from other sources. Of the 0 articles considered for inclusion, 0 randomized trials and 0 systematic studies met the inclusion criteria.*

MICROCURRENT ELECTRICAL STIMULATION

Microcurrent electrical stimulation is a type of electrotherapy. Proponents believe that it will relieve pain and contribute to healing while using lower currents than are used in TENS or interferential and galvanic stimulation.

Recommendation: Microcurrent Electrical Stimulation for Acute, Subacute, or Chronic Cervicothoracic Pain with or without Radiculopathy
Microcurrent electrical stimulation is not recommended for acute, subacute, or chronic cervicothoracic pain with or without radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation

There are no sham controlled or quality trials of microcurrent electrical stimulation in cervicothoracic pain. There are no quality trials in other spinal conditions either (see Low Back Disorders guideline).

Evidence for the Use of Microcurrent Electrical Stimulation
There are no quality studies incorporated into this analysis.

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Microcurrent Stimulation, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies. In PubMed we found and reviewed 740 articles, and considered 0 for inclusion. In Scopus, we found and reviewed 4 articles, and considered 0 for inclusion. In CINAHL, we found and reviewed 0 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 0 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 0 articles considered for inclusion, 0 randomized trials and 0 systematic studies met the inclusion criteria.*

TRANSCUTANEOUS ELECTRICAL NEUROSTIMULATION (TENS) AND NEUROMUSCULAR ELECTRICAL STIMULATION (NMES)
Transcutaneous electrical nerve stimulation (TENS) is a modality to control pain through electrical stimulation delivered by pads placed on the surface of the skin thought to relieve pain of both non-inflammatory and inflammatory disorders through distraction or alternate nerve pathway conduction (gate theory).(1098, 1099) Two of the more commonly utilized protocols are either a low-intensity prolonged (30 plus minutes) stimulation through an active electrode over the painful area or a higher intensity over the painful area for 15 to 30 minutes (commonly referred to as hyperstimulation analgesia).(1100) High-frequency stimulation is generally 80 to 200 Hz, whereas low frequency is generally 4 to 8 Hz. Some studies do not report the frequency of the stimulation.(1101)

1. *Recommendation: TENS for Acute or Subacute Cervicothoracic Pain or Acute Radicular Pain Syndromes*
   TENS is not recommended for acute or subacute cervicothoracic pain or acute radicular pain syndromes.

   Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendation
There are no sham controlled trials in acute or subacute cervicothoracic pain patients with or without radicular pain. There is one moderate-quality trial comparing TENS (15 to 30 minutes, 3 times a week for 4 weeks) versus manual therapy vs cervical collar for treatment of acute cervicothoracic pain. It suggested a minimal statistical improvement in range of motion. However, there was no significant difference in pain with TENS therapy at one week compared to manual therapy and neck collar use alone and all patients in the trial were recovered by 6 weeks.(1089) TENS is not invasive, has low adverse effects and is moderate to high cost depending on numbers of treatments. There are other interventions with documented efficacy for treatment of acute and subacute cervicothoracic and radicular pain syndromes.

2. *Recommendation: TENS for Chronic Cervicothoracic Pain*
   TENS is recommended for select use in patients with chronic cervicothoracic pain as an adjunct for more efficacious, active treatments.

   Indications – TENS (single or dual channel) is recommended as a treatment choice for chronic cervicothoracic pain when clear objective and functional goals are being achieved that include increased physical activity and/or reductions in medication use. TENS is recommended to be utilized as adjunctive treatment in chronic cervicothoracic pain to support graded strengthening and aerobic exercises.(9, 894) For patients who are not involved in a conditioning program or who are non-compliant with graded increases in activity levels, this intervention is not recommended. It is recommended TENS units be trialed (rented) prior to purchase to demonstrate efficacy and increase function.

Frequency/Duration – One or 2 sessions to instruct patient in use of TENS. Subsequent use is self-applications.

Indications for Discontinuation – Resolution, intolerance, or non-compliance including non-compliance with progressive strengthening and aerobic exercises.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
There is one sham-controlled RCT evaluating efficacy of TENS in chronic cervicothoracic pain and suggested improvement in trigger point tenderness with microcurrent when compared to sham treatment after 6 treatments over 2 weeks.(1102) Since trigger points are only palpated during physical exam, this is not a useful measure of functional outcome. A moderate-quality trial compared TENS plus infrared therapy, exercise plus infrared therapy, and infrared irradiation in patients with >3 months of intermittent cervicothoracic pain. They reported decreased pain scores, increased isometric strength, decreased analgesic use, less sick days for neck pain, and reduction in Northwick Park Cervicothoracic Pain Questionnaire in the TENS and exercise group up to 6 months after therapy.(575) Thus it is not clear whether the benefit is due entirely to exercise, or whether TENS facilitated exercise. TENS is not invasive, has no significant adverse effects, but is moderate to high cost. The balance of quality studies of the cervicothoracic spine, as well as the highest quality studies performed on the lumbar spine suggest efficacy; thus, TENS is recommended for select chronic cervicothoracic pain cases as an adjunct to an active exercise program.

Evidence for the Use of TENS
There is 1 high-(962) and 9 moderate-quality(575, 582, 894, 996, 1089, 1102-1105) RCTs incorporated into this analysis. There is 1 low-quality RCT in Appendix 1.(1106)

A comprehensive literature search was conducted using PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: Transcutaneous electrical nerve stimulation, TENS, Neuromuscular Electrical Stimulation, NMES, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 70 articles, and considered 12 for inclusion. In Scopus, we found and reviewed 163 articles, and considered zero for inclusion. In CINAHL, we found and reviewed 25 articles, and considered zero for inclusion. In Cochrane Library, we found and reviewed 20 articles, and considered zero for inclusion. We also considered for inclusion zero articles from other sources. Of the 12 articles considered for inclusion, 11 randomized trials and 1 systematic study met the inclusion criteria.*

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Gonzáles-Iglesias 2009 RCT No mention of sponsorship or COI.	9.0	N = 45 with acute mechanical neck pain, age range 23-42 (34 ± 5 years) for experimental group, and age range 24-44 (34 ± 6) for control	Experimental group, thoracic manipulation, once a week for three weeks (N = 23) vs Control group, no thoracic manipulation (N = 22). Both groups: electrotherapy program, 6 session of TENS (frequency 100 Hz; 20 minutes), superficial thermotherapy (15 minutes) and soft tissue massage Follow-up: baseline and 1 week after discharge from physical therapy	Patients receiving thoracic thrust manipulation experienced greater increases in all cervical motions with between group differences of 10.6° for flexion (95% CI 8.8-12.5); 9.9° for extension (95% CI 8.1-11.7); 9.5° for right lateral flexion (95% CI 7.6-11.4) 8° for left lateral flexion (95% CI 6.2-9.8); 9.6° for right rotation (95% CI t.t-11.6); and 8.4° for left rotation (95% CI 6.5-10.3).	"We found that the inclusion of thoracic manipulation combined with a standard electrotherapy/thermal program results in significantly greater reductions in neck pain and disability as well as increases in neck mobility in the short-term in patients with acute mechanical neck pain."	Combination therapy (thoracic spine manipulation plus electrotherapy thermal program) increased cervical mobility and decreased acute neck pain on a short term (1 week post intervention) basis.
Chiu 2005 RCT Sponsored by the Area of Strategic Development Fund of the Hong Kong Plytechnic University, and Health Services Research fund of the Hong Kong Government. No mention of COI.	7.0	N = 218 with chronic neck pain, mean age 44.31 ± 9.77 for control; 42.70 ± 9.77 for TENS, and 43.28 ± 9.69 for exercise.	TENS applied to acupuncture sites plus infrared (IR) for 20 minutes, then conventional TENS for 30 minutes (N = 73) vs IR plus intensive neck exercise program (multi cervical rehab unit), twice a week for 6 weeks, active exercises, resistance (N = 67) vs IR plus neck care advice, control (N = 78). Follow up at baseline, 6 weeks, and 6 months.	Lowest Northwick Park Neck Pain Questionnaire scores for exercise group; highest neck muscle strength also in exercise group. Numbers of patients taking sick leave at 6 months: 5.5% TENS vs 3% exercise vs 9% for controls.	"After the six-week treatment, patients in the TENS and exercise group had a better and clinically relevant improvement in disability, isometric neck muscle, strength, and pain. All the improvements in the intervention groups were maintained at the six-month follow-up."	Data suggest exercise superior to TENS or infrared for chronic neck pain. TENS placed over acupuncture sites for neck pain.
Maayah 2010 RCT No mention of sponsorship or COI.	6.0	N = 30 with neck pain that existed for most days in the last month, month; mean age 58 ± 8 for control group, and 53 ± 7 for treatment group.	TENS group, received 1-hour treatment at maximum tender area + pulse-rate with adjustable frequency and amplitude or voltage (N = 15) vs Control group, TENS stimulator in which contact was broken at wire connection (N = 15). Follow up before, during treatment, after switch off, and again a week after using Myometer machine.	Pain relief after 2 hours and after more than 2 hours; 20 % vs 13.33% and 26.67% vs 73.33".	"The present study demonstrated that TENS has shown an effective means of providing a sustained pain relief in terms of Myometer machine in subject complaining from neck pain due to musculoskeletal disorders."	Allocation, method unclear. Baseline differences. Appear to be blinded for participant although not described. Duration of symptoms not clear. Study weaknesses and small sample size limits conclusions of efficacy of single TENs use for neck pain.
Dusunceli 2009	5.5	N = 60 with neck pain of at least 6-	Physical Therapy Agents or PTA, TENS (30 minutes),	Mean ± SD for VAS score: group 1 vs group 2 vs group 3: 1 month:	"This study demonstrates the superiority of the neck	This might be used for exercise, also.

RCT No mention of sponsorship or COI.		week duration, age range 18 to 55, mean 53.4(6.8) for PTA group, 52.50(5.80) for PTA and isometric, and 50.2(4.8) for PTA and stabilization	infrared radiation (20 minutes), ultrasound (10 minutes, 5 times a week for three weeks) (N = 20) vs PTA and isometric and stretching exercises (N = 20) vs PTA and stabilization exercises, groups of 4-5 patients, guided by physiotherapist 3 times a week; exercise cards, showing all exercises;3 times per week, 1-1.25 hours (N = 20). Follow-up: baseline, and months 1, 3, 6, 9, and 12 months	5.8±1.4 vs 3.9±1.9 vs 3.3±1.6; 3 months: 5.6±1.9 vs 4.0±1.8 vs 3.3±1.5; 6 months: 5.8±1.4 vs 4.0±2.2 vs 3.6±7.1, $p < 0.05$; ROM: sagittal plane: group 1 vs group 2 vs group 3: 1 month: 107.6±13.9 vs 120.85±9.2 vs 117.5±9.10; group 2 vs group 3: 3 months: 118.3±9.6 vs 119.3±12.13; 6 months: 118.0±12.2 vs 118.0±9.33; 9 months: 114.3±10.3 vs 120.1±8.93; 12 months: 111.5±11.0 vs 119.2±9.01, $p < 0.01$; frontal plane: group 2 vs group 3: 1 month: 74.7±10.0 vs 72.8±7.7; 3 months: 71.6±10.0 vs 75.9±4.9; 6 months: 70.0±9.4 vs 75.4±7.7, $p < 0.01$; Transverse plane: 1 month: group 1 vs group 2, vs group 3: 117.1±21.6 vs 134.8±12.7 vs 133.6±14.6; 3 months: 119.2±15.0 vs 129.5±12.8 vs 136.7±16.3; 6 months: group 2 vs group 3: 127.2±15.7 vs 136.8±14.6; 9 months: 129.0±12.2 vs 136.8±16.1; 12 months: group 1 vs group 2 vs group 3: 103.1±9.1 vs 123.5±13.0 vs 137.2±13.8, ($p < 0.01$).	stabilization exercises, with some advantages in the pain and disability outcomes, compared with isometric and stretching exercises in combination with physical therapy agents for the management of neck pain."	Interventions poorly described. Differences between groups poorly analyzed.
Chee 1986 RCT No mention of sponsorship or COI.	5.0	N = 25 volunteer students, neck and shoulder pain, age range between 20-40 years.	TENS, plus bilateral stimulation with roller electrode continually slowly (N = 10) vs. Placebo treatment for trigger points, plus bilateral stimulation with the roller electrode continually slowly (N = 10). Follow-up for 2 weeks.	Significant improvement in trigger point pain from 1st and 5th sessions in TENS group, ($p = 0.001$).	"This study has clearly shown that microamperage stimulation is effective in the treatment of trigger point."	Study details and outcomes sparse. Chiropractic students select group that is difficult to generalize beliefs and education.
Vitiello 2007 RCT Sponsored by Enlightened Therapies PTY Ltd. No COI.	5.0	N = 24 with chronic neck pain, mean age 40.5 ± 7.79 years.	Electro Neuro Adaptive Regulator ENAR, for 10 minutes (N = 9) vs TENS for 10 minutes (N = 7) vs Controls for 10 minutes, ENAR therapy group except that unit turned on then immediately off before being applied to skin (N = 8). Each group recieved 10 minutes of	ENAR therapy participants reported a significant reduction in intensity of neck pain and disability, as well as a significant increased function and overall quality of life than TENS or control intervention participants.	"[P]articipants who received ENAR therapy experienced greater reductions in the intensity of neck pain and disability, and increased function and overall quality of life, compared with participants receiving either TENS therapy or placebo electrotherapy."	Baseline differences significant, concerning for randomization failure.

			therapy. Follow-up at baseline, 6, 12, 18 and 24 weeks.			
Nordemar 1981 RCT No mention of sponsorship or COI.	5.0	N = 30 acute cervical pain, mean age 43±16 for neck collar, 34±9 for TENS, and 42±17 for manual therapy.	Neck collar of semi-soft material vs neck collar plus transcutaneous nerve stimulation, 15 minute treatments (N = 15) vs Neck collar plus analgesics plus manual therapy, soft tissue treatment, gentle traction and mobilization for 30 minutes 3 times a week (N = 15). Neck collar group seen at 1, 2, 6, 12 week. TNS and mobilization seen at 2 weeks.	Age: NC 43+/-16, TNS 34+/-9, MT 42+/-17. Total mobility range after 1 week: NC 243+/-115, TNS 323+/-47, MT 316+/-84. Pain index after 1 week: NC 35+/-45, TNS 17+/-19, MT 18+/-25. Differences in mobility and pain after 1 week showed no significant changes between groups. At 6 weeks and 3 months all pain free. Pain <3 days.	"[T]ranscutaneous nerve stimulation is a valuable pain reducer and gives a more rapid restoration of cervical mobility in acute cervical pain."	Variable follow-up duration. Used cervical mobility as measurement for improvement. Only used data from 1 week of treatment because of rapid improvement seen in all groups. At one week saw increase in mobility in TENS group, but no difference in pain. Only 10 participants in each group.
Rodriguez-Fernandez 2011 RCT No sponsorship or COI.	5.0	N = 76 with latent myofascial trigger point (MTrP) in 1 upper trapezius muscle, aged 18 to 41 years (23±4)	TENS with verum electrotherapy treatment, BTL 5000 burst TENS with pulse frequency of 100Hz, burst frequency of 2Hz, 10 minutes, induce contraction of trapezius muscle (N = 38) vs Placebo, sham electrotherapy TENS, 10 minutes (N = 38). Follow-up 1 and 5 minutes after intervention	Between group differences were small at 1 minute (0.3 kg.cm; 95% CI, 0.1-0.4) and at 5 minutes (0.6kg/cm; 95% CI, 0.3-0.8). No statistically significant p-values to report.	"A 10-minute application of burst-type TENS increases in a small but statistically significant manner the RPPT over upper trapezius latent MTrPs and the ipsilateral cervical range of motion."	Results favor treatment over sham. Short duration of follow-up. Population was latent, i.e. no symptoms.
Escortell-Mayor 2011 RCT Study sponsored by the Instituto de Salud Carlos III, Fondo de Investgacion Santaria/ Fondos Europeos de Desarrollo Regional. No COI.	5.0	N = 90 with subacute or chronic mechanical neck disorders without neurological damage, aged between 18 and 60; mean 40.1 (10.7)	Manual Therapy (MT), neuromuscular technique, post-isometric stretching, spray and stretching, and Jones technique (N = 47) vs. TENS, portable, 80Hz (N = 43). Both groups: 10 treatment session of 30 minutes on alternate days; provided information on postural skills, isometric exercises and neck exercises Follow-up: before the intervention, when the intervention finished and 6 months.	No statistically significant p-values to report.	"Both analyzed physiotherapy techniques produce a short-term pain reduction that is clinically relevant."	Both intervention produced short term pain reduction, but at 6 months, only one-third of the patients reported benefits.
Carlsson 1990 RCT Sponsored by grants from Renee Eanders Hjälpfond and the	4.5	N = 62 females with chronic tension headache, mean age 34 years.	Acupuncture, each treatment session lasted 20 minutes, 2-4 weeks (n = 31) vs. Physiotherapy, individualized 10-12 sessions, 30-45 minutes over 2-3 months (N = 31) vs. Control group (undefined) (N	"The headache intensity had become significantly lower in the physiotherapy group compared with the acupuncture group ($p < 0.05$). A significant correlation was found between the intensity of headache and the tenderness of the temporal, masseter ($p < 0.05$) and	"The headache was more improved in the physiotherapy group, and there was a marked reduction in the intake of analgesics. The tenderness was reduced in all muscles tested in the physiotherapy group but only in some of the	Physiotherapy included a more intense interaction between participant and provider compared to acupuncture, biasing against acupuncture. Control group ill defined, uncertain if they had

Swedish Fund for Scientific Research Without Animal Experiments. No mention of COI.			= 30). Follow-up for 3 to 8 weeks.	trapezius muscles ($p < 0.01$). Physiotherapy group significantly better than acupuncture group after treatment with respect to tenderness of t3ssessmentstor, orbicularis occuli and masseter muscles ($p < 0.005$)."	muscles after acupuncture. The limitations of neck rotation was not influenced by either treatment."	headaches to compare to interventional groups. Many different medications taken by participants; only ASA and acetaminophen recorded and analyzed. Baseline characteristics are unclear.

PERCUTANEOUS ELECTRICAL NERVE STIMULATION (PENS)
See Low Back Disorders Guideline.

HIGH-VOLTAGE GALVANIC THERAPY
High-voltage galvanic is an electrical therapy that uses a twin-spike, monophasic pulsed current waveform with peak spike amplitudes of up to 500 V and pulse durations of about 50 to 200m sec at frequencies ranging from 1 to approximately 120 twin-spike pulses per second. Most devices allow the user to select and manually switch the polarity of the output leads.

Recommendation: High-voltage Galvanic Therapy for Chronic Cervicothoracic Pain
High-voltage galvanic therapy is not recommended for treatment of chronic cervicothoracic pain.
Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation
High-voltage galvanic is not proven efficacious for the treatment of chronic cervicothoracic pain. The single quality study suggests possible minimal, brief improvement for neck pain.(1107) While high-voltage galvanic is not invasive and not low cost, there are other interventions shown to be effective.

Evidence for the Use of High-voltage Galvanic
There is 1 moderate-quality RCT incorporated into this analysis.(1107)

A comprehensive literature search was conducted using multiple search engines including PubMed, Scopus, CINAHL and Cochrane Library without date limits using the following terms: high voltage galvanic therapy, high voltage galvanic, pulsed frequency electromagnetic therapy, high voltage galvanic stimulation, high voltage pulsed current, direct current stimulation, cervicalgia, pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, postop, postoperative*, postoperative, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. In PubMed we found and reviewed 5 articles, and considered 2 for inclusion. In Scopus, we found and reviewed 1 article, and considered 0 for inclusion. In CINAHL, we found and reviewed 0 articles, and considered 0 for inclusion. In Cochrane Library, we found and reviewed 161 articles, and considered 0 for inclusion. We also considered for inclusion 0 articles from other sources. Of the 167 articles considered for inclusion, 1 randomized trial and 2 systematic studies met the inclusion criteria.*

Author/ Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Foley-Nolan 1990 RCT No mention of sponsorship or COI.	6.5	N = 20 with subacute and chronic persistent neck pain (at least 8 weeks duration), middle aged.	6 weeks of pulsed high frequency (27MHz) electromagnetic therapy (PEMT) (N = 10) vs. 3 weeks of placebo followed by 3 weeks of active treatment (N = 10). Follow-up for 6 and 3 weeks.	3 subjects much better or completely well with active treatment after 3 weeks vs. 1 subject in placebo group. At end of study, 75% graded their response as "moderately better" or "much better" on subjective evaluation. Many gained little benefit in initial week, by 2 weeks had noted a definite improvement. Median pain score after 3 weeks of PEMT decreased in PEMT group to 4.0, ($p < 0.005$) vs no change for placebo. After 6 weeks difference in pain scores between 2 groups. After 3 weeks, a significant difference between groups for ROM scores, ($p < 0.008$).	"[T]he significant patient improvement, as judged by both patient and clinician, implies a role for PEMT in the treatment of persistent neck pain."	Patients' mean ages younger in those receiving active units for entire study (mean 38 vs 47 years); however mean durations of symptoms longer in that group (22 vs 17 months). Requirements to wear a device for 8 hours a day as per this study's protocol are considerable and are to be weighed vs degree of improvement which appeared mild even if statistically significant.

Injection Therapies……..

BOTULINUM INJECTIONS

Botulinum injections have been used to produce muscle paresis and have antinociceptive properties.(670, 1108) They have also been used in myofascial pain syndrome (see Shoulder Disorders guideline). This treatment is also used for cervical dystonia (spasmodic torticollis), although that is beyond the scope of this guideline.(1109-1112)

Recommendation: Botulinum Injections for Non-specific Acute, Subacute, or Chronic Cervical Pain, Cervical Myofascial Pain or Cervicogenic Headaches

Botulinum injections are moderately not recommended for treatment of non-specific acute, subacute or chronic cervical pain, cervical myofascial pain,(1113-1120) **or cervicogenic headaches**.(1121-1125)

Strength of Evidence – **Moderately Not Recommended, Evidence (B)**
Level of Confidence – Moderate

Rationale for Recommendation

High and moderate quality studies evaluating botulinum injections for the management of neck pain or tension headaches demonstrate no clear benefits greater than placebo (1126-1131), although a few lower-quality studies suggest some potential efficacy (1541, 1542). These injections are invasive, have high adverse effects including reported deaths, are costly, have no quality evidence of efficacy and are not recommended.

Evidence for the Use of Botulinum Injections

There are 5 high-(1108, 1114, 1126, 1128, 1132) and 14 moderate-quality RCTs incorporated into this analysis.(1113, 1115-1125, 1127, 1129) There are 7 low-quality RCTs in Appendix 1.(1133-1139)

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

Botulinum, botox, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies*

to find 1398 articles. Of the 1398 articles, we reviewed 78 articles and included 33 articles (27 randomized controlled trials and 6 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Silberstein 2006 (8.5)	Botulinum toxin injection	RCT	No mention of sponsorship or COI.	N = 300 chronic tension-type headaches	Mean age: 42.6 years; 113 males, 187 females;	Botulinum toxin A (50U, n = 50/86Usub, n = 51/100Usub, n = 52/100U, n = 51/150U, n = 49) vs. placebo normal saline (n = 50) for single injection.	Follow-up at 30, 60 90, 120 days.	Patients in 100 U group had significantly higher incidence in cervical region vs. other groups (p = 0.015). Placebo favored in mean frequency of headache-free days. At 90 days, significantly more patients in BoNTA 100 U group (p = 0.017), BoNTA Usub group (p = 0.024) and BoNTA 86 Usub group (p = 0.017) reported a 50% decrease in TTH days compared with placebo group.	"BoNTA treatment of CTTH in a dose range of 50 U to 150 U was shown to be safe and well tolerated. For tension headache-free days per month, all group improved at the day 60 primary endpoint. There was no statistically significant difference between placebo and four BoNTA groups, but a significant difference favoring placebo vs. BoNTA 150 U was observed."	Lack of dose-response relationships is concerning for a potential lack of an effect.
Padberg 2007 (8.0)	Botulinum toxin injection	RCT	Sponsored by Dr. Eduard Hoelen Foundation, the Hague. The authors declared no COI.	N = 40 whiplash-type neck distortion defined as a soft tissue injury of neck lasting more than 6 months	Mean age: 36.5 years; 13 males, 27 females.	Botulinum toxin max of 100 units (n = 20) vs. placebo, n = 20 (saline).	Follow-up at 4, 8, 12 weeks.	No significant differences found between 2 groups.	"Based on present evidence BTX cannot be recommended as treatment for neck pain in chronic whiplash patients. Future studies directed on possible	Small numbers. No mention of co-interventions. Data suggest lack of efficacy.

									central mechanisms of this complicated chronic pain syndrome are warranted."	
Seo 2013 (Score=7.0)	Botulinum toxin A injection	RCT	Sponsored by Ipsen Ltd grant A3852120104. No mention of COI.	N=76 patients with neck and shoulder chronic myofascial pain syndrome.	Mean age: 47.5 years; 11 males, 64 females.	Motor group: patients received Botox injection and followed by three daily 30 minutes electrical stimulation for muscle contraction (n=37) vs. Sensory group: patients received Botox injection and followed by three daily 30 minutes electrical stimulation for above sensory threshold intensity (n=38).	Follow-up at baseline, 1 and 3 days, 1, 2, 4, 8, 12, and 16 weeks.	The primary outcome VAS score indicated significant reduction in the two groups from 4th week to 16th week follow-up ($p<0.05$). The VAS score also showed significant between both groups during follow-up at 16th week ($p=0.043$).	"[I]t seems that sensory electrical stimulation was superior to motor electrical stimulation as an adjuvant therapy to BTX-A injection in patients with chronic MPS."	No meaningful differences between electrical stimulation groups for almost all outcomes at each time point. Any significant differences occurred near end of follow up period (week 16).
Schmitt 2001 (6.5)	Botulinum toxin A injection	RCT	No mention of sponsorship or COI.	N = 60 chronic tension-type headaches	Mean age: 34.8 years; 24 males, 36 females.	Botulinum toxin A, n=39 (20 U BTX-A, 100 U in 2 mL saline, each injection 2.5 U) vs. same amount of saline (n = 29) 2 injections.	Follow-up at 4 weeks and 8 weeks.	No statistically significant differences found.	"[T]here is some evidence that BTX-A injections in craniofacial muscles may have a positive effect in the treatment of chronic tension-type headache. However, variables such	Non-significant baseline differences, such as longer disease duration in botulinum group (27.7 vs. 19.4 years). Data on self-report of

									as patient selection, dosage, and injection sites must be elucidated. Most probably, individualized therapeutic regimens with repeated injections will provide the best benefit, as in the botulinum toxin A treatment of cervical dystonia. Duration until improvement seems to be more than 8 weeks, and perhaps multiple treatments are necessary until desensitization of central neurons occurs."	improvements suggest there are either not meaningful differences, or they are slight.
Wheeler 2001 (5.5)	Botulinum toxin injection	RCT	Supported by Allergan Pharmaceutical Corporation. No mention of COI.	N = 50 chronic neck pain and all had pain for at least 3 months	Mean age: 43.6 years; 12 males, 38 females.	Botulinum toxin A, n = 25 (mean dose of 231.20) vs. placebo, n = 25 (saline) for 4 months.	Follow-up at 4, 8, 12, and 16 weeks.	No significant differences found.	"A single BTXA injection session without physical therapy is not an effective treatment for chronic neck pain…BTXA has been demonstrated as an effective	No mention of co-interventions. Data suggest lack of efficacy.

									treatment for some disorders. However, the procedure that appears most effective in clinical practice for neck pain is one that includes low-dose applications with one or two repeat injection sessions."	
Truong 2010 (Score=5.0)	Botulinum toxin A injection	RCT	Sponsored by the Ipsen Group, Slough, UK. One or more of the authors have received or will receive benefits for personal or professional use.	N=116 patients with diagnosis of cervical dystonia (CD) from the US and Russia.	Mean age: 53 years; 41 males, 75 females.	Dysport group: patients received 12 weeks 500 units Dysport treatment (n=55) vs. Placebo group: patients received placebo (n=61).	Follow-up at baseline, 4, 8, and 12 weeks.	At 4th week, the primary outcome Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) in Dysport group (TWSTRS=-15.6±2.0) significantly decreased (P<0.001), comparing with placebo group (TWSTRS=-6.7±2.0). At 12th week, mean TWSTRS scores improved significantly in both groups: Dysport:-9.1±1.7 vs. Placebo: -4.9±1.7 (p=0.019).	"Dysport demonstrated a good long-term safety profile; most adverse events were mild or moderate and typical of the known safety profile of Dysport in this indication. These results confirm that Dysport (500 units) is safe, effective, and well-tolerated in patients with CD."	Meaningful dropout and discontinued for placebo group for non-response. Meaningful differences between treatment and placebo for most outcomes at most time points.
Mordin 2014 (Score=4.0)	Botulinum toxin A injection	RCT	Sponsored by Ipsen Biopharmaceut	N=116 patients with 18	Mean age: 53 years; 41	Abobotulinumtoxin A group: patients	Follow-up at baselin	The treatment group indicated higher portion in	"CD has a marked impact on HRQOL.	Significant differences between Tx

			ical Inc. in Basking ridge, New Jersey, USA. One author has received or will receive benefits for personal or professional use.	months of cervical dystonia symptoms and diagnosis.	males, 75 females.	received 500 units Dysport treatment (n=55) vs. Placebo group: patients received placebo (n=61).	e, 4, 8, and 12 weeks.	responding improvement in Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) than that in placebo group (30% vs. 16%). Patients responded to TWSTRS also reported significant improvement in physical functioning, vitality and social functioning, and pain visual analogue scale ($p \leq 0.03$).	Treatment with a single abobotulinumtoxinA injection results in significant improvement in patients' HRQOL."	and placebo at 3 weeks for SF-36 domains of physical functioning mental, physical, bodily pain and general health. Other SF 36 topics were trending toward significance. All results favoring active Tx.

CERVICAL EPIDURAL INJECTIONS

Epidural glucocorticosteroid injections (ESI) are performed in an attempt to deliver the active medication as close to the target tissue as possible, whether most commonly a herniated disc or spondylosis.(1140-1146)) For transforaminal ESI, complications rarely occur, but include infection (meningitis, epidural abscess, etc.) and hemorrhage related to penetration of an anatomical variant artery, nerve root injury, vertebral artery dissection, paralysis, and stroke.(1147, 1148) Due to proximity of the spinal cord, ESIs in the cervical spine are thought to have a higher adverse effect profile. A resulting epidural hematoma may compress the nerve or spinal cord (1140) and generally requires emergency surgery. Intralaminar ESI may have a disadvantage in not getting the medication anteriorly (the site of inflammation), but have less risk of inadvertent arterial injection of particulate steroid.(1147-1152) There have not been quality trials reported comparing transforaminal vs. intralaminar cervical ESIs.(1153)

1. *Recommendation: Epidural Glucocorticosteroid Injections for Acute, Subacute, or Chronic Cervical Radicular or non-Radicular Pain*

Epidural glucocorticosteroid injections, including selective nerve root injections, are not recommended for acute, subacute, or chronic radicular or non-radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I) –** Radicular pain
Strength of Evidence – **Not Recommended, Evidence (C) –** Non-Radicular pain
Level of Confidence –Moderate

2. *Recommendation: Continuous Infusion of Local Corticosteroids and Local Anesthetic for Acute, Subacute, or Chronic Cervicothoracic Pain with or without Radiculopathy*

Continuous infusion of local corticosteroids and local anesthetic for acute, subacute, or chronic cervicothoracic pain with or without radiculopathy.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence –Moderate

Rationale for Recommendation

There is a lack of quality trials for treatment of patients with acute or subacute cervicothoracic radicular pain. There is quality evidence documenting relatively weak efficacy for lumbar radiculopathy (see Low Back Disorders guideline). However, the risks of adverse effects are greater in the cervical spine than in the lumbar spine and have included quadriplegia.(1154, 1155) Thus epidural, intralaminar, and transforaminal approaches for epidural steroid injections and selective nerve root injections for radicular pain are not recommended.(1156)

Regarding non-radicular pain, there are no quality saline controlled trials although there are two trials with local anesthetic injections. A moderate-quality RCT compared methylprednisolone 40mg with 0.5ml carbocaine to 0.5ml carbocaine and 1ml saline. The authors reported a between-group difference of a 17% reduction in pain symptoms in the steroid group and 16% reduction of pain in the non-steroid group. They performed fluoroscopically guided transforaminal injections in patients who had positive diagnostic nerve root blocks performed before randomization. They included patients with MRI diagnoses of foraminal stenosis and hard disc disease.(1157) Another study compared 5ml lidocaine with 5ml lidocaine and 6mg betamethasone and reported no significant difference between groups at 12 months.(1158) A moderate-quality study compared triamcinolone 10mg/ml (dose was variable and dependent on volume injected) plus 0.5% lidocaine with triamcinolone, 0.5% lidocaine and 2.5mg morphine without any significant difference between the groups. They included patients who had x-rays, myelography, CT scan, and electrophysiology tests that did not reveal any pathology. The patients had undergone medical treatment for at least 12 months including NSAIDs, activity restrictions, physiotherapy, and other medical treatments and failed to respond. The overall improvement was 79.2% improvement to complete, excellent, or good pain control at 12 months.(1159) Another moderate-quality study comparing methylprednisolone 80mg with 5ml 1% lidocaine into the cervical epidural space to injection of the same medications into posterior neck muscles reported decreased pain and increased range of motion at 12 months in the epidural injection group.(1160) Thus, there is quality evidence that epidural steroid injections are not successful for treatment of chronic cervical radiculopathy and these injections are not recommended.

There are no sham-controlled studies of continuous infusion into the cervical spine. There is a moderate-quality study comparing continuous 0.25% bupivacaine with boluses of methylprednisolone 40mg every 4 to 5 days via catheter with 0.25% bupivacaine with epinephrine with 80mg methylprednisolone acetate with a 4 to 5 day interval between injections. Patients were classified as "resistant" to conventional therapy. They had CT or MRI exams with evidence of herniated nucleus pulposes or cervical spondylosis. Follow up at 6 months did not find statistical difference for the patients with pain <180 days duration. In patients with >180 days duration of pain the study reported improved pain control and number of pain-free hours compared to injection treatment.(1161) These procedures are quite invasive on a cumulative basis and thus are not recommended pending reporting of quality trials, particularly with placebo or sham control.

Evidence for the Use of Cervical Epidural Injections
There is 1 high-(1162) and 14 moderate-quality RCTs (1157-1159, 1161, 1163-1172) incorporated into this analysis. There are 3 low-quality (1160, 1173, 1174) RCTs and 3 other studies(1175, 1176) in Appendix 1.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

epidural injection, glucocorticoid, steroid injection, dexamethasone, betamethasone, methylprednisolone, triamcinolone, neck pain, cervicalgia, cervical pain, cervical radiculopathy, radicular pain, postoperative neck pain, postoperative cervical pain, herniated disk, controlled clinical trial, controlled trails, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies*
to find 815 articles. Of the 815 articles, we reviewed 83 articles and included 30 articles (20 randomized controlled trials and 10 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Manchikanti 2010a (score=9.0)	Epidural Injections	RCT	No sponsorship or COI.	N=70 with chronic neck pain and no disc herniation or radiculitis and negative facet joint pain.	Mean age: 44.5 years; 24 males, 46 females	Group I (n=35) Cervical epidural with Local anesthetics vs. Group II (n=35) Cervical Epidural with local anesthetics and steroids. Follow-up Baseline, 3, 6 and 12 months.	3, 6, 12 months	Results for Pain Relief Characteristics: Mean ± SD for (Group I; Group II) and p-value, are as follows. Baseline: (7.8 ± 0.8; 7.4 ± 0.9) P = 0.059, 3 Months: (3.4* ± 1.4; 3.1* ± 1.0) P = 0.313, 6 Months: (3.5* ± 1.5; 3.2* ± 1.0) P = 0.457, 12 Months: (3.5* ± 1.3; 3.2* ± 1.1) P = 0.372. Results for Functional assessment evaluated by Neck Disability Index: Mean ± SD for (Group I; Group II) and p-value, are as follows. Baseline: (30.0 ± 4.8; 28.5 ± 7.0)P = 0.302, 3 Months: (15.1* ± 5.9; 13.1* ± 4.9) P = 0.134, 6 Months: (14.5* ± 5.8; 13.1* ± 5.2) P = 0.266, 12 Months: (14.4* ± 5.6; 12.7* ± 4.9) P = 0.185. *indicates	"Assessment of the preliminary results…demon strated significant pain relieving effectiveness in 80% of patients with improvement in functional status as well."	Data suggests no differences between epidural injection with and without steroid in this population. Lack of "no injection" control group limits conclusions of efficacy for epidural injections.

								significant difference with baseline values (P < 0.001).		
Manchikanti 2010b (score=9.0)	Epidural Injections	RCT	No sponsorship or COI.	N= 70 with chronic neck pain with cervical disc herniation or radiculitis of at least 6 months duration.	Mean age: 46.1 years; 25 males, 45 females	Group I (n=35) cervical epidural with local anesthetics vs. group II (n=35) cervical epidural with local anesthetics and steroids. Follow-up at baseline, 3, 6 and 12 months.	3, 6, 12 months	Results for Pain Relief Characteristics: Mean ± SD for (Group I; Group II) and p-value, are as follows. Baseline: (7.8 ± 0.92; 7.6 ± 0.91) P = 0.302, 3 Months: (3.2* ± 1.06; 3.4* ± 1.12) P = 0.445, 6 Months: (3.2* ± 1.13; 3.4* ± 1.01) P = 0.320, 12 Months: (3.3* ± 1.19; 3.5* ± 1.20) P = 0.485. Results for Functional assessment evaluated by Neck Disability Index: Mean ± SD for (Group I; Group II) and p-value, are as follows. Baseline: (29.8 ± 5.6; 28.7 ± 8.4)P = 0.514, 3 Months: (14.6* ± 5.67; 14.1* ± 5.60) P = 0.735, 6 Months: (13.1* ± 5.46; 13.9* ± 5.71) P = 0.580, 12 Months: (13.5* ± 5.33;	"The assessment of preliminary results…demon strated significant pain relief in 77% of patients with improvement in functional satus, requiring 3.7 procedures per year and providing almost 38 weeks of relief during a 52 week period in appropriately selected patients."	Data suggest no difference in outcomes with addition of steroid in this population. No comparison group of "no epidural injection" limits conclusion of efficacy, although both injection groups had significant improvement over 12 month period.

								13.8* ± 5.46) P = 0.825. *indicates significant difference with baseline values (P < 0.001). Result for Opioid Intake (Morphine Equivalence mg): Mean ± SD for (Group I; Group II) and p-value, are as follows. Baseline: (61.9 ± 54.1; 54.5 ± 63.2)P = 0.602, 3 Months: (50.5# ± 47.9; 42.8# ± 43.9) P = 0.484, 6 Months: (48.5# ± 47.3; 42.1# ± 44.4) P = 0.563, 12 Months: (48.5# ± 47.3; 41.6# ± 44.9) P = 0.531. # indicates significant difference with baseline values (P < 0.05)		
Manchikanti 2010c (score=8.0)	Epidural Injections	RCT	No sponsorship or COI.	N = 120 cervical disc herniation or radiculitis. N=70 completed one year follow-up.	Mean age: 46.1 years; 25 males, 45 females	Cervical interlaminar epidural injections of lidocaine (n = 35) 0.5%, 5 ml vs. lidocaine (n = 35) 0.5%, 4ml plus non-particulate	3, 6, 12 months	No significant differences for any outcome measurements between the two groups at all follow up points.	"The assessment of preliminary results …demonstrated significant pain relief in 77% of patients with improvement in functional status, requiring 3.7 procedures	Data suggest in this highly specific population, no difference in outcomes from block with and without steroid. Both groups showed significant improvement. Lack of comparison to non-injection or

						betamethasone 1mL. Follow-up at 0, 3, 6, and 12 months.			per year and providing almost 38 weeks of relief during a 52-week period in appropriately selected patients"	placebo group limits conclusions.
Manchikanti 2012 (score=7.5)	Epidural Injections	RC T	No sponsorship or COI.	N=56 with cervical post-surgery syndrome; >18 yrs. of age; chronic function-limiting neck and upper extremity pain of >6 months duration.	Mean age: 48.7 years; 10 males, 18 females	Group 1: 5 mL of 0.5% lidocaine (N=28). vs. Group 2: 4 mL of 0.5% lidocaine mixed with 1 mL or 6 mg of nonparticulate betamethasone (N=28). Post treatment assessment at 3, 6, and 12 months.	3, 6, 12 months	Significant pain relief was seen in both groups with 71% of Group 1 participants and 68% of Group 2 participants reporting > 50% reduction in Numeric Rating Score (NRS) from baseline. Group 1 and Group 2: baseline NRS 8.0 + 1.23 and 7.8 + 0.9 (p=0.534) respectively; 12 month NRS 3.6 + 1.1 and 3.8 + 1.4 (p=.465) respectively.	"The assessment of the preliminary results of this randomized, controlled, double-blind trial of cervical interlamar epidural injection in chronic function-limiting neck pain and upper extremity pain in cervical postsurgery syndrome demonstrated significant pain relief in over 72% of patients with improvement in functional status, requiring 4 procedures per year and providing almost 40 weeks of relief during a 52-week period in appropriately	No placebo. Similar results in both groups.

									selected patients."	
Terzi 2002 (score=7.0)	Epidural Injections	RCT	No mention of sponsorship or COI.	N = 60 consecutive patients with primary headache disorder (migraine or TTH) or cervicogenic headache	Mean age: 35.1 years; 21 males, 39 females	1-ml injection of 2% prilocaine in physiological (0.9%) saline (treatment group) (n = 10) vs. 1ml injection of saline (placebo control group) (n = 10).	5, 10, 30 minutes	Pain decreased after local anaesthetic (LA) injection in both OF and ON areas at 5, 10 and 30 minutes compared to placebo; p <0.01.	"[G]ON blockade is a diagnostic tool if it is effective in the ON and OF areas."	Single injection, diagnostic study no long term follow-up. Study of limited use to evaluate treatment.
Anderberg 2007 (score=6.5)	Epidural injections	RCT	Sponsored by grant from Swedish Society for Spine Surgeons. No mention of COI.	N = 40 cervical radiculopathy	Mean age: 51 years; 20 males, 20 females	Carbocaine and methylprednisolone vs. carbocaine and saline. Chronic pain patients with cervical radiculopathy and positive response to nerve block at same level.	3 weeks	No significant difference for any of measured parameters when comparing results between 2 treatment groups at 1, 2, or 3 weeks after treatment.	"Using a single transforaminal injection for the treatment of cervical radiculopathy presenting with radicular pain, the combination of steroids and local anaesthetics did not provide more symptoms reduction than the combination of saline and local anaesthetics."	Mean duration of symptoms, 31 months. Diagnoses included foraminal stenosis, spondylosis and soft disc disease. Difference in diagnoses between 2 groups. Many other baseline characteristics missing. Injections fluoroscopically guided. Study needs to be repeated with better baseline randomization to conclude that steroids not necessary in

										cervical epidural injections.
McCormick 2017 (score=6.0)	Epidural Injections	RCT	Study was sponsored by the 2013 Midwest Pain Society Addison/Blonsky Research Grant. No COI.	N = 76 patients with unilateral C2-C6 radicular pain with MRI confirmation.	Median age: 48; 31 males, 45 females.	Group 1: received a targeted cervical interlaminar epidural steroid injection (CIESI) at the source of the pathology. (N =36) vs Group 2: (N =40) received the standard CIESI between C7 and T1.	Baseline, 2 weeks, 1, 3, and 6 months.	Group 1 vs Group 2, number (%) of patients with >30% reduction in Oswestery Neck Disability Score, 1, 3, and 6 months (p-value): 23 (58) vs 24 (67) (p=0.48), 16 (40 vs 21 (58) (p=0.17), 22 (55) vs 21 (58) (p=0.64). No significant difference between groups in patients global improvement scale at 1 month (p=0.35), 3 months (p=0.50), and 6 months (p=0.83).	"In conclusion, this trial showed no statistically significant differences in clinical outcomes between a targeted and standardized image-guided cervical interlaminar epidural steroid injections for the treatment of unilateral radicular pain at the C5 or C6 level."	No significant differences between treatment groups for any outcome at any time point.
Ji 2016 (Socre=4.5)	Epidural injection	RCT	Sponsored by the Industrial R&D program of MOTIE/KEIT. The authors declared no COI.	N=80 patients with single level cervical disease with neck pain.	Mean age: 55.1 years; 40 males, 40 females.	C-PEN group: patients received cervical lumbar percutaneous epidural neuroplasty (n=40) vs. C-ESI group: patients received cervical epidural	Follow-up at baseline, 6 and 12 months.	VAS score decreased in both groups from baseline to 12-month follow-up (p<0.001), and C-PEN group indicated lower VAS score than that in C-ESI group (2.7 vs. 3.5 in 6-month follow-up; 3.1 vs. 3.6 in 12-month follow-	"C-PEN was superior to C-ESI in terms of better NDI recovery (at 6 months) and greater reduction in VAS score (until 12 months) in treating single level cervical disc herniation."	Both treatments had meaningful improvement from baseline for both main outcomes.

						steroid injection (n=40).		up). Greater improvement in symptom relief showed in C-PEN group rather than C-ESI group (p<0.001).		
Choi 2015 (score=4.0)	Epidural Injections	RCT	No mention of sponsorship. No COI.	N=62 patients with unilateral radicular pain or axial neck pain caused by hemiated nucleus pulposus.	Mean age: 51.06; 33 males, 29 females.	Group 1: received fluoroscopically guided modified paramedian interlaminar (mPI) cervical interlaminar epidural steroid injection (CIESI) (N =31) vs Group 2: (N =31) received fluoroscopically guided transforaminal CIESI.	Baseline, 2 weeks, 1 and 3 months.	Group 1 vs Group 2, contrast flow grade 1, 2, and 3 (p-value): 3 (9.7%) vs 5 (16.1%), 6 (19.4%) vs 14 (45.2%), 22 (71.0%) vs 12 (38.7%) (p<0.036). Group1 vs Group 2, number of vascular uptakes (p-value): 0 (0%) 12 (38.7%) (p<0.001). Group 1 vs group 2, patients who indicated discomfort (p-value): 7 (22.6%) vs 21 (67.7%) (p<0.001). No differences at 2 weeks, 1 and 3 months in neck pain between groups.	"In conclusion, we determined that the mPI approach suggested in this study is able to deliver drugs suitably into the anterior epidural space through many levels of the cervical spine and is also safer and more convenient for patients when compared with the TF approach"	Data suggest that modified paramedian interlaminar approach is superior to transforaminal approach. Methodological details sparse.
Castagnera 1994 (score=4.0)	Epidural Injections	RCT	No mention of sponsorship or COI.	N = 24 chronic cervical radicular pain	Mean age: 47.7±8 years; 12 males, 12 females	Single cervical epidural steroid injection (CESI) with morphine vs.	1 day, 1, 3, 6, 8, 12 months	S + M group showed higher proportion of complete and excellent results day after CESI; p <0.03. No further	"We conclude that in patients suffering from chronic CRP unrelated to a compressive or malignant	Cervical radicular pain patients who failed more conservative therapies. Return to work evaluated; similar between

						without morphine.		p-values presented for pain relief. Total drug consumption before/ after CESI: Permanent or episodic NSAID use (24 vs. 4) vs. never used NSAID (0 vs. 20). Permanent or episodic anxiety relieving medication (20 vs. 13) vs. never used anxiety medication (4 vs. 11).	origin and not needing surgery, a single CESI could be helpful when medical treatment remains ineffective."	groups. At 12 months 79.2% complete, excellent, or good pain control from 1 injection. Lack of study details raises questions as to quality. Study suggests that single cervical epidural steroid injection can reduce cervicothoracic pain as long as 12 months.
Pasqualucci 2007 (score=4.0)	Epidural Injections	RCT	Sponsored by Department of Anesthesiology and Intensive Care, University of Udine, Italy. No mention of COI.	N = 160 cervical brachial radicular pain	Mean age: 64.5 years; 71 males, 89 females	Epidural steroid injections vs. continuous epidural steroid infusion.	1, 6 months	Patients in single injection: Group A required median 4 blocks vs. Group B, median 5 blocks vs. Group C, median 6 blocks vs. Group D, median 7 blocks. Continuous epidural: Group A average duration of continuous epidural 13.84±4.33 days vs. 16.94±5.67 days vs. 22.83±4.82 days vs. 24.23±4.64 days. At 1 month/ 6months, PC with	"Therapy with continuous epidural local anesthetic and methylprednisolone provides better control of chronic cervicobrachial pain compared with Single injection."	Patients with radicular pain and/or neuropathy. Duration of symptoms varied. No placebo controlled group. Average of 5 injections and 20 days of continuos infusion to obtain pain control of >80% in all patients. Assessments done up to 6 months after enrollment. Limited functional assessment done.

								continuous epidural and in single injection: 75.34±15.21/73.71±16.03 vs. 58.97±20.68/58.49±22.97 (p = 0.0065/p = 0.016).		
Stav 1993 (score=3.0)										Injections not done with fluoroscopy. Treatment discontinued if "complete" failure of 1st injection. Patients had pain >6 months with or without radiculopathy. Diagnoses were cervical arthritis and or degenerative disk disease. They did not find any impact on sensory or motor nerve dysfunction with the injections.

RADIOFREQUENCY NEUROTOMY, NEUROTOMY, AND FACET RHIZOTOMY

Facet joints ("zygapophysial joints") are thought the source of pain for some patients with chronic cervicothoracic pain.(1177) Patients who experience pain relief from the injection of anesthetic along the nerve roots innervating the joints ("diagnostic blocks") are thought by some to be candidates for various neurotomy procedures. Radiofrequency neurotomy involves the use of a radiofrequency electrode to create a heat lesion to coagulate (destroy) the nerve supplying the facet joint, and some surrounding muscle.(1178-1182) If the theory is correct and the patient correctly diagnosed, the procedure should result in complete or near-complete relief of cervicothoracic pain.(1183)

1. *Recommendation: Radiofrequency Neurotomy, Neurotomy, or Facet Rhizotomy for Chronic Cervicothoracic Pain*

   There is no recommendation for or against the use of radiofrequency neurotomy, neurotomy, or facet rhizotomy for the treatment of chronic cervicothoracic pain confirmed with diagnostic blocks, but who do not have radiculopathy and who have failed conservative treatment. (64% panel agreement; 36% of panel agreed with limited indications as indicated below.)

   Indications- Chronic cervicothoracic pain patients without radiculopathy who failed conservative treatments and who have had a confirmed diagnosis by medial branch blocks.(69)

   Frequency/Duration – One procedure might be tried after failure of non-invasive treatments including NSAIDs and a quality exercise program or as a means to help with participation in an active rehabilitation program. There is no recommendation for repeated procedures. It is reasonable to attempt a second lesion after 26 weeks in patients who had greater than 80% improvement in pain from first procedure for the first 8 weeks with a late return of pain.(1184) There is no recommendation for a third or for additional procedures. There is logically a limit as to how many times it is possible to permanently destroy the same nerve.

   Indications for Discontinuation – Resolution of symptoms. If there is no response to the first procedure, there is no evidence that a second lesion will be beneficial.

   Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
   Level of Confidence – Low

2. *Recommendation: Radiofrequency Neurotomy for Cervicogenic Headache*

   Radiofrequency neurotomy is moderately not recommended for the treatment of cervicogenic headache.

   Strength of Evidence- **Moderately Not Recommended, Evidence (B)**
   Level of Confidence - Low

Rationale for Recommendations

A moderate-quality, sham controlled trial evaluating patients with cervical zygapophyseal-joint pain diagnosed with anesthetic blocks, but without any radicular symptoms, showed improvement in pain over a sham procedure at 12 months. However, there were statistically more patients in the sham group involved in litigation over the accident that caused their pain ($p = 0.04$) than in the intervention group.(1184) Thus, even though the study's methodology scores were good, it has a potential fatal flaw or bias. Another moderate-quality study assessing radiofrequency denervation of facet joints C2-C6 for cervicogenic headache (CH) compared to a sham procedure did not have any significant improvements at 12 or 24 months.(1177) A study evaluating radiofrequency versus occipital nerve block did not find any benefit of radiofrequency lesions over nerve block in cervicogenic headache patients.(1185) Studies in the lumbar spine are increasingly suggesting lack of efficacy (1543–1547), including the largest-sized trial that found neurotomy to be ineffective compared with an exercise program for treatment of LBP, SI joint pain, or intervertebral disc pain (1548). The initial study for the cervical spine (1187) suggesting efficacy was small-sized, is now more than 20 years old, and has not been reproduced in a quality study, which is concerning.

As results can be permanent, there should be good evidence of long-term benefit prior to recommending this procedure. Radiofrequency lesioning is invasive, has adverse effects, and is costly. There is evidence of a lack of efficacy for treatment of lumbar pain, thus there is an unreconciled dispute in the literature (ineffective in the lumbar spine, but perhaps some efficacy in the cervical spine). This is not recommended as a first or second line procedure and is recommended only in the setting of participation in an active rehabilitation program in a patient who is motivated to increase his/her daily functioning.

Evidence for the Use of Radiofrequency Neurotomy, Neurotomy, and Facet Rhizotomy
There is 1 high-(1186) and 4 moderate-quality RCTs (1177, 1184, 1185, 1187) incorporated into this analysis.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

radiofrequency neurotomy, neurotomy, facet rhizotomy, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies. to find 369 articles. Of the 369 articles, we reviewed 369 articles and included 11 articles (6 randomized controlled trials and 5 systematic reviews).*

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Wallis 1997 (8.5)	Radiofrequency neurotomy, neurotomy, facet rhizotomy	RCT	Sponsored by the Motor Accident Authority of New South Wales, Australia. No mention of COI.	N = 24 chronic neck pain following and attributed to a motor vehicle accident (duration >3 months); all conventional resources must have been exhausted	Mean age: 46.5±11; 9 males, 8 females.	Active treatment inserting radiofrequency electrode under local anaesthesia and image intensifier guidance, to lie parallel and adjacent to nerves that mediated pain (n = 12) vs. operative, placebo-control equivalent radiofrequency procedure performed exactly as for active treatment except under double-blind conditions, no radiofrequency current delivered to patient (n = 20).	Baseline and 3 months.	Median change in SCL-90-R subscale scores for pain free patients vs. those still in pain: Global Severity Index: 0.30 vs. -0.02; p = 0.008. Obsessive-compulsive: 0.40 vs. -0.05; p = 0.002.	"[P]sychological distress exhibited by these patients was a consequence of the chronic somatic pain."	Pain a result of MVA and patients had tried and failed "conservative therapy." Main outcome was to see the relation of pain and psychological distress, not to evaluate if RF therapy worked vs. sham, nevertheless 6/9 RF patients had relief of pain at 3 months compared to 3/8.
Lord 1996a (7.5)	Radiofrequency neurotomy, neurotomy, facet rhizotomy	RCT	Supported by a grant from the Motor Accidents Authority of New South	N = 24 chronic cervical zygapophyseal joint pain	Mean age: 43.5±12; 9 males, 15 females.	Percutaneous radiofrequency neurotomy vs. a sham procedure.	Baseline and 3 months.	Patients included if pain thought from C3-4 to C6-7 required to successfully confirmed pain through 3	Authors found that in patients with chronic cervical zygapophysial-joint pain, percutaneous	Baseline differences in litigation status concerning in this population,

			Wales. No mention of COI.					placebo (saline)-controlled, diagnostic blocks of medial branches of 2 dorsal rami supplying putative joint. Baseline differences in litigation status active treatment (33%) vs. placebo (83.3%). Pain from procedure lasted 13.5 vs. 3.5 days. Median time to return of 50% of pre-op pain 263 days active treatment vs. 8 days in placebo.	radio-frequency neurotomy with multiple lesions of target nerves can provide lasting relief. Baseline demographic data demonstrate differences between two groups (e.g., 33% procedure vs. 83.3% in the sham group involved in litigation).	but authors report having found no differences during analyses. Most patients eligible for this trial excluded due to a lack of relief with confirmatory blocks or due to relief with saline.
Stovner 2004 (7.0)	Radiofrequency neurotomy, neurotomy, facet rhizotomy	RCT	No mention of sponsorship or COI.	N = 12 patients suffering from cervicogenic headache	Mean age: 48; 6 males, 6 females.	Radiofrequency vs. sham.	Baseline, 3 months, 12 months, and 24 months.	Days with headache decreased at 1 month 49% in RF group vs. 30% in sham. At 6 months, no change from baseline in RF, but -16% in sham. At 12 and 24 months, these values were 0% vs. +5% and 0% vs. -50%. Headache intensity showed a similar pattern.	Authors concluded that there is not "much evidence that RF-treatment is a promising procedure for most patients fulfilling purely clinical criteria for CeH. It is of some concern to us that many such patients are treated with facet joint neurotomy, despite lack of robust evidence	Cervical RF done on symptomatic side from C2-C6. There was a sham procedure involving local anesthesia as in treatment group and needle insertion without a lesion being made.

									for a beneficial effect. Since results are so dubious, we would recommend that RF-treatment for CeH is not performed on a routine basis, but is restricted to research protocols."	
Lord 1996b (5.5)	Radiofrequency neurotomy, neurotomy, facet rhizotomy	RCT	Sponsored by a grant from the Motor Accidents Authority of New South Wales. No mention of COI.	N=52 patients with chronic whiplash neck pain.	Mean age: 41±10; 26 males, 42 females.	Cervical zygapophysial joint block: series of local and placebo injections to localize pain.	No mention of follow up.	Group presenting with dominant headache: 50% responded to known local anesthetic at C2-C3 location. Group not responding to C2-C3 and dominant neck pain group: 20/41 satisfied criteria for cervical zygapophysial joint pain below C2-C3 level.	"Cervical zygapophysial joint pain is common among patients with chronic neck pain after whiplash. This nosologic entity has survived challenge with placebo-controlled, diagnostic investigations and has proven to be of major clinical significance."	Lack of details on randomization, allocation, baseline characteristics; 26% withdrawal rate in 1 arm. Study design unclear for total number of subjects randomized; 68 enrolled, 27 screened by symptoms of headache to C2-C3 block. Non-responders plus enrollees with primary symptoms of neck pain received series of blocks, 1st block with local, than

										local or placebo, followed by remaining block (all with 3 blocks).
Jee 2013 (4.5)	Radiofrequency neurotomy, neurotomy, facet rhizotomy	RCT	No mention of sponsorship or COI.	N = 120 patients with radicular pain from cervical spinal stenosis or cervical herniated disk.	Mean age: 57.2; 47 males, 63 females.	Group 1: patients received neural block (lidocaine) guided fluoroscopically (N = 55) vs Group 2: patients received neural block (lidocaine) guided utilizing ultrasound (N =55)	Baseline, 2 and 12 weeks.	Both Group 1 and Group 2 showed improvement in numeric pain scale and neck disability index at 2 and 12 weeks. No statically different variables between both groups at any follow up time.	"In conclusion, intravascular injections were only observed in five cases with the fluoroscopy-guided approach. The ultrasound-approach may aid in identifying atypical vessels at unexpected locations proximal to the intervertebral foramen. Although these advantages may support the utility of the ultrasound-approach, confirmation on the absence of the critical vessels that are small in size still require caution with the current ultrasound technology."	No differences between treatment groups. Methodological details sparse. Excluded participants who had meaningful (>50%) pain decrease or no pain decrease after first treatment.

Haspeslag 2006 (4.0)	Radiofrequency neurotomy, neurotomy, facet rhizotomy	RCT	No mention of sponsorship. No COI.	N = 30 patients with cervicogenic headache	Mean age: 48.3; 8 males, 22 females.	Local injections with steroid vs. anaesthetic.	Baseline, 4, 6, 8, 10, and 12 months.	Changes in VAS scores: (8 weeks/12 months) Group I (30.5/30.2) vs. Group II (32.4/26.8); 8 weeks after initial treatment (T1), 80% in RF-group (Group I) and 66,7% in local injection group (Group II) reported a successful treatment in terms of a positive global perceived effect and/or an VAS reduction of at least 50% compared to initial VAS. Meant no statistically significant difference in success rate between groups.	"We did not find evidence that RF treatment of cervical facet joints and dorsal root ganglion is an effective treatment for patients fulfilling the clinical criteria of cervicogenic headache."	Lack of some study details makes evaluation difficult. Patients were able to receive additional treatments after 8 weeks if the first intervention did not help. They followed up symptoms for 12 months.

DORSAL ROOT GANGLIA RADIOFREQUENCY LESIONING

Radiofrequency lesioning of the dorsal root ganglia has been attempted for treatment of chronic cervical radiculopathy.

Recommendation: Radiofrequency Lesioning for Chronic Cervical Radiculopathy

There is no recommendation for or against radiofrequency lesioning of the dorsal root ganglia for chronic cervical pain with or without radiculopathy.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

A moderate-quality study evaluated 67°C radiofrequency lesion compared to sham therapy. Patients were diagnosed with chronic cervicobrachial pain for at least 1 year with positive diagnostic segmental nerve blocks. Assessment was done at 8 week after a single segmental lesion or sham was conducted. They reported a significant decrease in pain in the intervention group over the sham therapy group ($p < 0.01$). They also reported a higher incidence of adverse effects with the intervention group, including burning nerve pain and hypesthesias.(1188) A moderate-quality study evaluated 67°C radiofrequency lesion compared to 40°C radiofrequency lesion at a single level. The participants had chronic cervicobrachial pain (mean duration 7 plus years) that had failed conservative therapy and had a positive diagnostic block with local anesthetic. They found improvement in both groups, but no statistical difference between the groups. They also reported side effects of neuritis and decreased pinch strength in the treated side.(1189) Thus a small study (n = 20) found some benefit at 8 weeks, with some complications, but a larger study (n = 61) found no benefit at 3 months. If effective despite some significant side effects the duration of relief appears to be too short to justify a recommendation in patients with chronic pain.

Radiofrequency lesioning is invasive, has adverse effects, and is costly. It is not recommended as a first of second line therapy and only in patients who have failed conservative therapy. The patient should be committed to participation in active rehabilitation after the procedure as the pain relief has not been shown to be permanent and there is no evidence for repeated lesioning.

Evidence for the Use of Radiofrequency Lesioning of the Dorsal Root Ganglia

There are 3 moderate-quality RCTs incorporated into this analysis.(1188-1190)

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

Dorsal root ganglia radiofrequency, cervical discectomy, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies*
to find 901 articles. Of the 901 articles, we reviewed 8 articles and included 7 articles (3 randomized controlled trials and 4 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Slappendel 1997 (score=7.5)	Dorsal Root Ganglia Radiofrequency lesioning	RCT	Sponsored by Dutch Ministry of Health. No mention of COI.	N = 61 intractable cervico-brachialgia	Mean age: 45.2 years; 21 males, 40 females	Radiofrequency lesion at a temperature of 67°C for 90 seconds (Group I) vs. radiofrequency lesion at a temperature of 40°C for 90 seconds (Group II or placebo treatment).	8 weeks, 3 months	After 3 months, significant reduction in VAS scores demonstrated both groups. Outcome of treatments identical (VAS reduction: Group I, 1.7; Group II, 1.9; p = 0.001). Group I, VAS reduction of 3 or more in 11/31 (34%) and Group II in 11/29 (38%) of patients. VAS reduction of 2 or more in Group I in 15/31 (47%) and in Group II in 15/29 (51%) of patients.	"This study suggests that treatment with 40°C radiofrequency application of the dorsal root ganglion is equally effective as treatment at 67°C."	Study suggests that treatment with 40°C radiofrequency application of dorsal root ganglion (sham treatment) is equally effective as treatment at 67°C.
van Kleef 1996 (score=7.0)	Dorsal Root Ganglia Radiofrequency lesioning	RCT	No mention of sponsorship or COI.	N = 20 intractable chronic cervico-brachial pain	Mean age: 45.7 years; 8 males, 12 females	Radiofrequency lesion of dorsal root ganglion (10 patients) vs. sham radiofrequency lesion (10 patients).	1 week, 8 weeks	Intervention vs. sham group had improvement in VAS at 8 week follow-up. (p <0.01) No long-term follow up reported.	"Radiofrequency lesions may be considered in the treatment of chronic cervical brachial pain if there is a segmental distribution of nociceptive pain, which does not respond to conservative therapy."	Pain duration at least 1 year with failure of conservative treatment. Follow-up 8 weeks. More adverse effects in treatment group including hypethesias and burning. Each patient had a positive diagnostic segmental nerve block. No long-term follow-up lessens ability to make recommendations. Study suggests RF DRG lesions an option for chronic cervicobrachial pain that has failed conservative therapy and to enable participation in a more active rehab program.

FACET JOINT HYALURONIC ACID INJECTIONS

Facet joint injections with hyaluronic acid are being attempted for treatment of facet degenerative joint disease.(1179, 1191) These injections are analogous to similar injections in the knee and other arthritic joints.

Recommendation: Facet Joint Hyaluronic Acid Injections for Acute, Subacute, or Chronic Cervicothoracic Pain with or with Radicular Pain Syndromes

Facet joint injections with hyaluronic acid are not recommended for acute, subacute, or chronic cervicothoracic pain with or without radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation

There are no sham controlled or quality trials of hyaluronic facet joint injections in cervicothoracic pain. There is one moderate-quality trial evaluating facet hyaluronic facet joint injection compared to steroid facet joint injections that reported some benefit; however, the comparison group has not been shown to be beneficial.(1191) This procedure is invasive, requiring a series of 18 injections performed at 3 levels, so radiation exposure is significant, and is high cost. Additional studies need to be conducted in spinal conditions (see Low Back Disorders guideline).

Evidence for the Use of Facet Joint Hyaluronic Acid Injections

There are 2 high- (1192, 1193) and 1 moderate-quality (1191) RCT incorporated into this analysis. There are 2 low-quality (1194, 1195) RCTs in Appendix 1.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

Zygapophyseal Joint, Facet Joints, Facet Joint injections, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies.*
to find 909 articles. Of the 909 articles, we reviewed 909 articles and included 4 articles (3 randomized controlled trials and 1 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Manchikanti 2008 (score=9.0)	Facet Joint Hyaluronic Acid Injections	RCT	No sponsorship or COI.	N = 120 non-specific cervical facet joint pain (duration ≥6months)	Mean age: 44.5 years; 31 males, 89 females	Group I: medial branch blocks with bupivacaine (n = 60) vs. Group II: consisted of cervical medial branch blocks with bupivacaine and steroid (n = 60).	3, 6, 12 months	Mean±SD pain scores comparing Group 1 vs. Group 2 at 3 months: 3.8±1.0 vs. 3.7±0.9; p = significant difference with baseline values (no p-values given). At 12 months: 3.7±1.2 vs. 3.4±0.9; p = significant difference with baseline values.	"Therapeutic cervical medial branch nerve blocks, with or without steroids, may provide effective management for chronic neck pain of facet joint origin."	Eighty-three percent improvement but no change in opioid intake, slight improvement in employment status. Not placebo control for MBB. Data suggest lack of efficacy of steroid.
Barnsley 1994 (score=8.5)	Facet Joint Hyaluronic Acid Injections	RCT	Sponsored by grant from Motor Accidents Authority of New South Wales. No mention of COI.	N = 41 chronic cervical pain thought from C2-3 through C6-7 joint(s) after motor vehicle crashes	Mean age: 43 years; 16 males, 25 females	Compared intraarticular injection of 0.5% bupivacaine vs. betamethasone 5.7mg.	2, 12 weeks, 20 weeks	A joint identified as sole source of neck pain after a median of 3 blocks, randomly selected to receive either 2% lidocaine or 0.5% bupivacaine; not told which agent administered. (Details of initial randomization trial somewhat sparse as not main thrust of study. However, authors did note there was an independent observer to assess effects). One cervical zygapophysial joint was felt responsible for sole source of neck pain in 27/42 (64.3%) of patients. A double-blind RCT then	Authors concluded that "intraarticular injection of betamethasone is not effective therapy for pain in cervical zygapophysial joints after whiplash injury."	Data suggest lack of efficacy.

								conducted on primary joint in each patient. Median time for return of 50% of more pain was 3 days in corticosteroid group vs. 3.5 days in bupivacaine group. Less than 20% had substantial pain relief after 1 month.		
Fuchs 2005 (score=7.0)	Facet Joint Hyaluronic Acid Injections	RCT	No mention of sponsorship. No COI.	N = 60 chronic non-radicular lumbar pain	Mean age: 65.4 years; 18 males, 42 females	Weekly, tri-level, bilateral injections of hyaluronic acid vs. triamcinolone acetonide under CT guidance.	3, 6 months	Chronic LBP of at least 3 months and x-ray evidence of facet joint degenerative joint disease. VAS scores decreased 69.2±14.2mm to 38.0±26.5mm at 6 months (45.1%) in hyaluronic acid group. In triamcinolone group, decreased 68.7±11.5 to 33.4±20.7 (56.2%). Oswestry scores decreased for hyaluronic acid and triamcinolone groups.	Authors concluded that intraarticular sodium hyaluronate is a promising new option for treating patients with chronic nonradicular lumbar symptoms. "Graphic representations suggest there are no meaningful differences in efficacy between the two injections."	Article states that patients received 6 injections, however 3 bilateral levels with weekly injections for 3 weeks is 18 injections per subject.
Park 2012 (score=3.0)										Lack of study details for randomization, allocation, concealment, compliance to intervention, blinding.
Hinderaker 1995 (score=2.0)										Controls not randomized, were "last patients to

										enter" study. Different areas injected based on clinical presentation. No mention of co-interventions. No baseline characteristics given, however patients received both lidocaine and bupivacaine, dosages not mentioned.

Intrathecal Drugs

See Low Back Disorders Guideline.

INTRADISCAL ELECTROTHERMAL THERAPY (IDET)

Intradiscal electrothermal therapy (IDET) involves the heating of an intradiscal probe through electrical current. The goal is to coagulate tissue and theoretically result in improvement in pain thought to be derived from the disc or surrounding structures.(1196, 1197) Techniques have not been standardized.

Recommendation: Intradiscal Electrothermal Therapy for Acute, Subacute, or Chronic Cervicothoracic Pain with or with Radicular Pain Syndromes

Intradiscal electrothermal therapy is not recommended for acute, subacute, or chronic cervicothoracic pain with or without radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

There are no sham controlled or quality trials of intradiscal electrothermal therapy in cervicothoracic pain. In low back pain there are two high-quality RCTs (1198, 1199) that unequivocally conflict regarding whether IDET has any value in treating chronic low back pain. IDET has not been clearly shown to be beneficial. It is costly and invasive, although it may have a relatively low complication rate.(1200) Thus, there is not adequate evidence to recommend this procedure for any spinal indication (see Low Back Disorders guideline).

Evidence for the Use of Intradiscal Electrothermal Therapy (IDET)

There are no quality studies incorporated into this analysis.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:Intradiscal electrothermal therapy, IDET ; cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies.*

to find 1398 articles. Of the 1398 articles, we reviewed 1398 articles and included 0 articles (0 randomized controlled trials and 0 systematic reviews).

PERCUTANEOUS INTRADISCAL RADIOFREQUENCY THERMOCOAGULATION (PIRFT)

Percutaneous intradiscal radiofrequency thermocoagulation involves the same principle as that of IDET; however, the heating of an intradiscal probe is through radiofrequency instead of electrical current.(1201) The theoretical mechanisms of efficacy are essentially the same as for IDET.

Recommendation: Percutaneous Intradiscal Radiofrequency Thermocoagulation for Acute, Subacute, or Chronic Cervicothoracic Pain with or without Radicular Pain Syndromes

Percutaneous intradiscal radiofrequency thermocoagulation is not recommended for acute, subacute, or chronic cervicothoracic pain with or without radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

There are no sham controlled or quality trials of percutaneous intradiscal radiofrequency thermocoagulation therapy in cervicothoracic pain. In low back pain, a high-quality trial of 28 patients compared PIRFT versus placebo for

chronic discogenic LBP with at least 50% pain relief on analgesic discography was conducted. At 8 weeks, there were two successes in the sham group and one in the PIRFT group.(1201) A moderate-quality trial compared different lengths of PIRFT (120 versus 360 seconds) and suggested there is no long-term benefit from PIRFT(1202) (see Low Back Disorders guideline).

Evidence for the Use of PIRFT

There are no quality studies incorporated into this analysis.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

percutaneous intradiscal radiofrequency thermocoagulation, PIRFT, intradiscal annulopathy, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies.*
to find 1074 articles. Of the 1074 articles, we reviewed 1074 articles and included 0 articles (0 randomized controlled trials and 0 systematic reviews).

PROLOTHERAPY INJECTIONS

Prolotherapy involves repeated injections of irritating, osmotic, and chemotactic agents (e.g. dextrose, glucose, glycerin, zinc sulphate, phenol, guaiacol, etc.), combined with an injectable anesthetic agent to reduce pain, into back structures, especially ligaments. The theory is that the injections will stimulate a healing response and thus strengthen the tissues.(1203-1206) A retrospective case series found prolotherapy to improve pain and disability in patients with chronic spinal pain.(1207)

Recommendation: Prolotherapy Injections for Acute, Subacute, or Chronic Cervicothoracic Pain with or without Radicular Pain Syndromes

Prolotherapy injections are not recommended for acute, subacute, or chronic cervicothoracic pain with or without radicular pain syndromes.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation

There are no sham controlled or quality trials of prolotherapy injections in cervicothoracic pain. In low back pain the highest quality trial reported no benefit of prolotherapy injections (1203) (see Low Back Disorders guideline).

Evidence for the Use of Prolotherapy Injections

There are no quality studies incorporated into this analysis.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:proliferation therapy, regenerative injection therapy, proliferative injection therapy, prolotherapy injections, prolotherapy injection, prolotherapy, postop, postoperative, postoperative, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies*
to find 1103 articles. Of the 1103 articles, we reviewed 1103 articles and included 3 articles (0 randomized controlled trials and 1 systematic reviews).

TRIGGER POINT INJECTIONS
See Shoulder Disorders guideline.

Surgical Considerations. . . . . .

This guideline will address only the non-emergent surgical treatment of the most common acute, subacute, and chronic neck and thoracic spine problems. The indications for emergent surgery for red flag conditions including acute spinal cord compression (myelopathy), unstable fractures, epidural abscess, or hematoma, etc., will not be discussed, as treatment of these conditions is outside the scope of these guidelines, as are other indications for surgery (e.g., neoplasms). Early recognition of red flag conditions that require expedited referral to a surgeon qualified to deal with spine emergencies is recommended (see Red Flags).

Within the first 3 months after onset of acute neck or thoracic spine symptoms, surgery is considered for serious spinal pathology, nerve root compression not responsive to an adequate trial of conservative therapy generally considered to require at least 6 weeks, or the development of a documented, progressive neurological deficit. Disc herniation, characterized by protrusion (or extrusion, which is also referred to as a "free fragment") of the central nucleus pulposus through a defect in the outer annulus fibrosus, may impinge on a nerve root typically causing mostly referred shoulder and arm symptoms accompanied by nerve root dysfunction. However, the presence of a herniated disc on an imaging study is common and in isolation, does not imply nerve root dysfunction.(1208) Studies of asymptomatic adults commonly demonstrate intervertebral disc protrusions that apparently do not cause symptoms. Many middle aged individuals with radiculopathy have nerve root syndromes due to a combination of disc protrusion and degenerative osteophytes ("disc-osteophyte complex"). One key feature associated with the development of neurological impingements, including spinal stenosis particularly with myelopathy, is having a congenitally narrow cervical spinal canal diameter.

Studies have strongly suggested spontaneous disc resorption without surgery in the lumbar spine (348) (A retrospective case series suggested most thoracic herniations, while rare, also do not require surgery.(1209)) Many patients with strong clinical findings of nerve root compression due to disc herniation and/or spinal stenosis recover activity tolerance within 1 month. There is no quality evidence that delaying surgery for this period worsens outcomes in the absence of progressive nerve root compromise. With or without surgery, most patients with apparent surgical indications eventually recover to their pre-morbid activity level, (512) including those with severe initial presenting signs of neurological compromise. Spine surgery for patients with clear indications appears to speed short- to mid-term recovery (see Low Back Disorders guideline). However, spine surgery also statistically increases the risk for future spine procedures with higher complication rates. In older patients (1210) and repeat procedures, the success rate is lower and rate of complications is higher. Patients with comorbid conditions such as smoking, cardiac or respiratory disease, diabetes, or mental illness, may be poorer candidates for surgery.(1211-1213) Comorbidity should be weighed and discussed carefully with the patient.

Therefore, referral for surgical consultation is recommended for patients who have the following:

- Severe and disabling arm or shoulder symptoms ("brachalgia") referred from the neck (radiculopathy) in a distribution consistent with nerve root compression on imaging studies, preferably with accompanying objective signs of neural compromise; *and*
- Activity limitations due to radiating brachalgia pain for more than 6 weeks; (361-364) *and*
- Imaging evidence of a lesion (disc herniation, spinal stenosis, spondylolisthesis) with clear clinical correlation to the patient's symptoms and physical findings (at the correct level and on the correct side); (361-364) *and*
- Failure of time and an adequate trial of conservative treatment to resolve disabling radicular symptoms; (361-364) *or*
- Evidence of chronic spinal cord compression (myelopathy) by physical exam, or bowel or bladder control symptoms/studies, with imaging evidence of spinal cord compression; *or*
- Documented progressive neurologic deficit, particularly motor loss.

If surgery is a consideration, counseling regarding likely outcomes, risks, and benefits and especially expectations is important. Patients with cervical pain/headache alone, without findings of serious spinal pathology (such as tumor, fracture, infection, hematoma), rarely derive benefit from surgery, although a second opinion from a spine surgeon to the effect that surgery is not recommended and is unlikely to be helpful may be reassuring to the patient.

Before surgery, physicians may consider referral for psychological evaluation to improve surgical outcomes, including evaluation for predictive variables.(57, 1214-1216) In addition, physicians may look for non-organic signs (similar to Waddell's non-organic signs in the lumbar spine) during the physical exam.(121)

CERVICAL AND THORACIC NERVE ROOT DECOMPRESSION

Cervical nerve root decompression is performed for symptomatic nerve roots compression by disc herniation and/or spinal stenosis.(361-364, 512) Thoracic nerve root decompression is an infrequent condition and surgery is rarely required. A population based study found very low rates of thoracic spine surgery in Japan.(1217) A retrospective case series found few thoracic spine cases.(1218) A retrospective case series suggested most thoracic herniations, while anatomically common (64) but clinically rare, also do not require surgery.(1209) Direct methods of nerve root decompression include standard open discectomy, laminotomy/foramenotomy, facetectomy, and laminectomy.

The number of different surgical procedures performed for cervical spine disorders has increased with time. Well designed, high-quality randomized controlled clinical trials with sufficient follow-up time are mostly unavailable [comparisons with sham procedures, no treatment groups, non-operative treatment, or comparisons between surgical procedures (see evidence table;(512)]. Thus, the overall quality of the literature limits robust conclusions regarding appropriate procedures for cervical disorders with radiculopathy or myelopathy. The increased variety of procedures to address the same diagnosis suggests quality trials are strongly needed to assist in better defining specific procedures for particular patients.

DISCECTOMY, MICRODISCECTOMY, SEQUESTRECTOMY, ENDOSCOPIC DECOMPRESSION

There are multiple surgical techniques that have been used to surgically relieve pressure on cervical nerve roots causing radicular pain syndromes, and these largely parallel studies of the lumbosacral spine. These include open anterior (361-364, 1219, 1220) or posterior discectomy (with or without microscope), (1221-1225) sequestrectomy, and foramenotomy. Additional techniques include percutaneous laser disc ablation or decompression, (1226-1232) automated percutaneous discectomies (also known as nucleoplasty), (1233-1236) and disc coblation.(400, 1237, 1238)

The same surgical approaches are also sometimes used to address less common spinal pathology (e.g., facet joint arthropathy with consequent nerve root impingement). This section reviews the indications for discectomy for a herniated cervical disc.

In contrast with the lumbar spine, cervical discectomy has been frequently combined with fusion as an initial surgical approach, (410, 1239-1241) although more recently, endoscopic approaches are being increasingly utilized.(1242) Cervical discectomy with fusion with allografts and plate fixation has been advocated for treatment with comparable clinical outcomes, but no iliac crest morbidity.(1240, 1243) Use of polyetheretherketone (PEEK Cages with demineralized bone matrix) has been used to produce fusion without the need for harvesting an iliac crest bone graft.(1244-1246) Similary, use of an anterior cervical plate yields a very high rate of fusion. Some particularly advocate a combined discectomy plus fusion approach for 'hard" disc (osteophyte) disease, or degenerative changes with osteophytes where discectomy is felt to be insufficient to relieve neurological impingement. Nevertheless, posterior discectomy alone for either soft or hard discs continues to be performed and has been found to have shorter operative times, hospital stays, and work absences, but no difference in arm pain relief or anatomical fusion compared with discectomy with fusion.(361-364, 1247, 1248) Patients treated with isolated anterior discectomy without fusion have similar relief of arm pain compared to patients treated with anterior cervical discectomy and fusion, but they have more severe and more prolonged cervical pain. Thus anterior discectomy without fusion is now uncommonly performed.

1. *Recommendation: Cervical Discectomy for Subacute or Chronic Radiculopathy*
   Cervical discectomy is recommended to speed recovery in patients with subacute or chronic radiculopathy due to ongoing nerve root compression who continue to have significant pain and

functional limitation after at least 6 weeks of time and appropriate non-operative therapy.(361-364, 1242, 1249-1251) Patients who are candidates for discectomy should be informed that (other than rare cases with significant and/or progressive neurological deficit or surgical emergencies), there is evidence there is no need to rush surgical decisions as there appear to be no differences in long-term functional recovery whether the surgery is performed early or delayed. Open discectomy, microdiscectomy, and endoscopic discectomy are all potentially appropriate ways to perform discectomy. The decision as to whether to use an anterior or a posterior approach, and what technique to achieve a fusion (which procedure to choose) should be left to the surgeon and the patient until quality evidence becomes available to provide evidence-based guidance. **Percutaneous discectomy (nucleoplasty), laser discectomy, and disc coblation are discussed in recommendation #4.**

Indications **–** All of the following present: 1) radicular pain syndrome with current dermatomal pain and/or numbness, or myotomal muscle weakness, or ongoing denervation changes by needle EMG consistent with radiculopathy from a herniated disc; 2) imaging findings by MRI, or CT with or without myelography, that confirm persisting nerve root compression at the level and on the side predicted by the history and clinical examination; and 3) continued significant pain and functional limitation after at least 6 weeks of time and appropriate non-operative treatment.(361-364, 1242)

Benefits – Earlier pain relief
Harms **–** Operative complications that very rarely include severe adverse effects or fatality comparable with other moderate surgical procedures.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence –High

2. Recommendation: Cervical Discectomy for Acute Radiculopathy
Cervical discectomy is not recommended for acute radiculopathy (under 4 week's duration) unless objective evidence of a progressive neurological deficit or myelopathy is present. Sufficient time for natural resolution and non-operative therapy is required. The excellent outcomes reported in the quality studies strongly suggest there is no need to rush surgery other than surgical emergencies.(361-364)

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

3. Recommendation: Discectomy for Acute, Subacute, or Chronic Cervical or Thoracic Spine Pain without Radiculopathy
Discectomy is not recommended for treatment of acute, subacute, or chronic cervical pain or thoracic pain without radiculopathy.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – High

4. Recommendation: Alternative Forms of Discectomy for Cervical or Thoracic Radicular Pain Syndrome
Percutaneous discectomy (nucleoplasty), laser discectomy, and disc coblation therapy are not recommended as treatment for any spine or radicular pain syndrome.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendations
There are no quality studies comparing discectomy with non-operative treatment, and non-operative resolution demonstrably occurs.(348, 1252, 1253) There are many methodological weaknesses in the existing literature, (1239) and not one single high-quality study has been identified for this area (see evidence table). The rapid pace of change in surgical technique and technologies has added additional major hurdles to have sufficient moderate- to high-quality studies that are technologically current. This literature analysis found most trials have major methodological issues generally including failures to report details on randomization processes, few data for evaluating between group baseline differences, lack of blinded assessors, nearly universal absence of recognition or controls on co-interventions, and some including lack of detailed reporting of dropout rates.

The available literature demonstrates moderate quality evidence of short to longer-term efficacy of nerve root decompression surgery for patients with radicular symptoms from disc herniation insufficiently responsive to non-operative treatment.(361-364, 1212, 1242, 1249-1251) Demonstrated favorable outcomes include marked improvements in radicular pain and work capacity.(361-364, 1249) Radicular pain due to a herniated intervertebral disc that does not decrease over a period of at least 6 weeks is thus considered a surgical indication for open discectomy and microdiscectomy.(361-364) However, because up to 75% of patients with radicular symptoms from herniated lumbar discs may become minimally symptomatic or asymptomatic without surgical intervention and there is no strong rationale or quality evidence of significant differences between the lumbar and cervical or thoracic spine, it is important to allow sufficient time to pass prior to consideration of surgery. (A population-based study found very low rates of thoracic spine surgery in Japan.(1217) A retrospective case series found few thoracic spine cases.(1218) A retrospective case series suggested most thoracic herniations, while rare, also do not require surgery (1209). Also, the evidence is strong that there is no need to rush patients into spine surgery in the absence of progressive neurological deficit, surgical emergencies, and catastrophic situations, as there is no quality evidence of differences in functional recovery whether the surgery is early or delayed, and there is quality evidence of spontaneous recoveries.(512) Discectomy is invasive, has complications and adverse effects (failure to improve, hoarseness, tongue paralysis, swallowing difficulty, Horner's syndrome esophageal perforation and fistulae, spinal cord/root injury, and vertebral artery injury) (1239, 1254) and is costly; however in select patients, surgery is recommended.

The rare patient with muscle weakness or sensory deficit that gets progressively worse over serial physical examinations is a potential candidate for relatively immediate discectomy.(361-364) Upper extremity muscle weakness and sensory deficits that do not change on serial physical examination are not absolute indications for discectomy as the prognosis for recovery of strength and sensation depends of many factors other than surgery. While non-progressive weakness and sensory deficit are not absolute indications for surgery, many patients with significant functional impairment from cervical radiculopathy who have weakness and/or sensory deficit are candidates for discectomy.(361-364)

5. *Recommendation: Thoracic Discectomy for Subacute or Chronic Radiculopathy*
   Thoracic discectomy is recommended for treatment of patients with ongoing nerve root compression who continue to have significant pain and functional limitation after at least 3 months of time and appropriate non-operative therapy. The decision as to which type of discectomy procedure to perform should be left to the surgeon and the patient until quality evidence becomes available to provide evidence-based guidance.

   Indications – All of the following present: 1) radicular pain syndrome with current dermatomal pain and/or numbness consistent with a herniated disc; 2) imaging findings by MRI, or CT with or without myelography that confirm persisting nerve root compression at the level and on the side predicted by the history and clinical examination; and 3) continued significant pain and functional limitation after at least 3 months of time and appropriate non-operative treatment.

   Strength of Evidence – **Recommended, Insufficient Evidence (I)**
   Level of Confidence – Low

Rationale for Recommendation
There are no quality studies on treatment of symptomatic herniated thoracic discs. However, the same indications are believed to be necessary for treatment of patients with these relatively less common issues. There is no significant muscle weakness problem with thoracic disc herniations. The issues are pain, and potentially spinal cord compression with leg spasticity and ataxia, and bowel or bladder control impairment. The current literature does not permit a conclusion that open discectomy, microdiscectomy, or endoscopic discectomy should be the preferred procedure as there are no quality comparative trials for treatment of the cervical or thoracic spine. There is no quality evidence that automated percutaneous discectomy, laser discectomy, or coblation therapy is an effective treatment for any cervical or thoracic spine problem. There are no quality studies for this issue, which is relative uncommon. Patients who are candidates for discectomy should be informed that (other than likely for progressive neurological deficits and the rare progressive major neurologic deficit), there is evidence that there is no need to

rush surgical decisions. The decision as to which type of discectomy procedure to perform should be left to the surgeon and the patient until quality evidence becomes available to provide evidence-based guidance.

Evidence for the Use of Discectomy, Microdiscectomy, Sequestrectomy and Endoscopic Decompression
There are 17 moderate-quality (361-364, 860, 1223, 1224, 1242, 1249-1251, 1255-1260) RCTs incorporated into this analysis. There are 27 low-quality (643, 865, 1261-1285) RCTs and 4 other studies (1286-1289) in Appendix 1.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

discectomy, microdiscectomy, microdiskectomy, micordiscetomies, microdiskectomies, sequestrectomy, sequestrectomies, endoscopy, endoscopic, decompression, endoscopic decompression, endoscopic decompressions, 'diskectomy, percutanenous', percutaneous diskectomy, percutaneous, nerve root decompression, nerve root decompressions, nerve root, thoracic discectomy, thoracic discectomies, thoracic diskectomies, thoracic, diskectomy, spinal fusion, autologous platelet gel, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies.*
to find 3437 articles. Of the 3437 articles, we reviewed 3437 articles and included 74 articles (61 randomized controlled trials and 12 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Hauerber 2008 (6.5)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopic Decompression	RCT	No sponsorship. No COI.	N = 86 with 1-nerve root level C4-T1 over at least 6 weeks	Median Age: 45; 43 males, 43 females.	Discectomy vs. discectomy plus interbody fusion with titanium cage.	Baseline, 2 years.	Duration of surgery longer for fusion (median 60 vs. 55 minutes, p = 0.05). Subjective assessment of "Full" recovery (3/12/24 months): fusion 15/39 (38.5%) vs. discectomy 19/46 (41.3%, p = 0.25)/48.6% vs. 40.5% (p = 0.06)/41.7% vs. 34.9% (p = 0.62). Neck pain NS. Radiological fusion at 2 years for 83.3% vs. 81.0%. Return to work 33.3% vs. 50.0%/27.5% vs. 46.0%/27.5% vs. 43.5% (all p >0.16).	"[N]o statistically significant difference between simple discectomy and discectomy followed by interbody fusion with a titanium cage in the surgical treatment of cervical radiculopathy caused by disc herniation."	Claims to have included hard and soft herniation, but no data provided. No difference in radiological fusion at 2 years. Suggests fusion does not add to discectomy for simple, 1-level radiculopathy.
Wirth 2000 (5.5)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopic Decompression	RCT	No mention of sponsorship or COI.	N=72 unilateral C-radiculopathy	No specifics on age or sex. Only specified that all groups had similar demographics.	Posterior cervical foraminotomy vs. ACD vs. ACDF	Baseline, 1 day, 2 months, ave. 60 month phone interview.	Pain improvement in all groups at day 1. Pain improvement at 2months 100% vs. 100% vs.96% (NS). RTW at 2 months 91% FOR vs. 88% ACD vs. 92% ACDF (NS). 60	"All three of the procedures were successful for treatment of cervical radiculopathy caused by a herniated cervical disc. Although the numbers in this study were	Some baseline differences. Suggest procedures comparable, although likely underpowered.

								months follow-up phone call working status FOR 79% vs. ACD 92% vs. ACDF 81%. Total reoperations 27% vs. 12% vs. 28%.	small, none of the procedures could be considered superior to the others."	
Hisey 2014 (5.5)	Discectom, Microdisc ectomy, Sequestrec tomy, Endoscopi c Decompre ssion	RCT	No mention of sponsorship. Multiple authors have stock or hold patents in Mobi-C or LDR spine products.	N=222 patients with diagnosis of degenerative disc disease (DDD) with radiculopath y or myeloradicul opathy from C3 to C7.	Mean age: 43.67; 114 males, 131 females.	Group 1: patients received ProDisc-C cervical total disc replacement (TDR) (n=164) vs. Group 2: patients received anterior cervical discectomy and fusion (n=81).	Baseline, 6 weeks, 3, 6, 12, 18, and 24 months.	Group 1 vs group 2, success rate; 6 months: 75% vs 41.4% (p=0.0021). Group 1 showed greater improvements in Neck Disability Index at 6 weeks (p=0.0141) and 3 months (p=0.0026).	"This prospective, randomized trial comparing TDR to fusion showed that the TDR is a viable alternative to ACDF, with some advantages in early recovery and potentially some advantage to reduce adjacent segment degeneration."	This is a non-inferiority 2:1 study comparing TDR to ACDF which showed comparable efficacy at 12 months and 24 month, radiography shows increased adjacent level disc disease in ACD7 compared to TDR. ($p<0.05$)
Davis 2013 (Score=5.0)	Discectom, Microdisc ectomy, Sequestrec tomy, Endoscopi c Decompre ssion	RCT	Sponsored by LDR medical. One or more of the authors have received or will receive benefits for personal or professional use.	N=330 patients with diagnosis of intractable symptomatic cervical degenerative disc disease.	Mean age: 45.6 years; 158 males, 172 females.	Mobi-C group: patients received the Mobi-C cervical artificial total disc replacement (n=225) vs. ACDF group: patients received anterior cervical	Follow-up at baseline, 3, 6, 12 and 24 months.	VAS neck and arm pain scores improved in both groups ($p<0.0001$). TDR group (VAS=54±25) indicated higher improvement in VAS neck pain score than that in the ACDF group (VAS=53±25), and group difference was	"These results continue to support the use of cervical arthroplasty in general, but specifically demonstrate the advantages of 2-level arthroplasty over 2-level ACDF."	A 2:1 matched study showing similar efficacy study showed some advantages of Mobi-C over ACDF in terms of fewer numbers of reoperations.

						discectomy and fusion (n=105).		statistically significant at 3-month and 6-month follow-up period (p<0.05).		
Zigler 2013 (Score=5.0)	Discectom, Microdisc ectomy, Sequestrec tomy, Endoscopi c Decompre ssion	RCT. Post-hoc analysis of Murrey 2009.	Sponsored by Synthes funds. No mention of COI.	N=209 patients with symptomatic cervical disc disease.	Mean age: 42.8 years; 95 males, 114 females.	ProDisc-C group: patients received ProDisc-C cervical total disc replacement (n=103) vs. ACDF group: patients received anterior cervical discectomy and fusion (n=106).	Follow-up at baseline, 2, 5, and 7 years.	ProDisc-C group showed higher improvement rate of neck and arm pain than that in ACDF group (p=0.0112 vs. p=0.0263), and the group difference was statistically significant.	"Five-year results show that TDR with ProDisc-C is a safe and effective treatment of single-level symptomatic cervical disc disease. Clinical outcomes were comparable with ACDF."	Follow-up for 5 years of prior report. Significant differences between treatment groups at 5 years for neck VAS scores, favoring ProDisc-C. But no difference in disability scores or arm VAS scores.
Van den Bent 1996 (5.0)	Discectom y, Microdisc ectomy, Sequestrec tomy, Endoscopi c Decompre ssion	RCT	No mention of sponsorship or COI.	N = 81 cervical radicular syndrome without response to conservative treatment	Mean age: 47.5 years; 53 males, 28 females.	Discectomy only (n = 39) vs. discectomy with insertion of polymethyl-methacrylate (n = 42).	Follow-up at baseline, 2 years.	Good clinical outcome in 70% PMM vs. 77% discectomy (NS). Better relief of neck pain if neck pain before surgery in PMM group (p=0.04). Bony union in 63% discectomy vs. 28% PMM (p<0.005).	"No relevant clinical differences between treatments were found. Based on these results, the use of polymethacrylat e to obtain fusion after anterior discectomy is not recommended."	Baseline more severe neck pain in PMM group may invalidate conclusions. Data suggest radiological fusion may not be well related to clinical outcomes.
Kim 2009 (4.5)	Discecto my, Microdisc ectomy, Sequestrec tomy,	RCT	No mention of sponsorship or COI.	N = 41 cervical radiculopath y with foraminal stenosis or	Mean age: 54.3; 26 males, 15 females.	Open foraminotomy plus discectomy vs. Tubular retractor	Baseline, 1 days, 5 days, 1 month, 3 months, 6 months, 1	Excellent results for 57.9% non-vs. 59.1% tubular retractor assisted procedures. Post-	"TAF/TAFD is a minimally invasive procedure using a tubular	Data suggest use of retractors reduced hospital stay, post-op analgesics and patients had less

	Endoscopic Decompression			C-posterolateral disc herniation and >6 weeks conservative care		assisted foraminotomy plus discectomy	year, 2 years.	operative transverse and vertical foramen diameters identical. Less neck pain days 1, 5, 4 wks in the retractor group ($p<0.05$). Hospital stay 6.7±2.1 vs. 4.1±1.7 days, $p<0.05$. Less post-operative analgesia time at 3.6 vs. 2.6 weeks, $p<0.05$.	retractor system, which allows for a smaller skin incision and far less muscle injury. It also reduces the amount of postoperative discomfort and shortens the length of hospital stays and the postoperative analgesic using time."	neck pain for 4 weeks after surgery. Lack of details. Small sample. Korean population. Suggests no long-term differences in outcomes between 2 procedures, but may have short-term benefit in reducing hospital stay and duration of analgesic.
Xie 2007 (4.5)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopic Decompression	RCT	No mention of sponsorship or COI.	N = 45 cervical radiculopathy at least 6 weeks, C4-T1	Mean age: 42.3±8; 28 males, 14 females.	Discectomy vs. discectomy with fusion (Aspen collar for 3 months) vs. Discectomy with fusion and Codman Plate. Iliac crest grafts used. 2 year follow-up.	Baseline, 3 and 6 weeks, 3 and 6 months, 1 and 2 years.	No clinical differences in any outcome at any time interval (see Figure 3). Fusion in 67% vs. 93% vs. 100% ($p<0.05$).	"Neither ACD, ACDF, nor ACDFI provide any advantage to the patient in terms of symptomatic relief; all three procedures result in excellent pain relief immediately postoperatively and continuing throughout a 2-year follow-up period."	Some baseline differences. Author statement that patient selection is key not tested by design; 75% of ACD patients post-op vs. 17% pre-op had kyphosis vs. ACDF patients with or without instrumentation had no changes in sagittal balance. Suggests no difference in outcomes.
Savolaine 1998 (4.5)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopi	RCT	No mention of sponsorship or COI.	N = 91 "long lasting" 1 level C-radiculopathy from soft or hard disc. C3-T1	Mean age: 47.8 years; 63 males, 28 females.	Discectomy (n=31) vs. Discectomy with fusion (Smith-Robinson) (n=30) vs.	Follow-up at baseline, 4 years.	"Good" surgical outcomes at 6 months/2 years in 67/76% discectomy vs. 70/82% discectomy plus	"[S]atisfactory results can be achieved by performing simple discectomy to treat single level	Baseline duration of symptoms unclear. Data suggest no benefits of fusion over discectomy for 1-

	c Decompression					Discectomy with fusion plus plating (Caspar) (n=30).		fusion vs. 77/73% plating (NS). Bony fusion in 100% fusion groups and 90% discectomy. Severe iliac crest pain in 24/30 each fusion group; prolonged pain in 5/60 fusion patients combined.	cervical root compressive disease."	level radiculopathy.
Bärlocher 2002 (4.5)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopic Decompression	RCT	No mention of sponsorship or COI.	N = 125 cervico-brachialgia "refractory to nonoperative treatment." C3 to T1; Soft disc herniation with or without osteophytes	Mean age: 50.2 years; 74 males, 51 females.	1) Micro-discectomy (n=33) vs. 2) microdiscectomy with autologous bone graft (n=30) vs. 3) microdiscectomy with polymethyl-methacrylate (n=26) vs. 4) microdiscectomy with titanium cage (n=36). All soft collar for 3 weeks.	Follow-up at baseline, 1 year.	Improvements (%) in neck VAS (2/6/12 months): Group 1 (45.5/53.6/64) vs. 2 (20/53.4/50) vs. 3 (27/58.4/62.5) vs. 4 (47.3/72.3/72.3). Improvements in radicular pain VAS: Group 1 (78.8/78.8/81.9) vs. 2 (66.7/76.7/86.7) vs 3 (88.5/79.2/87.5) vs. 4 (86.2/91.7/97.3). Work incapacity 6/12 months: Group 1 (18.1/12.1) vs. 2 (27.2/16.7) vs. 3 (8.3/4.2) vs. 4 (5.5/2.8) (p <0.05 Groups 1, 2 vs. cage at 6	"[F]usion with interbody cages yields a significantly better short- and intermediate-term outcome than (MDO) in the treatment of single level DDD of the cervical spine in terms of the following parameters: 1) return to work, 2) radicular pain, 3) Odom criteria, and 4) earlier fusion…These results suggest that interbody cage-assisted fusion is a promising therapeutic option in patients with	Randomization process unclear. Some baseline differences. Data suggest microdiscectomy results in faster improvement in neck pain than other groups except cage; however 'work capacity' better in cage group at 6 wks and cage group overall generally trended towards best clinical outcomes.

								months). Odom Excellent/Good at 6/12 months: 72.7/75.5 vs. 66.6/80 vs. 91.6/87.5 vs. 91.6/94.4% (p <0.05 comparing Group 2 to cage). Fusion rates 6/12 months: Group 1 (60.6/93.3) vs. 2 (65.3/93.3) vs. 3 (0/0) vs. 4 (86.1/97.2).	single-level disc disease.	
Oktenoglu 2007 (4.5)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopic Decompression	RCT	No mention of sponsorship or COI.	N = 20 c-radiculopathy patients, C3-C7; at least 2 weeks conservative treatment	Median age: 40 years; 11 males, 9 females.	Anterior cervical microdiscectomy (n=11) vs. anterior cervical microdiscectomy with fusion (n=9). Soft collars for 2 weeks.	Follow-up at baseline, 14 months.	Arm VAS (baseline/postop): ACMD (8.18/3.27) vs. Fusion (8.0/3.11). Neck VAS: ACMD (3.18/2.81) vs. Fusion (3.22/2.0).	"[T]he ACD technique offers satisfactory result with or without fusion where radiculopathy is the major complaint."	Small sample size. Baseline gender difference (4/11 vs. 7/9 males). Variable follow-up period. Blinded assessor. Suggests no differences.
Ruetten 2008 (4.0)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopic Decompression	RCT	The authors declared no sponsorship or COI.	N = 175 C-radiculopathy C2-T1	Mean age: 43 years; 68 males, 132 females.	Endoscopic posterior foraminotomy plus discectomy (n=91) vs. A DF (PEEK cage) (n=84).	Follow-up at baseline, 1 day, 3, 6, 12, and 24 months.	Overall 87.4% had relief of arm pain and 9.2% occasional pain. No differences in clinical outcomes between groups, including VAS arm pain, neck pain, NASS pain, neurology scores. Mean operative time: ACDF 68 minutes v. FPCF 28 minutes, p<0.001. Recurr	"[T]he the full-endoscopic posterior foraminotomy is a sufficient and safe supplement and alternative to conventional procedures when the indication criteria are fulfilled. At the same time, it offers the advantages of a	Pseudorandomization (every other). Sparse details on patients. Data suggest posterior foraminotomy plus discectomy results in the same clinical outcomes but is less invasive. Quasi-randomized. Population is not well described. 2 year follow up. Data suggest

								ences/revisions: NS. VAS scores: NS. Postoperative pain: significantly reduced in FPCF group (no p-value). Mean postoperative work disability: ACDF 34 days v. FPCF 19 days, p<0.01.	minimally invasive intervention."	comparable results.
Rosenorn 1983 (4.0)	Discectomy, Microdiscectomy, Sequestrectomy, Endoscopic Decompression	RCT	No mention of sponsorship or COI.	N = 63 herniated C-disc C3-T1	Mean age: 51.9 years; 40 males, 23 females.	Discectomy without interbody fusion (DE) (n=32) vs. Discectomy with interbody fusion (DEF) (n=31).	Follow-up at baseline, 3 and 12 months.	Clinical condition (excellent plus good): 3 months ACDF 19/31 (61.3%) vs. ACD 28/32 (87.5%). 12-months ACDF 20/29 (69.0%) vs. ACD 27/31 (87.1%).	"The prognosis is significantly better for men than for women after DEF (p<0.005), while no difference can be shown after DE."	Sparse details. Trends of less pain and less sick leave in ACD.
Jackson 2016 (3.5)										5yr follow-up. Non non-surgical control. Data suggest 2nd surgeries in 1-level (4.5 vs 17.3%) and 1-level (7.3-21.0%) favoring disc replacement.
Radcliff 2016 (3.5)										Methodological details sparse.
Bartels 2006 (3.5)										Trial reported in progress. Per initial report will not control well for co-interventions,

										however eventual quality score appears likely to be at least moderate.
Martins 1976 (3.5)										Sparse details. Dropout high at 1 year.
McGuire 1994 (3.5)										Sparse details. Very small numbers in experimental group. Suggests iliac crest autograft superior.
Coric 2006 (3.5)										Sparse details. Suggests disc replacement may be superior to fusion.
Grob 2001 (3.5)										Sparse details. Data suggest minimal differences between groups. Somewhat more fusion in the plated group.
Riina 2008 (3.5)										Small sample size. Sparse details. Data appear to favor disc replacement. Results of both groups declined over time.
Hacker 2005 (3.5)								.		Sparse details. Part of study results reported above

										(Hacker, Sasso, Heller)
Hacker 2009 (3.5)										Details sparse. Some baseline differences. 390 one and 98 2-level procedures, but were not randomized on it. High dropout rate at 2 years. Data suggest does not reduce risk of adjacent disease.
Cho 2005 (3.5)										Somewhat more 2-level disease in Group B, presumably biases in favor of Group A. Shorter hospital stay in A (4.4±2.4 vs. 7.0±3.8, p = 0.001). Data suggest autograft superior to biphasic calcium phosphate ceramic for fusion, but inferior for EBL, operative time and donor site pain. Data suggest slower fusion with calcium phosphate ceramic, but no differences in clinical outcomes.
Phillips 2013 (3.0)										Methodological details sparse. Multiple comparisons without measurement.

										Composite "overall success" outcome was significantly different between groups favoring PCM @ 24 months.
Panchal 2016 (3.0)										No patient demographics presented. Methodological details sparse.
Hacker 2000 (3.0)										Total study population reported in Nabhan J Long Term Eff Med Implants 2007. Data suggest disc replacement not superior for pain relief.
Nabhan 2007 (3.0)										Total study population reported in Nabhan J Long Term Eff Med Implants 2007. Data suggest disc replacement not superior for pain relief.
Phillips 2015 (2.5)										Long term follow up (60 months). Most outcomes, including (???) score significantly better for PCM intervention @ 60 months.
Abd-Alrahman										Many baseline differences, different sizes of groups (50 vs. 40)

1999 (2.5)										suggest randomization failure or not truly randomized. Most variables appear to bias against fusion. Conclusion regarding which patients for discectomy not directly tested. Data suggest no difference but potential bias against fusion in baseline data.
Hwang 2004 (2.5)										Sparse details. Unclear if RCT. Appears to be comparative clinical trial, as group sizes differ and some baseline differences. Variable follow-up periods from 13-28 months.
Sasso 2011 (2.5)										Lack of study details. Allocation unclear. No blinding, no data or co-intervention control, completions rates. Data suggest similar outcomes in alignment and ROM.
Chen 2011 (2.0)										Lack of study details. No comparison of kyphoplasty with other treatments or

										sham limits conclusions of efficacy.
An 1995 (2.0)										Randomization by every other. Compliance with assignment unclear.
Loumeau 2016 (2.0)										Methodological details sparse.

DECOMPRESSIVE SURGERY FOR SPINAL STENOSIS (LAMINOPLASTY, LAMINECTOMY)

Spinal stenosis means insufficient room for neural elements in the spinal canal and/or neural foramina. It can be congenital (e.g., short pedicles) or acquired (degenerative enlargement of facets and ligaments and in addition the formation of osteophytes), or both. Stenosis can be in the central canal, in the lateral recess, or in the neural foramen. These degenerative changes are also referred to as cervical or thoracic spondylosis, although cervical stenosis is a more common term. The typical symptoms of cervical spinal stenosis are radiating pain into one or both upper limbs on movement of the neck. Patients may have symptoms and signs of multiple nerve root impingements, including dermatomal and myotomal findings. When the changes involve the cord and include findings such as spastic gait, ataxia, clonus, atrophy and incontinene, it is termed myelopathy.(335, 1244, 1256, 1290-1293) Cervical spinal stenosis when combined with lumbar stenosis may include symptoms of neurogenic claudication, or leg pain that develops during walking and that is promptly relieved by rest, although those symptoms are more typical of lumbar stenosis.(1294) Acquired cervical and thoracic spondylosis are natural aging phenomena with strong genetic components that may become symptomatic. Decompressive surgery for cervical spinal stenosis is infrequently performed in the US, as decompression combined with fusion is generally performed (see below). Decompressive surgery for thoracic spinal stenosis is infrequently performed due to the relatively uncommon occurrence of this condition, although decompression without fusion is more common in the thoracic spine than cervical spine.

Decompressive surgery for spinal stenosis involves techniques that remove bone from one or more structures to expand a narrowed spinal canal/neural foramen that impinges on neural structures. **Laminoplasty** involves freeing or partially freeing lamina without complete removal of the laminae. (1295-1304) **Foraminotomy** involves surgically opening the nerve root foramen, usually compressed due to degenerative osteophytes and disc changes.(1223) Percutaneous laminoforaminotomy can also be used.(1305) **Laminectomy** refers to the complete removal of the lamina. Unilateral laminotomy was traditionally performed as part of a discectomy, but is not generally performed any longer for sole treatment of cervical radiculopathy due to poorer outcomes in comparative studies, (1306) although not all authors report poor results and a skip laminectomy procedure has been reported.(1298, 1307) Laminectomy with posterior cervical plating has been developed to address the potential instability from laminectomy alone and has been utilized for treatment of posterior longitudinal ligament ossification.(1308) **Hemilaminectomy** refers to removal of the left half or the right half of the lamina. **Facetectomy** is removal of part of or at times all of a facet joint. **Posterior decompression** is a term usually used to include any of the above surgeries for spinal stenosis. **Fusion** is frequently recommended at the same time as a spinal stenosis decompression. The fusion section of these guidelines should be consulted for the indications for spine fusion performed simultaneously with decompression.

Fusion has been more popular in the US and slightly higher rates of success have been reported for fusions compared with laminoplasty.(1306) Anterior cervical discectomy and fusion is the most commonly performed decompression procedure for cervical stenosis in the United States. Laminoplasty has been particularly utilized for neurological compromise thought to be due to ossification of the posterior longitudinal ligament.(1309-1311) Laminoplasty was developed after concerns about instability from laminectomy (1309, 1312) and there are various specific laminoplasty procedures.(1309, 1312) Laminoplasty has also been advocated for treatment of failed ACDF due to inadequate decompression.(1313) It has also been reportedly superior to laminectomy (1296) and long term studies suggest good results.(1314, 1315)

Recommendation: Decompression Surgery for Spinal Stenosis

Decompression surgery is recommended for treatment of patients with symptomatic spinal stenosis that is intractable to non-operative management.

Indications – All of the following should be present: 1) neurogenic symptoms (e.g., upper extremity pain on neck movement, upper or lower limb ataxia, etc.) or objective neurologic deficit from cervical spinal stenosis; 2) imaging findings, by MRI, or CT/myelogram that confirm the nerve roots and/or the spinal cord are compressed consistent with the neurological symptoms; and 3) lack of responsiveness or unsatisfactory response(s) to adequate non-operative treatment over a minimum 6 to 8 week period. (1223) Myelopathic changes are associated with worse outcomes prognoses.

Benefits – Relief of spinal stenosis-related symptoms.
Harms – Rare, but serious complications include infection, paralysis and death.
Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation
There are no quality studies to provide evidence-based guidance on the effectiveness of decompressive surgery for cervical or thoracic spinal stenosis compared with other procedures. Thus, until quality evidence is available, the choice of surgical procedure for symptomatic spinal stenosis is to be decided by the surgeon and patient. One moderate quality study compared laminoplasty with skip laminectomy and found no differences.(1304) Another moderate-quality study found French door laminoplasty modestly superior to open door.(1316) There are no quality studies comparing one type of decompressive surgery with another. These procedures are effective for treatment of the lumbar spine (see Low Back Disorders Guideline). These procedures are invasive, have adverse effects, but may be less invasive than fusion and thus are recommended for select patients (see Fusion below).

Evidence for the Use of Decompressive Surgery for Spinal Stenosis
There are 7 moderate-quality RCTs incorporated into this analysis. (1242, 1304, 1316-1320) There is 1 low-quality RCT(1321) and 2 other studies(1322, 1323) in Appendix 1.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:
: laminectomy, foraminotomy, laminoplasty, facetectomy, decompressive surgery, neck pain, cervicalgia, cervical pain, cervical, radiculopathy, radicular pain, postoperative neck pain, postoperative cervical pain, herniated disk, controlled clinical trial, controlled trails, randomized controlled trial, randomized controlled trials, random allocation, random, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Nonexperimental Studies.*
to find 1155 articles. Of the 1155 articles, we reviewed 1155 articles and included 30 articles (16 randomized controlled trials and 14 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Hida 2017 (Score=5.5)	Collar fixation/ cervical compressiv e myeopathy	RCT	The authors declared no sponsorship or COI.	N=74 patients with cervical compressive myelopathy and had had double-door laminoplasty.	Mean age: 72.7 years; 52 males, 22 females.	CF group: patients received collar (n=39) vs. NC group: patients received no collar (n=35).	Follow-up at 1 year.	The primary outcome of the study VAS score indicated no significant difference between two groups (p=0.487). VAS score in CF group showed no significant improvement before and after surgery (p=0.735), same as that in NC group (p=0.837).	"The VAS scores of cervical pain with the postoperative treatment without collar fixation were not inferior to those when using Philadelphia collars for 2 weeks."	There was no difference between treatment aims at 1 year, suggesting collar not necessary. However, this is not an equivalence trial.
Yukawa 2007 (5.0)	Decompress ive surgery for spinal stenosis	RCT	Sponsored by Japan Labor Health and Welfare Organization. The authors declared no COI.	N = 41 cord compression only at disc levels from C3 to C7.	Mean age: 64.2 years; 13 males, 28 females.	Modified double-door laminoplasty (n = 21) vs. skip laminectomy (n = 20).	Follow-up at baseline, 12, 28, and 48 months.	No significant difference between groups for ROM and recovery rate. Mean VAS scores for Lamino vs. Skip at 1 day/4 weeks/6 months/ final: 50.0±27.4/ 57.8± 22.2, 9.9±14.1/15.0± 11.1, 8.7±13.2/13.8± 12.1, 9.0±10.5/12.2± 10.4. No significant difference between mean VAS scores at each collection time.	"No significant differences were seen between Lamino and Skip groups, in terms of operative invasiveness, axial neck pain, cervical alignment, and ROM, and clinical results in the patients of CSM without developmental stenosis."	Quasi-randomization on birth month. Suggests comparable outcomes.
Kadanka 2000 (5.0)	Decompress ive surgery for spinal stenosis	RCT	Sponsored by Internal Grants Agency of the Ministry of Health of the Czech Republic. No	N=48 with clinical signs and symptoms of mild to moderate Cervical spondylotic myelopathy,	Mean age: 54.3 years; 37 males, 11 females.	Surgical Therapy with anterior decompression + osseous graft in nine patients (n=27) vs.	Follow-up at baseline, 6, 12, and 24 months.	Recovery / Daily activity / Timed 10 m walk / Self-evaluation; (binominal test p<0.05) /	"The current study, comprising patients with no or very slow, insidious progression only, showed, on average, no	Details for randomization, allocation, compliance, control of cointerventions, missing or unclear. Data suggest similar outcomes

			mention of COI.	duration of 6.4 ± 9.9 years.		Conservative The340ssessments340on immobilisation with a soft collar + anti-inflammatory medications + intermittent bed rest if pain is present + active discouragement of high-risk activities) (n=21).		(p<0.05 i“ the cate”ory "no change") / (no statistical significant differences) / (group B at 6-12 and 6-24 months, p<0.05; and between group biominal “est, p<0.05).	significant deterioration in objective parameters (mJOA score, recovery ratio, quantified gait time,) within the two groups during the 2 year” of follow-up."	for both groups. Outcomes measures may not be applicable in US.
Cesaroni 2010 (4.5)	Decompressive surgery for spinal stenosis	RCT	No mention of sponsorship or COI.	N= 115 patients with cervical disc herniation. Patients had neck/arm pain VAS score of >50 on a scale of 0-100.	Mean age: 46.14 years; 48 males, 67 females.	Plasma disc decompression (PDD) (n= 62) vs. Conservative care (CC) (n= 53).	Follow up at baseline, 6 weeks, 3, 6, and 12 months.	VAS pain scores were significantly decreased in PDD compared to CC at 6 weeks, 3-months, 6-months, and 1-year (p<0.0001). Neck disability index scores were significantly decreased in PDD compared to CC at 6-	“We have found PDD to offer improved pain relief as well as superior immediate and longterm gains in functional ability and quality of life when compared to conservative therapies. PDD is a minimally invasive treatment option for symptomatic contained disc herniation that provides an excellent medium for both resu”ts and safety."	Randomization method not well described. Baseline differences in outcomes measures. Compliance data not described. Conservative care measures received not described. Data suggest some benefit in pain relief of measured intervals and mixed improvements in disability index over 1-year follow-up.
Bae 2015 (Score=4.0)	Anterior cervical discectomy and fusion (ACDF)/ total disc replacement	RCT. Secondary analysis of Davis 2013.	The authors declared no sponsorship or COI.	N=575 patients (1-level arm=245, 2-level arm=330) with symptomatic degenerative disc disease.	No mention of mean age or age range; no mention of sex.	TDR group: patients received total disc replacement (n=389; 1-level arm=164 vs. 2-level arm=225) vs. ACDF group: patients	Follow-up at baseline, 6 weeks, 3, 6, 12, 18, 24, 36, and 48 months.	Both 1-level arm and 2-level arm TDR groups indicated statistically significant improvement in VAS arm and neck pain scores (P<0.0001). No	“A 4-year *post hoc* comparison of 1- and 2-level TDR patients concurrently enrolled in a 24-center, Food and Drug Administration Investigation	There are no meaningful difference between treatment arms. All groups improved over time.

						received anterior cervical discectomy and fusion (n=186; 1-level arm=81 vs. 2-level arm=105).		group difference was found between 1-level arm TDR group (VAS neck pain score=52.3±32.8) and 2-level arm TDR group (VAS neck pain score=52.6±30.2).	Device Exemption clinical trial indicated no statistical differences between groups in clinical outcomes, overall complication rates, and subsequent surgery rates."	
Okada 2009 (4.0)	Decompressive surgery for spinal stenosis	RCT	The authors declared no sponsorship or COI.	N = 35 cervical myelopathy from spondylosis, C-disc herniation, and PLL ossification. C1-T1, mostly C3-C7	Mean age: 60.5 years; 23 males, 12 females.	Group A: patients received open-door laminoplasty (n=17) vs. Group B: patients received French-door laminoplasty (n=18).	Follow-up at baseline, 12 months.	Longer op times for French door, but more EBL for open. Japanese Orthopedic Association (JOA) scores: 14.2±1.6 vs. 13.2±2.7 (NS). Recovery rates 52.8±28.1 vs. 42.0±35.4% (NS). Axial pain (pre/post): Open 14.3±31.0/39.8±30.4 vs. 32.0±33.5/26.7±30.4mm. SF36 scores favored French door, with some subscales statistically different.	"JOA scores and recovery rates suggested that both open-door and French-door laminoplasties could be similarly effective in decompressing the spinal cord. Axial pain was improved in French-door laminoplasty but became worse in open-door laminoplasty. SF-36 suggested that French-door laminoplasty could be more beneficial than open-door laminoplasty for patients with cervical compressive myelopathy."	Some details sparse. Modest sample size. Data suggest overall French-door laminoplasty has slightly better results.
Ying 2007 (4.0)	Decompressive surgery for spinal stenosis	RCT	The authors declared no sponsorship or COI.	N = 178 cervical spondylotic myelopathy with 2 or 3 adjacent levels requiring decompression	Mean age: 49 years; 117 males, 61 females.	Corpectomy with preserved posterior vertebral wall vs. conventional corpectomy for 2 or 3 adjacent levels.	Follow-up at baseline, 6 months.	JOA scores (baseline/3/6/12 months): CPW (13.3±3.0/15.0±1.4/15.9±1.0/16.1±0.75) vs. Corpectomy (12.5±3.2/15.2±1.4/ 15.8±0.92/16.3±0.72) (NS). No difference in	"CPW is a feasible procedure for anterior decompression and fusion, with safety, complete decompression, and high fusion rate, as long as indicative patients are selected."	High dropouts. Cage vs. iliac crest graft not controlled. Trend towards more use of cages in corpectomy group (58 vs. 49). No differences between groups in outcomes. No comparison with

								radiographic fusion.		procedures with known success/ complication rates.
Lian 2010 (3.5)										Quasi-randomization (consecutive admissions) lack of method details on blinding. Data suggest no difference in scoring decompression. Significant differences in clinical measures were most likely clinically significant.

SPINAL FUSION

Cervical fusion to treat symptomatic disc herniation (anterior cervical discectomy and fusion) and spinal stenosis are discussed above.(361-364, 512, 1242, 1249-1251, 1324-1335)

Cervical fusion involves the surgical fusion of one or more vertebral segments by inserting bone grafts (with or without instrumentation) so that the previously mobile involved segments heal together to form a single bone mass. A spinal motion segment consists of 2 adjacent vertebrae, the connecting ligaments, 2 facet joints, and the interposed disc– (the occiput - C1 level and the C1-C2 level do not have discs). The proposed goal of cervical fusion is similar to that in fusing other joints in the body – that instability and pain will be improved. However, quality studies document fusion is not a reliable indicator for resolution of pain.(361-364, 512, 1210, 1244, 1249-1251, 1256, 1290-1292, 1336-1355)

There are numerous methodological issues affecting the quality of the literature, particularly on non-radicular cervical pain indications for fusion. These methodological issues impair the ability to draw robust evidence-based conclusions.(1247, 1356) Many of these conflicts likely originate from the problem that case series tend to show benefits while subsequent RCTs may or may not support the original impressions from the uncontrolled or less well designed studies, although not all authors support this supposition.(1357)

Diagnoses for which fusion is felt to be indicated include unstable vertebral fractures, stenosis with myelopathy, recurrent radiculopathy, failed discectomy treatment, surgery for tumor, infection, or other disease processes with spinal motion segment instability. However, some surgeons perform cervical fusion for cases of axial cervical pain without radicular pain, and there are no quality studies identified to support surgery for those patients.(211, 402, 407, 410, 1356, 1358-1360)

1. Recommendation: Cervical Discectomy with Fusion for Chronic Radiculopathy

Cervical discectomy with fusion is recommended for patients with chronic radiculopathy due to ongoing nerve root compression who continue to have significant pain and functional limitation after at least 6 months of time and appropriate non-operative treatment. The decision to use an anterior or posterior approach and what technique to achieve a fusion (which procedure) to use should be left to the surgeon.

Benefits – Reduction in spine and extremity pain and neurological compromise if present.
Harms – Operative complications, rare severe outcomes (e.g., paralysis, fatalities), increased further re-operative risk, cost, increased risk of disability.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence –Moderate

2. Recommendation: Decompression Surgery for Spinal Stenosis/Myelopathy

Decompression with fusion is recommended for treatment of patients with symptomatic spinal stenosis that is intractable to non-operative management. The decision to use an anterior or posterior approach and what technique to achieve a fusion should be left to the surgeon.

Benefits – Reduction in spine and extremity pain and neurological compromise if present.
Harms – Operative complications, rare severe outcomes (e.g., paralysis, fatalities), increased further re-operative risk, cost, increased risk of disability.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence –Moderate

3. *Recommendation: Fusion for Degenerative Spondylolisthesis*

Fusion is recommended for treatment of degenerative spondylolisthesis.
Benefits – Reduction in spine and extremity pain and neurological compromise if present.
Harms – Operative complications, rare severe outcomes (e.g., paralysis, fatalities), increased further re-operative risk, cost, increased risk of disability.

Strength of Evidence – **Recommended, Evidence (C)**
Level of Confidence –Moderate

4. Recommendation: Spinal Fusion with Simultaneous Discectomy

Spinal fusion is recommended as an option at the time of discectomy if a patient is having a simultaneous discectomy on the same disc.

Indications – Meeting indications for a discectomy on the same disc.
Benefits – Theoretical reduced risk of later surgery on the same disc.
Harms – Longer recovery, greater rate of complications, higher costs.

Strength of Evidence – **Recommended, Insufficient Evidence (I)**
Level of Confidence –Low

5. Recommendation: Pulsed Electromagnetic Field Stimulation for Cervical Spine Fusion Patients

Pulsed electromagnetic field stimulation for cervical spine fusion is not recommended as a routine treatment for these patients, including patients with multiple spine fusion levels or in smokers.(1210)

Strength of Evidence – **Not Recommended, Evidence (C)**
Level of Confidence –Low

6. Recommendation: Autologous Platelet Gel for Cervical Spine Fusion Patients

Autologous platelet gel for cervical spine fusion is not recommended.(1354)

Strength of Evidence – **Not Recommended, Evidence (C)**
Level of Confidence –Low

Rationale for Recommendations

There are quality studies on fusion, although most are somewhat handicapped as they have heterogeneous populations of patients and insufficient sample sizes with which to assess differences between diagnostic entities. However, as considerable numbers of subjects often migrate out of the non-operative group assignments, a conclusion that there is no long term difference between surgery and non-operative management is currently unable to be supported with quality data.

There are no RCTs on patients with what are generally accepted as unequivocal indications for cervical fusion surgery such as unstable fracture, spinal infections, or tumors, and none on thoracic spine fusions. There are no quality studies of cervical or thoracic spondylolisthesis which are believed to be relatively uncommon, although there are a few in the lumbar spine. There are no quality RCTs using cervical fusion for either acute, subacute, or chronic non-specific cervical pain. Cervical fusion has been proposed as treatment for spondylolisthesis, disc herniation, spinal stenosis, and chronic non-specific cervical pain (also referred to as degenerative disc disease, discogenic cervical pain, micro instability, black disc disease, and cervical spondylosis).

The available quality studies suggest cervical fusion for radiculopathy results in improvements in arm pain more than cervical pain, because nerve root decompression is done at the time of fusion (see evidence table), thus fusion appears to be an option, although discectomy appears to be equally effective. (361-364, 1242, 1249-1251) One trial suggests fusion did not provide additive benefit to a rehabilitation program (1549). There is no quality evidence to evaluate cervical fusion for persisting upper extremity and/or cervical pain in those who have had a prior discectomy.

Chronic cervical pain patients can be extremely difficult to manage, particularly when the pain is severe, narcotic and other drug issues are present, adherence to exercise regimens is weak, psychosocial stressors are present, and coping skills are poor. Fusion is often viewed as one of the last resort options for treatment of these individuals. Similarly, patients often come to view these surgical procedures as potential cures. However, there are no quality studies documenting improved results with fusion compared with other treatments including non-operative treatments for these patients.

Pulsed electromagnetic field stimulation has been used to increase radiological fusion rates in high risk patients, particularly including fusion of multiple levels or in smokers (who are more likely to have non-unions than are non-smokers).(1210) However, a large, moderate quality study found that while there was increased fusion in these patients at 6 months, there were no differences at 12 months and there were no differences at any point in clinical outcomes, thus this treatment is not recommended. This treatment may still have some value, however the patient

population would seem to be those with an extremely high risk of nonunion where PEMF is thought to be helpful and there is no quality study currently available and supportive among such a small, highly defined patient population.

Autologous platelet gel has been proposed to increase radiological fusion rates in ACDF patients;(1354) however, a moderate quality, double-blinded study found no differences in intermediate to long term fusion rates or clinical outcomes, thus, this treatment is not recommended.

Cervical fusion is among the more invasive of the commonly performed spine surgeries. It is high cost and has significant risks of complications. However, for a select few chronic radicular pain patients, particularly those who have recurrence after discectomy, it may be recommended.

Evidence for the Use of Spinal Fusion
There are 36 moderate-quality RCTs (two with multiple reports) incorporated into this analysis.(361-364, 512, 860, 1210, 1224, 1244, 1249-1251, 1256, 1257, 1259, 1290-1292, 1336-1352, 1354, 1361-1365) There are 16 low-quality RCTs(643, 865, 1266, 1275-1277, 1279-1281, 1284, 1285, 1321, 1353, 1366-1368) in Appendix 1.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

discectomy, microdiscectomy, microdiskectomy, micordiscetomies, microdiskectomies, sequestrectomy, sequestrectomies, endoscopy, endoscopic, decompression, endoscopic decompression, endoscopic decompressions, 'diskectomy, percutanenous', percutaneous diskectomy, percutaneous, nerve root decompression, nerve root decompressions, nerve root, thoracic discectomy, thoracic discectomies, thoracic diskectomies, thoracic, diskectomy, spinal fusion, autologous platelet gel, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies.*
to find 1740 articles. Of the 1740 articles, we reviewed 1740 articles and included 119 articles (90 randomized controlled trials and 29 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Hauerber 2008 (Score=6.5)	Spinal fusion	RCT	The authors declared no sponsorship or COI.	N = 86 1-nerve root level C4-T1 over at least 6 weeks	Median age: 45.5 years; 43 males, 43 females.	Discectomy (n=47) vs. Discectomy plus interbody fusion with titanium cage (n=41).	Follow-up at baseline, 3, 12, and 24 months.	Duration of surgery longer for fusion (median 60 vs. 55 minutes, p = 0.05). Subjective assessment of "Full" recovery (3/12/24 months): fusion 15/39 (38.5%) vs. discectomy 19/46 (41.3%, p = 0.25)/48.6% vs. 40.5% (p = 0.06)/41.7% vs. 34.9% (p = 0.62). Neck pain NS. Radiological fusion at 2 years for 83.3% vs. 81.0%. Return to work 33.3% vs. 50.0%/27.5% vs. 46.0%/27.5% vs. 43.5% (all p >0.16).	"[N]o statistically significant difference between simple discectomy and discectomy followed by interbody fusion with a titanium cage in the surgical treatment of cervical radiculopathy caused by disc herniation."	Claims to have included hard and soft herniation, but no data provided. No difference in radiological fusion at 2 years. Suggests fusion does not add to discectomy for simple, 1-level radiculopathy.
Persson 1997 (Score=6.0)	Spinal fusion	RCT	Sponsored by the Land and Sean Foundation, the Einar Bjorkelunds Foundation, and University of Lund Neurosurgery Institution Foundation.	N = 81 cervicobrachial pain >3 months from C-root compression spondylotic spurs +/-disc bulging	Mean age: 47 years; 44 males, 37 females.	Anterior cervical discectomy and fusion (Cloward) (n=27) vs. rigid cervical collar for 3 months (n=27) vs. physiotherapy ("decided by the	Follow-up at baseline, 1 year.	ACDF surgery vs. physiotherapy vs. cervical collar; mean present pain intensity VAS (average baseline/ 14-16 weeks/12 months): ACDF (47/27/30) vs. PT (50/41/39) vs.	"In treatment of patients with long lasting cervical radicular pain, it appears that a cervical collar, physiotherapy, or surgery are equally effective in the long term."	Some baseline differences. Compliance unclear and 5/27 collared treated surgically. PT unstructured and individualized, precluding assessment of

			No mention of COI.			physiotherapist according to preferences and symptoms," 30-45 min sessions, 1-2/wk, may have included TENS, moist heat, U/S, cold, massage, traction, gentle mobilization, heat relaxation, stretching, flexibility, isometric neck strengthening (n=27).		collar (49/48/35). Surgery superior to collar at 14-16 weeks (p <0.01). No differences at study end between groups. Subjective estimation of restored (surgery/PT/ collar) vs. improved vs. unchanged vs. improved vs. worse: N = 2/3/2, 5/11/9, 11/4/9, 8/9/6. At 12 months, no difference between any group for pain intensity or function (SIP) and mood (MACL) outcomes.		program elements or ability to replicate PT in composite. 8/27 had second surgery. Unclear how 1 year data analyzed with crossovers and most co-intervention procedures.
McConnel 2003 (Score=6.0)	Spinal fusion	RCT	The authors declared no sponsorship or COI.	N = 29 radiculopathy, myelopathy, discogenic pain, spondylosis, segmental instability	Mean age: 47 years; 15 males, 14 females.	ProOsteon 200 hydroxyapatite blocks (n=13) vs. Tricortical iliac crest graft (n=16). 1 to 3 level fusions. Smith Robinson approach. Cervical spine locking plates (Stratec	Follow-up at baseline, 2 years.	16/18 (89%) of hydroxyapatite grafts vs. 2/19 (11%), p = 0.001, fragmented within 3 months. No differences in SF-36 scores, Oswestry Disability scores between groups (p = 0.70, p = 0.59).	"ProOsteon 200 does not possess adequate structural integrity to resist axial loading and maintain disc height or segmental lordosis during cervical interbody fusion."	Study stopped because of radiographic outcomes of fragmentation and collapse, although no clinically significant differences in outcomes. Study results mixed, and based on small sample size are

						Medical) all patients.				inconclusive on clinical outcomes.
Villavicencio 2011 (Score=6.0)	Spinal fusion	RCT	The authors declared no sponsorship. Two of the authors have received or will receive benefits for personal use.	N= 122 patients undergoing 1- to 3-level anterior cervical diskectomy and fusion.	Mean age: 54.4 years; 63 males, 59 females.	Cervical sagittal alignment lordotic (n=57) vs. parallel allograft (n=65).	Follow-up at baseline, 12, 37.5, and 54 months.	Both groups improved in VAS pain and neck disability s348ssessments there was no satistical difference (p=0.93 and 0.83). Segmental and cervical sagittal alignment was not different between both groups at post-operation"or follow-up (p>0.05).	"The use of lordotically shaped allografts does not increase CSA or SSA and does not correlate with improved clinical outcomes."	Data suggest no difference in clinical outcomes and use of lordotic or parallel allografts.
Lenzi 2017 (Score=5.5)	Surgery / Spinal fusion	RCT	No mention of sponsorship. The authors declared no conflict of interest.	N=80 patients with reflex reduction or loss, motor weakness, and sensory deficit.	Mean age: 45.5 years; 46 males, 34 females.	Surgical group: patients received posterior cervical transfacet fusion (n=40) vs. Traction group: patients received mechanical cervical tractions (n=40).	Follow-up at baseline, 1, 6, and 12 months.	Both groups indicated good results, and surgical group showed better results in VAS score than traction group (VAS neck score before interventions: surgical group=5.725 vs. traction group=5.475; VAS neck score at 1 year follow-up: surgical group=0.33 vs.	"Posterior cervical transfacet fusion is a safe and effective procedure to treat single-level cervical radiculopathy."	Patients' details sparse. Surgical intervention superior for pain & disability but not function.

								traction group=1.05).		
Wirth 2000 (Score=5.5)	Cervical spine/ discectomy/ fusion	RCT	No mention of sponsorship or COI.	N = 72 unilateral C-radiculopathy	Mean age: 43.5 years; 36 males, 36 females.	Posterior cervical foraminotomy (n=22) vs. anterior cervical discectomy without fusion (ACD) (n=25) vs. anterior cervical discectomy with fusion (ACDF) (n=25).	Follow-up at baseline, 2, 53, 56, and 69 months.	Pain improvement in all groups at day 1. Pain improvement at 2months 100% vs. 100% vs.96% (NS). RTW at 2 months 91% FOR vs. 88% ACD vs. 92% ACDF (NS). 60 months follow-up phone call working status FOR 79% vs. ACD 92% vs. ACDF 81%. Total reoperations 27% vs. 12% vs. 28%.	"All three of the procedures were successful for treatment of cervical radiculopathy caused by a herniated cervical disc. Although the numbers in this study were small, none of the procedures could be considered superior to the others."	Some baseline differences. Suggest procedures comparable, although likely underpowered.
Vavruch 2002 (Score=5.5)	Spinal fusion	RCT	The authors declared no sponsorship or COI.	N = 89 patients with more than 6 months neck pain and radiculopathy of degenerative origin	Mean age: 47.5 years; 45 males, 44 females.	ACDF with Cloward procedure (n=41) vs. carbon fiber cage with autograft (CIFC, AcroMed) (n=48). All Philadelphia collar for 6 weeks.	Follow-up at baseline, 24, 36, and 72 months.	Fusion rate 86% Cloward vs. 62% cage ($p < 0.05$). Pseudoarthrosis rate 14% Cloward vs. 38% cage ($p < 0.05$). CIFC group with greater reduction in segmental kyphosis and greater disc height. RTW 41% vs. 38% (NS).	"Except for reduced donor site pain, the clinical outcome for the carbon fiber intervertebral fusion cage is the same as for the Cloward procedure."	Participation rate 100%. Some baseline differences (gender) of unclear impact. Data suggest Cloward superior for radiologic fusion, but functional results not different at 2 years. Neither strongly successful for

										RTW (33% before surgery vs. 40% after).
Peolsson 2007 (Score=5.5)	Spinal fusion	RCT	Sponsored by the Research Council of Southeastern Sweden (FORSS), and the Faculty of Health Sciences at Linköping University. No mention of COI.	N = 83 patients with neck pain for at least six months and radiculopathy of degenerative origin.	Mean age: 53 years; 40 males, 43 females.	Anterior cervical decompression and fusion with AcroMed cage (n = 43) vs. Cloward procedure with autograft (n = 40).	Follow-up at baseline, 6 years.	Change in NDI from baseline to 6 years was ACDF 14 (18%) better, 16 (20% worse vs. Cloward 7 (18%) better and 7 (18%) worse vs. CIFC 7 (18%) better and 9 (22%) worse. Results also not different from 2 to 6 years of follow-up. 70% with persistent pain and disability at 6 year follow-up.	"Before undergoing ACDF, patients should be informed that they have an approximate 50% probability of achieving pain relief and little chance of functional improvement. The findings suggest that these outcomes are stable between 2 and 6 year follow-ups, and that there is poor evidence for difference between the surgical techniques CP and CIFC."	Data suggest cage fusion not superior to Cloward procedure over long term with mean follow-up 76 months. Data suggest long-term disability common. Suggests long-term outcomes include significant percentage that worsens.
Peolsson 2004 (Score=5.5)	Spinal fusion	RCT	Sponsored by the Faculty of Health Sciences at Linköping University. No mention of COI.	N = 89 patients with neck pain for at least six months and radiculopathy of degenerative origin.	Mean age: 47±8 years; 45 males, 44 females.	CIFC group: patients received anterior cervical decompression and fusion with cervical carbon-fiber intervertebral fusion cage (n=47) vs. CP group:	Follow-up at baseline, 2 years.	65 with healed fusion had mean pain intensity 33±30mm vs. 24 with pseudarthrosis 49±30mm, p = 0.04.	"Overall, the study shows that the importance of radiological factors as predictors for fusion as well as clinical outcome is limited."	Modestly lower pain scores for those with fusion vs. pseudarthrosis.

						patients received anterior cervical decompression and fusion with the Cloward procedure (n=42).				
Peolsson 2003 (Score=5.5)	Spinal fusion	RCT	Sponsored by the Faculty of Health Sciences at Linköping University. No mention of COI.	N = 74 patients with neck pain for at least six months and radiculopathy of degenerative origin.	Mean age: 48±8 years; 37 males, 37 females.	CIFC group: patients received anterior cervical decompression and fusion with cervical carbon-fiber intervertebral fusion cage (n=40) vs. CP group: patients received anterior cervical decompression and fusion with the Cloward procedure (n=34).	Follow-up at baseline, 1 and 2 years.	Multivariate analyses presented. Stepwise regression for predicting NDI after surgery found current pain, smoking, flexion to be significant. For pain intensity, factors were kyphosis, gender, age and smoking.	"[T]he multivariate analysis shows that male sex, non-smoking, greater segmental kyphosis and a low pain and disability level are preoperative predictors of a good outcome in ACDF."	Scores inferred from other study reports.
Thomé 2006 (Score=5.5)	Spinal fusion	RCT	Sponsored by Signus GmbH in Alzenau, Germany. The authors declared no COI.	N = 100 with 1 or 2-level spondylosis and/or herniation refractory to conservative treatment	Mean age: 47.5 years; 58 males, 42 females.	Ilac crest autograft (ICAG n = 50) vs. rectangular titanium cage (RTC n = 50).	Follow-up at baseline, 1 year.	ICAG vs. RTC 12 month follow-up exam of reduced arm pain: 1.3±2.2 (p <0.001), 1.1±2.0 (p <0.001). Neck pain at 12 month follow-up: 2.7±2.5, 1.9±2.1.	"Fusion rates and clinical outcome at 12 months after ACD were comparable between patients who underwent	Trends suggest cage is better.

								Overall pain at 12 month follow up: 3.3±2.5, 2.2±2.4. Neck pain resolved at 12 month follow-up: 67%, 48%. Radiologically assessed fusion status at 12 month follow up: 81%, 74%.	ICAG and RTC fusion."	
Wigfield 2003 (Score=5.5)	Spinal fusion	RCT	Sponsored by Medtronic Sofamor Danek. No mention of COI.	N = 24 intractable radiculopathy or myelopathy C3-C7	Mean age: 54.3; 17 males, 7 females.	ACDF (Smith Robinson) with Novus block (n=6) vs. Novus ring (n=11) vs. autologous iliac crest bone graft (n=7). Surgery individualized, generally including ACD, osteophytectomy, resection of PLL. Post-op soft/hard collars individualized.	Follow-up at baseline, 6 weeks, 2, 6, 12, and 24 months.	Radiolucent lines seen on flexion/extension films resulted in cessation of enrollment due to possibility of elevated non-union. However, found to not have clinical meaning and lucency disappeared at 12 months. NDI improvement >15 14.3% controls vs. 40% ring and 60% Novus blocks. SF-36 physical improvement 66.7% controls vs. 50% vs. 100%.	"No statistically significant difference in clinical effectiveness could be demonstrated between either of the implants used in this study and autologous bone graft. Had greater recruitment into the study been achieved any differences of clinical relevance may have become apparent."	Small sample size. Baseline differences, block older (58 vs. 47 years) vs. controls 63 years. Study enrollments stopped prematurely due to radiological features.
Nabhan 2009 (Score=5.5)	Spinal fusion	RCT	The authors declared no sponsorship or COI.	N = 40 single level radiculopathy, after not responding to	Mean age: 48 years; 23 males, 17 females.	ACDF with Cages were MC+, PEEK with Tribone. Trial compared plates that	Follow-up at baseline, 6 weeks, 3 and 6 months.	Both groups decreased motion, but no significant difference at any time p >0.05. No differences in	"(O)ur study shows clearly that a bioresorbable plate has a number of unique	Baseline population(s) not well described. Data suggest no clinical differences in

				conservative treatment		were bioresorbable INION S-1 (n=19) vs. titanium ABC plate (n=18).		bone density (p = 0.805). VAS arm pain scores (pre/post): resorbable 8.1±1.4/2.1±1.6/ 1.4±1.2/1.4±1.3/ 1.4±1.4 vs. Ti 8.0±1.3/2.2±1.4/ 2.0±1.4/1.7±1.8/ 1.2±1.4 (NS).	advantages over traditional metallic implants mentioned in this Study."	outcomes. Advantage is no need for, or ability to remove.
Foley 2008 (Score=5.5)	Spinal fusion	RCT	No mention of sponsorship. The authors declared no COI.	N = 323 mostly multi-level ACDF C3-T1 fusion patients (Smith-Robinson) or smokers thought at risk of non-union; 1 week soft collars.	Mean age: 46.8 years; 175 males, 148 females.	Pulsed electromagnetic field stimulation device (begun 7 days post-op, 4 hours a day for 3 months) (n=163) vs. usual care (n=160).	Follow-up at baseline, 12 months.	At 6 months, 68.6% controls fused vs. 83.6% PEMF treated (p = 0.0065). At 12 months, 86.7% vs. 92.8% (0.11). No differences in VAS pain scores. NDI scores baseline/6/12 months: control (45.6/23.0/22.8) vs. PEMF (48.0/31.0/25.6) (NS).	"PEMF stimulation significantly improved the fusion rate at 6 months postoperatively in patients undergoing ACDF with an allograft and an anterior cervical plate…At 12 months postoperatively, however, the fusion rate for PEMF patients was not significantly different from that of the control group."	No sham treatment. Suggests modestly earlier fusion but did not translate into functional differences and no longer term difference in fusion.
Feiz-Erfan 2007 (Score=5.5)	Spinal fusion	RCT	Sponsored by Johnson & Johnson, DeBuy, and	N = 50 ACDFP patients – 29 hard disc	Median age: 46 years; 21	Anterior cervical fusion with allograft bone	Follow-up at baseline, 6 and 12	Overall fusion rates at 6 weeks/12 weeks/1 year:	"[N]o consistent early fusion was obtained with the use of the	Patients not well described, however

			Raynham, Massachusetts. No mention of COI.	disease with osteophytes and 21 soft herniations.	males, 29 females.	and internal fixation with (n=29) vs. without autologous platelet gel (n=21).	weeks, 1 and 2 years.	47%/59%/84%. Fusion rates (6 weeks/12 weeks/1 year/2 year): gel (48/55/79/79%) vs. controls (46/64/85/87%).	platelet gel preparation in patients with a soft herniation."	study is double blinded. Suggests autologous platelet gel effective at 12 weeks for degenerative disc disease, but no prolonged effect and ineffective for soft herniations.
Baskin 2003 (Score=5.5)	Spinal fusion	RCT	Sponsored by Medtronic Sofamor Danek. One or more of the authors have received or will receive benefits for personal or professional use.	N = 33 treated with anterior cervical discectomy and fusion.	Mean age: 49.4 years; 15 males, 18 females.	Recombinant Human Bone Morphogenic Protein-2 (rhBMP-2) implanted on bovine collagen sponge (n=18) vs. Iliac crest bone in allograft ring (n=15).	Follow-up at 6 weeks, 3, 6, 12, and 24 months.	rhBMP-2 vs. Allograft Mean hospital days 1.1 vs. 1.4 (NS) Mean Improvement NDI scores: 52.7% vs 36.9%, p <0.03 although no difference in final scores (10.1 vs. 14.5). No increase in antibodies to rhBMP.	"This pilot study demonstrates the feasibility of using rhBMP-2 safely and effectively in the cervical spine."	Investigational study for FDA approval. Small sample. Allocation unclear. Baseline comparability not clear, but data suggest differences. Study suggests no differences in complications, with comparable outcomes.
Lind 2007 (Score=5.0)	Spinal fusion	RCT	No mention of sponsorship or COI.	N = 24 with 1-level radiculopathy and MRI and/or spondylosis C4-C7	Mean age: 41.5 years; 11 males, 13 females.	ACDF with iliac crest autograft (n=12) vs. fusion cage (BAK/C) with bone	Follow-up at baseline, 2, 6, and 12 weeks, 6 months,	No differences in fusion rates. Odom's Excellent/Good results in 67% autograft vs. 93% cage. Less	"By using radiostereometry (RSA) to study migrations between vertebrae,	Small sample size. Longer duration and higher baseline arm/neck VAS scores

						from end plates, both without plate fixation (n=12).	1 and 2 years.	VAS arm pain at 2 years in cage group (p = 0.03) (graphic data). No difference (p = 0.15) in neck pain VAS.	ACDF with smith-Robinson autografts was compared with a fusion cage (BAK/C)…No significant differences were found between the two surgical techniques after 2 years…The cage group could have a significantly better clinical outcome in terms of pain reduction in both neck and arm as well as in a better Odom's score 2 years after surgery."	in Cage group. Differences in scores persisted throughout study precluding analysis of clinical differences.
Zoëga 1998 (Score=5.0)	Spinal fusion	RCT	Supported by the Inga Britt and Arne Lundberg Research Foundation, the Göteborg Medical Society, the Bertha and Felix Neubergh Foundation, and the Greta and Einars	N = 18 with 2 adjacent cervical discs; pain plus neurological symptoms	Mean age: 44 years; 7 males, 11 females.	Fusion with autologous bone grafting and CSLP plate fixation (n=9) vs. fusion without fixation for 2-levels, Smith Robinson approach (n=9).	Follow-up at baseline, 1 year.	Arm pain (baseline/3 months/12 months): plate 5.1 (range 3.1-8.6)/2.4 (0-6.5)/1.7 (0-3.7) vs. no plate 5.8 (3.7-7.8)/3.2 (0.5-8.3)/4.6 (0.4-6.5) (p <0.05 at 12 months). Neck pain: plate 6.3 (3.7-8.3)/2.1 (0-6.0)/2.4 (0-6.7) vs. no plate 6.3	"[P]late fixation could not be demonstrated to increase the healing rate, promote more rapid fusion or influence the frequency of graft complications."	Small sample size. Primary emphasis on radiological fusion, not function. Patients not well described. More post-op arm pain in plated group.

			Askers Foundation. No mention of COI.					(3.3-9.9)/3.3 (0.1-8.7)/4.6 (0.5-7.7) (NS).		
Celik 2007 (Score=5.0)	Spinal fusion	RCT	No mention of sponsorship. The authors declared no COI.	N = 65 with 87 levels with C-radiculopathy C2-C7	Mean age: 44.8 years; 40 males, 25 females.	ACDF with iliac crest autograft Smith-Robinson (n=30) vs. ACDF with PEEK cages (n=35).	Follow-up at baseline, 18 months.	No clinical differences. Mean foraminal heights (pre-op/Day 2/18 months): ACDF (8.2±2.7/10.8±2.6/8.1± 1.5mm) vs. PEEK (8.4±2.8mm/10.3 ±1.1/9.6±1.2mm) (p <0.05). VAS arm and neck pain scores not different between groups.	"In both groups the foraminal height increased sufficiently and the nerve root was decompressed postoperatively. The PEEK cages may provide sufficient preservation of foraminal height even 1.5 years after the operation."	Data suggest differences in radiological but not clinical outcomes.
Xie 2007 (Score=4.5)	Discectomy/ spinal fusion	RCT	No mention of sponsorship or COI.	N = 45 cervical radiculopathy at least 6 weeks; C4-T1	Mean age: 42.76±7.57 years; 28 males, 14 females.	Discectomy vs. Discectomy with fusion (Aspen collar for 3 months) vs. discectomy with fusion and Codman Plate. Iliac crest grafts used.	Follow-up at baseline, 2 years.	No clinical differences in any outcome at any time interval. Fusion in 67% vs. 93% vs. 100% (p <0.05).	"Neither ACD, ACDF, nor ACDFI provide any advantage to the patient in terms of symptomatic relief; all three procedures result in excellent pain relief immediately postoperatively and continuing throughout a 2-year follow-up period."	Some baseline differences. Author's statement that patient selection is key not tested by this design. Suggests no difference in outcomes.
Savolainen 1998 (Score=4.5)	Spinal fusion	RCT	No mention of sponsorship or COI.	N=91 patients with "long lasting" l	Mean age: 47.8 years; 63 males,	Discectomy (n=31) vs. Discectomy with fusion	Follow-up at baseline, 4 years.	"Good" surgical outcomes at 6 months/2 years in 67/76%	"[S]atisfactory results can be achieved by performing	Baseline duration of symptoms unclear. Data

				level C-radiculopathy from soft or hard disc. C3-T1.	28 females.	(Smith-Robinson) (n=30) vs. Discectomy with fusion plus plating (Caspar) (n=30).		discectomy vs. 70/82% discectomy plus fusion vs. 77/73% plating (NS). Bony fusion in 100% fusion groups and 90% discectomy. Severe iliac crest pain in 24/30 each fusion group and prolonged pain in 5/60 fusion patients combined.	simple discectomy to treat single level cervical root compressive disease."	suggest no benefits of fusion over discectomy for 1-level radiculopathy.
Bärlocher 2002 (Score=4.5)	Spinal fusion	RCT	No mention of sponsorship or COI.	N = 125 cervico-brachialgia "refractory to nonoperative treatment." C3 to T1. Soft disc herniation with or without osteophytes	Mean age: 50.4 years; 74 males, 51 females.	1) Micro-discectomy (n=33) vs. 2) Microdiscectomy with autologous bone graft (n=30) vs. 3) Microdiscectomy with polymethyl-methacrylate (n=26) vs. 4) Micro-discectomy with titanium cage (n=36). All soft collar for 3 weeks.	Follow-up at baseline, 1 year.	Improvements (%) in neck VAS (2/6/12 months): Group 1 (45.5/53.6/64) vs. 2 (20/53.4/50) vs. 3 (27/58.4/62.5) vs. 4 (47.3/72.3/72.3). Improvements in radicular pain VAS: Group 1 (78.8/78.8/81.9) vs. 2 (66.7/76.7/86.7) vs 3 (88.5/79.2/87.5) vs. 4 (86.2/91.7/97.3). Work incapacity at 6/12 months: Group 1 (18.1/12.1) vs. 2 (27.2/16.7) vs. 3	"[F]usion with interbody cages yields a significantly better short- and intermediate-term outcome than MDO (microdiscectomy only) in the treatment of single level DDD of the cervical spine in terms of the following parameters: 1) return to work, 2) radicular pain, 3) Odom criteria, and 4) earlier fusion…These results suggest that interbody	Randomization process unclear. Some baseline differences. Data suggest microdiscectomy results in faster improvement in neck pain than other groups except cage; however "work capacity" better in cage group at 6 weeks and cage group overall generally trended towards best

								(8.3/4.2) vs. 4 (5.5/2.8) (p <0.05 Groups 1, 2 vs. cage at 6 months). Odom Excellent/Good at 6/12 months: 72.7/75.5 vs. 66.6/80 vs. 91.6/87.5 vs. 91.6/94.4% (p <0.05 comparing Group 2 to cage). Fusion rates 6/12 months: Group 1 (60.6/ 93.3) vs. 2 (65.3/93.3) vs. 3 (0/0) vs. 4 (86.1/97.2).	cage-assisted fusion is a promising therapeutic option in patients with single-level disc disease."	clinical outcomes.
Oktenoglu 2007 (Score=4.5)	Spinal fusion	RCT	No mention of sponsorship or COI.	N = 20 C-radiculopathy patients, C3-C7; at least 2 weeks conservative treatment	Mean age: 40 years; 11 males, 9 females.	Anterior cervical microdiscectomy (n=11) vs. anterior cervical microdiscectomy with fusion (n=9). Soft collars for 2 weeks.	Follow-up at baseline, 14 months.	Arm VAS (baseline/postop): ACMD (8.18/3.27) vs. Fusion (8.0/3.11). Neck VAS: ACMD (3.18/2.81) vs. Fusion (3.22/2.0).	"[T]he ACD technique offers satisfactory result with or without fusion where radiculopathy is the major complaint."	Small sample size. Baseline gender difference (4/11 vs. 7/9 males). Variable follow-up period. Blinded assessor. Suggests no differences.
Löfgren 2000 (Score=4.5)	Spinal fusion	RCT	Sponsored by the County Council of Jönköping. The authors declared no COI.	N = 43 cervical disc protrusion, stenosis or both with radiculopathy with/without myelopathy	Mean age: 47 years; 26 males, 17 females.	ACDF with iliac crest autograft (n = 15) vs. allograft (n = 14) vs. bovine xenograft (n = 14). Cloward procedures.	Follow-up at baseline, 6, 12, 24, and 50 months.	Total pain change compared with baseline: autograft -78 vs. allograft -62 vs. xenograft -50. Final neck pain ratings 2.5/3.4/4.1. Final arm pain	"Most of the patients healed with a rigid fusion no matter which graft was used, but the healing process took longer than expected. The clinical results	Some baseline differences. Suggests autograft superior to allograft or xenograft.

								1.1/3.7/4.2. No differences in mobility.	were not influenced by whether mobility could be demonstrated."	
Siddiqui 2003 (Score=4.5)	Spinal fusion	RCT	No mention of sponsorship. The authors declared no COI.	N = 42 including 25 brachalgia, 3 neck pain plus brachalgia, 8 myelopathy, 6 brachalgia plus myelopathy	Median age: 50.5 years; 25 males, 17 femlaes.	Fusion with cage (Ostapek) (n=22) vs. tricortical graft Smith-Robinson technique for cervical interbody fusion (n=20).	Follow-up at baseline, 6 weeks, 3 and 6 months, and 1 year.	No difference in time to fuse (4.7 vs. 6.0 months, p >0.05), Percentage of pre-op NDI at 6 months (67% vs. 51%, p >0.05). Percentage pre-op pain favored graft (mean 70% vs. 35%, p <0.05).	"Overall, the results of fusion using a tricortical graft are equal to, if not slightly superior to those achieved with a cage."	Pseudo-randomization by date of birth. Patients not well described. Data favor tricortical graft over cage.
Fernandez-Fairen 2008 (Score=4.5)	Spinal fusion	RCT	The authors declared no sponsorship or COI.	N = 61 with at least 6 weeks neck pain, brachalgia and clinical cervical nerve root compression at 1 level C3-C7	Mean age: 48.5 years; 22 males, 39 females.	Fusion with interbody tantalum (n = 28) vs. Autologous iliac crest graft with Alpha Plate (n = 33). Smith Robinson approach.	Follow-up at baseline, 6 weeks, 3, 6, 12, and 24 months.	Duration of surgery 53 (tantalum) vs. 98.5 minutes. Fusion rates (6/12/24 months): tantalum (82.1/89.3/89.3%) vs. ACDF plated (78.7/84.8/ 84.8%) (NS). NDI pre/24 months: tantalum 46.8/ 19% vs. plating 48.9/ 20.9% (NS). VAS also improved, but not different	"[T]he tantalum cervical interbody implant achieved a rate of fusion and patient outcome similar to that of ACDF with autologous graft and plating, avoiding graft requirements/risks and requiring generally fewer hospital resources."	No significant differences between group differences in pain. Functional outcomes trend towards tantalum, but not statistically significant.

								between groups. Favorable outcomes in 78.6% tantalum vs. 57.5% plated patients (p>0.1).		
Cho 2004 (Score=4.5)	Spinal fusion	RCT	Sponsored by CMCH financial support. No mention of COI.	N = 180 radiculopathy, ± myelopathy V3-C7	Mean age: 53.8 years; 111 males, 69 females.	A) PEEK fusion (Stryker) (n = 60) vs. B) AICG fusion and plate fixation (n = 50) vs. C) AICG fusion only. Smith Robinson approach. 2 or 3 level fusions. All Miami cervical collar for 8 weeks.	Follow-up at baseline, 1, 2.5, and 4 years.	Complication rates 3.3% (PEEK), 16% (AICG with plate), vs. 54.3% (AICG only), but mostly asymptomatic. Instrument complications only in plated group (8%). Peek fusion statistically superior to AICG on Prolo scale but not AICG with plate. Prolo scale for function/ work status: 6.12±1.54/ 8.83± 1.36 vs. 6.33±2.01/ 8.14 ±2.22 vs. 6.25±2.17/ 7.15±2.31, A vs. C. Satisfactory outcomes 90% vs. 88% vs. 66%, p = 0.0024 for C vs. A.	"Both the PEEK cage and AICG with plating are good methods for interbody fusion in multilevel cervical degenerative disease."	Number and levels of fusions uncontrolled and differed somewhat. Data suggest AICG without plating modestly inferior for rate of fusion and work status. Data suggest cage fusion not superior to Cloward procedure over long term with mean follow-up 76 months. Data suggest long term disability common.
Zoëga 1998 (Score=4.5)	Spinal fusion	RCT	Sponsored by IngaBritt and Arne	N = 27 pain plus neurological	Mean age: 41 years; 15 males,	ACDF CLSP plated (n=15) vs. non-plated	Follow-up at baseline,	No differences in arm (p = 0.4) or neck pain (p =	"The use of an anterior plate in degenerative	Baseline not well described.

			Lundberg Research Foundation, Berthda and Felix Neuberghs Foundation, the Gothenburg Medical Society, and the Greta and Einars Askers Foundation. No mention of COI.	symptoms and correlate 1-level MRI	12 females.	for 1 level, Smith Robinson method (n=12).	1 and 2 years.	0.6) at 2-years. Kyphosis more associated with non-plate fusion vs. lordosis associated with plated fixation.	cervical spine surgery clearly prevented postoperative kyphosis, but did not, in this study, improve the clinical outcome."	Suggests plating results in no improvements in clinical outcomes.
Dai 2008 (Score=4.5)	Spinal fusion	RCT	Sponsored by Shanghai Natural Science Foundation. No mention of COI.	N = 62 upper extremity radicular and/or myelopathy symptoms.	Mean age: 45.3 years; 40 males, 22 females.	Fusion with or without osteophytectomy with interbody cage (carbon fiber or PEEK cages supplemented with β–tricalcium phosphate) with anterior plate (n=33) vs. without anterior plate at 1 or 2 adjacent levels C3-C7. Smith Robinson approach (n=29).	Follow-up at baseline, 2 years.	At 3 months, fusion rate 98.1% plated vs. 72.3% non-plated ($p < 0.05$). At 6 months, all fused. Less cage migration with plate. JOA scores (baseline/final): plated 8.1±2.7/14.3±2.7 vs. unplated 7.8±2.4/13.8±1.9 (NS).	"Supplemented anterior plate fixation can promote interbody fusion and prevent cage subsidence but do not improve the 2-year outcome when compared with those treated without anterior plate fixation."	Suggests plate slightly accelerated fusion but no differences in functional outcomes or long term fusion rates.
Nunley 2009 (Score=4.5)	Spinal fusion	RCT	No mention of sponsorship.	N = 66 cervical radiculopath	Mean age: 51 years; 37 males,	ACDF with static plate (fixed holes)	Follow-up at baseline,	VAS (baseline/final): 63.1/30.0, no	"Although clinical improvement is	Aggregated data not well presented by

			The authors declared no COI.	y with neck and/or arm pain for at least 4-6 weeks	29 females.	(n=33) vs. dynamic plate (slotted holes) (n=33).	12, 16, and 24 months.	differences between groups. NDI 44.2/22.6, no differences between groups. "In the overall population, the plate design (static vs. dynamic) did not significantly affect the reduction in VAS (p=.49) or NDI scores (p=.31). It is therefore a logical conclusion that the plate design does not have any effect on the clinical outcome of patients receiving ACDF when number of levels fused was not taken into consideration."	a good predictor of successful ACDF, radiological evidence of fusion alone is not reliable as a parameter of success. The design of plate does not affect the outcomes in single-level fusions but statistical trends indicated that multiple-level fusions may have statistically better functional outcome when a dynamic plate is used."	treatment allocation. Follow-up time varied 12-24 months. Few baseline data and some differences in multilevel disease. No randomized on levels of disease, raises questions about those conclusions. Suggests no differences between static and dynamic plates.
Engquist 2013 (Score=4.0)	Surgery / fusion	RCT	Sponsored by Medical Research Council of Southeast Sweden funds. No mention of COI.	N=63 patients with cervical radiculaopth y, without motor and sensory deficit.	Mean age: 46 years; 33 males, 30 females.	Group 1: Surgical intervention in which patients received Anterior cervical decompressio n and fusion (ACDF) (n=31) vs.	Follow-up at baseline, 6, 12, and 24 months.	The primary outcome self-reported disability in both groups indicated no significant group difference (p=0.23). However, Neck Disability Index in both groups indicated significant	"[I]t was shown that surgery with physiotherapy resulted in a more rapid improvement during the first postoperative year, with significantly greater improvement in neck pain and	No significant differences between groups for most outcomes at most time points.

						Group 2: a nonsurgical intervention group that participated inphysical and psychological exercises (n=32)		reduction (p<0.001).	the patient's global assessment than physiotherapy alone, but the differences between the groups decreased after 2 years."	
Rosenorn 1983 (Score=4.0)	Spinal fusion	RCT	No mention of sponsorship or COI.	N = 63 herniated C-disc C3-T1	Mean age: 51.9 years; 40 males, 23 females.	DE: discectomy without inter-body fusion (n=32) vs. DEF: discectomy with interbody fusion (n=31).	Follow-up at baseline, 3 and 12 months.	Clinical condition (excellent plus good): 3 months ACDF 19/31 (61.3%) vs. ACD 28/32 (87.5%). 12-months ACDF 20/29 (69.0%) vs. ACD 27/31 (87.1%).	"The prognosis is significantly better for men than for women after DEF (p<0.005), while no difference can be shown after DE."	Sparse details. Trends of less pain and less sick leave in ACD.
Dowd 1999 (Score=4.0)	Spinal fusion	RCT	No mention of sponsorship or COI.	N = 84 with 1 or 2 level spondylosis with radiculopathy and/or myelopathy	Mean age: 52 years; 38 males, 46 females.	ACD: anterior cervical discectomy (n=44) vs. ACDF: anterior cervical discectomy with fusion (modified Cloward) (n=40); soft collar for 6 weeks.	Follow-up at baseline. 1.5 to 8 years.	Two level procedures in 59% ACD vs. 50% fusion. Medical complications in 4/44 (10%) ACD vs. 10/40 (25%) ACDF (p <0.05). Resolved in 34/44 ACD vs. 20/40 ACDF. Fewer narcotic shots in ACD. Radiological fusions in 22/31 ACD vs. 30/31 ACDF.	"Analysis of the results suggests that the addition of a fusion procedure may be unnecessary."	Fewer complications in ACD. ACD more satisfied. More radiological fusions in ACDF.
Ryu 2006 (Score=4.0)	Spinal fusion	RCT	No mention of sponsorship or COI.	N = 40 neck pain or upper extremity	Mean age: 48 years; 22 males,	ACDF with carbon fiber cage (I/F Cage) (n=20)	Follow-up at 6, 12, and	Pain scores (baseline/12 months/24 months): Cage	"Although the two groups saw similar outcomes both	Baseline longer duration neck pain in AP

				radicular symptoms with/out myelopathy from cervical DDD, 1 or 2 adjacent levels	18 females.	vs. ACDF with allograft and DOC plating, Smith-Robinson technique (n=20).	24 months.	(3.9±1.3/1.8±0.9/ 1.7±1.1) vs. fusion with plate (4.5±0.7/2.4±1.3/ 1.6±1.1), NS. NDI scores: Cage (38.6±19.6/15.8± 16.6/ 12.4±17.0) vs. fusion with plate (35.2±18.2/18.0± 16.6/ 19.6±15.6), NS. No difference in "clinical evaluation" or radiological fusion.	improved greatly, the increased morbidity inherent in bone graft collection should be factored against any such fusion procedure. The cage technique is without these risks and did achieve a higher fusion rate at 3 months, suggesting that it may facilitate quicker fusion, although no difference was seen at 12 months."	(36 vs. 17 months) may bias against AP. Heterogeneou s population. 19/40 treated 2 levels. Large loss to follow up especially at 24 months.
Löfgren 2010 (Score=4.0)	Spinal fusion	RCT	Partly sponsored by Zimmer Inc. The authors declared no COI.	N= 80 patients with cervical radiculopath y with or without myelopathy due to degenerative disc disease.	Median age: 49 years; 50 males, 30 females.	Fusion with trabecular metal (n=40) vs. fusion with Smith-Robinson technique (n=40).	Follow-up at baseline, 2 years.	There was no statistically significant differences between the two techniques for pain, neck disability, and patients' global assesments for all follow-ups.	"This study of uninstrumented single-level ACDF showed a lower fusion rate with Trabecular Metal than with the Smith-Robinson technique with autograft after single-level anterior cervical"fusion without plating."	Data suggest no difference in clinical outcomes between the two fusion techniques. Conclusions on efficacy of fusion are limited due to lack of control group.

Ruetten 2009 (Score=4.0)	Spinal fusion	RCT	No mention of sponsorship or COI.	N= 103 patients with clinically symptomatic cervical mediolateral soft disc herniations.	Median age: 45 years; 43 males, 77 females.	Investigational group: Full-endoscopic anterior cervical discectomy or FACD (n= 54) vs. Control group: anterior cervical decompression and fusion or ACDF (n= 49).	Follow-up at baseline, 3, 6, 12 and 24 months.	The mean operating time in the ACDF was 62 min vs. 32 min in the FACD, (p< 0.001). The height of the intervertebral space decreased in ACDF: 6.1 to 5.0 mm vs. FACD: 5.3 to 4.1 mm, (p<0.05). The absolute height of the intervertebral space was significantly higher in the ACDF group (Ø 0.9 mm, p<0.05). At 3 months, patients had returned to work ACDF= 62.6 %(30) vs. FACD= 84.3% (p<0.01).	"The full-endoscopic technique afforded advantages in operation technique, rehabilitation and soft tissue injury. The recorded results show that FACD is a sufficient and safe alternative to conventional procedures when the indication criteria are fulfilled. At the same time, it offers the advantages of a minimally invasive intervention."	Lack of details for allocation, baseline comparison. Data suggests no short or long-term differences in outcomes between techniques.
Peolsson 2013 (Score=3.5)										Both groups demonstrated improvements but there were no differences between treatment arms.
Abbott 2012 (Score= 3.5)										Small sample size (N=33). Cervical collar use limited only differences between

										groups were for neck pain SF-36 for bodily pain and SF 36 PC 3 Physical component scale.
Anderson 2008 (Score=3.5)										Lack of study details limits conclusions.
Kwon 2007 (Score=3.5)										Relatively small sample size and likely underpowered. No clear preference between two approaches in these data. Allocation unclear, baseline comparisons sparse without table, lack of blinding. Each intervention had multiple types of surgical techniques. Data suggest no significant differences between approaches.

Hisey 2015 (Score=3.0)										The only significant difference was range of motion. Methodological details sparse.
Engquist 2017 (Score=2.5)										Follow-up details sparse.
Brenke 2015 (Score=2.5)										Methodological details sparse. No significant differences between groups at 3 or 12 months.
Sasso 2011 (Score=2.0)										Lack of study details. Allocation unclear, no blinding. No data on co-interventions in control, completion rate. Data suggest similar outcomes in alignment and ROM.
Hermansen 2013 (Score= 0.5)										Analysis of positive predictions of post-surgical fusion.

Non-specific Chronic Cervical Pain: Cervical Fusions
The terms "degenerative disc disease," "discogenic cervical pain," "black disc disease," "micro instability," and "cervical spondylosis" are used interchangeably to describe the same group of patients with chronic cervical pain in whom the pain generating structure is not defined. Discography has been used to attempt to define the neck disc as the pain source, although without studies showing a change in outcome (no construct validity). Chronic cervical pain is complex and can be difficult to treat. Current surgical treatment modalities are controversial. Since there is no reliable method to identify the source of a patient's pain, surgery for pain is unlikely to be helpful.

There is no comparable study in the neck, but higher quality studies of non-specific low back pain treatments found fusion failed to improve the outcomes seen with either cognitive intervention and exercise or an intensive rehabilitation program in two different populations studied.(1369-1371) There is no clear reason to expect differences in the neck if similar studies were conducted.

The effects of workers' compensation on fusion patients suggests workers' compensation conveys a worse prognosis in the cervical spine,(1212, 1372-1383) as it also does in the lumbar spine (427, 1384, 1385) In summary, cervical fusion does not have clear evidence of efficacy for chronic non-specific cervical pain. It has a significant rate of serious complications, and is high cost.

Recommendation: Cervical or Thoracic Fusion for Chronic Non-specific Cervical or Thoracic Pain
Cervical fusion is not recommended for chronic non-specific cervical or thoracic pain.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Moderate

Rationale for Recommendation
There are no quality trials comparing fusion with either a quality functional restoration program or with non-operative treatment for management of chronic non-specific cervical pain. Chronic back pain has been shown to have comparable outcomes at one year with either fusion or a quality rehabilitation program.(1370) Thus, the same results could be expected in the cervical or thoracic spine. There is controversy in the medical literature about the definition of proven spinal instability. The Evidence-based Practice Cervical and Thoracic Spine Panel recognizes the controversy (1386) and recommends the following definition be used with flexion-extension bending films done standing with a 72 inch tube to film distance: These films should be taken digitally, and a CD with the films and the software to permit viewing and computer measurement of the translation distance should be retained and kept available for review. The first criterion would be ≥4 mm of translation of the superior vertebral body on the inferior body from the full extension film to the full flexion films. The other criterion would be having a total angular movement during flexion and extension at the unstable level that is at least 12 degrees greater than the motion present at an adjacent disc.(1387)

DISC REPLACEMENT
Cervical disc replacements have been developed as an alternative to fusion for treatment of intractable radiculopathy and myelopathy patients (see evidence table).(1258, 1260, 1335, 1388-1396) An argument used to support disc replacement surgery is that it allows more natural movement of the vertebral segments, thus reducing biomechanical forces on the neighboring segment and presumably reducing the risk of adjacent segments becoming clinically diseased.(1397) A comparative study found no differences in kinematics.(1398) The term "adjacent segment disease" is used to describe patients with degenerative changes (that are presumed to be painful) at the spinal level above or below a spinal motion segment that has been treated, for example by spinal fusion. Disc replacement has also been reportedly used to treat adjacent level disc disease.(1399)

1. Recommendation: Disc Replacement for Subacute or Chronic Cervical Radiculopathy or Myelopathy
Artificial disc replacement is moderately recommended as a treatment for subacute or chronic radiculopathy or myelopathy.

Indications – Select patients with symptomatic cervical radiculopathy with or without myelopathy that is resistant to at least 6 weeks of non-operative care.(361, 362, 1400) Symptoms should have a consistent dermatomal or myotomal pattern. MRI, CT or myelogram findings should correlate with clinical findings. Patients should be thought to be better candidates for this procedure than simple discectomy or traditional anterior cervical discectomy

and fusion (see evidence table). **Caution should be noted particularly for surgery in younger workers as there are few reports of long-term follow-up (10 to 20 years) after this surgery.**[xvi]

Benefits – Reduction in neck pain and neurological compromise. Somewhat faster recovery than with fusion surgery.

Harms – Operative complications, rare severe outcomes (e.g., paralysis, fatalities), increased further re-operative risk, cost, increased risk of disability.

Strength of Evidence – **Moderately Recommended, Evidence (B)**

Level of Confidence – Moderate

2. Recommendation: Disc Replacement for Chronic Non-specific Cervical Pain

Disc replacement is not recommended as a treatment for chronic non-specific cervical pain or other spinal pain syndrome.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**

Level of Confidence –Moderate

Rationale for Recommendations

There are quality studies of short to intermediate term durations of up to 7 years for treatment of cervical radiculopathy or myelopathy patients (see evidence table). However, there are no quality trials comparing disc replacement with non-operative treatments, particularly including a quality rehabilitation program. All 4 of the highest quality studies document superiority of the disc replacement over fusion particularly in the first 3 months, and at least one study documented trends towards earlier return to work in the disc replacement group.(1401) However, there are no quality studies comparing disc replacement with either simple discectomy or non-operative treatments. A few trials included two-levels with disc replacement, but not more than two levels. Cervical disc replacement is invasive, has adverse effects, is costly, but trends towards faster recovery and studies have now been reported out to 3 years of follow-up sufficient to warrant a recommendation for consideration of this treatment for select patients. In all published series and RCTs the indications for cervical disc replacement surgery were patients who were candidates for discectomy or anterior discectomy and fusion for radiculopathy with or without myelopathy, and not patients with non-specific cervical pain. Additional research including demonstrated long-term safety and efficacy would be needed prior to a recommendation in support.

Evidence for the Use of Disc Replacement

There are 17 moderate-quality RCTs (two with multiple reports) (1258-1260, 1320, 1389-1393, 1397, 1401-1414) incorporated into this analysis. There are 9 low-quality RCTs(643, 1278, 1281, 1282, 1284, 1285, 1415-1417) and 9 other studies(1287, 1289, 1418-1424) in Appendix 1.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

Disc Replacement, Total Disc Replacement, replacement and replantation, disorder terms-cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, and Non-experimental Studies.*

to find 857 articles. Of the 857 articles, we reviewed 857 articles and included 42 articles (37 randomized controlled trials and 5 systematic reviews).

[xvi]A case report by Devin et al of a lumbar disc replacement patient who at age 30 was reported in a case series as having a "good" early post-operative result, but at age 50 was reported to have total mechanical failure of the implant and a difficult salvage surgery is concerning when considering disc replacement in young individuals with long predicted life expectancies. The authors state this case is the longest published follow up of a lumbar disc replacement patient.

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Murrey 2009 (score=6.0)	Disc replacement	RCT	Sponsored by Synthes Spine (West Chester, Pennsylvania). Four of the authors have received or will receive benefits for personal or professional use.	N = 209 1-level intractable radiculopathy C3-C7.	Mean age: 42.8 years; 95 males, 114 females.	ProDisc C (n=103) vs. ACDF with allograft with plate (n=106).	Follow-up at baseline, 24 months.	Intraoperative times 107.2 Disc vs. 98.7 (ACDF), p = 0.0078. Neurological success 6/24 months: 94.6%/90.9% vs. 85.1%/88.0%, p = 0.046, p = 0.64. NDI favored disc at 3 months (p = 0.05). SF-36 borderline favored disc at 24 months (p = 0.09); 9 re-ops in fusion patients vs. 2 discs. Narcotic use pre-op: ACDF 48.1% vs. 48.5%, at 24 months, 13.0 vs. 11.2%. Combined strong narcotic or muscle relaxant use at 24 months favored disc replacement (p = 0.05).	"Disc arthroplasty is shown to be similar of better than ACDF on a number of outcome measures."	Suggests disc replacement superior to ACDF for single-level disease particularly in short term for some measures and no outcomes worse in disc replacement group. (Editors comment: "Longer-term follow-up is needed as late failure of arthroplasty is a reasonable concern.
Mummaneni 2007 (score=5.0)	Disc replacement	RCT	Sponsored by Medtronic Sofamor Danek. The authors has received or will receive	N = 541 intractable C-radiculopathy myelopathy; at least 6 weeks treatment unless	Mean age: 43.6 years; 250 males, 291 females.	Prestige ST cervical disc arthroplasty (n=276) vs. decompressive ACDF (n=265).	Follow-up at baseline, 2 years.	Mean operative time: ACDF 1.6 vs. disc 1.4 hours (p <0.001). Mean blood loss not different (60.1 vs. 57.5mL). Hospital time 1.1	"[T]he prestige ST disc replacement is as safe and effective as the current standard of care for the treatment of	Some baseline differences. 100% compliance reported, which seems unlikely for

			benefits for personal or professional use.	worsening neurological status with non-operative treatment.				vs. 1.0 days (p = 0.041). External orthosis in 59.1 vs. 31.2%, p <0.009. Secondary surgery with hardware removal in 9 vs. 5 patients (p = 0.29), revision in 5 vs. 0 (p = 0.03). NDI scores (baseline/1.5/3/6/ 12/24 months): ACDF (56.4/32.1/ 26.8/24.5/23.4/2 2.4) vs. disc (55.7/27.1/20/7/2 1.7/20.6/ 19.3) (p ≤0.0014 Months 1.5, 3; p >0.05 other months). Working status (baseline/24 months): ACDF 63%/74.7% vs. disc 66/75.4% (NS). Median RTW 61 vs. 45 days.	cervical DDD. In addition, motion preservation associated with arthroplasty has the potential to reduce long-term consequences of fusion surgery while improving outcomes."	large sample size. Data support disc replacement superior to ACDF particularly for first 3 months. Borderline faster RTW with disc.
Nabhan 2011 (score=5.0)	Disc replacement	RCT	No mention of sponsorship. The authors declared no COI.	N=20 suffering from symptomatic degenerative soft disc disease with single-level radiculopathy	Mean age: 43±9 years; 13 males, 7 females.	ACDF or Anterior cervical discectomy and fusion with single-level with ABC=advanced biomechanical	Follow-up at baseline, 6, 12, 24, and 60 months.	ROM in prosthesis group in comparison to fusion after / axial rotation / segmental motion for bending; (p=0.001,	"[There] is no significant difference of the segmental motion of the adjacent level, either treated with prostheses	Baseline comparison details not provided. No blinding. Data suggest no significant differences in segmental

				not responding to a trial of conservative treatment.		concept, titanium plate fixation (n=10) vs. Study group received single level disc replacement with ProDisc-C prostheses (n=10).		p=0.01, p=0.02) / (p=0.0002, p=0.021, and p=0.013) / (p=0.3 , p=0.1, and p=0.06) at 1 week, 6 months, and 1 year, respectivelly. No significant difference between both groups in pain relief for neck and arm pain for all time points, p>0.05.	or fusion, 1 year after surgery."	mobility of adjacent levels or in clinical outcomes at 1-year. Small sample size limits conclusions.
Cheng 2008 (score=4.5)	Disc replacement	RCT	No mention of sponsorship or COI.	N = 65 spondylotic myelopathy or cervical radiculopathy	Mean age: 46 years; 33 males, 32 females.	Two-level cervical disc (Bryan) (n=31) vs. ACDF with iliac crest autograft and Orion plating (n=34).	Follow-up at baseline, 1 and 2 years.	NDI (pre/12 months): ACDF (51/18/19) vs. disc (50/12/11), p = 0.030, p = 0.023. Arm pain VAS: ACDF (7.2/2.4/2.7) vs. Disc (7.1/1.8/1.4), (NS at 12 months), p = 0.013. Odom's scale at 24 months (Excellent): ACDF 22/32 vs. disc 24/30.	"Although both groups showed significant improvement, the Bryan group improved to a greater degree in pain scores and range of motion at 24 months follow-up." "[L]ong term outcome data collected five to ten years after prosthesis implantation will be necessary to demonstrate the putative advantages of disc arthroplasty in two-level	Data suggest disc replacement modestly superior to ACDF for pain.

									cervical disc disease."	
Zhang 2012 (score=4.5)	Disc replacement	RCT	Sponsored by Chinese Medical Doctor Association. The authors declared no COI.	N= 120 with degenerative disc disease. Average age 45 years.	Mean age: 45.17 years; 67 males, 53 females.	Total disc replacement (n=60) vs. anterior cervical decompression and fusion (ACDF) (n=60).	Follow-up at baseline, 6, 12, and 24 months.	Both groups improved significantly in neck disability index, range of motion, and VAS pain scores from before surgery to post-surgery ($p<0.05$). Mean change from baseline of ROM at 24-month follow-up was different between the TDR and ACDF group ($p<0.001$).	"Our findings suggest that TDR is associated with significantly better maintenance of ROM at the index level than ACDF as determined at 2-year follow-up."	Possible differences at baseline in primary outcome ($p=0.055$). Data suggest no differences in pain, disability index. Disc arthroplasty may have better ROM at one and two years post-op.
Manzano 2012 (score=4.5)	Disc replacement	RCT	No mention of sponsorship. The authors declared no COI.	N= 16 with myelopathy with and without radiculopathy.	Mean age 59 years; 7 males, 9 females.	Expansile cervical laminoplasty (ECL) (n=9) vs. cervical laminectomy and fusion (CLF) (n=7).	Follow-up at baseline, 3 months, 1 year.	The reduction of the spinal canal was not significantly different between both groups (CLF -0.262 +/- 0.12; ECL -0.03 +/- 0.09 cm2). The cervical ROM between C2 and C7 was reduced by 75% in the CLF and 20% in ECL from pre-operative to 1-year follow-up. Pre-operative and post-operative scores on SF-36 and	"…The results suggest that patients may benefit from both procedures and that the complication rates are low. The relatively small number of patients in each treatment arm limits the strength of the comparative aspects of the study; however ECL demonstrated improvements in several outcome	Small sample size limits power, conclusions. Lack of study details for randomization method, baseline characteristics, cointerventions, lack of blinding.

								NDI were significantly improved for those receiving laminectomy ($p<0.05$).	measures, including pain, NDI, SF-36, and ROM. Improvements in neurological function were seen in both groups despite a statistically greater increase in canal area in the CLF group."	
Cheng 2011 (score=4.5)	Disc replacement	RCT	No mention of sponsorship. The authors declared no COI.	N= 83 patients with cervical myelopthy. Mean age 47 years +/- 6 years.	Mean age: 47.5 years; 44 males, 39 females.	Bryan® cervical disc prosthesis (n=41) vs. anterior cervical decompression and fusion (n=42).	Follow-up at baseline, 3 years.	Patients in the Bryan® group had better scores than ACDF in NDI ($p<0.001$), SF-36 ($p<0.05$), and the Japanese Orthopedic Association (JOA) ($p=0.016$). At 3-year follow-up ROM was retained in the Bryan group compared to ACDF.	"We showed arthroplasty with implantation of the Bryan® cervical disc prosthesis is effective and safe for the treatment of patients with cervical myelopathy and comparable to ACDF in improving the functional outcomes of patients 1 year and to 3 years after surgery."	Lack of study details for allocation, concealment, blinding absent. In Chinese population, disc prosthesis resulted in quicker return to work (20 days vs 84 days), higher functional scores on NDI, SF-36 on long term follow-up. Data suggests benefit of disc prosthesis vs. fusion.
Kim 2009 (score=4.0)	Disc replacement	RCT	No mention of sponsorship or COI.	N = 105 with 1 or 2 level symptomatic cervical disc disease	Mean age: 47.3 years; 63 males;	Single level ACDF (n=26) vs. single level Bryan (n=39) vs. Bi-level ACDF (n=28)	Follow-up at baseline, 12, 19, 20, 38,	Single level procedures NDI (baseline/post-op/follow-up): ACDF (25.5±1.5/16.6±2	"Clinical status of both groups, showed improvement. Although clinical	Single vs. Multiple levels and varied numbers fused by

					52 females.	vs. Bi-level Bryan (n=12).	and 40 months.	.0/7.2±1.6), vs. disc (25.3±1.8/17.1±1.7/7.6±0.9), p = 0.29. VAS single level: ACDF (8.3±0.9/6.2±0.8/3.8±1.1) vs. Disc (8.3±1.0/6.4±0.7/3.7±0.9), p = 0.84; 2-level differences also not significant. Results stratified by numbers of levels treated, but appears not randomized for that purpose.	outcomes between the two groups were not significantly different at final follow-up, radiographic parameters, namely ROM and intervertebral heights at the operated site, some adjacent levels as well as FSU and overall sagittal alignment of the cervical spine were relatively will maintained in our Bryan group compared to our ACDF group... could reduce adjacent level disease."	treatment (>1 level in 28/54 (51.9%) ACDF patients vs. 12/51 (23.5%) Bryan). Uncontrolled plates and cages in comparison group. Clinical data suggest Bryan not superior to ACDF for NDI. Due to numbers of methodological limitations, utility of this study questionable.
Heller 2009 (score=4.0)	Disc replacement	RCT	Sponsored by Medtronic. One or more of the authors have received or will receive benefits for personal or professional use.	N = 463 symptomatic radiculopathy and/or myelopathy C3-C7; at least 6 weeks non-operative treatment.	Mean age: 44.5 years; 223 males, 240 females.	Microdiscectomy with Bryan cervical disc (n=242) vs. ACDF with plating (Atlantis) (n=221). Bryan disc treated postop 2 weeks with NSAIDs.	Follow-up at baseline, 6 weeks, 3 and 6 months, 1 and 2 years.	NDI decreased at 24 months in both groups: Bryan 34.7±20.5 at 24 months vs. ACDF 30.6±19.8. NDI also significant at all 4 other intervals vs. baseline (p ≤0.007). Return to work 48 days in disc replacement patients vs. 61	"Bryan cervical disc treatment achieved statistically superior results…the investigational group returned to work sooner."	Baseline SF-36 mental and ROM differences. Allowed 12 subjects to crossover without randomization. Study claim of no co-interventions other than disc replacement

								days fusion (p = 0.015). Overall success in 82.6% vs. 72.7%. (p = 0.01).		group treated with NSAID for 2 weeks post-op, thus presumably no other post-op medication or treatment, appears dubious. Data suggest disc replacement superior to ACDF.
Sasso 2008 (score=4.0)	Disc replacement	RCT	No mention of sponsorship or COI.	N = 22 patients with Bryan cervical disc arthroplasty.	Mean age: 42.4±5.4 years; 13 males, 9 females.	Atlantis single-level anterior cervical plate (n=13) vs. Bryan artificial cervical disc prosthesis (n=9).	Follow-up at baseline, 3 and 6 months.	Angular motion: mean (pre-op/24 years): Disc (6.34± 3.42/+7.95±4.70 °) vs. ACDF (8.39±4.54/-0.87±0.62°). "[N]o consistent correlation between angular range of motion at adjacent levels and NDI, Arm pain, or Neck Pain score."	"Significantly more motion was retained in the disc replacement group than the plated group at the index level."	Same population as above, however this study emphasized motion.
Sasso 2007a (score=4.0)	Disc replacement	RCT	Sponsored by Corporate/Industry funds. One or more of the authors have received or will receive benefits for personal or professional use.	N = 115 patients with single-level aymptomatic cervical myelopathy or radiculopathy.	Mean age: 44.3 years; 62 males, 53 females.	Bryan group: patients received single-level cervical arthroplasty with Bryan cervical disc prosthesis (n=56) vs. Fusion group: patients received single-level allograft	Follow up at baseline, 1 and 2 years.	Appears to be subset of above. VAS neck pain (baseline/12, 24 months): Disc (72/17/16) vs. ACDF (73/28/32) (p ≤0.05). Arm pain VAS: Disc (70/12/14) vs. ACDF	"The Bryan artificial disc replacement compares favorably to anterior cervical discectomy and fusion for the treatment of patients with 1-level cervical disc disease."	Sparse details. Appears to be subset of above study.

						and plate ACDF (n=59)		(71/23/28) (p ≤0.031).		
Sasso 2007b (score=4.0)	Disc replacement	RCT	No mention of sponsorship or COI.	N = 115 patients with single-level aymptomatic cervical myelopathy or radiculopathy.	Mean age: 44.3 years; 62 males, 53 females.	Investigational group: patients received single-level cervical arthroplasty with Bryan cervical disc prosthesis (n=56) vs. Control group: patients received single-level allograft and plate ACDF (n=59).	Follow-up at baseline, 12 and 24 months.	Hospital stay 0.9±0.4 vs. 0.6±0.6. (Data reported as significant, however appears impossible). External orthosis not used in 60.7% Disc vs. 8.5% ACDF. Mean SF-36 physical component scores 50 vs. 45 ACDF, p = 0.016.	"At 24 months, cervical arthroplasty with the BRYAN Cervical Disc Prosthesis compares favorably with ACDF as defined by standard outcomes scores."	Same study population.
Nunley 2012 (score=4.0)	Disc replacement	RCT	The authors declared no sponsorship or COI.	N = 170 with established symptomatic cervical disc disease at 1 or 2 levels.	Mean age: 44 years; 76 males, 94 females.	Total disc arthroplasty (TDA or treatment group) (n = 113) vs. anterior cervical fusion (ACDF or control group) (n = 57).	Follow-up at baseline, 6 weeks, 3, 6, 12, 24, 36, and 48 months.	Adjacent segment disease (ASD) was established in 28 patients. No significant differences were seen in the incidence of ALD in the 2 groups. Survival analysis for the ALD-free period shows the actuarial rate for nonosteopenic group as 82.3% ± 0.42% and for the osteopenic group (T score > -1.5) as 54.0% ± 1.76% (P = 0.04; 95% CI: 0.007-0.223). A 4 year	"At a projected follow-up of up to 54 months, the risk of developing symptomatic ASD after anterior surgery for 1 or 2 levels of the cervical spine does not significantly vary between patients receiving TDA or anterior fusion. Other factors including bone mineral density and presence of concurrent lumbar	Data suggest TDA not superior re. adjacent segment disease. Lum bar DDD conferred significant risk over 4yrs for adjacent segment disease (25 v 44%).

								ALD-free survival rate of 74.5% ± 0.6% for patients with no lumbar disease and 55.5% ± 0.12% for those with lumbar DDD (P = 0.023; 95% CI: 0.003-0.196) is reflected in the mean actuarial ALD-free survival times, which are 50.3 ± 0.8 month (95% CI: 48.6-52.3 months) for patients without lumbar disease and 45.7 ± 1.2 months (95% CI: 43.2-48.2 months) with those with lumbar DDD.	degeneration have a more significant effect in the incidence of adjacent segment degeneration."	
Lanman 2017 (score=4.0)	Disc replacement	RCT	Sponsored by Medtronic Inc. One or more of the authors have received or will receive benefits for personal or professional use.	N=397 patients with cervical degenerative disc disease.	Mean age: 47.2 years; 182 males, 215 females.	Investigational group: patients received 2 level prestige LP artificial cervical disc replacement (n=209) vs. Control group: patients received 2 level anterior cervical discectomy and fusion	Follow-up at baseline, 6 weeks, 3, 6, 12, 24, 36, 60, and 84 months.	The primary outcome overall efficacy success rate in artificial disc replacement (ADR) group was superior to that in anterior cervical discectomy and fusion (ACDF) group. The overall success rate at 36 months follow-up in ADR group was	"The low-profile artificial cervical disc in this study, Prestige LP, implanted at 2 adjacent levels, maintains improved clinical outcomes and segmental motion 84 months after surgery and is a safe and	At 84 months, data suggest 2-level Prestige LP device is non-inferior to ACDF but superior to ACDF for serious device related adverse events, neck disability, neurosurgical success and

						procedure (n=188).		81.6%, compared with 70.5% in ACDF group.	effective alternative to fusion."	fewer second surgeries.
Kouyoumdjian 2009 (score=4.0)	Disc replacement	RCT	The authors declared no sponsorship or COI.	N=20 with herniated disc-induced cervicobrachial neuralgia resistant to medical treatment.	Mean age: 44 years; 11 males, 9 females.	Lateral fluorscopic or L guidance (n=10) vs. Lateral + AP or anteroposterior fluoroscopic guidance (n=10).	No mention of follow up.	There were no significant differences between either in the control plane p=0.26 or horizontal plane p=0.19.	"The unci are reliable landmarks for proper positioning of cervical TDRs in the coronal plane. AP fluoroscopic guidance does not improve this positioning."	Small sample zise limits conclusions, but data suggests no benefit in fluoroscopic alignment intraoperatively of prosthesis.
Peng-Fei 2008 (score=3.5)										Lack of study details. Randomization, allocation not explained. No blinding. No baseline comparison presented, Data suggest no differences between clinical measures of fusion or prosthesis.
Anderson 2008 (score=3.5)										Lack of methods details limits conclusions. This may be reposted elsewhere,

										since this is a secondary analysis.
Sasso, 2017 (Score=3.5)										Crossover due to "randomization errors". Questionable study execution.
Peng 2009 (Score=3.5)										While minimal difference in ROM in patients with disc height < 4 mm. No functional clinical outcome differences at 2 years. Concerns about need for more procedures after TDR in 7-15% of patients.
Burkus 2014 (Score=3.0)										Methodological details sparse.
Zhang 2014 (score=3.0)										Methods poorly described and sparse data.
Park 2011 (score=2.5)										Lack of study details limits conclusions.
Delmarter 2013 (score=N/A)	Disc replacement	Post-hoc analysis of	Sponsored by Synthes Spine (West Chester,	N = 209 1-level intractable	Mean age: 42.8 years;	ProDisc C (n=103) vs. ACDF with	Follow-up at baseline,	Compared with patients in anterior cervical discectomy and	"Five-year follow-up of a prospective randomized	At 5 years, reoperation rates were 5 times higher

		Murrey 2009.	Pennsylvania). Four of the authors have received or will receive benefits for personal or professional use.	radiculopathy C3-C7.	95 males, 114 females.	allograft with plate (n=106).	24 months.	fusion group (85.5%), patients in ProDisc-C group (97.1%) indicated higher possibility of no second surgery 5 years after the surgery (p=0.0079).	clinical trial revealed 5-fold difference in reoperation rates when comparing patients who underwent ACDF (14.5%) with patients who underwent TDR (2.9%). These fi ndings suggest the durability of TDR and its potential to slow the rate of adjacent-level disease."	in ACDF patients versus TDR patients suggesting the durability of TDR and its apparent ability to retard adjacent-level segment disease.
Garrido 2010 (Score=N/A)	Disc replacement	RCT	No mention of sponsorship or COI.	N=47 with single level cervical spine disease (C3-7) manifesting as radiculopathy or myelopathy and failed nonoperative treatment for at least 6 weeks.	Mean age: 41.7 years; 30 males, 17 females.	Cervical arthroplasty group with Bryan disc arm-milling jig 2 concave surfaces that accept titanium alloy metal, long term fixation (n=21) vs. Arthrodesis high-speed burr appropriately sized Cornerstone SR fibural allograft ACDF group or Anterior cervical discectomy and fusion (n=26).	Follow-up at 24, and 48 months.	Preoperatively Neck Disability Index / Neck Pain Scores / Arm Pain Score / SF-36 PCS & MCS; (51.1 vs. 51.5 ACDF group) / (76.2 vs. 80.6, at 6 weeks 32.3 vs. 39.2) / (78.8 vs. 77.1, at 6 weeks 16.3 vs. 22.8) / (33.1 vs. 31.4 and 43.2 vs. 46.3, at 6 weeks 26% Bryan vs. 33% ACDF & 52.4 vs. 47.2). Postoperatively NDI at 6 weeks / 48 months; (22.2	"At 48 months, cervical arthroplasty with the Bryan cervical disc prosthesis continues to compare favorably to ACDF at our institution."	Single site report of a multicentre trial.

								vs. 26.4 in ACDF group). At 4 years, 24% improvement in SF-36 MCS in Bryan group vs. 13% in ACDF group.		
Anakwenze 2009 (Score=N/A)	Disc replacement	RCT	Sponsored by Corporate / Industry funds. One or more of the authors have received or will receive benefits for personal or professional use.	N=180 with 1-level disease treated surgically at C3-4, C4-5, C5-6, and C6-7.	Mean age: 41.9 years; 89 males, 91 females.	TDR-C or total disc replacement (n=89) vs. ACDF or Anterior cervical discectomy and fusion (n=91).	Follow-up at baseline, 2 years.	Total level lordosis C2-C6 increased in TDR-C by 3.1º (p=0.001) vs. ACDF by 3.8º (p<0.001). Loss of lordosis was greater in TDR-C vs. ACDF,0.39º (p=0.05).	"In both TDR-C and ACDF, lordosis increased at the device-level, cranial adjacent level, and in total cervical lordosis, while lordosis decreased at the caudal adjacent level."	Secondary analysis of ProDisc-C trial. Clinical relevance of results are unknown.
Jawahar 2010 (Score=N/A)	Disc replacement	RCT	No mention of sponsorship or COI.	N=93 with established symptomatic one or two-level cervical disc disease who failed to responded to conservative treatment.	No mention of age; 37 males, 56 females.	TDA or total disc arthroplasty (n=59) vs. ACDF or Anterior cervical discectomy and fusion (n=34).	Follow-up at baseline, 24, 37, and 49 months.	VAS and NDI / VAS; (p=0.693, similar for both groups) / (61.6±4.1 vs. 61.7±3.5).	"Total disc arthroplasty demonstrates equivalence of safety and efficacy when compared with anterior cervical fusion in the management of symptomatic DDD of the cervical spine."	Data presented is analysis from 3 RCTs for 3 separate types of artificial disc replacements vs. pooled fusion results. Methods for each trial not described, limiting ability to make conclusions.
Coric 2010 (Score=N/A)	Disc replacement	RCT	No mention of sponsorship or COI.	N=98 with 1-and-2 level cervical disc disease producing	Mean age: 46.5 years; 38	Cervical arthroplasty including Bryan, Kineflex/C and	Follow-up at baseline, 24, 38,	NDI scores improvement / NPI/VAS / Angular Motion; (94%, 89%, and	"Patients treated with the artificial discs showed significantly	Data is pooled analysis of 3 separate trials from one

				radiculopathy or/and myelopathy.	males, 52 females.	Discover cervical disc (n=57) vs. ACDF or Anterior cervical discectomy and fusion with plate or artificial disc placement (n=41).	and 67 months.	91% vs. 81%, 87, and 85%) / (27.8, 26.9, and 26.7 vs. 31.9, 29.8, and 31.6), at 6, 12, and 24 months / (combined arthroplasty group 0.91 vs. 7.8 reduction in ACDF group). All groups showed significant improvement from the preoperative to the minimum 2-year follow-up, p<0.0001.	better clinical results, maintained motion at the treated level, and trended toward less adjacent-level disease."	investigational site that is included in large trials for the Bryan Disc, Kineflex/C disco, and the discover disc.
Burkus 2010 (Score=N/A)	Disc replacement	Secondary analysis of Mummaneni 2007 RCT	Sponsored by Medtronic Spinal and Biologics. All of the authors have received or will receive benefits for personal or professional use.	N=541 with symptomatic degenerative cervical disc disease.	Mean age: 44.6 years; 238 males, 303 females.	Investigational group received cervical disc prosthesis (n=276) vs. Control group received instrumented inter-body fusion (n=265).	Follow-up at baseline, 2 and 5 years.	NDI / Neck Pain / Arm Pain / SF-36; (36.3 and 38.4 vs. 31.3 and 34.1) / (53.8 and 56 vs. 49.2 and 52.4) / (47.1 and 52.5 vs. 45.0 and 47.7) / (13.6 and 14.7 vs. 11.1 and 12.9) scores improvement at 36, 60 months.	"Cervical disc arthroplasty has the potential for preserving motion at the operated level while providing biomechanical stability and global neck mobility and may result in a reduction in adjacent segment degeneration."	Secondary analysis. Data presented included only 50% of original sample.

VERTEBROPLASTY

Vertebroplasty, first reported in 1987, (1425) involves using imaging guidance to inject polymethylmethacrylate within the vertebral body, in order to stabilize vertebral fractures caused by osteoporosis, vertebral osteonecrosis, or malignancies of the spinal column.(1426-1434) This procedure is most common among elderly osteoporotic patients who have delayed healing of compression fractures of the vertebral body(ies),(1435) but it is sometimes performed on younger patients with acute vertebral fractures due to osteoporosis. A work-related minor trauma may be the event that caused the osteoporotic pathologic fracture.

1. *Recommendation: Vertebroplasty for Cervical or Thoracic Pain Due to Vertebral Compression Fractures*
   Vertebroplasty is not recommended as a routine treatment for patients with cervical or thoracic pain due to vertebral compression fractures.(1436, 1437)

   Strength of Evidence – **Strongly Not Recommended, Evidence (A) [Subacute, Chronic]**
   Level of Confidence –High

   Strength of Evidence – **Not Recommended, Evidence (C) [Acute]**
   Level of Confidence –Moderate

2. *Recommendation: Vertebroplasty for Select Patients with Cervical or Thoracic Pain Due to Vertebral Compression Fractures*
   There is no recommendation for or against the use of vertebroplasty for treatment of highly select patients with cervical or thoracic pain due to unusual vertebral compression fractures.

   Indications – Patients who are not included in the two available high-quality trials. These include patients who have had fractures despite bisphosphonate therapy, pathologic fractures due to neoplasms in the vertebral body, or multiple simultaneous compression fractures (three or more). Candidates for vertebroplasty should have these types of unusual vertebral body compression fractures, should generally have severe pain, passage of at least 2 months, and failure of other treatment options including medical management.

   Strength of Evidence **– No Recommendation, Insufficient Evidence (I)**
   Level of Confidence –Low

Rationale for Recommendations

There are two recent high-quality, sham-controlled RCTs available that evaluated the efficacy of vertebroplasty and both failed to find any significant improvements in the patients who underwent vertebroplasty compared with a sham procedure.(1436, 1437) Both trials included patients with thoracic fractures. These results are in contrast with other low-quality studies that had reported pain relief and other functional improvements that had appeared promising.(1429, 1433, 1434, 1438-1444) Carragee's review chronicles how the apparent benefit of this procedure disappeared as low-quality evidence (case series) was replaced by high quality evidence RCTs.(1445) There is one other quality trial which reported pain relief and increased mobility; however, that trial is of lower quality, was short (2 weeks), and had a substantially lower sample size than the recent studies, and appears biased against pain treatment. In addition, substantial complications occur with this procedure including deaths.(1429, 1436, 1446-1449) The results of these high quality trials have not been universally supported.(1450)

The results of the two high-quality RCTs indicate that vertebroplasty is strongly not recommended for nearly all patients with vertebral compression fractures. It remains unclear whether there are selected unusual patients – such as severely affected patients, patients with 3 or more simultaneous compression fractures, or patients with pathologic fractures due to neoplasms (1433) – who were outside the scope of these two quality trials, who might still derive benefit from this procedure. This procedure is invasive, has complications,(1451, 1452) and is costly. Therefore, vertebroplasty is not recommended other than for select patients who have failed other interventions (including quality medical management) and for whom there are no other options available, whose significant pain is not resolving, and especially those for whom bisphosphonate therapy has failed.

Evidence for the Use of Vertebroplasty

There are 2 high-(1436, 1437) and 2 moderate-quality(1453, 1454) RCTs incorporated into this analysis.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

Vertebroplasty, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies.*

to find 1162 articles. Of the 1162 articles, we reviewed 1162 articles and included 7 articles (4 randomized controlled trials and 3 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Buchbinder 2009 (score=9.5)	Vertebroplasty	RCT	Sponsored by grants from the National Health and Medical Research Council of Australia, Arthritis Australia, the Cabrini Education and Research Institute, and Cook Australia. COI: One or more of the authors have received or will receive benefit for personal or professional use.	N = 78 with 1 to 2 painful compression fractures up to 12 months old	Mean age: 76.6 years; 16 males, 62 females	Vertebroplasty vs. sham (blunt needle used)	1 week, 1, 3, 6 months	Overall pain score changes (1 week/1 month/3 months/6 months): vertebroplasty (1.5±2.5/2.3±2.6/ 2.6±2.9/ 2.4±3.3) vs. placebo (2.1±2.8/ 1.7±3.3/1.9±3.3/ 2.1±3.3), all p >0.05. Perceived status 1 week: vertebroplasty 6 (16%) better, 5 (14%) worse vs. placebo 13 (35%) better, 1 (3%) worse; 1 month vertebroplasty 12 (34%) better, 2 (6%) worse vs. placebo 9 (24%) better and 9 (24%) worse. At 6 months, vertebroplasty 16 (46%) better, 7 (20%) worse vs. sham 15 (42%) better and 5 (14%) worse.	"We found no beneficial effect of vertebroplasty as compared with a sham procedure in patients with painful osteoporotic vertebral fractures, at 1 week or at 1, 3, or 6 months after treatment."	Co-interventions unclear, as noted usual care. Overall 141/468 declined to participate. Data suggest no benefit.
Kallmes 2009 (score=9.0)	Vertebroplasty	RCT	Sponsored by grant from National Institute of Arthritis and Musculoskelet	N = 131 with 1 to 3 painful compression fractures T4-L5 up to	Mean age: 73.8 years; 32 males, 99 females	Vertebroplasty vs. control group (sham, no needle)	3 days, 14 days, 1 month, 3 months	At 14 days, 63% vertebroplasty vs. 51% controls correctly guessed assignment; 1 patient	"Improvements in pain and pain-related disability associated with osteoporotic	Co-interventions not mentioned, but appear likely; 300 of 1682 exclusions were declinations. Allowed crossover

			al and Skin Diseases. COI: One or more of the authors have received or will receive benefits for personal or professional use.	12 months old				hospitalized with thecal sac injury. Rolland-Morris Disability scores (baseline/3 days/14 days/1 month): vertebroplasty (16.6±3.8/13.0±5.2/12.4±5.8/12.0±6.3) vs. sham (17.5±4.1/12.5±5.5/12.3±5.9/13.0±6.4), p = 0.30, 0.35, 0.49. Pain intensity scores: vertebroplasty (6.9±2.0/4.2±2.8/4.3±2.9/3.9±2.9) vs. sham (7.2±1.8/3.9±2.9/4.5±2.8/4.6±3.0), p = 0.37, 0.77, 0.19. No significant differences by pain duration (<13 weeks, 14-26 weeks, 27-52 weeks).	compression fractures in patients treated with vertebroplasty were similar to the improvements in a control group."	after 1 month for both groups [8(12%) of vertebroplasty group vs. 27(43%) controls crossed over], precluding assessment of long-term effects. Data suggest no benefit.
Voormolen 2007 (score=5.5)	Vertebroplasty	RCT	No mention of sponsorship or COI.	N = 34 compression fractures and "refractive to medical therapy for at least 6 weeks and	Mean age: 73 years; 6 males, 28 females	Vertebroplasty vs. pain management (NSAID or opioid). Study terminated early as nearly all pain management	1 day, 2 weeks	VAS pain scores (baseline/day 1/2weeks): PV 7.1/4.7/4.9 vs. OPM 7.6/7.1/6.4. Analgesic use: PV 1.9/1.1/1.2 vs. OPM 1.7/2.5/2.6.	"Pain relief and improvement of mobility, function, and stature after PV is immediate and significantly better in the	Short 2-week trial after which able to crossover. Small sample; baseline differences. Required at least 6 weeks prior treatment (likely including pain

				no longer than 6 months."		patients asked to be treated with vertebroplasty after 2 weeks (suggests bias).			short term compared with OPM treatment."	management) appears to bias in favor of other intervention as pain management would then be "more of the same."

KYPHOPLASTY

Kyphoplasty, first introduced in 1998, has been used similarly to vertebroplasty to restore vertebral body height and improve sagittal alignment of the spine.(1433, 1434, 1455, 1456) Kyphoplasty involves injection of polymethylmethacrylate within a cavity in the vertebral body that has been created by percutaneous insertion of a balloon through the involved pedicle(s).(1433, 1434, 1457)

Recommendation: Kyphoplasty for Cervical and Thoracic Pain Due to Vertebral Compression Fractures

There is no recommendation for or against the use of kyphoplasty as a treatment for patients with cervical or thoracic pain due to vertebral compression fractures.

Indications – Vertebral body compression fractures among patients with severe pain; patients who have had fractures despite bisphosphonate therapy may be candidates.

Strength of Evidence – **No Recommendation, Insufficient Evidence (I)**
Level of Confidence –Low

Rationale for Recommendation

There are no quality randomized controlled trials comparing kyphoplasty with a sham procedure. There is one moderate-quality study comparing kyphoplasty with an unstructured, unblinded non-interventional control that included cancer patients.(1458) That study also differentially utilized passive treatments between the two groups, such as bed rest and braces, and that may have confounded the results. The other moderate-quality study compared two types of cement and found the calcium phosphate cement to be inferior for burst fractures.(1457) There are other non-randomized comparative clinical trials and other low-quality studies suggesting benefit.(1433, 1459-1461) These have been compiled into meta-analyses with a conclusion of efficacy (as well as efficacy of vertebroplasty) that have been supported by others.(1433, 1434, 1462-1464) Yet, as kyphoplasty is similar to vertebroplasty, and two high-quality sham-controlled trials for vertebroplasty are now reported documenting a lack of benefit, (1436, 1437) and despite the Wardlaw study which included patients with neoplasia, it appears reasonable to assume the same lack of benefit will eventually be shown for kyphoplasty for treatment of non-cancer patients. It remains unclear whether there are selected patients such as those severely affected, patients with 3 or more simultaneous compression fractures, or patients with pathologic fractures due to neoplasms,(1433) who may derive benefit from this procedure. Kyphoplasty is invasive, has complications, and is costly. There is no recommendation for or against kyphoplasty other than highly selected patients who failed other interventions (including quality medical management), and in whom there are no other options available, whose significant pain is not resolving, and especially those for whom bisphosphonate therapy has failed. A systematic review found kyphoplasty patients to have outcomes and pain reduction compared to patients receiving conservative treatment.(1465)

Evidence for the Use of Kyphoplasty

There are 2 moderate-quality RCTs incorporated into this analysis.(1457, 1458) There is 1 low-quality RCT in Appendix 1.(1466)

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

kyphoplasty, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies.*

to find 1125 articles. Of the 1125 articles, we reviewed 1125 articles and included 2 articles (2 randomized controlled trials and 0 systematic reviews).

Author Year (Score):	Category:	Study type:	Conflict of Interest:	Sample size:	Age/Sex:	Comparison:	Follow-up:	Results:	Conclusion:	Comments:
Wardlaw 2009 (score=6.0)	Kyphoplasty	RCT	Sponsored by Medtronic Spine LLC. COI: Sponsor contributed to study design, data monitoring, and reporting of results, and paid for statistical analysis.	N = 300 with 1-3 compression fractures T5-L5, <3 month fracture age.; included malignancies ; 12 month follow-up	Mean age: 73.2 years; 68 males, 232 females	Kyphoplasty plus non-operative care vs. non-operative alone. Non-operative care unstructured and included analgesics, bed rest, back braces, physiotherapy, rehabilitation programs, walking aids, vitamin D, calcium, anti-resorptive or anabolic agents.	1 month, 12 months	Mean improvement in SF-36 physical component improved at 1 month 5.2 points more than for non-operative group ($p < 0.0001$). Differences decreased over time (4.0, 3.2, 1.5 at 3, 6, 12 months) and not different at 12 months. Roland Morris improved 4.0 pts at 1 month and 2.6 at 12 months ($p < 0.0001$ and $p = 0.0012$); 2.9 fewer days of restricted activity per 2 weeks than non-operative at 1 month ($p = 0.0004$).	"[C]ompared with non-surgical management, balloon kyphoplasty resulted in improvements in quality of life and disability measures and reduction of back pain in patients with acute painful vertebral fractures; however, differences in improvement… diminished by 1 year."	No sham treatment arm. Somewhat more multiple fractures in kyphoplasty group (32.9% vs. 23.8%). Heterogeneous and unstructured non-operative care precludes assessment of comparison with specific treatments. Some non-operative treatments more utilized in non-operative group and questionable: bed rest (42 vs. 23%), back braces (20 vs. 7%), possibly worsening clinical case, potentially confounding results.
Blattert 2009 (score=4.5)	Kyphoplasty	RCT	No sponsorship or COI.	N = 56 osteoporotic with 60 fractures; excluded those under age 65	Mean age: 74 years; no mention of sex.	Kyphoplasty with polymethylmethacrylate (PMMA) vs. calcium phosphate cement (CaP)	6 weeks, 1 year	VAS pain ratings (pre/1 year): A1.3 fractures CaP (7.9/2.1) vs. PMMA (8.2/2.3). A3 fractures CaP (8.2/7.4) vs. PMMA (8.1/2.5).	"The routine use of the CaP tested is not currently recommended for kyphoplasty."	Baseline data not well described. Long-term dropout rate unclear. Results worse for CaP A3 fractures. Study does not compare kyphoplasty with sham procedure, non-interventional control, or control group with a known success/failure rate.

CERVICAL SPINAL CORD STIMULATORS

Spinal cord stimulators (SCS) deliver electrical impulses to the spinal cord area through electrodes that are implanted in the epidural space.(1467, 1468) While most commonly utilized in the lumbar spine, they are utilized for treatment of the cervical spine for chronic cervicothoracic spinal pain patients with or without radiculopathy.

Recommendation: Spinal Cord Stimulators for Treatment of Chronic Cervicothoracic Pain with or without Radiculopathy

Spinal cord stimulators are not recommended for chronic cervicothoracic pain with or without radiculopathy.

Strength of Evidence – **Not Recommended, Insufficient Evidence (I)**
Level of Confidence – Low

Rationale for Recommendation

There are no quality trials of SCS in cervicothoracic pain with or without radiculopathy. There is one case series of cervical SCSs in only 5 chronic cervicothoracic pain patients who had failed to improve with conservative therapies and cervical fusion surgeries. Eighty-percent of the patients indicated at least 50% pain reduction during a trial implantation lasting 5 to 7 days. After implantation, follow-up ranged from 1 to 9 months in 4 patients. They reported pain relief of >50% at 6 months. They did not report any serious adverse events during their follow-up period.(1468) (See Low Back Disorders and Chronic Pain guidelines for discussion of spinal cord stimulators.) SCS are invasive, have high adverse effects, and are high cost. They are not recommended for treatment of cervicothoracic pain with or without radiculopathy.

Evidence for the Use of Cervical Spinal Cord Stimulators

There are no quality studies incorporated into this analysis.

We searched PubMed, EBSCO, Google Scholar, and Cochrane Review with no limits on publication dates and then an updated search was conducted using PubMed for publications between 1/1/2013 and 11/15/2017. We used the following search terms:

spinal cord stimulation, spinal stimulation, spinal cord stimulators, cervicalgia, neck pain, cervical pain, neck, cervical, vertebrae, vertebral, spine, radiculopathy, radiculopathies, radicular pain, intervertebral disc displacement, herniated, herniat, displacement, displacements, displaced, disk, disc, disks, discs, pain, controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly, systematic, systematic review, retrospective studies, prospective studies, epidemiological studies, epidemiological research, Nonexperimental Studies.*
to find 2475 articles. Of the 2475 articles, we reviewed 2475 articles and included 0 articles (0 randomized controlled trials and 0 systematic reviews).

Rehabilitation for Delayed Recovery……

See Chronic Pain Guideline for recommendations on the following:

- Work Conditioning, Work Hardening, Early Intervention Programs and Back Schools for Chronic Pain
- Tertiary Pain Programs: Interdisciplinary Pain Rehabilitation Programs, Multidisciplinary Rehabilitation Programs, Chronic Pain Management Programs, and Functional Restoration Programs
- Psychological Evaluation for Chronic Pain Patients
- Cognitive Behavioral Therapy for Patients with Chronic Pain
- Fear Avoidance Belief Training
- Biofeedback

APPENDIX 1: EVIDENCE TABLES FOR EXCLUDED STUDIES (LOW-QUALITY RANDOMIZED CONTROLLED TRIALS AND NON-RANDOMIZED STUDIES)

The following low-quality randomized controlled studies (RCTs) and other studies were reviewed by the Evidence-based Practice Cervical and Thoracic Spine Panel to be all inclusive, but were not relied upon for purposes of the development of this document's guidance on treatments because they were not of high quality due to one or more errors (e.g., lack of defined methodology, incomplete database searches, selective use of the studies and inadequate or incorrect interpretation of the studies' results, etc.), which may render the conclusions invalid. ACOEM's Methodology requires that only moderate- to high-quality literature be used in making recommendations.(1536) (Harris 08)

SPECT

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Type of SPECT	CT used	MRI Used	More than one rater	Blinding of rater	Myelography	Surgery Performed	Clinical outcomes assessed	Long term follow-up (mean when noted)	Results	Conclusion	Comments
Makki 2010 Diagnostic	3.5	534	C, L	Patients who underwent a SPECT scan for spinal pain over 7.5 years. Any cervical or lumbar spinal pain were included.	SPECT	-	-	-	-	-	-	-	-	486 (91.1%) patients had at least one abnormality. This included 42.8% increased uptake in facet joint 29.8% in the vertebral bodies/end plates, and 5.9% in sacroiliac joints. There was a prevalence of increased uptake in both lumbosacral (44%) and cervical facet joints (37%). Significantly higher increased uptake in the older group ($p<0.05$).	"In a hospital-wide population with spinal pain, there is a 42.88% prevalence of increased uptake in the facet joint on SPECT. The incidence increases significantly with advancing age. SPECT can play a role in investigating patients with spinal pain."	Data suggest that as a person ages and has spine pain the prevalence of positive SPECT scan for facet joint pathology increases.

MYELOSCOPY

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Injected Medications	Intradiscal Local Anesthetic	Sedation Used	Fluoroscopy/imaging	Pressure Readings	MRI	CT	CT Myelography	X-ray	More than one rater	More than one level	Surgery Performed	Long term follow-up (mean when noted)	Results	Conclusion	Comments
Uchiyama 1998 Diagnostic	NA	N=18	C	18 patients exhibiting pain or other self-reported neurological symptoms for whom there was either no diagnosis or a doubtful diagnosis.	n/a	-	+	-	-	+	-	+	-	-	-	-	4 years and 3months	The spinal cord, cauda quina, nerve roots, small vessels, and features of the arachnoid membrane with its trabeculations were seen clearly and were vibrating with the pulsating of the spinal fluid. In four patients	"Myelosopy providers detailed information about the subarachnoid space and even reveals dynamic conditions that cannot be identified during	Small numbers and wide age range and wide diagnostic purpose.

				Stenotic patients were excluded														whose condition closely resembled a thoracic arachnoin cyst or spinal cord herniation on clinical and radiologic examination, spinal cord compression attributable proliferation of soft fibrous tissues, with characteristics similar to those of cotton candy, was confirmed.	open surgery or at autopsy. It will bring new concepts to the diagnosis of spinal disease.	

THERMOGRAPHY

Author/Year Study Type	Score	N	Area of Spine	Diagnoses	Type of Thermography	CT used	MRI Used	More than on rater	Blinding of rater	Myelography	Surgery Performed	Clinical outcomes assessed	Long term follow-up (mean when noted)	Results	Conclusion	Comments
Zhang 1999 Diagnostic	2.5	115 patients and 50 controls	C	Cervical disc herniation (CDH)	Digital Infrared Thermographic Imaging device (DITI).	-	-	-	-	-	-	-	-	CDH $C_{3/4}$ patients (9 cases) had thermal differences vs. control group. Significant thermal change in CDH $C_{3/4}$ patients in areas of posterior upper back and shoulder ($p < 0.01$), and areas of anterior shoulder ($p < 0.01$). CDH $C_{4/5}$ patients (11 cases) had significant thermal change in areas of middle and lateral aspect of triceps muscle and proximal radius ($p < 0.01$), and areas of posterior medial aspect of forearm and distal forearm ($p < 0.05$). CDH $C_{5/6}$ patients (57 cases) had significant thermal change in the areas of the anterior aspect of the thenar, thumb, and second finger ($p < 0.01$), and areas of anterior aspect of pararadial region ($p < 0.05$). CDH $C_{6/7}$ patients (30 cases) had significant thermal change in areas of	"In conclusion, the areas of the thermal change in CDH can be helpful in diagnosing the level of disc protrusion and in detecting the symptomatic level in multiple CDH patients."	Sparse methods, suggests some efficacy in the use of thermatomal changes for diagnosing CDH patients but study did not clearly define case definition.

														posterior aspect of ulnar and palmar regions (p <0.01), and areas of anterior aspect of ulnar region and some fingers (p <0.05).CDH $C_{7/T1}$ patients (8 cases) had significant thermal change in the areas of scapula and posterior medial aspect of arm (p <0.01) and areas of anterior medial aspect of arm (p <0.05).		

EDUCATION

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Lamb 2012 2 linked, pragmatic, RCTs Funded by the NIHR Health Technology Assessment programme. No mention of COI.	Trial 1: 2.0 Trial 2: 3.5	N = 3851 with an acute whiplash injury of whiplash-associated disorder grades I–III were eligible for Step 1, and those who attended emergency departments or EDs with whiplash injuries and had persistent symptoms 3 weeks after ED attendance were eligible for Step 2.	Step I: Usual care advice or UCA (N = 1598). Psycho-educational intervention or The Whiplash Book advice (WBA/active management advice) (N = 2253). Step II: Experimental Intervention or physiotherapy package, 6 sessions of therapy, over an 8-week period or a single session from a physiotherapist. Outcome measures; Neck Disability Index (NDI) including severity/frequency	NDI scores for physiotherapy group were on average 3.2% point lower than those of the advice group at 4-month follow-up and no difference at 8 and 12 months.	"MINT suggests that enhanced psycho-educational interventions in EDs are no more effective than UCA in reducing the burden of acute whiplash injuries."	Lack of details for randomization, allocation, control of cointerventions. Low compliance rates, no blinding. Conclusions are therefore limited.

			of pain and symptoms, plus range of activities including self-care, driving, reading, sleeping and recreation. Secondary outcomes; mental and physical health-related quality-of-life or HRQoL, subscales Short Form questionnaire-12 items (SF-12) and number of work days lost.			

REST AND RELATIVE REST

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Gennis 1996 RCT No mention of industry sponsorship or COIs.	3.5	N = 250 whiplash injury-related pain	NSAIDs with soft cervical collar vs. no collar	Only 74 subjects (38%) completely recovered. Soft cervical collar group did not have a significant different difference in pain (chi-square = 1.9; p = 0.59). Recovery (chi-square = 0.91; p = 0.34) and improvement (chi-square = 0.92; p = 0.34) between control and cervical collar group did not differ significantly either.	"[D]espite perceived temporary comfort in some patients during intermittent soft cervical collar use, there is no evidence for quicker injury resolution with their use."	Follow up done by telephone interview at 6 weeks. No benefit from collar was reported. Data suggest neck collars not helpful for acute whiplash patients.
Mealy 1986 RCT No mention of industry sponsorship or COIs.	3.5	N = 61 acute whiplash injuries	Standard treatment (soft cervical collar, rest, and initial mobilization) vs. alternative regimen of early active mobilization	"Results showed that eight weeks after the accident the degree of improvement seen in the actively treated group compared with the group given standard treatment was significantly greater for both cervical movement ($p < 0.05$) and intensity of pain ($p < 0.0125$)."	"Our results confirmed expectations that initial immobility after whiplash injuries gives rise to prolonged symptoms whereas a more rapid improvement can be achieved by early active management without any consequent increase in discomfort."	Lack of study details lowered score. Unsure of number of treatments or amount of time treatment given. Both groups improved during 8 week follow up. Active exercises appear beneficial vs. rest for acute whiplash injuries.
McKinney 1989 RCT	1.5	N = 170 acute whiplash injuries	Rest and analgesia vs. active out-patient physiotherapy vs.	Patients who received out-patient physiotherapy had significant improvement in severity of neck pain ($p < 0.01$) and cervical	"There appears to be no difference in effectiveness between outpatient	No blinding, lack of study details makes conclusions difficult. PT group had mostly passive modalities. No

No mention of industry sponsorship or COIs.			mobilization advice	movement (p <0.01) at 1 and 2 months post-injury vs. patients who received analgesia and cervical collar. Patients offered comprehensive advice for home mobilization by a physiotherapist showed similar improvement.	physiotherapy and home mobilization."	strengthening exercises performed. Data suggest cervical rest in a collar is not helpful for acute whiplash patients.

SLEEP PILLOWS AND SLEEP POSTURE

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Lavin 1997 Crossover trial Supported by funds and materials from Mediflow Water Pillow Ltd. COI, an organization with which one or more of the authors is associated has received financial benefits from a commercial party.	3.0	N = 41 benign cervical pain syndromes, free of cognitive impairment	Subjects used their usual pillows for 1st week of 5-week study. Subsequently randomly assigned to use each of other 2 pillows for 2-week periods.	Mean±SE pain relief roll pillow: morning: 2.42±0.42; p <0.01; evening: 2.76±0.44; p <0.05. Water pillow in morning: 3.87±0.41; p <0.1. Evening: 3.86±0.42; p <0.1.	"Proper selection of a pillow can significantly reduce pain and improve quality of sleep but does not significantly affect disability outcomes measured by the SIP."	Small numbers. No "washout" period before crossover between 2 study pillows. Low compliance rate for roll pillow; >50% stopped use before 2 weeks completed.
Erfanian 2004 RCT No mention of sponsorship or COI.	2.0	N = 36 with chronic neck pain with and without headache; mean age 34.1±9.5 for experimental group and 30.2±7.7 for non-experimental group.	Experimental group, cervical pillow prototype with foam quadrants of increasing height (N = 17) vs. Non-experimental group, continued using his/her usual pillow (N = 19). Follow-up at baseline and weeks 2, 3, and 4.	Mean ± SD for weekly NDI score: experimental vs. non-experimental: week 1: 14.18±7.77 vs. 11.21±6.42; week 2: 14.00±7.10 vs. 12.79±16.33; week 3: 11.09±5.54 vs. 13.21±16.28; week 4: 9.27±6.02 vs. 15.64±14.96, (p = 0.04). Weekly AM NRS scores: week 1: 2.29±2.13 vs. 1.32±1.24; week 2: 1.98±1.87 vs. 1.13±1.36; week 3: 1.82±1.71 vs. 1.22±1.27; week 4: 1.56±1.45 vs. 1.49±1.49, (p = 0.04).	"This study suggests that compared to conventional pillows, the experimental semi-customized cervical pillow in this study proved to be effective in reducing daily AM neck pain and weekly NDI scores in a group of chronic neck pain sufferers."	Methodological details sparse.

EXERCISES

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Directional Exercise						
Guzy 2011 RCT No mention of COI or sponsorship.	1.0	N = 61 with cervical derangement syndrome. Mean±SD age: McKenzie group 46.67±7.91 years. Rehab group: 49.03±8.77 years.	M Group: McKenzie method (N = 30) vs. T Group: Complex rehabilitation program (N = 31). 3 week follow-up.	Within group changes in pain intensity in the neck: M Group 103.39, p<0.001. T group 40.23, p<0.001.	"1) The McKenzie method seems to be more efficacious than traditional therapy in regard to centralization of symptoms, overall, head and upper extremities pain intensity, headache and number of pain-free days in treating patients with cervical derangement syndrome. 2) The movement which centralizes symptoms is more effective than a complex rehabilitation program."	Chronic LBP trial with sparse details. Trends towards worse pain in all body parts in the traditional group, concerning for randomization failure (randomization method not stated). Data suggest McKenzie may be more effective than a traditional approach of many methods.
Specific Stretching and Flexibility Exercises						
Ma 2011 RCT Sponsored by Hong Kong Polytechnic University. No mention of COI.	3.5	N = 60 with chronic neck/ shoulder pain from computer use. Mean±SD age: 33.3±9.7	Biofeedback machine for 2 hours daily while performing computer work (Group A; N=15) vs. Strengthening and stretching exercises using Thera-band for 20 minutes 4 times a day (Group B; N = 15) vs. Inferential therapy (20 minutes) and hot packs applied to neck and shoulder regions for 15 minutes twice a week (Group C, N = 15) vs. control group receiving education booklet about ergonomics (Group D; N = 15). Outcomes assessed	Mean±SD of Neck Disability Index for Group A vs. Group B vs. Group C vs. Group D: 7.50±2.83 vs. 11.30±2.59 vs. 13.55±2.18 vs. 16.40±2.59, at 6 weeks (p=0.000); and 7.70±2.79 vs. 11.88±2.36 vs. 15.55±2.87 vs. 16.7±2.94, at 6 months (p=0.000). Mean±SD for Visual Analogue Scale for Group A vs. Group B vs. Group C vs. Group D: 1.52±0.53 vs. 3.44±0.46 vs. 3.77±1.09 vs. 5.15±1.33 at 6 weeks (p=0.000); and 1.70±0.63 vs. 3.70±0.90 vs. 5.05±1.23 vs. 5.70±1.16 at 6 months (p=0.000).	"Biofeedback, active exercise, and passive treatment all improved NDI and EMG results after 6 weeks of treatment. Biofeedback yielded the greatest average improvement in neck and shoulder muscle activation patterns during typing… On the whole, the results indicate more favorable long-term outcomes from biofeedback training compared with conventional interventions such as active exercise or passive treatment modalities."	High dropout rate.

			at baseline, 6 weeks and at 6 month follow up.			
Hakkinen 2008 RCT No COI. Funded by Medical Research Foundation from Jyva¨ skyla¨ Central Hospital.	3.0	N = 1,051 non-specific neck pain (duration >6 months)	Strength training and stretching group supported by 10 group training sessions (n = 49) vs. stretching group instructed to perform stretching exercises only (n = 52) as instructed in 1 group session.	Neck disability indices were lower at the 12-month follow-up in both groups (p <0.001).	"No statistically significant differences in neck pain and disability were observed between the two home-based training regimens. Combined strength training and stretching or stretching only were probably as effective in achieving a long-term improvement although the training adherence was rather low most of the time."	No mention of co-interventions of baseline rate of exercise of previous PT. No mechanisms of injury. Exercises are beneficial for cervical spine pain.
Crawford 2004 RCT No mention of industry sponsorship or COIs.	3.0	N = 108 acute neck pain after motor vehicle accident	Early exercise vs. cervical soft collar for 3 weeks. All had soft collar, NSAIDs at enrollment until randomized at next clinic visit (not defined, presumably within 3-4 days).	Mobilization vs. soft collar 3, 12, 52 weeks Activities of Daily Living: no differences VAS (0-10): No differences ROM (0-380): No differences except at baseline. Return to work: 34 days vs. 17 days, p value not reported.	"[T]his study has shown that following soft tissue injuries to the neck, treatment in a soft collar had no clinical benefit compared to early mobilisation in terms of recovery of function, pain or range of neck movement but was associated with an increased time to return to work."	Lack of study details. Quasi-randomization. No blinding, no report of compliance to treatment regimen. Study suggests no difference in outcomes in pain or function. Soft collar group had more lost time from work than mobilization group.
Omer 2003 RCT No mention of sponsorship or COI.	2.0	N = 50 with "cumulative trauma disorder" Mobilization group mean age 27.4 and Training group 27.8 years.	Mobilization, stretching, strengthening and relaxation (N = 25) vs. Training course (N = 25). Follow-up assessments were made at 2 months.	At 2 months the treatment group had improvements in NRS Mobilization vs. Training 1.52 vs. 5.68 (p<0.001), pain disability index 8.16 vs. 16.68 (p<.05) and beck depression scale 8.52 vs. 12.08 (p<.05).	"Mobilization, stretching, strengthening, and relaxation exercises reduces pain and depression levels of CTD patients in the short term."	Lack of baseline characteristics and cointerventions. Diagnoses of CTS and MPS syndrome suspect causing conclusions to be uninterpretable.
Cunha 2008 RCT No mention of industry sponsorship or COI.	1.5	N = 31 females diagnosed with primary mechanical neck pain lasting > 12 weeks, mean (SD) age 44.4 (7.8) for GPR group and 48.7 (7.3) for conventional	Global posture reeducation group performing muscle chain stretching (GPR) (N = 15) vs. Conventional stretching group performing standard static muscle stretching (N = 16). Both groups underwent manual therapy.	Concerning health-related quality of life, improvement was observed after treatment, except for the GPR group in the general health domain. At follow-up, both groups reported more pain than immediately after treatment and improvements in all other domains. No significant differences were observed between groups (P>0.05)	"Conventional stretching and muscle chain stretching, in association to manual therapy, were equally effective in reducing pain and improving range of motion and quality of life in female patients with chronic neck pain, both immediately after treatment and at a follow-up six weeks later. Since muscle stretching is a low-cost treatment, it should be	Small sample size (N=31). Methodological details sparse

		stretching group	Assessments at baseline, post treatment and 6 weeks.		pursued more often for treating chronic neck pain."	
Allan 2003 RCT No mention of sponsorship or COI.	1.5	N = 16 with chronic mechanical neck pain. Mean ages for treatment groups 1, 2, and 3: 42, 45, and 39 years.	Treatment group 1 (control, N = 5) received cervical manipulation alone vs. Treatment group 2 (N = 5) received neck musculature stretching immediately prior to manipulation vs. Treatment group 3 (N = 6) received neck musculature stretching immediately post manipulation. Assessment before and immediately after intervention. No long-term follow-up.	Range of Motion (RoM): No statistical difference between groups for mid-study ($\chi 2 = 0.876$, d.f. = 2, (p = 0.645)) or end study ($\chi 2 = 0.101$, d.f. = 2, (p = 0.951)). Pain: No statistical difference between groups for mid-study ($\chi 2 = 1.616$, d.f.=2, p = 0.446) or end study ($\chi 2=2.447$, d.f. = 2, (p = 0.294)).	"(I)nter-group analysis failed to differentiate which treatment was the most effective with regard to RoM, pain and disability."	Small sample size (N=16). Methodological details sparse.
Salo 2012 RCT No mention of industry sponsorship. No COI.	NA	N = 101 with presence of non-specific neck pain for more than 6 months; mean age 40±10 for Stretching group and 41±9 for the CSSG group.	Combined Strength Training and Stretching group (CSSG); elastic rubber bands attached to a leather strap, forward, toward the right and left and directly backwards combined with a training program; 15 repetitions, 10 supervised sessions (N = 49) vs. Stretching group (SG); same stretching exercises as CSSG (N = 52). Both groups instructed	CSSG group increased weekly exercise frequency by 0.13 times a week (95% CI, 0.00-0.27, (p=0.05)). The SG group increased weekly exercising by 0.22 times a week (95% CI, 0.03-0.42, (p=0.03)). There were no statistically significant differences at any of the follow up times.	"Both the CSSG and CG training protocols were feasible and equally effective for home-based regimes that achieved improvement in HRQoL. The baseline HRQoL and pain values had only minor effects on training adherence."	Secondary analysis, not scored

			to repeat exercises at home 3 times a week and keep an exercise diary. Follow up baseline and 12 months.			
Strengthening and Stabilization Exercises						
Pedersen 2013 RCT Sponsored by the Danish Working Environment Research Fund. No COI.	3.5	N = 537 with repetitive work task, to evaluate long-term adherence and effects of workplace strength training intervention on back, neck and upper extremity pain, with the mean age of 42.	Training group 1 or TG1, supervised strength training for 20 minutes, three times per week, for 20 weeks (N = 282) vs Training group 2 or TG2, the same training and schedule as TG1, during the second half of year (N = 255). Follow-up for 12 months.	Intent-to-treat analysis at one year showed significant time effect for pain in neck, R-shoulder, R-elbow, R-hand, upper back and lower back and DASH to decrease, ($p < 0.01$-0.0001). Group by time effect for pain in the neck and DASH, ($p < 0.001$), and R-shoulder, R-hand and lower back, ($p < 0.05$).	"The pain reductions achieved during the intensive training phase with supervision appears to be maintained a half year later, i.e. follow up with self-administered training can keep pain on a low level but does not result in further pain reduction."	High dropout rate. Methodological details sparse. At 20 weeks there were some differences but at 1 year there were few.
Hamberg-van Reenen 2009 RCT No mention of sponsorship or COI.	3.0	N = 22 with regular or prolonged neck/shoulder or back pain in past 12 months, age mean 36.6 for training group and mean 37.8 for control group.	See Hamberg-van Reenen 2009 above	See Hamberg-van Reenen 2009 above	See Hamberg-van Reenen 2009 above	See Hamberg-van Reenen 2009 above
Kaya 2012 RCT No mention of industry sponsorship or COI.	3.0	N = 116 healthy volunteers who had not performed any regular physical activity for at least 2 years. Mean age was 21.26 years.	Cervical stabilization exercise Group (N = 23) vs. Lumbar exercise Group (N = 23) vs. Thoracic exercise Group (N = 23) vs. Combined Exercise Group (N = 23) vs. Control (No regular exercise/physical	At six weeks, the Thoracic group showed a significant difference compared to the other groups for Eyes Closed Postural Stability, -1.63 vs. 0.26 (vs. Control) (P=0.003). The Cervical group showed significant improvement compared to control for Weight Distribution, -1.35 vs. 1.19 ($p = 0.004$). At 12 weeks the difference between the Thoracic group and control for postural	"The study put forward the following outstanding findings: (i) Thoracic group showed the maximum decrease in SI among all groups after training and kept the improvement at the 12th week, (ii) Thoracic group had improvements in somatosensory reactions and SI in head rotated positions in long term, (iii) Cervical group had significant improvements	Methodological details sparse The ages were statistically different. Also, the age range was small (19-23 years)

			activity) (N = 24). Follow-up at 6 and 12 weeks.	stability remained significant, -1.67 vs. 0.75 (p = 0.005).	in WDI in head right rotated position after training."	
Ma 2011 RCT Sponsored by Hong Kong Polytechnic University. No mention of COI.	3.5	N=60 participants with chronic neck/ shoulder pain from computer use. Mean±SD age: 33.3±9.7	Biofeedback machine for 2 hours daily while performing computer work (Group A; N = 15) vs. Strengthening and stretching exercises using Thera-band for 20 minutes 4 times a day (Group B; N = 15) vs. Inferential therapy (20 minutes) and hot packs applied to neck and shoulder regions for 15 minutes twice a week (Group C, N=15) vs. control group receiving education booklet about ergonomics (Group D; N = 15). Outcomes assessed at baseline, 6 weeks and at 6 month follow up.	Mean±SD of Neck Disability Index for Group A vs. Group B vs. Group C vs. Group D: 7.50±2.83 vs. 11.30±2.59 vs. 13.55±2.18 vs. 16.40±2.59, at 6 weeks (p=0.000); and 7.70±2.79 vs. 11.88±2.36 vs. 15.55±2.87 vs. 16.7±2.94, at 6 months (p = 0.000). Mean±SD for Visual Analogue Scale for Group A vs. Group B vs. Group C vs. Group D: 1.52±0.53 vs. 3.44±0.46 vs. 3.77±1.09 vs. 5.15±1.33 at 6 weeks (p = 0.000); and 1.70±0.63 vs. 3.70±0.90 vs. 5.05±1.23 vs. 5.70±1.16 at 6 months (p=0.000).	"Biofeedback, active exercise, and passive treatment all improved NDI and EMG results after 6 weeks of treatment. Biofeedback yielded the greatest average improvement in neck and shoulder muscle activation patterns during typing… On the whole, the results indicate more favorable long-term outcomes from biofeedback training compared with conventional interventions such as active exercise or passive treatment modalities."	High dropout rate.
Falla 2008 RCT Sponsored by the National Health and Medical Research Council of Australia. No mention of COI.	3.5	N = 58 females with history of chronic neck pain >3-month duration, mean (±SD) age 33.7 (±10.1) for cranio-cervical flexion group and 38.1 (±10.7) for endurance-strength exercise group	See Falla 2008 above	See Falla 2008 above	See Falla 2008 above	Methodological details sparse.

Dellve 2011 RCT Sponsored by the Swedish Council for Working Life and social Research. No COI.	3.0	N = 60 females with chronic neck pain and at least 60 days sick leave from work due to neck pain. Age range: 35-60 years.	Myofeedback training for a minimum of 8 hours a week (2 hours for 4 days/week) for a 4 week period (N = 25) vs. Muscular Strength Training for 5-10 minutes for 6 days a week (N = 27) vs. Control group (N = 21). Follow up at 1- and 3- months	From baseline to 3 month follow-up the myofeedback group improved significantly in vitality (p = 0.021). The strength training group improved significantly in self-rated health and pain (p = 0.042) and work ability (p = 0.005).The control group improved significantly in neck pain scores (p = 0.046) and cutlery wiping performance (p = 0.006).	"The two interventions showed positive results, suggesting that they could be developed for use in health care practice to address pain and work ability. The intensive muscular strength training program, which is both easy to conduct at home and easy to coach, was associated with increased work ability."	Randomization and allocation method not described. No assessor blinding. No control of co-interventions. Loss to follow-up greater than 20%. Data suggest interventions may be of benefit.
Mongini 2012 RCT Sponsored by the Compagnia di San Paolo and the Regione Piemonte. No COI.	3.0	N = 1881 workers with neck and shoulder pain. Median age 47 years.	Shoulder and neck exercises plus relaxation and posture exercises (N = 909) vs. Control (N = 972). 3 months follow up.	The intracluster correlation (ICC) for neck and shoulder pain responders was 0.029 (95% CI 0.007 to 0.110). For neck/shoulder pain, mean change of frequency from baseline was -0.95 (-2.40 to 0.50) for low compliance, -3.46 (-4.43 to -2.49) for medium compliance, -4.67 (-6.14 to -3.20) for high compliance. When comparing high vs. low compliance for frequency of neck/shoulder pain -3.52 (-5.20 to -1.83).	"…Our study shows that a low-cost, low-intensity educational and physical program is effective in reducing head and neck/shoulder pain and possibly analgesic drug consumption in large working populations."	High dropout rate with low compliance. Randomization of participating city departments. No exclusion criteria. Data collected by participants on other participants. Intervention group had significantly more research contact time, (possible contact bias).
Murphy 2010 RCT Sponsored by the Australian Spinal Research Foundation. No COI.	2.0	N = 20 with chronic, non-specific neck pain. Mean age: 43± 12 years	See Murphy 2010 above.	See Murphy 2010 above.	See Murphy 2010 above.	Small sample size (N=20). Methodological details sparse.
Ylinen 2006 RCT Sponsored by the Social Insurance Institution,	2.0	N = 180 females diagnosed with chronic non-specific neck pain; age 25-53 years.	STG, specific neck exercises using an elastic band as a resistance; 1 set of 15 reps directly forward, left and right, and directly backward vs. ETG,	No statistically significant differences to report between the groups in any of the outcomes.	"Neck and shoulder muscle training was shown to be an effective therapy for chronic neck pain, resulting in early improvement in both the strength tests and subjective measures. The results can be	Methodological details sparse.

Finland. No mention of COI.			trained neck flexor muscles with a constant load; 3 sets of 20 reps. Follow up baseline, 2, 6, and 12 months.		maintained and even improved with long-term training."	
McKinney 1989 No mention of sponsorship or COI.	1.5	N = 170 with acute whiplash injuries. Mean age 30.6 years.	Active out-patient therapy physiotherapy for 40 minutes sessions for 6 weeks and posture exercises (N = 71) vs. Mobilization advice and encouragement of mobilization exercises for 30 minutes (N = 66) vs. Rest and analgesia for 10-14 days (N = 33). Follow up at 1 and 2 months.	Patients who received out-patient physiotherapy had significant improvement in severity of neck pain ($p < 0.01$) and cervical movement ($p < 0.01$) at 1 and 2 months post-injury vs. patients who received analgesia and a cervical collar. Patients offered comprehensive advice for home mobilization by a physiotherapist showed a similar improvement.	"We conclude that good advice and tailored practical instruction on early mobilization, when given by a suitably experienced physiotherapist, is as effective as out-patient physiotherapy in reducing pain and increasing mobility and would recommend this as an ideal alternative in the management of the increasing number of patients with acute neck sprains, within the constraints of limited physiotherapy resources."	No blinding, lack of study details. Physical therapy group had mostly passive modalities. No strengthening exercises performed. Cervical rest in a collar is not recommended for acute whiplash patients.
Umar 2012 RCT No mention of sponsorship. No COI.	0.5	N = 93 patients with cervical radiculopathy. Age range 40-70 years.	Cervical traction and core muscle strengthening vs. cervical traction only. Follow up at 6 months.	Experimental group had a significant improvement compared to control ($p<0.05$). After treatment the control group did not have significant improvement in numbness, the experimental group had 45% of patients with no numbness.	"Results of the present study also supported the fact that cervical traction is more useful when it is combined with core muscle strengthening exercises in the long term follow up."	Lack of study details for each point of analysis. Limited conclusions. Lack of details in the group sample.
Salo 2012 RCT No mention of sponsorship. No COI.	NA	N = 101 with a presence of non-specific neck pain >6 months; mean age 40±10 for Stretching group and 41±9 for the CSSG group.	See Salo 2012 above	See Salo 2012 above	See Salo 2012 above	See Salo 2012 above
Andersen 2013 RCT Sponsored by Danish Working	N/A	N = 537 women with severe neck pain. Calculated	Training group performed 4 high-intensity-specific strength training exercises for neck and 1 for forearm	From baseline to follow-up, significant difference in VAS ($p<0.01$) – Control group: 12mm decrease (95% CI: -19 to -5); Training group: 26mm decrease (95% CI: -31 to -20).	"In conclusion, 20 weeks with as little as 1 to 2 weekly strength training sessions of 20 minutes adhering to principles of periodization and progressive overload	Participants are all women. Not scored

Environment Research Fund and Danish Ministry of Culture Committee for Sports Research. No mention of COI.		mean age 42.4 years.	(N = 276) vs. Control group were offered usual care (N = 255). No long-term follow-up.		effectively relieves severe neck pain among women."	
Lidegaard 2013 RCT Sponsored by the Hygenic Corporation. COI, Lars L. Andersen received a grant from the Danish Rheumatism Association.	N/A	N = 30 female office workers suffering from chronic neck and shoulder pain, the mean age (± SD) 41.7 (± 10.8) for training group and 40.5 (± 7.27) for control group	Treatment group receiving high-intensity elastic training for 2 minutes per day (N = 15) vs. Control group receiving weekly general health information emails (N =15). Assessments at baseline and 10 weeks.	Training group improved isometric muscle strength and shoulder/neck pain intensity values over control: Strength- 6%; ($p < 0.05$), Shoulder/neck pain- 40%; ($p < 0.01$). Training group increased frequency of EMG gaps (more relaxed muscle activity) over control: 300%, 3.1 gaps per min to 12.3 gaps per min; ($p<0.05$).	"[W]e reported beneficial long-term changes in both the frequency and duration of the EMG gaps alongside with alterations in the time with minimal muscular activation. In summary, the acute response to a single session of resistance training appeared to generate an unfavorable muscle activity pattern. By contrast, the longitudinal changes were beneficial in terms of longer and more frequent periods of complete muscular relaxation and reduced pain."	Not scored. Secondary analysis.
Aerobic Exercise/Endurance Training						
Falla 2008 RCT Sponsored by the National Health and Medical Research Council of Australia. No mention of COI.	3.5	N = 58 females with history of chronic neck pain of greater >3-month duration, mean (±SD) age 33.7 (±10.1) for cranio-cervical flexion group and 38.1 (±10.7) for endurance-strength exercise group	Endurance-strength exercise group training of cervical flexor consisting of progressive resistance exercise program for cervical flexor muscles (N = 29) vs. Low load cranio-cervical flexion training group (N = 28). Both groups received 6 weeks of treatment. Assessments at baseline and 7 weeks.	There was no significant differences between groups for change in pain or perceived disability ($P>0.05$).	"This study demonstrates that 6 weeks of specific cervical flexor muscle training, which has been shown to improve parameters of muscle function and reduce the symptom of neck pain, may not automatically transfer to changes in muscle activity during an untrained functional upper limb task. These results suggest that rehabilitation of the cervical muscles should be extended to include training in functional postures and tasks."	Methodological details sparse

Hamberg-van Reenen 2009 RCT No mention of sponsorship or COI.	3.0	N = 22 with regular or prolonged neck/shoulder or back pain in the past 12 months, age mean 36.6 for training group and mean 37.8 for control group.	Training Group: warming up of 10 min on a cross-trainer, exercises to increase muscle strength of shoulder and trunk muscles during approximately 40 min (N = 9) vs Control Group, resistance-training program 2x a week during 8 weeks (N = 10). Follow-up for 8 weeks.	There were small differences between the training and control group, but these differences were not statistically significant, ($p > 0.05$).	"In a Randomized Controlled Experiment, we found no effects of a resistance-training program on muscle strength, muscle fatigue, and musculoskeletal discomfort during working tasks. However, at the follow-up measurement, trained workers performed the lifting tasks for a longer time period than the control group, before they reported considerable discomfort. In this study, no training effect was found."	Small sample size (N=22). Methodological details sparse
Søgaard 2012 RCT Sponsored by Danish Medical Research Council and the Danish Rheumatism Association. No mention of CI.	2.5	N = 39 females with clinical diagnosis of trapezius myalgia; aged 30-60 yrs.	General Fitness Training (GFT), leg bicycling with relaxed shoulders; 3 sessions, 20 minutes per week for 10 weeks (N = 15) vs. Specific Strength Training (SST), for the affected muscle; 3 sessions, 20 minutes per week for 10 weeks (N = 16) vs. Reference Intervention without physical activity (REF); 1 hour per week (N = 8). Follow up: baseline and after intervention.	Mean ± SD for pain intensity (VAS) at rest in mm: before vs. after: SST: 23.2±23.1 vs. 11.2±11.8, ($p<0.05$); rate of pain development: GFT: 0.65±0.37 vs. 0.37±0.34, ($p<0.05$).	"In conclusion, GFT performed as leg-bicycling decreased pain development during repetitive work tasks, possibly due to improved oxygenation of the painful muscles. SST lowered the overall level of pain both during rest and work, possibly due to a lowered relative exposure as evidenced by a lowered relative EMG. The results demonstrate differential adaptive mechanisms of contrasting physical exercise interventions on chronic muscle pain at rest and during repetitive work tasks."	Methodological details sparse. Short follow-up period.
Murphy 2010 RCT Sponsored by the Australian Spinal Research Foundation. No COI.	2.0	N=15 with chronic, non-specific neck pain. Mean age: 43± 12 years	Spinal manipulation 1-2 times per week, for 4 weeks (Group 1; N = 8) vs. 4 weeks waiting plus strength and endurance training 1-2 sets of 6-8	Average change for 12 weeks (±SD) of Neck Disability index MG vs. EG: 10.75±9.56 vs. 8.29±7.06 (effect size: 0.293). Average change for 12 weeks (±SD) for "pain now" of MG vs. EG: 16.75±21.14 vs. 12.71±24.84 (effect size: 0.175). Average change for 12 weeks (±SD) for "pain worst" of MG vs. EG:	"This pilot study showed that both exercise and exercise combined with manipulation can improve pain and disability in people with long-term neck pain. The study indicates that the FRR changes had an ES of .636, and 32 subjects per group would be needed to show a	Small sample size and high dropout rate (25%).No difference between groups (ie, exercise alone and exercise plus chiropractic care).

			repetitions for isometric exercises and 1-2 sets of 12-15 repetitions for dynamic exercises 3 times per week for 8 weeks (N = 7). Outcomes assessed at week 1, 4, and 12.	9.5±18.62 vs. 19.8±32.4 (effect size: 0.392).	difference between the 2 treatments with and α of .05 and a power of 0.8."	
Salmon 2013 RCT No mention of sponsorship or COI.	1.5	N = 42 helicopter pilots at a higher risk of suffering from neck pain; mean age 37.8±4.5 for ETP, 35.40±8.22 for CTP, and 37.12±6.31 for control group.	Endurance Training Program (ETP); elastic rubber tubing (flexion, extension, right flex and left flex); 3 sets of 10 reps (N = 15) vs. Coordination Training Group (CTP); guidance of a certified physiotherapist, low-load exercises focused on muscle control (N = 10) vs. Non treatment, Control group (N = 8). Follow up pre and post tests	Mean ± SD for Maximal Voluntary Contractions (MVC) measurements: CTP: flexion: pre vs. post: 155.82±50.89 vs. 177.26±45.15, delta: 21.44, ($p \leq 0.05$); Right flex: pre vs. post: ETP: 163.02±45.50 vs. 186.42±52.93, delta: 23.40, ($p \leq 0.05$), CTP: 169.34±64.68 vs. 196.30±68.15, delta: 26.96, ($p \leq 0.05$.)	"The provision of an ETP and CTP resulted in a positive trend toward improved maximal force and muscular endurance. The greatest improvements in endurance and strength were found for those subjects assigned to the CTP treatment. Our research demonstrates the importance of including a designed and supervised training program into the daily routine of helicopter aviators."	Methodological details sparse.
Yoga						
Yogitha 2010 RCT Sponsored by members of SVYASA and Ebenezer Orthopedic Center. No COI.	3.5	N = 60 with chronic neck pain. Age range 20-70 years.	Mind sound resonance technique (MSRT) Yoga (N = 30) vs. Relaxation control (N = 30). Outcomes assessed at 1- and 10 days.	Both groups showed improvement in pain ($p<0.01$), tenderness ($p<0.01$), extension ($p<0.01$), and spinal flexibility ($p<0.01$). The yoga group had a 95% reduction of pain, 92% reduction of tenderness, and neck disability scores improved by 93%.	"[Y]oga relaxation through MSRT adds significant complimentary benefits to conventional physiotherapy for CNP by reducing pain, disability and state anxiety and improving flexibility."	Lack of details for allocation method, compliance, control of co-interventions. Baseline data for duration of pain not specified, inclusion criteria was non-specific. Data suggest yoga is somewhat beneficial when added to PT.
Spence 1995 RCT No mention of industry	1.5	N = 48 chronic pain patients with history of musculoskeletal pain problems in upper limbs, neck, and/or	Applied EMG biofeedback (EMG) (N = 12) vs. Applied Relaxation Training (ART) (N = 12) vs.	No significant differences between treatments for any of the outcome measures from pre-treatment to follow-up to report.	"In summary, the prediction that a combined approach would produce superior results to either applied relaxation training or EMG biofeedback alone was not supported. Applied relaxation training,	Methodological details sparse.

sponsorship or COI.		shoulders associate with repetitive tasks in the workplace; mean age 43.27±9.40 for ART, 43.41±6.52 for EMG, 40.00±6.57 for CO, and 41.55±9.21 for WLC	Combined EMG biofeedback and relaxation (CO) (N = 12) vs. Waiting List Control (WLC) (N = 12). Follow up pre, post, and 6 months.		EMG biofeedback and a combined procedure were all found to be associated with reductions in pain, symptoms of depression, distress and interference caused by pain, which were continued through to follow-up. The improvements shown were also found to be clinically significant and meaningful. Short-term reductions in anxiety were found during the treatment phase, but were not generally maintained. In the short term, the applied relaxation training group manifest the strongest benefits, but by follow-up there was little difference in outcome between the 3 treatments. It is concluded that treatments that aim to increase awareness of muscle tension levels and to reduce muscle tension in stressful situations offer promise as a therapy component in the rehabilitation of chronic, upper extremity CTDs."	
Cramer 2013 RCT (Cross-over) Sponsored by the Karl and Veronica Carstens Foundation. No COI.	1.5	N=51 with chronic non-specific neck pain for at least 5 days a week lasting >12 weeks, pain intensity >40mm (100mm VAS scale), mean age (±SD) 47.8 (± 10.4)	Yoga Group treated with 90 minute lyengar yoga sessions weekly for 9 weeks (N = 25) vs. Control group receiving self-directed home manual for the first 10 weeks and participation in the same 9-week yoga program at 10 weeks (cross-over) (N = 26). Assessments at baseline, 1 week,	From baseline to 12-month follow-up, pain intensity improved from 48.81 ±17.71 to 32.31 ± 20.68 ($p < 0.001$)), neck-related disability decreased from 25.26 ± 9.02 to 19.49 ± 11.52 ($p = 0.001$)), and bodily pain in the SF-36 improved from 49.37 ± 12.40 to 59.26 ±17.57 ($p = 0.005$)). Improvements in pain intensity were predicted by weekly minutes of yoga practice during the past 4 weeks ($r2 = 0.12$, ($p = 0.028$)); improved neck-related disability ($r2 = 0.24$, ($p = 0.001$)) and bodily pain ($r2= 0.26$, ($p = 0.006$)) were predicted by regular yoga practice during the past 12 months.	"In conclusion, a 9-week yoga intervention appears to be effective in relieving pain and functional disability in patients with chronic nonspecific neck pain for at least 12 months. Sustained yoga practice seems to be the most important predictor of long-term effectiveness. Further, more rigorous studies are needed that compare yoga with active control groups before the long-term effectiveness of yoga for chronic neck pain can be conclusively judged"	Methodological details sparse.

			10 weeks and 12 months.			
Cramer 2013 Qualitative Study Sponsored by the Karl and Veronica Carstens Foundation. No COI.	0.5	N = 18 invited back from above study with chronic non-specific neck pain for at least 5 days a week lasting >12 weeks, pain intensity >40mm (100mm VAS scale), ages 18-60 years	See above. Participants completed drawing of their neck and shoulder regions to reflect their subjective body perceptions before/ after their yoga program. Semi standardized interviews used to explore their body perception, emotional status, everyday life and coping skills, as well as any perceived changes in these dimensions post participation. An interdisciplinary group analyzed the study data using content analysis techniques.	Participants reported change on five dimensions of human experience: physical, cognitive, emotional, behavioral, and social. Physically, most participants cited renewed body awareness, both during their yoga practice and in their daily lives. Such change was echoed in their post-participation body drawings. Cognitively, participants reported increased perceived control over their health. Emotionally, they noted greater acceptance of their pain and life burdens. Behaviorally, they described enhanced use of active coping strategies. Finally, socially, they reported renewed participation in an active life.	"Yoga was seen as a multidimensional intervention linked to change in all dimensions of human experience. Body awareness seems to be a key mechanism in these changes. Further qualitative research should focus on exploring perceived differences between yoga and other exercise or between different yoga styles. Quantitative studies might assess changes in, for example, body awareness or fear-avoidance using standardized instruments or even changes in cortical representations after yoga practice using imaging techniques"	Methodological details sparse.
Other Exercises						
Jellad 2009 RCT No mention of sponsorship or COI.	3.5	N = 39 with cervical radiculopathy (onset within the previous 3 months), the mean (± SD) age 42.08 (± 11.8) for Group A, 38.54 (± 3.6) for Group B, 44.23 (± 4.5) for Group C	Group A, standard rehab program+ cervical spine mobilization + muscle strengthening via isomatic contraction of flexor and extensor muscle + stretching exercise + self-expansion for the spinal muscles (N = 13) vs. Group B, standard rehabilitation + mechanical traction with	Neck pain / Radicular pain / Self-perceived disability / Analgesic consumption at baseline and 6 months; ((p = 0.009) vs. (p <0.0001) vs. (p = 0.23), & (p = 0.002) vs. (p < 0.0001) vs. (p = 0.70) in Group C, at 6 months)/((p = 0.008) vs. (p < 0.0001) vs. (p = 0.51), & (p=0.0001) significance for groups A and B vs. C, at 6 months) /((p = 0.044) vs. (p < 0.0001) vs. (p = 0.67), & (p<0.0001) vs. (p = 0.001) vs. (p = 0.75), at 6 months) / ((p = 0.012) vs. (p <0.0001) vs. (p=0.012), & (p <0.0001) for groups A and B vs. (p = 0.003) for group C, at 6 months).	"Manual or mechanical cervical traction appears to be a major contribution in the rehabilitation of CR particularly if it is included in a multimodal approach of rehabilitation."	Small sample size, lack of study details for compliance, dropout rate, allocation, and methods limits conclusions.

			weight bearing pulley system (N = 13) vs. Group C, standard rehab alone (N = 13). Assessments at baseline, post-treatment, 1 month, 3 months and 6 months.			
Masiero 2014 RCT No sponsorship. No mention of COI.	3.0	N = 69 nean age 46.37 years	Rehabilitation program group with (N = 22) vs. Educational group (N = 24) vs. Control group (N = 23). 12 months follow up.	Intra-group changes in the rehabilitation group from baseline to 12 months yielded statistically significant gains ($p < 0.05$) for all outcomes. At 12-months follow-up, compared with the control and educational-behavioural, the rehabilitation group exhibited significant differences in chest expansion ($p = 0.001$ and $p < 0.001$), Bath Ankylosing Spondylitis Disease Activity Index ($p = 0.012$ and $p = 0.050$), and in some goniometric measurements as cervical rotation ($p = 0.007$ and $p = 0.014$), thoracolumbar rotation ($p = 0.009$ and $p = 0.050$), and total cervical movements ($p = 0.009$ and $p = 0.001$).	"In comparison with the educational-behavioral programme or no intervention, supervised training and home exercises improved long-term outcome in patients with ankylosing spondylitis"	Not randomized, sequential allocation. Methodological details sparse.
McLean 2013 RCT Sponsored by the Arthritis Research UK and Hull and East Yorkshire Hospitals NHS Trust. No COI.	2.5	N = 151 with subacute or chronic mechanical pain. Mean age 53.85 years.	Graded exercise treatment for 12 sessions, in a 6 weeks period. (N = 75) vs. Physiotherapy sessions of 40-60 minutes, and follow up treatment for 20-30 minutes (N = 76). Follow up at 6 weeks, 6 months and 12 months.	Treatment main effects were found to be non-significant: {NPQ GET minus UP estimated difference 1.91 (95% CI (-3.14,6.96); p = 0.74); DASH GET minus UP estimated difference 4.54 (95% CI (-1.10, 10.2); p = 0.16)}. Time main effect significant for NPQ (p = 0.005) but not for DASH (p = 0.80) with estimates: {NPQ 6 week minus 12 month difference 5.62 [95% CI (3.16,8.09)]; NPQ six month minus 12 month difference 3.12 [95% CI (0.768,5.47)]; DASH six week minus 12 month difference 2.07 (95% CI (-0.480,4.62); DASH 6 month minus 12 month difference 1.39 (95% CI (-0.676,3.46))}.	"This study demonstrated that GET and UP produced modest but significant reductions in pain and disability for patients with nonspecific neck pain at six and 12 month follow-up. Both approaches are appropriate for use in clinical practice although both interventions had high levels of non-adherence. Patients should be assessed to establish whether either of these interventions is likely to meet their clinical needs and whether they have a preference for either of the interventions. Health professionals should attempt to identify possible	Utilized multiple imputation for intent to treat analysis. Interventions poorly described. Methodological details sparse.

					cognitive, behavioral, demographic, organizational or practical barriers which may impact on patient adherence with treatment. Supporting patients to overcome their barriers may help patients to optimize treatment outcome, though strategies to improve adherence require further investigation."	
Sandsjö 2010 RCT Sponsored by the EC and from the Swedish Council for Working Life and Social Research. No mention of COI.	2.5	N = 65 with neck and shoulder complaints for more than 3 months; mean age 45±11 years.	Intervention group; myofeedback-based tele-treatment, 4 weeks, 8 hours a week (up to 2 hours), 2 days a week vs. Control group; no treatment but were allowed to continue activities and medication, except muscle relaxants. Follow up baseline, 4 weeks and 3 months.	No statistically significant differences to report between the two groups in any of the outcomes.	"The treatment appears to be as effective in terms of reduction of pain, pain-related disability and improved work ability as conventional treatment among a working population reporting neck and shoulder problems. We conclude that the myofeedback-based teletreatment service has great potential in occupational health services."	Methodological details sparse.
Aslan Telci 2012 RCT No mention of sponsorship or COI.	2.0	N = 60 participants with cervical arthritis and neck pain > 6 months. Mean ages for groups 1, 2, and 3: 50.45+7.78, 48.35+8.92, and 52.35+9.96 years.	Group 1 (N = 20) received active and passive physical therapy and exercise with supervision of physiotherapist vs. Group 2 (N = 20) received active physical therapy only and home exercise program. vs. Group 3 (N = 20) received drug treatment including NSAIDs and muscle relaxants from a physician. Follow-up at 3 and 6 months.	VAS groups 1 vs. 3 – 3 months: 3.48+1.43 vs. 5.08+1.89 ($p<0.05$); 6mths: 3.16+1.51 vs. 5.31+2.05 ($p<0.05$). NDI groups 1 vs. 3 – 6 months: 8.75+5.57 vs. 13.65+6.59 ($p<0.05$). NHP groups 1 vs. 3 – 3 months: 168.08+100.37 vs. 229.97+132.29 ($p<0.05$); 6mths: 146.29+96.74 vs. 257.63+136.04 ($p<0.05$). BDE groups 1 and 2 vs. 3 – 3 months: 10.15+7.45, 6.75+4.94 vs. 10.70+8.46 ($p<0.05$); 6 moonths: 9.00+5.46, 8.30+5.69 vs. 11.75+8.74 ($p<0.05$).	"In conclusion, we found that the results with pain, disability, and quality of life, psychological state, and patient satisfaction were higher in the two groups than in the drug treatment groups."	Methodological details sparse.

Diab 2012 RCT No sponsorship or COI.	3.5	N = 96 with unilateral lower cervical spondylotic radiculopathy (C5–C6 and C6–C7) and craniovertebral angle measured less than or equal to 50º , mean age (±SD) 46.3 (±2.05) for study group and 45.9 (±2.1) for control group	Control group receiving ultrasound and infrared radiation (N = 48) vs. Exercise group receiving a posture correcting exercise program with ultrasound and infrared radiation (N = 48). Assessments at baseline, 10 weeks post treatment and 6 months.	Values significantly different for groups adjusted to baseline value of outcome at 10 weeks post-treatment for craniovertebral angle, pain, C6 and C7 peak-to-peak amplitude of dermatomal somatosensory evoked potentials p = 0.000, 0.01, 0.000, 0.001 respectively and at follow-up for all previous variables (p = 0.000).	"In conclusion, the effectiveness of forward head correction in reducing pain and improving the nerve root function in cases of cervical spondylotic radiculopathy introduces yet another treatment option to a list that already includes physical agent modalities and manual therapies such as massage and myofascial stretch. Its unique appeal lies in its long-lasting effect."	Results suggests that experimental intervention is superior to study control after 6 months.
Mongini 2010 RCT Sponsored by the Compagnia di San Paolo and the Regione Piemonte. No COI.	3.0	N = 2,895 workers. Median age 47 years.	Shoulder and neck, and relaxation exercises 8-10 times repetition each (N = 1457) vs. Control group (N = 1438). Follow up at 6- and 12-months.	IG showed a higher responder rate [risk ratio, 95% confidence interval (CI)] for headache (1.58; 1.28 to 1.92) and for neck/shoulder pain (1.53; 1.27 to 1.82), and a larger reduction of the days per month with headache [95% CI 21.72; (22.40 to 21.04)] and with neck/ shoulder pain [95% CI 22.51 (23.56 to 21.47)].	The program effectively reduced headache and neck/shoulder pain in a large working community and appears to be easily transferable to primary-care settings. Further trials are needed to investigate the program effectiveness in a clinical setting, for highly selected patients suffering from specific headache types.	Population description missing. Data suggest intervention superior to control however high dropout at baseline may limit findings.
Gustavsson 2006 RCT Sponsored by grants from the Swedish National Social Insurance Board and Centre of Clinical Research. No mention of COI.	2.5	N = 37 with various neck disorder and were eligible if they had musculoskeletal neck pain great than 3 months and no signs of neurological symptoms or cervical facet joint pathology. Age range 18-65.	Applied Relaxation (AR) had 7, 1.5-hour sessions for 7 weeks. 4 body awareness exercises, and information about pain and stress management (N = 18) vs. Treatment As Usual (TAU) group, 11 treatment sessions: consisted of: acupuncture, massage, spinal mobilization techniques, hot-	Pain levels at (baseline/7 weeks/ 20 weeks) AR:(6/6/5) TAU: (6.5/6/7) No significant in pain between the 2 groups at (p = 0.928) for AR and (p = 0.867) for TAU. Neck pain levels at (baseline/7 weeks/ 20 weeks) AR:(2/1/1); TAU: (1/1/2) No significant in neck pain between the 2 groups at (p = 0.008) for AR and (p = 0.017) for TAU.	"The design and methods of this pilot study were feasible and will be suitable for a larger randomized controlled study. The intervention program, AR, had an impact on control over pain, although there was no difference in self-rated pain."	Methodological details sparse. Data suggest minimal differences between groups.

			pack, TENS, ultrasound and/or introducing the patient to different exercise programs (N = 19). Follow–up for both at 7 and 20 weeks.			
Wani 2013 RCT No mention of sponsorship or COI.	2.5	N = 30 with cervical spondylosis (with or without radiculopathy); mean age 51.53±9.48 for group A and 47.06±8.72 for group B.	Group A, heat packs and cervical retraction exercises (McKenzie) (N = 11) vs. Group B, heat pack and cervical retraction exercises with instructions to use the pressure biofeedback (N = 19) 10 cervical retraction exercises, once per day for 2 weeks. Follow up: baseline and 2 weeks.	Mean ± SD for NPRS: pre vs. post: Group A: 7±0.81 vs. 4±1.09, p=0.0001; NPQ: 13.13±3.09 vs. 5.8±1.32, (p=0.0001); Group B: NPRS: 7.06±0.99 vs. 2.4±0.8, (p=0.0001); NPQ: 13.66±2.08 vs. 3.8±0.83, (p=0.0001). Intergroup comparison: NPRS: group A vs. group B: 4±1.09 vs. 4.2±0.8, p = 0.0001; NPQ: 5.8±1.32 vs. 3.8±0.83, (p = 0.0001).	"This study has demonstrated the effectiveness of cervical retraction exercise with or without pressure biofeedback for the treatment of pain in cervical spondylosis. The study also concluded that the group using cervical retraction exercises with pressure biofeedback (Group B) experienced more pain reduction and functional disability improvements associated with cervical spondylosis than the group using cervical retraction exercises without pressure biofeedback."	Methodological details sparse.
Beer 2012 RCT No mention of sponsorship or COI.	2.0	N = 20 participants with persistent neck pain. Mean age 29.3+11.4 years.	Exercise group received functional exercises training deep cervical flexor muscles vs. Control group did not receive any treatment. No long-term follow-up.	Stage of CCFT for Exercise vs. Control – 24mmHg: 7.5+6.3 vs. 19.4+16.1 (p = 0.04); 26mmHg: 11.1+7.9 vs. 27.7+22.3 (p = 0.04). No significant differences for NDI, VAS, or PSFS scores between the groups pre to post.	"[T]hese observations suggest the worth of including such an exercise in the rehabilitation of patients with neck pain disorders."	Methodological details sparse.
Cleland 2010 RCT No mention of industry sponsorship or COI.	2.0	N=98 with cervical pain, mean age (SD) 39.4 (11.9) for all participants	Thoracic manipulation group (N=52) vs. Exercise group (N=46). Assessments at baseline, 1, 4, and 26 weeks.	Patients receiving thrust manipulation experienced greater improvements in disability (NDI) with a between group difference at 1-week of 5.7% (95% CI: 2.1, 9.7; *P* = .007), 4-weeks of 5.8% (95% CI: 1.1, 10.6; *P* = .016), and 6-months of 8.1% (95% CI: 3.1, 13.2; *P* = .002). The group receiving thoracic spine thrust manipulation also experienced significantly greater between group improvements in pain at 4-weeks	"The results of this study provide evidence that the addition of thoracic spine thrust manipulation to a program of exercise results in significantly greater benefits in pain and disability as compared to a program consisting solely of therapeutic exercise."	Abstract only.

				(.78 points; 95% CI: 0.08, 1.5; *P* = .03) and 6-months (1.5 points; 95% CI: 0.62, 2.4; (*P* = .001)) than the exercise only group.		
Peolsson 2007 RCT Sponsored by the Faculty and Health Sciences of Linkoping University. No mention of COI.	1.5	N = 116 with nonspecific neck pain or NP with or without radiation, with cervical disk disease or ACDF, and healthy controls or C age ranging from 18 to 65 years.	NP group randomized either to General exercise, McKenzie treatment, or Control group (N = 45) vs ACDF treatment included Philadelphia collar for 6 weeks (N = 47) vs Control group had different work with different physical demands (N = 43). Follow-up for 2 months.	For those with ACDF, there was a significant correlation between NME and pain intensity both before treatment and at follow-up, r = -0.54 to -0.66, (p < 0 .01), except for dorsal NME, r = 0.39, (p = 0.06), at follow-up. There was an improvement in pain intensity and NDI in the NP group, (p < 0.0001), and NDI, (p = 0.0005) in the ACDF group. NDI both before, (p = 0.0001), and after treatment, (p = 0.006), were worse in ACDF group compared to the NP group.	"[M]any patients with NP and ACDF have impaired NME compared with healthy controls before and also after rehabilitation."	Methodological details sparse.
Pesco 2006 Random-selection No mention of sponsorship or COI.	N/A	N = 24 randomly selected females with complaints of pain and stiffness in neck, shoulder, or both, from 20-29 years of age.	All received medical exam and x-ray before and after study: Student participants received education and exercise instructions to be continued daily (n = 12) and custodial workers received once-per-week hands-on treatment (n = 12). Follow-up for 4 months.	Significant reductions in perceived shoulder stiffness, (p < 0.000) and neck stiffness, (p < 0.000), and headache, (p <0.000), and general irritation, (p <0.000).	"Treatment of repetitive stress injuries that combines maintenance of daily active exercises prescribed and modeled by a professional therapist, which emphasize postural awareness to correct poor posture and provide a basic physiological understanding of the disorder, is as crucial to reducing upper back and neck pain and stiffness as hands-on therapy with active exercise provided in a clinical setting."	Not RCT, only pre-post
Lewis 2007 Economic Evaluation Sponsored by Arthritis Research Campaign and West Midlands R & D NHS. No COI.	N/A	See Dziedzic's et al. 2005 (Under Diathermy table)	See Dziedzic's et al. 2005 (Under Diathermy table)	See Dziedzic's et al. 2005 (Under Diathermy table)	"The cost-effective intervention is likely to be A&E or MT, depending on the economic perspective and preferred outcome, but not PSWD."	This is an economic evaluation of Dziedzic's 2005 article summarized under Diathermy. Not scored.

NSAIDs

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Heikkila 2000 RCT No mention of industry sponsorship or COIs.	2.5	N = 14 with complaint of dizziness or vertigo of suspected cervical origin	Acupuncture for 3 sessions during 2-week period vs. cervical manipulation (acupuncture; cervical manipulation; NSAID-gel (ketoprofen); and no therapy vs. NSAID-gel (ketoprofen) 2-3 times a day (60g total) vs. no therapy for 2 weeks.	Mean repositioning error before manipulation 4.47cm (SD = 3.27) vs. 3.93cm (SD = 2.85) after treatment (p = 0.007). Vertical plane movements (flexion and extension) mean repositioning error before acupuncture 4.45cm (SD = 3.38) vs 3.91cm (SD = 2.93) after treatment (p<0.011).	"The results of this study suggest that spinal manipulation may be most effective in influencing the complex process of proprioceptive sensibility and dizziness of cervical origin. The preliminary findings of this study must be viewed in the light of certain inherent design weaknesses."	Small sample size. No mention of co-interventions or compliance to treatment.

ANTI-EPILEPTIC AGENTS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Salinas 2012 RCT Sponsored by Colciencias and the Universidad de Antioquia. No COI.	7.0	N = 46 with spinal cord injury sustained within 2 weeks before enrollment and without evidence of neuropathic pain or NP, older than 18 years of age.	Carbamazepine (up to 600 mg/day) (N = 24) vs Placebo (N = 22). Follow-ups were at 1, 3, and 6 months.	At 1 month, 8 patients in the placebo and 2 patients in the carbamazepine group reported moderate-intense pain (VAS, ≥ 40, p = 0.024), this was not seen at 3 or 6 months. No differences were seen between groups in the number of participants receiving some treatment for NP or the occurrence or intensity of depression. No differences were seen in any of the SF-36 subscales or in bodily pain.	"Early intervention with carbamazepine decreased NP incidence at the 1 month but not at the 3 and 6 month follow-ups in the group of patients with acquired spinal cord injury."	Exclude, article specific to spinal cord injury – not relevant to this guideline's subjects.

CAPSAICIN

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Cho 2012	3.5	N = 57 with >3-month	Capsaicin 0.1% hydrogel patches	Mean ± SD for VAS: 2 weeks vs 4 weeks: treatment: 3.86± 1.64 vs	"Future research may help to discern specific effects of	Methodological details sparse.

RCT Sponsored by KyungHee University. No COI.		duration of neck pain and myofascial pain, mean age 40.33±14.15 for treatment group, and 42.22±11.91 for control group.	(N = 30) vs. Control hydrogel without capsaicin (N = 27). Follow-up: at baseline, 2 and 4 weeks.	2.89±1.71, p < 0.001; control: 4.34 ± 2.71 vs 3.77±2.52, (p < 0.001); NDI: 2 weeks vs 4 weeks: treatment: 17.47 ± 9.31 vs 14.17 ± 8.37, (p < 0.001); control: 20.04 ± 13.17 vs 17.04 ± 12.36, (p < 0.001); BDI: 2 weeks vs 4 weeks: treatment: 28.27 ± 4.88 vs 27.40±6.05, (p < 0.001).	capsaicin, trigger point stimulation by application of the patch, and the placebo effect."	

SKELETAL MUSCLE RELAXANTS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Goi The 1982 RCT No mention of sponsorship or COI.	3.0	N = 40 with acute cervical muscle spasm, age range 30-70	Tizanidine 4mg 1 capsule 3 times daily (N = 20) vs Diazepam 5 mg 1 capsule 3 times daily (N = 20). Treatment period: 7 – 9 days.	Mean for Efficacy Assessment Parameters: tizanidine vs diazepam: spontaneous pain: after 3 days: 1.60 vs 1.55, (p < 0.05); tenderness: 1.50 vs 1.65, (p < 0.05); muscle tension: 0.95 vs 1.25, (p < 0.05); neck flexion (cm): 1.55 vs 2.45, p < 0.05; neck rotation left (degrees): 44.75 vs 45.75, (p < 0.05): neck rotation right (degrees): 46.25 vs 45.50, (p < 0.05); daily living: 1.16 vs 1.22, (p < 0.05); self-assessment of disability: 1.25 vs1.40, p < 0.05. after 7 – 9 days: spontaneous pain: 1.32 vs 1.10, (p < 0.05); tenderness: 1.21 vs 1.10, p < 0.05; muscle tension: 0.84 vs 0.75, (p < 0.05); neck flexion (cm): 1.55 vs 2.45, p < 0.05; neck rotation left (degrees): 50.79 vs 50.50, (p < 0.05); neck rotation right (degrees): 51.05 vs 50.25, (p < 0.05); daily living: 0.72 vs 0.53, (p < 0.05); self-assessment of disability: 1.05 vs 0.85, (p < 0.05). Median VAS: tizanidine vs diazepam: day 3: 66 vs 56, (p < 0.05); day 4: 65 vs 55, (p < 0.05); day 5: 543 vs 53, (p < 0.05); day 6: 60 vs 50, (p < 0.05); day 7: 40 vs 50, (p < 0.05).	"It can be concluded that, like diazepam, tizanidine is a useful drug for the treatment of acute muscle spasm associated with cervical spine disorders."	Small sample size. Methodological details sparse.

OPIOIDS

Author/Year Study Type	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Yeganeh 2010 RCT No mention of COI. Funded by the Kermanshah University of Medical Sciences and Health Services.	N/A	N = 22 with documented cervical spinal injury, risk of hyperextension and mandiblomaxillofacial surgery candidates.	Target-controlled Infusion (TCI) group (N = 11) vs. Manually-controlled Infusion group (MCI) (N = 11). All patients premeditated with intramuscular scopolamine 20 mg butylbromide for 30 minutes + 0.03 kg-1 midazolam, intravenously for 10 minutes before procedure.	Recall + pain sensitivity / Infusion rate / Intubation condition; (10 patients pain free, p=0.02 vs 4 patients, p = 0.02 in MCI group) / (p = 0.07) / (5.2 ± 2.0 vs 5.5 ± 1.9 in MCI, p=0.66).	"Remifentanil infusion could be recommended to provide good conscious sedation in procedures such as awake nasotracheal intubation, but target-controlled remifentanil infusion seems to provide better conditions compared with manually controlled remifentanil infusion and is easier to use."	

PHYSICAL AND OCCUPATIONAL THERAPY

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Chiropractic vs. Physiotherapy						
Skargren 1998 RCT Sponsored by the County Council of Östergötland and Vårdalstiftelsen. No mention of COI.	2.0	See Skargren 1997	See Skargren 1997	Multiple regression analysis showed that the five prognostic factors: duration of current episode, Oswestry score at entry, number of localizations, expectations of treatment and well-being, were all significantly associated with Oswestry score at 12 month follow up.	"The factors 'duration of current episode' and 'Oswestry score at entry' that emerged strengthen previous results and the factors 'number of localisations, expectations of treatment' and 'well-being' add new factors. Clinical decision models for managing patients with back pain visiting primary care that consider prognostic factors need to be implemented and prospectively evaluated."	Methodological detail sparse.
Surgery vs. Physical Therapy						
Peolsson 2013 RCT Sponsored by Medical Research Council of	2.0	N = 49 with cervical radiculopathy for at least 8 weeks, mean age 46±8.9	Group A, ACDF with postoperative PT (N = 24) vs Group B, PT, educational lectures, medical exercise therapy, twice a week for 14 weeks	Mean ± SD for NME flexion: PT vs. ACDF plus PT: baseline: 33±38 vs. 41±39, p=0.01; 12 month: 58±45 vs. 59±45, p = 0.01; 24 month: 43±42 vs. 55±41, p=0.01; extension: PT vs. ACDF plus PT: baseline: 82±68 vs. 78±62, p=0.006; 12 month: 81±54 vs. 103±66, p=0.006; 24 month: 86±71	"Compared with a structured physiotherapy program alone, ACDF followed by physiotherapy did not result in additional improvements in neck active range of motion, neck muscle endurance, or hand-related function in	Methodological details sparse.

Southeast Sweden (FORSS) funds. COI, one or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to subject of this manuscript.			(N = 25). Follow up at baseline, 3, 6, 12, and 24 months.	vs. 108±64, p=0.006. Mean ± SD for right hand strength: baseline vs 24 month: PT vs. ACDF plus PT: 34±17 vs. 36±15, p = 0.01; 38±21 vs. 42±13, p = 0.01.	patients with radiculopathy. We suggest that a structured physiotherapy program should precede a decision for ACDF intervention in patients with radiculopathy, to reduce the need for surgery."	
Physiotherapy vs. Manipulative Therapy						
Koes 1992 Results of 1 year follow up RCT Sponsored by the Dutch Ministry of Welfare, Health, and Cultural Affairs and by the Dutch National Health Insurance Council. No COI mentioned.	3.5	See Koes 1991.	See Koes 1991.	Mean ± SD for improvement in main complaint: Manipulative therapy vs. physiotherapy: 3 weeks: 2.3±2.1 vs. 2.0±2.3; 12 months: 4.5±2.2 vs. 3.8±2.3; manipulative therapy improved after 12 month follow up.	"Manipulative therapy and physiotherapy are better than general practitioner and placebo treatment. Furthermore, manipulative therapy is slightly better than physiotherapy after 12 months."	Short term follow up. Another report of 1 year follow up.
Koes 1991 Results of 3, 6 and 12 week follow ups RCT	2.5	N = 256 with non-specific neck back and neck complaints of at least six weeks duration, mean age of 43	Physiotherapy, exercise, massage, physical therapy modalities (N = 66) vs Manipulative Therapy, manipulative techniques (N = 65)	Mean ± SD for improvement in main complaint: Manual Therapy vs. Physiotherapy: 3 weeks: 2.3±2.1 vs. 2.0±2.3; 12 weeks: 4.0±2.6 vs. 3.8±2.3; both groups improved more than the GP group.	"We conclude that it seems useful to refer patients with non-specific back and neck complaints lasting for at least 6 weeks for treatment with physiotherapy or manual therapy."	Wide variability in compliance and specific interventions with in treatment arms.

Sponsored by the Dutch Ministry of Welfare, Health, and Cultural Affairs and by the Dutch National Health Insurance Council. No COI mentioned.		for all participants.	vs Continued Treatment by the general practitioner, prescribed drugs, advice (N = 61) vs Placebo treatment, diathermy, ultrasound, twice a week for 6 weeks (N = 64). Follow up at 3, 6, and 12 weeks.			
McKenzie System vs. Goal Setting						
Moffett 2006 RCT Sponsored by the Arthritis Research Campaign. No COI.	3.5	N = 315 with back pain or neck pain of more than 2 weeks duration, mean age 45.0, range of 18-90	SFA (Solution Finding), help patients identify main problems, work out solutions and then agree realistic goals for what they wanted to achieve (N = 154) vs McKenzie system, repeated movements of spine, direction specific exercises (N = 161). Follow-up at 6 weeks, 6 and 12 months.	Patients with neck pain attended more session with the McKenzie technique compared with SFA: 4.6 vs. 3.2, respectively. McKenzie patients reported higher satisfaction compared to the SFA group: 90 vs. 70, respectively	"The McKenzie approach resulted in higher patient satisfaction overall, but the SFA could be more cost-effective, as fewer (three vs. four) sessions were needed."	Methodological details sparse. High crossover from brief intervention.
Intensive training vs. Physiotherapy vs. Manipulative Therapy						
Jordan 1998 RCT Supported by the Danish Medical Research Council, the Danish Arthritic Association, the Medical Research Fund for Copenhagen, the Faroe	2.5	N = 119 with chronic neck pain of greater than 3 months' duration, age range 20-70.	Intensive Training, groups of four or 5 patients, physiotherapy guided, stationary bike, muscle stretching, 12 repetitions, 1 h to 1 h and 15 min, 2 training sessions per week for 6 weeks vs. Physiotherapy Treatment, active and passive elements, hot packs, massage, manual	Mean (95% CI) for pain scale: baseline vs. 12 month: intensive: 12(10-15) vs. 6(4-9), $p<0.05$; physiotherapy: 12(10-15) vs. 8(6-11), $p<0.05$; manual: 13(10-15) vs. 6(6-8), $p<0.05$. Disability Scale: intensive: 8(7-10) vs. 5(4-7), $p<0.05$; physiotherapy: 9(8-11) vs. 6(4-7), $p<0.05$; manual: 8(7-10) vs. 5(3-6), $p<0.05$.	"There was no clinical difference between the three treatments. All three treatment interventions demonstrated meaningful improvement in all primary effect parameters. Improvements were maintained at 4 and 12 month follow-up."	Methodological details sparse.

Islands and Greenland, the Foundation for the Chiropractic Research and Education, and The Fund to Promote Chiropractic Research and Postgraduate Education. No mention of COI.			traction, manipulation, 45 minutes, twice a week for a period of 6 weeks vs. Manipulative Therapy, chiropractor guided, high velocity, low amplitude spinal manipulation, manual traction of cervical spine, 45 minutes, twice a week for 6 weeks. Follow up at baseline, 4 and 12 months after treatment.			
Multimodal Rehabilitation vs. Usual Care						
Hudson 2010 RCT Supported by North of Scotland National Health Service Research and Ethics Committee. No mention of COI.	2.5	N = 12 with reported non-specific, recurrent or chronic neck pain of greater than 3 months duration, mean age 42.7±16.1 for usual care, and 42.3±19.8 for multimodal group.	Multimodal Group Rehabilitation, 40 minute initial assessment, cervicothoracic stability training, relaxation training, postural control training, 1 hour, once a week for 6 weeks (N = 6) vs. Usual Care Group, physiotherapist guided physiotherapy management (manipulations, mobilizations, exercises, education or acupuncture), 40 minute initial appointment, follow up of 20 minutes (N = 6). Follow-up at pre and post.	Mean NDI score: pre: multimodal vs. usual care: 28 vs. 16, $p<0.05$; multimodal vs. usual care: pre vs. post: 28 vs. 16, $p<0.01$; usual care: pre vs. post: 16 vs. 8, $p<0.01$. Mean NRS score for pain: pre vs. post: multimodal: 7.5 vs. 3, $p<0.01$; usual care: 6.5 vs. 2, $p<0.01$.	"This pilot study found that multimodal group rehabilitation brought about significant improvements in pain and function to a similar level as usual care physiotherapy management for patients with CNP. These results should be treated with caution due to the small sample size and lack of long-term follow-up."	Small sample size. Methodological details sparse.
Physiotherapy vs. Acupuncture						

David 1998 RCT No mention of sponsorship or COI.	1.5	N = 70 with non-inflammatory neck pain of > 6 weeks duration and with no abnormal neurology, aged 18-75	Physiotherapy (N = 35) vs Acupuncture (N = 35). Follow up at baseline, 6 weeks and 6 months.	Mean for VAS score: acupuncture vs. physiotherapy: baseline: 50 vs. 50 (no p-value to report); 6 weeks: 31 vs. 21, (p <0.01).	"Both acupuncture and physiotherapy are effective forms of treatment. Since an untreated control group was not part of the study design, the magnitude of this improvement cannot be quantified."	Methodological Details sparse.
Manual Physical Therapy vs. Therapeutic Exercises						
Ragonese 2009 RCT No mention of sponsorship or COI.	2.5	N = 30 with a chief complaint of neck/or upper extremity symptoms,	Group 1, Manual Physical Therapy alone, cervical lateral glides, thoracic mobilizations, neural dynamic techniques for the median nerve, 30-45 seconds each (N = 10) vs Group 2, Therapeutic Exercises, deep neck flexor strengthening (10 sec for 10 reps), trapezius and serratus anterior strengthening (15 reps for 2 sec) (N = 10) vs Group 3, Manual Physical Therapy and Therapeutics Exercises. Each participant treated 3 times per week for 3 weeks.	Mean ± SD for pain: initial vs. final: Manual: 5.3 ± 1.6 vs. 2.4 ± 1.1; Therapeutic Exercises: 4.9 ± 1.4 vs. 1.6 ± 1.5; Combination: 4.1 ± 1.5 vs. 0.9 ± 1.2, (p < 0.01). NDI score: initial vs. final: Manual: 39.6 ± 17.2 vs. 17.2 ± 10.3; Therapeutic Exercises: 28.7±13.3 vs. 10.2 ± 7.1; Combination: 25.5 ± 10.9 vs. 7.8 ± 5.5, (p < 0.05).	"When treating patients with a diagnosis of cervical radiculopathy, an approach that combines manual therapy and therapeutic exercise appears to be superior to treatment when compared to either intervention alone."	Small sample size. Methodological details sparse, poor baseline comparability.

MAGNETS AND MAGNETIC STIMULATION

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Kanai 2011 Randomized, Double-blind,	3.5	N = 62 with chronic neck and shoulder stiffness or pain	Magnetotherapeutic Device (MTD) (N = 31) vs. non-MTD	Significant increase 1,2, and 7 days post-treatment in the MTD vs. non-MTD for percent VAS improvement; skin surface and	"[T]he present study showed that a subjective parameter (VAS improvement) and objective parameters (skin temperature and	Lack of study details. Results reported in percentage change of variable. Clinical

placebo controlled COI, Norimasa Taniguehi and Hideyuki Okano, PhD, are employed by PIP Co, Ltd, Osaka, Japan, manufacturer of magneto-theraputic device used in this study.		including myofascial pain and cervical spondylosis. Age range 21-58 years; mean, 34 years	sham control (N = 31).	deep body temperature; and mean muscle stiffness (p<0.05).	deep body temperature in the painful area) were significantly greater, and the muscle stiffness was significantly lower in the MTD group than in the non-MTD group during the 7-day treatment period."	significance of results is unclear, limiting conclusions.
Thuile 2002 RCT No mention of industry sponsorship or COIs.	2.0	N = 92 with whiplash syndrome	Conventional treatment with diclofenac and tizanidine vs. Conventional treatment plus additional treatment with magnetic fields	Patients given magnetic therapy showed more improvement than the control group (p<0.03). Mobility in all three planes also improved in the magnetic group (p <0.05).	"Magnetic therapy is a non-invasive method. Provided it is correctly applied, it is practically devoid of side effects, extremely well tolerated by patients and therefore has a high degree of compliance."	Poorly described study. Unsure of many aspects.

ACUPUNCTURE

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Acupuncture vs NSAIDs						
Heikkilä 2000 RCT Single-subject No mention of sponsorship or COI.	2.5	N = 14 with complaint of dizziness or vertigo of suspected cervical origin. Mean age 36 (range: 22-54) years old.	Acupuncture for 3 sessions during 2-week period (N = NA) vs Cervical manipulation (acupuncture; cervical manipulation; NSAID-gel (ketoprofen); and no therapy (N = NA). Treatments randomly alternated in 14 subjects, for 2 weeks.	Mean repositioning error before manipulation 4.47cm (SD = 3.27) vs 3.93cm (SD = 2.85) after treatment, (p = 0.007). Vertical plane movements (flexion and extension) mean repositioning error before acupuncture 4.45cm (SD = 3.38) vs 3.91cm (SD = 2.93) after treatment, (p < 0.011).	"The results of this study suggest that spinal manipulation may be most effective in influencing the complex process of proprioceptive sensibility and dizziness of cervical origin."	Small sample size. No mention of co-interventions or compliance to treatment.
Acupressure						

Wong 2012 RCT No mention of sponsorship or COI.	3.5	N = 60 with neck pain. Age Mean (SD): 32.2 ± 2.2 (for CMAT) and 29.7 ± 2.0 (for Control).	Collateral Meridian Acupressure Therapy or CMAT (N = 30) vs Control for one session (N = 30). Follow-up not specified.	VAS (before/after, mean ± SD): CMAT (3.4 ± 0.7/0.7 ± 0.6) v. control (3.2 ± 0.8/2.8 ± 0.9), (p < 0.0001).	"The CMAT seems to have a satisfactory therapeutic effect for patients suffering from neck pain."	Multiple study weaknesses limit conclusions. Mixture of acute and chronic pain. Randomization by coin flip. No details for sham interventions, compliance. Duration of effects not described. Timing of outcomes not described. Power calculation not described. Subjects had low average pain VAS scores to start study.
Hohmann 2012 RCT Supported by the Karl and Veronica Carstens Foundation. No mention of COI.	3.0	N = 40 with nonspecific neck pain. Age range 18-75 years.	Home based, self-administered needle stimulation pad (acupressure pad) for 10 minutes once a daily for 14 days (N = 20) vs Waiting list controls or WL (N = 20). Follow up at 14 days.	Mean (SD) for pain intensity comparing control group vs needle stimulus pad: 4.4 (1.8) vs 4.9 (2.0) pretreatment; 4.5 (2.2) vs 3.4 (2.7) post treatment [95% CI: -1.6 (-2.8 to -0.3), (p = 0.021). Mean (SD) for function (NPQ or ODI) comparing control group vs needle stimulus pad: 33.2 (11.1) vs 36.3 (13.5) pretreatment; 32.5 (9.2) vs 26.5 (15.7) post treatment [95% CI: -7.4 (-13.7 to -1.1), (p < 0.001). Mean (SD) for log pressure pain threshold (PPT) area of maximum pain comparing control group vs needle stimulus pad: 2.303 (0.168) vs 2.193 (0.211) pretreatment; 2.311 (0.182) vs 2.314 (0.264) post treatment [95% CI: 0.106 (0.013 to 0.198), (p = 0.032).	"The needle stimulation pad revealed a substantial potential for the alleviation of chronic NP and BP. Furthermore, psychophysical data support the assumption that the pad reveals its effects at least partly on a subcortical level of the pain processing system."	Data suggest intervention may be superior to waiting controls.
Dry needling vs Placebo						
Tsai 2009 RCT No mention of sponsorship or COI.	2.5	N = 35 with myofascial trigger points in upper trapezius muscle. Mean age: 43.9±11.4 years.	Dry-needling (N = 17) Vs Sham needling (N = 18). Outcome assessed immediately after treatment.	Mean±SD of percentage change in pain intensity for sham needling vs dry needling: 10.0±8.1 vs 28.5±21.8, (p <0.05). Mean±SD of percentage change in pain threshold (kg/cm^2) for sham needling vs dry needling: 15.8 ±11.3 vs 67.8±38.8 (p < 0.05). Mean±SD of percentage change in range of motion for sham needling vs dry needling: 9.5±13.2 vs 25.8±16.8, (p <0.05).	"In this study, we demonstrated that dry needling of a distal MTrP in the extensor carpi radialis longus muscle could reduce the irritability of a proximal MTrP in the upper trapezius muscle."	Methodological details sparse.

Karakurum 2001 RCT No mention of sponsorship or COI.	2.0	N = 30 women with tension type headache (TTH).	Intramuscular stimulation carried out by a 30-gauge, 1-inch needles to 6 pre-designated trigger points for 30 minutes (N = 15) vs Placebo received needles were inserted only subcutaneously (N = 15). Follow up at 4 weeks.	Mean±SD for neck movement limitation for the left and right sides at pretreatment for placebo vs treatment group: 1.03±0.85 vs 0.87±0.94 for right side; 0.87±0.74 vs 0.80±1.08 for left side. And at 4 weeks: 1.07±0.70 vs 0.47±0.83 for right side; 0.80±0.68 vs 0.33±0.49 for left side ($p < 0.05$) difference only in needle group).	"We conclude that the dry-needle technique in chronic TTH is effective in improving headache and symptoms such as muscle tenderness and ROM limitation that accompany and contribute to the pain in TTH, but we were unable to demonstrate significantly different effect compared with placebo in relieving the headache itself."	Methodological details sparse.

CRYOTHERAPIES

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Frozen vs Non-Frozen						
Sprouse-Blum 2013 RCT Sprouse-Blum designed the neck wrap and was the lead investigator. No mention of sponsorship.	3.0	N = 55 with migraine headaches, age range 18-65, 43.1 ± 11.4.	Frozen, keep wrap frozen (not well described) (N = N/A) vs Non-Frozen, room temperature (not well described) (N = N/A). Participants educated that cold therapy is most common self-care treatment and how to apply the neck wrap. Each participant wore wrap for first 30 minutes then removed it for another 30 minutes to report pain score. Follow-up baseline, 15, 30, and 60 minutes after treatment.	Mean ± SD for VAS pain score: baseline vs 60 minutes: frozen: 2.83 ± 0.26 vs 1.83 ± 0.33, ($p < 0.001$).	"The application of a frozen neck wrap at onset of migraine targeting the carotid arteries at the neck significantly reduced recorded pain in participants with migraine headaches."	Number of participants in each group was not described well: "odd numbered participants started in the treatment arm and even numbered participants started in the control arm",… "55 participants were included in the data analysis." Methodological detail sparse. Short follow up time of 1 hour.

ULTRASOUND

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments

Moodley 2002 RCT No mention of industry sponsorship or COIs.	2.5	N = 30 neck pain	Spinal manipulation vs. ultrasound pulsed mode for 5 min twice a week for 4 weeks.	First treatment group achieved improvements in extension and right lateral flexion at 1-month follow-up ($p < 0.05$); 2nd treatment group achieved improvements in left flexion at final and 1 month follow-up consultations ($p < 0.05$).	"From the results, it appears that both ultrasound and adjustments are useful in treating mechanical neck pain; however, it appears that adjustments were more effective in restoring overall mobility and in decreasing cervical disability than ultrasound alone."	Recruited by advertisements. Lack of study details makes it difficult to assess clinical significance of outcomes. Says there was no improvement on pain, but no data presented. Need more details to draw conclusions.
Unalan 2011 RCT No mention of industry sponsorship. No COI.	3.5	N = 49 who had active myofascial trigger point injections of upper trapezius muscle. Average age HPPTUS (high-power pain threshold ultrasound) group 41.0±12.4 years, average age local injection group 42.6±13.8 years.	The study group received the high-power pain threshold static ultrasound technique (n = 25) vs control group which was treated with 1 session of injection of 1 mL of 0.5% local anesthetic lidocaine (n = 24). Follow-up at weeks 1 and 4.	Mean numbers of therapy sessions were 1 and 1.5 in the local injection and HPPTUS groups, respectively. No statistically significant difference between groups. After treatment VAS, ($p = 0.860$); ROM, ($p = 0.250$).	"No treatment differences were found between the HPPTUS technique and local injections in the treatment of patients with TrPs in the upper trapezius. Both techniques could be considered equally as treatment options when treating patients with MPS."	Methodological details sparse.

MANIPULATION AND MOBILIZATION

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Vasseljen 1995 RCT Supported by Norwegian Fund for Postgraduate Education in Physiotherapy and by Norwegian Research Council. No	3.5	N = 33 female office workers with shoulder and neck pain at or above 3 on a pain rating scale from 0 to 6	Group 1: individual physiotherapy (n = 12) vs. group exercise (n = 12) vs. individual physiotherapy (n = 9) were people evaluated before and after treatment.	Decreases in pain levels and perceived general tension in all groups from test 1 to 2; $p<0.05$.	"[N]o correlation was found between upper trapezius muscle activity and shoulder and neck pain or perceived general tension. Good test-retest reliabilities were seen for some of the EMG variables."	Significantly baseline differences in age, employment time, health care, randomization done on 24 women; 9 non-randomized. Different amount of therapy time between groups. No mention of co-interventions. Unable to draw conclusion because of weaknesses.

mention of COI.						
Allison 2002 RCT No mention of industry sponsorship or COIs.	3.0	N = 30 chronic cervico-brachial pain syndrome	Neural manual therapy (cervical lateral glide, shoulder girdle oscillation, muscle reeducation, home mobilization) vs. articular manual therapy (gleno-humeral and thoracic mobilization, home exercises) vs. control (no treatment, than crossed over to Neural. Therapy for 8 weeks.	Neural vs. articular vs. control; Short Form McGill Pain: NT, AT improved significantly from baseline, no differences between groups and control. Northwick Park Questionnaire: NT, AT improved significantly from baseline, no differences between groups and control; VAS (0-10): No differences between groups except at 4 weeks. NT had lower scores than AT, p = 0.03	"The findings suggest that both manual physiotherapy interventions combined with home exercises are effective in improving pain intensity, pain quality scores and functional disability levels."	Lack of study details for allocation, co-interventions, compliance, drop-outs. Small sample size limits power of study. Not true crossover. Baseline differences in duration of symptoms. Comparisons to control not stated in statistics. Results of crossover of control into neural group unclear.
van Schalkwyk 2000 RCT No mention of industry sponsorship or COIs.	3.0	N = 30 diagnosed with mechanical neck pain.	Group A: cervical rotary manipulation(s) on the ipsilateral side of lateral flexion fixation(s), vs. Group B: supine lateral break manipulation(s) on contralateral side of lateral flexion fixation(s). Subjects received a maximum of 10 treatments over 4-weeks.	Intragroup analysis indicated a significant difference between initial consultation data and the final consultation data for the subjective data, indicating an effect.	"Statistically, the results suggested that both treatments had an effect but that neither group showed a benefit over the other. However, because of the unsatisfactory power of the study, conclusions are to be drawn with caution. Clinical significance supported the statistical outcomes where it was suggested that both treatments had an effect and that neither treatment had a greater effect. A larger sample size and the inclusion of a placebo group is recommended to reveal true treatment outcomes and trends."	Small numbers. Lack of study details. No blinding. No control group. Controlled for analgesic use, but no other co-interventions such as exercise. Duration of symptoms not compared between groups.
Fernandez-de-las-penas 2004 RCT No mention of industry sponsorship or COIs.	3.0	N = 88 from group of 120 volunteers with whiplash injury	Dorsal manipulation (high velocity, low amplitude) + PT vs. PT. PT included ultrasound, home exercises, stretches, electrotherapy, massage, manual therapy. Manipulation at 5th and 10th PT session of 15 total sessions.	Mean Group Pain Reduction: 1 week post 2nd reduction (Manipulation vs. PT). Cervical Pain (scale not defined) 100 vs. 73, p = 0.002. Thoracic Pain (scale not defined) 238 vs. 59, p = 0.001. Head Pain (scale not defined) 49 vs. 51, p = 0.834.	"Dorsal manipulation favours the clinical improvement in whiplash patients."	Possible selection bias as sample from 120 volunteers with whiplash injury. No baseline comparison data. No analysis of severity. Reported VAS improvements of unknown clinical significance as scale not reported. Not clear which PT modality each received or compliance to regimen. Study therefore of uncertain findings.
Karlberg 1996 RCT	3.0	N = 17 dizziness of suspected	Immediate physiotherapy (n = 9)	Mean±SD VAS cervical pain comparing before and after	"Patients with dizziness of suspected cervical origin are	Very small numbers. Treatment modalities depended on

Supported by grants from the Medical Faculty of the University of Lund, the Swedish Medical Research Council and the Mutual Group Life Insurance Company. No COI.		cervical origin in whom extracervical causes had been excluded	vs. delayed physiotherapy (wait 2 months, undergo repeat measurements) (n = 8).	physiotherapy: 55±19 vs. 33±26; p = 0.004. Median±quartile deviation dizziness frequency score (0-4): 4±0.5 vs. 2±1.125; p = 0.002.	characterized by impaired postural performance. Physiotherapy reduces neck pain and dizziness and improves postural performance. Neck disorders should be considered when assessing patients complaining of dizziness, but alternative diagnoses are common."	symptoms and therapist choice. Number of sessions varied from 5 to 23.
Ventegodt 2004 RCT Supported by grants from IMK Almene Fond. No mention of COI.	3.0	N = 87 with whiplash-associated disorder (WAD) for at least 37 months	2 day course on philosophy of life teachings followed by 6-10 individual sessions in Rosen gestalt physiotherapy and Cranio Sacral body therapy (n = 43) vs. no treatment (n = 43).	Groups comparable at baseline; no effect was found (p = 0.28).	"The above version of a quality of life intervention based on alternative therapy had no effect on patients with chronic WAD."	Chronic pain case definition did not require pain from MVA. High dropout rate (50%). Three month follow-up results in limited study interpretability. Variable number of treatments. Study results suggest lack of efficacy.
Savolainen 2004 RCT No mention of industry sponsorship or COIs.	2.5	N = 75 employees of Finnish Broad-casting company	Four thoracic manipulations vs. instructions for physiotherapeutic exercises.	Both treatment groups showed a statistically significant reduction in muscular tenderness (p <0.001) at 6 month follow-up. Thoracic manipulation group showed a significant (p <0.05) decrease in levels of perceived pain at 12 month follow-up.	"Both treatment groups showed marked reductions in pain ratings during the course of treatment, and these improvements persisted for at least 12 months. Manual therapy appeared to be more effective in treating the most intense pain."	All participants had significant decreases in pain including large drop out group (34). No difference between groups at 6 or 12 months. Thoracic manipulation done in manipulation group. Unsure duration or etiology of symptoms. Paper lacks many details.
Vernon 1990 RCT	Ex-cluded	N = 9 mechanical neck pain	Rotational mobilization with gentle oscillations into the elastic barrier (n = 4) vs. rotational high velocity, low amplitude thrust manipulation (n = 5).	Pressure pain threshold of tender points (TP) surrounding fixation pre-/post-treatment for oscillation manipulation vs. HVLA manipulation: at TP 1: 3.4±1.3/4.9±2.3 (p ≤0.0001) vs. 2.8±1.7/ 2.8±1.7 (NS), between group p ≤0.0001; at TP 2: 3.4±1.7/4.8±2.2 (p ≤0.0001) vs. 2.3±1.9/ 2.3±1.7 (NS), between group p ≤0.0001; at TP 3: 3.3±0.51/5.2±3.2 (p ≤0.0001) vs.	"This study confirms that manipulation can increase local paraspinal pain threshold levels. The use of the pressure pain threshold meter allows for the determination of such a beneficial effect in the deeper tissues."	Small sample size. Excluded

				2.3±1.4/ 2.4±1.7 (NS), between group p ≤0.0001; at TP 4: 3.5±0.99/4.9±2.8 (p ≤0.0001) vs. 2.4±1.5/ 2.6±1.5 (NS), between group p <0.0001.		
Yurkiw 1996 RCT	Ex-cluded	N = 14 subacute unilateral neck pain	Sacro-occipital technique vs. a mechanically assisted device.	Unable to report results because tables not attached to article found on line.	"This study did find a trend toward clinical improvement; however, the differences observed are not statistically significant."	Small sample size. Excluded.
Acute Neck Pain						
Soderlund 2000 RCT Sponsored by the Swedish Foundation for Health Care Sciences and Allergy Research. No mention of COI.	2.5	N = 66 with acute whiplash injury; mean age of participants was 34 years.	Regular treatment group-general exercise program (N = 32) vs Additional Treatment Group-same exercise program but complemented with an exercise to improve kinesthetic sensibility of the neck muscles. (N = 34). Assessments took place at immediate, 3 and 6 month follow-up.	No significant differences between groups for PHI (disability), SES (self-efficacy) and VAS (pain intensity) scores, (p > 0.05). Both groups showed a significant increase in SES, PDI, and VAS scores (p < 0.001). The whole group also showed improvement in cervical range of motion in all outcomes, (p < 0.05).	"In conclusion, the results of this study showed that a small number of common exercises seem to be sufficient treatment for some patients with acute WAD. However, the exercises should be done regularly."	Sparse methodology and long with a 41% compliance rate.
Shin 2006 RCT No mention of sponsorship or COI.	NA	N = 26 with a herniated cervical disc (HDC); CT group: mean age = 43.3, CMT group: mean age = 39.5.	Cervical traction (CT) group (N = 13) vs Chuna manual therapy (CMT), a soft-tissue manipulation and thrust technique (N = 13). Assessments took place at baseline and after 2 weeks of treatment (12 treatments total).	Mean pain level did not differ at baseline. The CMT group showed a significant improvement in pain levels from baseline (7.5 pre-treatment vs 2.7 post-treatment, p < 0.001). There was a significant difference in pain intensity between groups post-treatment CMT vs CT, 2.7 vs 4.2, (p < 0.05).	"The present findings suggest that both CT and CMT reduce the pain level of HCD patients. CMT was found to be more effective than CT, but since this was a preliminary study with several limitations (e.g., small sample size and subjective measures), future studies should examine different symptoms and different manual therapy techniques to assess the generalizability and interpretation of these findings."	Small sample size.
Vernon 2009 RCT Sponsored by the Ministry of Health and	Exclude d	N = 20 with frequent or disabling headaches defined as occurring between 10 to	Real cervical manipulation + Real amitriptyline (N = 4) vs Real cervical manipulation + placebo amitriptyline (N = 6) vs Sham	Primary outcome for the adjusted analysis neither the chiropractic nor amitriptyline were statistically significant (p > 0.05). Combined treatment of amitriptyline and chiropractic intervention showed significant improvement from	"However, in our small sample, a clinically important, statistically significant benefit was found in the combination therapy group."	No neck pain, exclude.

Long-Term Care and Canadian Memorial Chiropractic College. No mention of COI.		25 days per month. Calculated mean age 34.1 years.	cervical manipulation + real amitriptyline (N = 5) vs Sham cervical manipulation + placebo amitriptyline (N = 5). No long-term follow-up.	baseline (p = 0.03) There were no significant differences between groups (p > 0.05).Four subjects with chiropractic treatment and 5 with amitriptyline reported adverse events.		
Subacute Neck Pain						
Williams 2003 RCT Sponsored by all Wales primary care research network (CAPRICORN), which receives funding from National Assembly for Wales and North Wales Health Authority. No mention of COI.	3.5	N = 201 with mechanical spine pain lasting from 2-12 weeks; mean age not reported; target age range was 16-64.	Usual General Practitioner care group (N = 109) vs Osteopathic manipulation treatment group (N = 92). Questionnaire mailed out at 2 and 6 months post-intervention to assess outcome measures.	At the 2 month follow-up, Manipulation group showed a significant improvement in the EASPS pain scale rating compared to GP group. (13.9 vs 8.6, p = 0.02). Manipulation also showed a significantly better outcome for the SF-12 mental score (7.9 vs 1.2, p = 0.001). At 6 months, Manipulation continued to show a significant improvement in SF-12 mental score (6.8 vs 1.4, p = 0.02) as well as SMPQ total score (6.6 vs 3.7, p = 0.05) and SMPQ affective subscale (1.8 vs 0.7, p = 0.03). The EASPS pain scale difference was not significant at 6 months (p = 0.14)	"Osteopathic spinal manipulation is increasingly provided in primary care, but only occasionally by a member of the primary health care team. In this trial, provision of such a service yielded extra benefits at little extra cost."	A pragmatic study. Baseline comparability is sparse. High dropout rate. At 2 months, all measures improved in both groups, but more in osteopathic group. At 6 months, group differences were not significant, which included improvement in the control group.
Hemmilä 2005 RCT Sponsored by Finnish Cultural Foundation. No mention of COI.	3.0	N = 42 with tension neck syndrome with nonspecific pain between the shoulder and the occiput for 1 or more months; between the ages of 18-64 years. Excluded: any therapy in previous month, contraindication to manual therapy.	Bone setting using adjustments (non-chiropractic), rotations, or massage for 5 30 minutes sessions for 5 weeks (N = 22) vs Control, not offered or denied any therapy (N = 20). Follow-up at 5 weeks and 3, 6, and 12 months from baseline.	Cervical ROM (CROM) 5 weeks mean change: frontal plane – bone setting 18.9 vs control -1.0, p = 0.001; sagittal plane – bone setting 23.2 vs control 1.0, p = 0.000; horizontal plane – bone setting 18.1 vs 3.4, p = 0.02. Million index mean improvement 5 weeks/3 months/ 6 months/ 12 months: bone setting 18.5 vs control 4.0, (p = 0.002/21.2) vs (6.2, p = 0.01/22.9) vs (5.4, p = 0.005/NS).	"This study is the first to show effectiveness of bone setting on chronic neck pain. In spite of its limitations, it indicates that this type of traditional folk medicine provides at least transient relief of nonspecific neck pain, which seems rather stable when left untreated.	Article contains both subacute and chronic pain. Differences in baseline comparability (5.3v 8.4y neck pain) concerning for randomization failure. Small sample size.
Moretti 2004	2.0	N = 80 with benign	Experimental group received vertebral	Mean VAS scores for Experimental vs Control:	"The results obtained… showed the greater	Article contains both subacute and chronic pain. Manipulative

RCT No mention of sponsorship or COI.		cervicobrachialgia of mechanical origin lasting more than 6wks. Mean age of Experimental and Control groups: 31.9 years and 34 years.	manipulative therapy using R. Meigne semi-indirect method (N = 40) vs Control group received traditional physiotherapy based on segmental functional rehabilitation of spine and massotherapy (N = 40). Assessments at pre-treatment and 1 and 3 months post-treatment.	Pretreatment – 8.9 vs 8.5; 1-month – 1.2 vs 6.6 ($p < 0.01$); 3-month – 1.3 vs 7.1, ($p < 0.01$).	effectiveness of manipulative treatment, in the short term and in the long term."	therapy group performed better than physiotherapy group short term and at 3 months but weak methodology in study.
Chronic Neck Pain						
Youssef 2013 No mention of sponsorship COI.	3.5	N = 38 with recurrent headache and neck pain for at least 2 months; mean age was 31.7 years old.	Group 1-Low velocity passive upper cervical mobilization techniques (N = 20) vs Group 2- Massage therapy (N = 18). Treatment took place 12 times, 2 times per week for 6 weeks.	Functional activity and active neck range of motion were significantly improved in both groups compared to baseline, ($p < 0.05$). No significant difference between groups, however Neck extension was trending towards being significant for the mobilization technique group, ($p = 0.080$) as well as neck right trunk bending, ($p = 0.1$).	"The neck range of motion in flexion, extension, rotation, lateral flexion for patients with CGH significantly increased after upper cervical mobilization and to a greater extent than with massage therapy."	All participants had some form of treatment.
Sillevis 2010 RCT No mention of sponsorship or COI.	3.5	N = 101 with chronic cervical pain. Mean age data not provided; age range of 18-65.	Chronic cervical manipulation group (N = 50) vs Chronic placebo group (N = 51). Assessments made twice immediately after intervention.	VAS scores decreased significantly in placebo group ($p = 0.03$), but not significantly in manipulation group ($p = 0.06$) compared to baseline. Post-intervention measures did not show significant difference between groups, (32 vs 28) however, it was trending towards significance in favor of placebo group ($p = 0.076$).	"This study did not show a statistical difference in the subject's pain perception when comparing the effects of either the manipulation or a placebo intervention. This suggests that thrust manipulation was not effective in reducing pain in the chronic neck pain subjects of this study."	Study methods sparse. Baseline comparability not provided in detail. No change in sympathetic activity between groups.
Espi-Lopez 2014 RCT No sponsorship or COI.	3.5	N = 84 with chronic tension type headache (CTTH) or episodic tension type headache (ETTH); mean age 39.76±11.38, ranging from 18 to 65.	Group 1: Manual Therapy, supine position, therapist guided, 10 minutes (N = 20) vs Group 2: Manipulative Therapy, supine position, rotation and lateral flexion, thrust manipulation (N = 22) vs Group 3: Combination of	Mean ± SD for Cervical Range of Motion: Cervical Flexion: pre vs post: manual: 49.20±12.53 vs 59.85±11.61, ($p = 0.002$); per vs follow up: 49.20±12.53 vs 56.85±10.85, $p = 0.02$; control: pre vs post: 46.95±9.03 vs 50.29±9.81, $p = 0.02$; pre vs follow-up: 46.95±9.03 vs 49.40±9.47, $p = 0.04$. Cervical Extension: manual: pre vs post: 50.90±14.51 vs 57.05±13.33, ($p = 0.03$);	"Both treatments, administered both separately and combined together, showed efficacy for patients with tension-type headache with regard to pain perception. As for cervical ranges of motion, treatments produced greater effect when separately administered."	Methodological details sparse.

			Manual Therapy and Manipulative Therapy (N = 20) vs Group 4: No treatment (N = 22). Follow-up: baseline, 4 and 8 weeks.	manipulation: 49.36±10.36 vs 56.35±11.85, (p = 0.03); combination: 53.40±14.53 vs 57.80±14.53, (p = 0.06). Left Lateral Rotation: manipulation: pre vs post: 39.54±6.36 vs 44.05±5.59, (p = 0.01); pre vs follow-up: 39.54±6.36 vs 42.50, (p = 0.04); Control: pre vs post: 38.27±7.08 vs 41.14±6.46, p = 0.06; pre vs follow-up: 38.27±7.08 vs 40.20±5.81, p 0.04; **Right Rotation**: manual: pre vs post: 59.85±11.94 vs 64.35±12.28, p = 0.02; manipulation: pre vs post: 61.05±8.27 vs 68.70±7.86, p = 0.000; pre vs follow-up: 61.05±8.27 vs 66.45±7.51, p = 0.007; combination: pre vs post: 63.10±9.76 vs 67.95±9.96, p = 0.04; **Left Rotation**: manipulation: pre vs post: 56.50±14.34 vs 66.83±11.22, (p = 0.000); pre vs follow-up: 56.50±63.15, (p = 0.02); manipulation: pre vs post: 64.45±8.05 vs 64.15±13.47, (p = 0.006); pre vs follow-up: 64.45±8.05 vs 68.20±9.14, (p = 0.03); combination: pre vs post: 63.45±11.26 vs 71.50±7.61, (p = 0.02).		
Allan 2003 RCT No mention of sponsorship or COI.	2.5	N = 16 with chronic mechanical neck pain for a minimum of 12 weeks; mean ages were; 42 ± 13, 45 ± 15 and 39 ± 13 years for groups 1, 2 and 3 respectively.	Manipulation or control group 1 received cervical spinal chiropractic manipulation high-velocity only, low amplitude, which was given in accordance with the motion palpation findings (N = 5) vs Stretch before or group 2, before the cervical manipulation (N = 5) vs Stretch after or group 3, stretching the neck musculature immediately after the	NDIs measurements at Baseline: (± SD) point average scores of 5 ± 5 for group 1, 16 ± 9 for group 2, and 11 ± 4 for group 3. End-of-study intra group analysis showed, 80% decrease in disability in pre stretch group and 73% in post stretch group. NRS-101s Baseline: (± SD) point average scores of 30 ± 29% for group 1, 58 ± 30% for group 2, and 63 ± 24% for group 3. Mid-study and end-of-study showed similar findings: 58% decrease in pain in group 1, 88% decrease in group 2 and 84% in post stretch group. RoM Baseline: 296◦ for group 1, 263◦ for group 2, and 277◦	"[C]ombining manipulation with stretch in this study significantly decreased intra-group pain and disability, and may be considered possible useful in the management of chronic mechanical neck pain."	Small sample size. Methodological details sparse.

			cervical manipulation (N = 6). Follow-up for 4 weeks.	for group 3, not statistically significant differences. Mid-study and end-of-study intra group analysis showed no statistical significance, (p = 0.918).		
Murphy 2010 RCT Sponsored by Australian Spinal Research Foundation. No COI.	2.5	N = 20 with chronic nonspecific neck pain; mean age 43 ± 12 years.	Experimental group received 4-weeks chiropractic care followed by 8 weeks exercise intervention. (N = 10) vs. Control group waited 4 weeks prior to receiving 8 weeks exercise intervention (N = 10). Assessments performed at weeks 1, 4, and 12.	Mean changes after 12-weeks in Experimental vs Control: Neck disability (NDI) – 10.75 ± 9.56 vs 8.29 ± 7.06; Pain now (VAS) – 16.75 ± 21.14 vs 12.71 ± 24.84; Pain worst (VAS) – 9.5 ± 18.62 vs 19.8 ± 32.4.	"This pilot study showed that both exercise and exercise combined with manipulation can improve pain and disability in people with long-term neck pain."	Small sample size. Methodological details sparse, poor baseline comparability.
Palmgren 2006 RCT Sponsored by the Scandinivian College of Chiropractic. No mention of COI.	2.5	N = 41 with continuous cervical neck pain 3 months prior to study; mean age 31.9 ± 8.5 years.	Treatment group received high-velocity and low-amplitude manipulation, proprioceptive neuromuscular facilitation, ischemic compression of myofascial trigger points, and spinal rehabilitation exercises (N = 20) vs. Control group did not received any type of treatment (N = 21). Follow-up assessment at end of 5 week study.	Change in VAS score for Treatment vs Control: 29mm (p = 0.0002) vs No Change, (p = 0.3721).	"The results of this study support that chiropractic care can be effective in influencing the complex process of proprioceptive sensibility and pain of cervical origin."	Many study design and methodological weaknesses. Results for head repositioning accuracy were ambigious.
Ragonese 2009 RCT No mention of sponsorship or COI.	2.5	N = 30 with cervical radiculopathy; mean age not reported.	Manual Physical Therapy group received cervical lateral glides, thoracic mobilizations, and neural dynamic techniques for the median nerve (N = 10) vs Exercise group performed deep neck flexor strengthening, lower and middle trapezius	Numeric Pain Rating Scale Initial vs Final: Manual – 5.3±1.6 vs 2.4±1.1 Exercise – 4.9±1.4 vs 1.6±1.5 Combo – 4.1±1.5 vs 0.9±1.2. Combo had greatest difference (p < 0.01). Neck Disability Index Initial vs Final: Manual – 39.6±17.2 vs 17.2±10.3 Exercise – 28.7±13.3 vs 10.2±7.1 Combo – 25.5±10.9 vs 7.8±5.5.	"The results of this study suggest that a multimodal treatment approach using a combination of manual therapy and strengthening exercises is superior to treatment by either intervention alone."	Small sample size with sparse methodological details and poor baseline comparability.

			strengthening, and serratus anterior strengthening (N = 10) vs Combined group received both therapeutic exercises and manual physical therapy (N = 10). Follow-up for 3 weeks.	Combo had greatest difference ($p < 0.05$).		
Moretti 2004 RCT No mention of sponsorship or COI.	2.0	N = 80 with benign cervicobrachialgia of mechanical origin lasting more than 6wks; mean age of experimental and control groups: 31.9 years and 34 years.	Experimental group received vertebral manipulative therapy using R. Meigne semi-indirect method (N = 40) vs Control group received traditional physiotherapy based on segmental functional rehabilitation of spine and massotherapy (N = 40). Assessments at pretreatment and 1 and 3 months post treatment.	Mean VAS scores for Experimental vs Control: Pretreatment – 8.9 vs 8.5; 1-month – 1.2 vs 6.6 ($p < 0.01$); 3-month – 1.3 vs 7.1, ($p < 0.01$).	"The results obtained… showed the greater effectiveness of manipulative treatment, in the short term and in the long term."	Article contains both subacute and chronic pain. Manipulative therapy group performed better than physiotherapy group short term and at 3 months but weak methodology in study.
Mansilla-Ferragut 2009 RCT No mention of sponsorship or COI.	1.5	N = 37 women with mechanical neck pain for at least 6 months; mean age 35 $\pm$ 8 years.	Experimental group received spinal manipulation directed at atlanto-occipital joint (N = 18) vs Control group received a manual contact placebo intervention (N = 19). Assessment performed pre-treatment and 5 minutes post treatment.	Experimental vs Control pre and post treatment difference – Active mouth opening: 3.5 (95%CI 2.4-4.6) vs -0.3 (95%CI -0.4-1.2; Pressure pain threshold: 0.1 (95%CI 0-0.2) vs -0.1 (95%CI -0.2-0.1).	"Our results suggest that the application of an atlantoaxial joint thrust manipulation results in an immediate increase in active mouth opening and pressure pain thresholds over a trigeminal-related area (sphenoid bone) in women with mechanical neck pain."	Limited generalizability: subjects were all women. Weaknesses include only a qualitative description of baseline comparability. Limited details
Lee 2013 RCT No mention of sponsorship or COI.	1.0	N = 30 diagnosed with neck pain with forward head posture or FHP with 15 mm.	Cervical mobilization plus thoracic mobilization (N = 15) vs Control or Cervical mobilization only (N = 15). Both groups received joint mobilization 3x a week for 15 minutes	Cranial vertical angle (CVA) mean ± SD before/after: experimental group 46.6±3.3/48.9±3.1 vs control 45.8±2.5/46.7±2.4, $p < 0.05$. Cranial rotation angle (CRA) mean ± SD before/after: 155.3±3.1/152.6±3.1 vs 155.6±3.2/154.5±3.1, ($p < 0.05$).	"[C]ervical mobilization combined with thoracic mobilization was performed for patients with FHP, and changes in FHP were compared."	Methodological details sparse.

			for 4 weeks. Follow-up after treatment.			
Ko 2010 Non-RCT No mention of sponsorship or COI.	N/A	N = 53 females with chronic neck pain; mean age for the experimental and control groups: 36.56±9.82 and 38.65±12.50 years.	Experimental group received thoracic mobilization and performed cranio-cervical flexor exercises (N = 27) vs Control group performed cranio-cervical flexor exercises (N = 26). Pre- and post-treatment assessment. No long-term follow-up.	Endurance changed significantly between groups from pre to post-test 30.22 (95% CI 23.47-36.97) for experimental group and 15.96, 95% CI 9.08-22.83, $p < 0.05$). VAS pain scores improved significantly in the experimental group 3.44 (95% CI 3.39-3.49) compared to the control 1.42, 95% CI 1.37-1.47, ($p < 0.05$). Neck disability index scores improved significantly in the experimental group 7.96 (95% CI 7.28-8.63) compared to the control group 5.88, 95% CI 5.19-6.57, ($p < 0.05$).	"After comparisons of interventions and their results after mid- to long-term treatment are done, their positive and adverse effects over time should be studied."	Not randomized.
Non-specific Neck Pain						
Metcalfe 2006 RCT No mention of sponsorship or COI.	1.5	N = 67 accessing physical therapy for the treatment of neck pain or headaches; mean age 37 ± 11 years.	Treatment group received manipulation to dysfunctional segments in the upper (C0-C2) and lower (C2-C7) cervical spine (N = 41) vs. Control Group received manipulation to dysfunctional segments in the lower cervical spine only (N = 26). Assessments performed pre-treatment and 2 minutes post treatment.	Mean strength improvement between pre & post intervention for Treatment vs Control groups: Predicted weak side – 2.9 ± 3.0 ($p<0.05$) vs 1.9 ± 4.2 ($p<0.05$); Predicted strong side – 1.2 ± 2.5 ($p < 0.05$) vs 1.3 ± 4.1, ($p < 0.05$).	"Treatment of segmental dysfunctions in the upper and lower cervical spine by manipulation resulted in greater increase in neck strength on the weaker side compared to the stronger side. This effect was more pronounced than when treatment included only manipulation of lower cervical spine dysfunctions."	Little descriptive data on baseline comparability. Weak study methodology.
Parkin-Smith 1998 RCT No mention of sponsorship or COI.	1.5	N = 30 with mechanical neck pain without radiculopathy; mean age 35.4 years.	Treatment group received cervical manipulation only (n = 13) vs Combined group received cervical and upper thoracic manipulation (n = 17). Follow-up time is unclear.	Post-treatment comparison Treatment vs Combined: Numerical Pain Rating Scale – 17.71 vs 13.18 ($p = 0.39463$); McGill Short-Form Pain – 2.96 vs 2.77 ($p = 0.0527$); CMCC Neck Disability Index – 6.89 vs 4.71 ($p = 0.19226$).	"This study demonstrates that manipulating both the cervical and upper thoracic spines does not show any benefit over manipulating the cervical spine only, in terms of subjective and objective clinical findings, in subjects with mechanical neck pain."	No placebo (control) group. Both the cervical manipulation group and the cervical and thoracic spine manipulation group showed little (if any) difference. Pilot study
Other						
Fernandez-de-las-Peñas 2008	3.5	N = 30 asymptomatic	Experimental Dominant Group,	Mean (95% CI) for PPT levels: pre- post- differences: right side:	"The application of a cervicothoracic junction	Small sample size (N=30). Baseline comparability unclear.

RCT No mention of sponsorship or COI.		volunteers; mean age 25±5 for experimental dominant group, 27±6 for experimental non-dominant group, and 25±4.5 for the placebo group.	participants who received manipulative thrust directed at right side of C7-T1 joint (N = 10) vs Experimental Non-Dominant Group, manipulative thrust on left side of the C7-T1 joint (n = 10) vs Placebo, sham-manual procedure (n = 10). Follow-up pre- and post-intervention	experimental dominant vs experimental non-dominant: 53.1 (30.7 to 75.3) vs 80.7 (49.9 to 111.5), ($p < 0.05$).	manipulation induced changes in PPT in both right and left C5-C6 zygapophyseal joints in healthy subjects. In addition, the effect size for the groups that received C7-T1 manipulation was large, suggesting a clinically important increase in PPT after intervention."	Both experimental groups showed improvements over placebo in PPT.
Howe 1983 RCT No mention of sponsorship or COI.	2.5	N = 52 with pain in the neck, arm, or hand due to a lesion of the cervical spine; between the ages of 15-65 years.	Manipulation and/or injection of methylprednisolone or mixture of lignocaine and hydrocortisone, plus azapropazone (N = 26) vs. Control plus azapropazone (N = 26). Follow-up at 1 and 3 weeks after baseline.	Proportion of immediate improvement in neck pain, stiff neck, pain/paraesthesia of shoulder: better in manipulation vs control, ($p < 0.001$) for all. Rotation immediately, after 1 week and after 3 weeks: significant improvement for manipulation vs control, ($p <0.05$). Lateral flexion immediately: significant improvement for manipulation vs control, ($p <0.05$).	"Pain in the neck, pain or paraesthesia in the shoulder and stiffness of the neck were all improved significantly after manipulation."	Manipulation of cervical spine showed small improvement in rotation and worsening in pain in neck and shoulders and worsening of neck stiffness.
Oliveira-Campelo 2010 RCT No mention of sponsorship or COI.	2.0	N = 122 with diagnosis of latent trigger points (TrPs) in the masseter muscle on either the left or right side; mean age 20 $\pm$ 3 years.	Manipulative group received an atlanto-occipital joint thrust (N = 41) vs Soft tissue group received inhibition technique over suboccipital muscles (N = 41) vs Control group received no intervention or sham procedure (N = 40). Assessments performed pre-treatment and 2 minutes post treatment.	The 2 year 3 mixed ANOVA model showed a significant group by time interaction for pressure pain changes over masseter ($p<.01$) and temporalis ($p=.003$)muscle latent TrPs and also for active mouth opening ($p<.001$)	"The application of an atlanto-occipital technique targeted to the suboccipital muscles led to an immediate increase in pressure pain thresholds over latent TrPs in the masseter and temporalis muscles and an increase thrust manipulation or soft tissue in maximum active mouth opening."	The atlanto-occipital joint manipulation and suboccipital muscle inhibition led to an increase in pain. Between group sizes were small.

MASSAGE

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Youssef 2013 RCT No mention of sponsorship or COI.	3.5	N = 38 with recurrent headache and neck pain for at least 2 months. Mean age was 31.7 years old.	Group 1- Low velocity passive upper cervical mobilization techniques (N = 20) vs Group 2 - Massage therapy (N = 18). Treatment took place 12 times, 2 times per week for 6 weeks.	Functional activity and active neck range of motion were significantly improved in both groups compared to baseline, ($p < 0.05$). No significant difference between groups, however Neck extension trending towards being significant. ($p = 0.080$) as well as Neck right trunk bending, ($p = 0.1$).	"The neck range of motion in flexion, extension, rotation, lateral flexion for patients with CGH significantly increased after upper cervical mobilization and to a greater extent than with massage therapy."	All participants had some form of treatment.
Hohmann 2012 RCT No mention of sponsorship or COI.	2.5	N = 40 with non-specific neck pain lasting for more than 3 months. Mean age among participants was 46.1 years old.	Treatment group- Acupressure Pad—a needle stimulation pad (n = 20) vs Control group (N = 20). Pain and disability were measured pre and post-operatively.	The difference between groups according to the NPS pain scale postoperatively was -1.6 pts in favor of the treatment group, ($p = 0.021$). Neck pain disability was significantly improved in the treatment group compared to control with a -7.4 NPQ score difference, ($p = 0.028$)	"The needle stimulation pad revealed a substantial potential for the alleviation of chronic NP. Furthermore, psychophysical data support the assumption that the pad reveals its effects at least partly on a subcortical level of the pain processing system. A further benefit of the device is the fact that it is easy to use, safe, and does not require a therapist.	Methodological details sparse

MYOFASCIAL RELEASE

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Tozzi 2011 RCT No COI. No mention of sponsorship.	3.5	N = 60 with non-specific pain in the cervical or lumbar region and non-specific LBP at least for 3 weeks and no more than 6 months, tmean age 37.3 for experimental	Experimental Group (n = 30) received manual fascial techniques vs. Control Group (n = 30) received a sham treatment by someone w/o experience in manual therapy.	Experimental group reported an SF-MPQ reduced pain perception from 24.65 to 15.51 while the control group reported 24.88 to 25.05 (p,0.0001)	"MFTs appear to be a useful method to improve or even restore normal tissue mobility and function as well as to decrease pain perception."	Lack of study details. Outcomes, measures, and correlation of ultrasound findings difficult to understand. Small sample size with mixed acute, subacute, and chronic neck and lumbar pain.

		NP group, 39.1 for experimental LBP group, 39.1 for control NP group, and 39 for control LBP group.				
Fryer 2005 RCT No mention of sponsorship or COI.	1.0	N=37 volunteers without generalized primary fibromyalgia from a student population. Mean age 23.1±3.2 years.	Manual pressure release (MPR) slow pressure applied to myofascial trigger points (MTrP) until subject reported 7 out of 10 pain for 60 seconds, pressure readings recorded (n = 20) vs. control group: sham myofascial release procedure (n = 17). Study duration 60 seconds of pressure. No follow-up time.	Mean change in pressure pain threshold (PPT) pre-post: MPR - 2.05 vs. control 0.083 ($p<0.001$).	"Significant increases in PPT were observed following MPR applied to the pre-determined MTrP, but no significant change was demonstrated in the sham control group."	Small sample size (N=37). Details sparse.

SUBCUTANEOUS CARBON-DIOXIDE INSUFFLATIONS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Mouton 2001 RCT No mention of sponsorship or COI.	2.5	N = 40 with post-op pain following thoracoscopic procedures; mean age or range not provided.	Humidified CO2 group (N = 20) vs Standard dry CO2 group gas (N = 20). Postoperative analgesia administrated blinded to procedure, standardized prescription of intramuscular oral morphine sulphate 10mg/4hours + rectal Paracetamol 500mg for 6 hours. Follow-up for 14 days.	Humidified gas group reported less pain at 6 h , 1st day, 3rd and 14th post-operative day, ($p = 0.007$, 0.002, 0.005, and 0.006, respectively), when compared to control group.	"The use of humidified gas appears to reduce postoperative pain but not the rate of respiratory complications."	Methodological details sparse.

TRACTION

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Jellad 2009 RCT No mention of sponsorship or COI.	3.5	N = 39 with cervical radiculopathy; mean age 41.6 (8).	Group A, standard rehabilitation programme + cervical spine mobilization + muscle strengthening via isomatic contraction of flexor and extensor muscle + stretching exercise + self-expansion for the spinal muscles (N = 13) vs Group B, standard rehabilitation + mechanical traction with weight bearing pulley system (n = 13) vs Group C, standard rehabilitation alone (n = 13). Follow ups at end of treatment, 1, 3 and 6 months.	Neck pain / Radicular pain / Self-perceived disability / Analgesic consumption at baseline and 6 months; ($p = 0.009$ vs $p < 0.0001$ vs $p = 0.23$, & $p = 0.002$ vs $p < 0.0001$ vs $p = 0.70$ in Group C, at 6 months)/($p = 0.008$ vs $p < 0.0001$ vs $p = 0.51$, & $p = 0.0001$ significance for groups A and B vs C, at 6 months) /($p = 0.044$ vs $p < 0.0001$ vs $p = 0.67$, & $p < 0.0001$ vs $p = 0.001$ vs $p = 0.75$, at 6 months)/($p = 0.012$ vs. $p < 0.0001$ vs $p = 0.012$, and $p < 0.0001$ for groups A and B vs. $p = 0.003$ for group C, at 6 months).	"Manual or mechanical cervical traction appears to be a major contribution in the rehabilitation of CR particularly if it is included in a multimodal approach of rehabilitation."	Small sample size, lack of study details for compliance, dropout rate, allocation, and methods limits conclusions.
Myśliwiec 2011 RCT No mention of sponsorship or COI.	1.0	N = 45 with chronic neck pain caused by overload, which resulted from postural insufficiency and head protraction; mean age 39.4 (11.53) for group 1, 44.2 (10.67) for group 2, and 55.1 (10.82) for group 3.	Group 1, cervical spine traction, Home Track unit by Saunders, supine position with head locked in unit head-rest, 10 minutes of traction (n = 15) vs. Group 2, Saunders and TENS, 50ms and frequency of 100 Hz, 30 minutes per session (n = 15) vs. Group 3, only received TENS Hand grip strength: CMS 2 dynamometer, strength of painless grip and maximum strength, repeated 3 times (n = 15).	Mean ± SD for painless left arm flexion strength: initial vs final visit: group 1: 17.16±9.43 vs 19.28±8.97, $p = 0.013$; group 2: 15.42 ±13.4 vs 14.31±10.86, $p = 0.046$; painless right arm flexion strength: 17.86±11.48 vs 21.55±10.7, $p = 0.005$; strength of the left arm flexors: 23.21±9.31 vs 26.06±10.49, $p = 0.015$.	“The use of the Saunders cervical traction device produced an increase in painless hand grip strength in patients with cervical spine pain.”	“Overload-induced cervical pain,” ill-defined. Quasi-randomized every other. Attention bias and sparse methods.

			Follow-up not specified.			
Myśliwiec 2012 RCT No mention of sponsorship or COI.	1.0	N = 39 with chronic cervical spine pain of at least several months duration; mean age 41.92 (10.14) for group 1, 44.2 (10.67) for group 2 and 51.73 (10.72) for group 3.	Group 1, traction of the cervical spine, Home Track unit by Saunders, supine, 10 minutes per session (n = NA) vs. Group 2, Saunders device and TENS, pulse duration of 50 ms, frequency of 100 Hz, each session lasted 30 minutes (n = NA) vs. Group 3, only received TENS device (n = NA). Follow-up not specified.	Mean ± SD for extension flexion of cervical spine: baseline vs final: Group 1 (ex): 66.93±10.19 vs 76.67±14.01, p = 0.017; Group 2 (ex): 68.67±10.44 vs 76.4±11.19, p = 0.001; Group 2 (fl): 49.07±14.6 vs 52.13±7.94, p = 0.020; Group 3 (fl): 37.6±9.39 vs 42.27±5.6, p = 0.002. Mean ± SD for right and left lateral flexion of neck: baseline vs final: Group 1 (left): 41.33±12.34 vs 46.67, p = 0.004; Group 2 (left): 41.73±7.81 vs 48.4±7.68, p = 0.001; Group 3 (left): 36.13±7.91 vs 40.27±6.67, p = 0.012; Group 1 (right): 38.93±6.23 vs 46.67±7.2, p = 0.003; Group 2 (right): 39.2±9.4 vs 48.4±7.68, p = 0.002; Group 3 (right): 32.53±7.35 vs 38±5.76, p = 0.003. Mean ± SD for left and right rotation of neck: baseline vs final: Group 1 (left): 53.33±12.34 vs 70.77±8.75, p = 0.003; Group 2 (left) 65.07±12.35 vs 75.73±8.03, p = 0.000; Group 3 (left): 61.33±9.9 vs 68.27±8.45, p = 0.017; Group 1 (right): 66.13±7.87 vs 74.13±8.33, p = 0.002; Group 2 (right): 63.2±7.59 vs 72.53±5.32, p = 0.001; Group 3 (right): 60.4±9.66 vs 66.13±7.15, p = 0.003.	"The best therapeutics effect was obtained by combining traction with transcutaneous electrical nerve stimulation."	Pilot study with sparse methodology.
Lee 1996 RCT Supported by a grant from the National Science Council of Taiwan. No mention of COI.	0.5	N = 24 cervical radiculopathy and muscle spasm	Traditional open-loop traction (n = 12) vs. EMG biofeedback closed-loop traction device (n = 12).	Over 7-week treatment period, ANOVA scores significantly different in EMG activity (f = 19.57; p <0.001).	"The results of this study indicate that the use of intermittent, cervical traction in the sitting position produces relaxation of cervical paraspinal muscle. It also reveals that the average myoelectric activity of cervical paraspinal muscle during traction is reduced as traction force increases over a 7-week traction treatment duration. This study also finds that intermittent cervical traction with EMG biofeedback and adaptive traction force control is more effective in muscle	Lack of study details. Results are intriguing but without study details are not acceptable as evidence.

					relaxation than traditional open loop traction protocol."	
Wong 1997 RCT Supported by grant from National Science Council of Taiwan. No mention of COI.	0.5	N = 30 cervical radiculopathy included 6 health subjects in addition to 24 patients with cervical radiculopathy	Traditional open-loop traction vs. EMG biofeedback closed-loop traction device.	During 7-week trial, subjects with high neck muscle tension in conventional group showed a reduction in EMG activity of 47.8%, biofeedback group showed a reduction of 78%. For subjects with low neck muscle tension, conventional group showed EMG activity decrease of 54.6% and biofeedback a 59.5% decrease.	"The clinical trial for patients with cervical radiculopathy indicated that the raised traction force from start to optimum was shortened from 4 to 2 week in achieving the same effective outcome by the biofeedback to conventional traction modality."	Second report of Lee 1996. Lack of study details.

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Hou 2002 RCT No sponsorship or COI.	1.5	N = 62 with clinically active, palpable MTrPs in a single side or both sides of the upper trapezius muscle, age range 30 to 60	B1: hot packs plus active range of motion (ROM), control (n = 21) vs. B2, B1 plus ischemic compression (n = 13) vs. B3, B2 plus TENS (n = 10) vs. B4, B1 plus stretch and spray (n = 9) vs. B5, B4 plus TENS (N = 9) vs. B6, B1 plus interferential current and myofascial release. Follow up: baseline and posttreatment	Mean ± SD for Pain Threshold: pre-treatment vs post treatment: B1:3.07±0.96 vs 3.45±1.09; B2: 3.16±1.18 vs 3.58±1.16; B3: 2.68±0.75 vs 3.39±0.83; B4: 3.09±1.06 vs 3.69±0.83; B5: 3.09±1.10 vs 3.93±1.03; B6: 3.01±0.87 vs 3.94±1.40; pain tolerance: B1: 4.08±1.38 vs 4.36±1.33; B2: 4.65±1.76; B3: 3.80±0.95 vs 4.61±1.09; B4: 3.88±1.37 vs 4.36±1.46; B5: 4.25±1.29 vs 5.47±1.40; B6: 3.76±0.90 vs 5.00±1.56; VAS: B1: 5.10±1.78 vs 4.33±1.82; B2: 4.94±1.93 vs 3.35±1.66; B3: 4.69±2.24 vs 2.46±1.33; B5: 4.68±1.28 vs 2.43±0.65; B6: 5.68±1.34 vs 2.34±0.90, ($p < 0.05$).	"Ischemic compression therapy provides alternative treatments using either low pressure (pain threshold) and a long duration (90s) or high pressure (the average of pain threshold and pain tolerance) and short duration (30s) for immediate pain relief and MTrP sensitivity suppression. Results suggest that therapeutic combinations such as hot pack plus active ROM and stretch with spray, hot pack plus active ROM and stretch with spray as well as TENS, and hot pack plus active ROM and interferential current as well as myofascial release technique, are most effective for easing MTrP pain and increasing cervical ROM."	High number of females (107) compared to men (12). Baseline comparability not described. Sparse methods.

BOTULINUM INJECTIONS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Botulinum Injections for Neck Pain						
Sarifakioglu 2005 RCT No mention of sponsorship or COI.	3.0	N = 93 undergoing injections in the neck, face region and axillary areas	Group 1, dynamic hyperactive line formations, bilateral orbital area (n = 60) vs Group 2, more than 1 platysmal wrinkle in the neck vs (n = 15) Group 3, bilateral axillary hyperhidrosis vs (n = 18) Preservative-containing solution (PCS): Bacteriostatic sodium chloride solution containing benzyl alcohol. Unpreserved saline (UPS): 0.9% chloride BTX-A flacon: right and left sides of patients, 2 mL of PCS and UPS solutions, 5 MU of active drug/1mL. Total number of injections: 8-10 in lateral orbital area, 10-12 in neck, and 20-24 in axillary areas. Follow-up: 7 days by phone, 1, 3, 4, and 6 months.	Mean VAS score: PCS vs. UPS: group 1: 1.2 vs. 4.5, (p = 0.000); group 2: 0.6 vs. 3.9, (p = 0.000); group 3: 0.9 vs. 5.1, (p = 0.000).	"[C]onsequently, this clinical study has shown that by the administration of a PCS solution containing benzyl alcohol in BTX-A applications at different injection sites and for different purposes, patients felt less pain."	Methodological details sparse.
Botulinum Injections for Headaches						
Harden 2009 RCT Sponsored by Lawrence and Nancy Glick Pain Research Fund	3.0	N = 23 with chronic tension-type headache (CTTH) with myofascial trigger points (MTP's)	BT-A, diluted in 1mL saline, 25 units/trigger point, no more than 100 units/patient (n = 12) vs. Placebo, isotonic saline, 1 mL (n = 11). All patients received injections at 4 most sensitive trigger	Days/month headache frequency: BT-A vs. placebo: weeks 5-6: 23.5 vs. 27.5, (p = 0.013); weeks 7-8: 23 vs. 27, (p = 0.0013). No significant differences for secondary outcomes between two groups.	"The evidence for BT-A in headache is mixed, and even more so in CTTH. However, the putative technique of injecting BT-A directly into the ubiquitous MTPs in CTTH is partially supported in this pilot study. Definitive trials	Small sample size (N=23). Methodological details sparse.

and Allergan Pharmaceuticals. Harden received a grant from UCB, serves on an advisory board for Endo pharmaceuticals and GlaxoSmithKline and a consultant for Solstice Neurosciences, Houle received research grant form Endo Pharmaceuticals.			points. Follow-ups: baseline, 2 weeks, 1, 2, and 3 months.		with larger samples are needed to test this hypothesis further."	
Rollnik 2000 RCT Sponsored by Ipsen Pharma, Ettlingen, Germany. No mention of COI.	3.0	N = 21 with chronic tension-type headache (CTTH)	BTA, 20 MU per injection, diluted to 200 MU/mL (n = 11) vs. Placebo, 0.1 mL isotonic saline (n = 10). All received injections at 10 trigger points. Follow up at baseline, 4, 8, and 12 weeks.	No significant differences were reported between the two groups in primary or secondary measures.	"The findings of our study strongly support the hypothesis that peripheral mechanisms, such as increased muscle tenderness, only play a minor role in the pathogenesis of tension-type headache."	Small sample size. Details sparse.
Schnider 2002 RCT Sponsored by Österreichische National Bank. No mention of COI.	3.0	N = 33 with cervical headaches (CH)	BTX-A, 90 MU, 0.9 mL, 100 MU, diluted in 1 mL saline; 15 MU (N = 17) vs. Placebo, 0.15 mL (N = 16). All patients received injections at 6 trigger points of the cervical muscles. Both groups received physical therapy (massage and hot packs) for 9 sessions (weeks 6-8). Follow-ups: baseline, 4, 8, and 12 weeks.	Mean for Visual Analogue Scale (VAS): BTX-A vs. placebo: 5 to 8 weeks: 44 vs. 41, ($p < 0.05$); 9 to 12 weeks: 41 vs. 40, ($p < 0.05$); 13 to 16 weeks: 42 vs. 43, ($p < 0.05$). Number of days for headache free: BTX-A vs. placebo: 5 to 8 weeks: 8.9 vs. 9.0, ($p = 0.005$); 9 to 12 weeks: 10.1 vs. 9.1, ($p = 0.005$); 13 to 15 weeks: 12 vs. 8.9, ($p = 0.005$) (BTX-A group increased). Headache hours per day: BTX-A vs. placebo: 5 to 8 weeks: 7.2 vs. 9, ($p < 0.005$); 9 to 12 weeks: 7 vs. 8.5, ($p < 0.005$); 13 to 16 weeks: 7.9 vs. 8.9, ($p < 0.005$).	"In conclusion, the combined use of physical measures and adjunctive intramuscular injections of botulinum toxin type A is safe. Adjunctive BTX-A injections seem to further improve cervical headache-related pain. Repeated BTX-A treatments probably show a more marked improvement compared to physical therapy alone. These results warrant further studies including larger numbers of patients who receive physical therapy and adjunctive, repeated BTX-A treatment cycles."	Methodological details sparse. Multiple outcomes assessed. All patients also received physical therapy.

Relja 2004 RCT No mention of sponsorship or COI.	2.5	N = 16 with chronic tension-type headache (TTH)	BoNT/A (Botox), 40-95 units (100 units/1 mL saline) (n = 8) vs. Placebo (n = 8). All injected once throughout study. Follow-up: baseline, weeks 1, 2, 4, and 8.	Mean tenderness score (% of baseline): week 1: placebo vs. Botox: 110% vs. 70%, ($p<0.001$); week 2: 111% vs. 39%, ($p<0.001$); week 4: 112% vs. 50%, ($p<0.001$); week 8: 115% vs. 80%, ($p<0.001$).	"Our results as well as the data reported in the literature indicate the increasing evidence of the efficacy and safety of BoNT/A treatment in chronic TTH. However, further clinical and preclinical studies are needed not only to clarify the analgesic pharmacology of BoNT/A but also to establish the best dosing and the best choice of number and injection technique required to provide the best treatment outcome."	Methodological details sparse. Small sample size (N=16).
Botulinum Injections for Cervical Myofascial Pain						
Wheeler 1998 RCT Sponsored by Allerga Corporation. No mention of COI	2.5	N = 33 with myofascial pain syndrome (MPS)	BTX-A, 50 units in 2 cc of normal saline (NS) without preservative (n = 11); 100 units in 2cc (n = 11) vs. Placebo, normal saline, 2cc NS (n = 11). Follow-ups: 1, 3, 6, 9 weeks, 3 and 4 months.	No significant differences to report between groups.	"Although no statistically significant benefit of botulinum toxin type A over placebo was demonstrated in this study, the high incidence of patients who were asymptomatic after a second injection suggests that further research is needed to determine whether higher dosages and sequential injection in a larger cohort might show a botulinum toxin type A effect."	13 patients received additional injections. Methodological details sparse. Small sample size (N=33).

Kamanli 2005 RCT No mention of sponsorship or COI.	1.5	N = 29 with myofascial pain syndrome (MPS)	Lidocaine injection, 1 mL 0.5% lidocaine solution (LIG) (n = 10) vs. Dry needling (DNG) (n = 10) vs. BTX-A injection, 10-20 units (10 units in 1mL) (BTIG) (n = 9). All patients received injections at 7 trigger points. Follow-ups: baseline, week 4	Mean ± SD for VAS pain: before vs. after treatment: LIG: 6.90 ± 1.43 vs. 1.95 ± 1.67, (p = 0.005); VAS fatigue: 5.01 ± 2.16 vs. 1.99 ± 2.01, (p = 0.005); VAS work disability: 5.14 ± 2.48 vs. 2.04 ± 2.46, (p = 0.012); Nottingham Health Profile (NHP): 18.50 ± 6.59 vs. 6.40 ± 4.83, (p = 0.005). Mean ± SD for trigger point pain scale: BTIG: before vs. after treatment: 2.82 ± 0.39 vs. 2.04 ± 0.78 0.000; VAS pain: 6.09 ± 1.95 vs. 2.68 ± 1.04, (p = 0.012); VAS fatigue: 5.65 ± 2.86 vs. 3.54 ± 2.30, (p = 0.021); VAS work disability: 5.54 ± 2.28 vs. 2.58 ± 2.37, (p = 0.011); NHP: 16.55 ± 6.12 vs. 10.11 ± 5.13, (p = 0.021). Mean ± SD for trigger point pain scale: DNG: before vs. after treatment: 2.67 ± 0.54 vs. 2.15 ± 0.62, (p = 0.003).	"[B]otulinum toxin and lidocaine injections both had significant effects on VAS values such as pain, fatigue, and work disability, but this efficacy was more prominent with lidocaine, Although dry needling did not have any therapeutic efficacy on disability, lidocaine and BTX injections had effects of significant degree."	Methodological details sparse.

CERVICAL EPIDURAL INJECTIONS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Matsumoto 2001 RCT No mention of industry sponsorship. COI category 12.	3.5	N = 46 with a mean age of 60.6 years and diagnosis of cervical spinal cord injury by physicians associated with study, mean age 60.6 years.	Treatment Group received high-dose methylprednisolone sodium succinate or (MPSS, provided in 16-vial sets of 1g vials prepared with diluent, administered in 15-minute bolus, followed by a 45-minute pause then 23-hour maintenance infusion) (n = 23) vs. Placebo Group received placebo, administered in 15-minute bolus, followed by 45-minute pause then 23-hour maintenance infusion (n = 23). Follow-up up	Treatment Group had 8 cases of respiratory complication compared to 1 case in the Placebo Group, (p = 0.009) and 4 cases gastrointestinal complications compared to 0 for the Placebo Group, (p = 0.036). Pulmonary complications in patients > 60 years had borderline significance, (p = 0.029). There were no significant differences between the Groups with any other type of complication.	"In conclusion, the results of the present study indicate that aged patients with acute cervical spinal cord injury may be particularly susceptible to pulmonary complications after high-dose therapy with MPSS."	Methodological details sparse.

			to 2 months after injury.			
Stav 1993 RCT No mention of sponsorship or COI.	3.0	N = 50 chronic resistant cervico-brachialgia	Cervical epidural steroid with lidocaine vs. Posterior neck muscle injection with lidocaine and steroids.	"1 week after the last injection, very good and good pain relief was achieved in 76% of the patients in group A versus 35.2% in group B. One year later, pain relief was 68% versus 11.8% respectively. These differences were statistically significant (p=0.004) for 1 week very good and good pain relief and (p= 0.0002) for 1 year. The improvement in ROM 1 week and 1 year after treatment was also significantly better in group A than in group B, as were the DDA and RCW."	"[C]ervical epidural steroid local anaesthetic injection is an effective method for achieving immediate and long-standing pain relief and improvement in motion and performance in chronic resistant cervico-brachialgia."	Injections not done with fluoroscopy. Treatment discontinued if "complete" failure of 1st injection. Patients had pain >6 months with or without radiculopathy. Diagnoses were cervical arthritis and or degenerative disk disease. They did not find any impact on sensory or motor nerve dysfunction with the injections.
Dreyfuss 2006 RCT No mention of sponsorship or COI.	3.0	N = 30 with single-level, unilateral radicular pain with advanced imaging demonstrating single-level neural compression, the mean age 49.3±9.3 years.	Nonparticulate group received a single injection of 12.5mg dexamethasone sodium phosphate (n = 15) vs Particulate received a single injection of 60mg triamcinolone acetonide group (n = 15). Assessment was performed at baseline and during a phone interview at 4 weeks post injection.	For the primary outcome of pain reduction both groups reported clinical and statistical improvement at 4 weeks. Baseline and week 4 mean visual analog pain scores (0-100): Nonparticulate – Baseline: 48 vs Week 4: 29, (p = 0.006) Particulate – Baseline: 49 vs Week 4: 17, (p = 0.000). Thought he particulate group exhibited greater improvement, there was no statistical difference between the groups (Baseline: p = 0.933; week 4: p = 0.156). Proportion of group with at least 50% pain reduction: Nonparticulate group was 0.60 (95% CI: 0.35-0.85). Particulate group was 0.67 (95% CI: 0.43-0.91).	"The study found that the effectiveness of dexamethasone was slightly less than that of triamcinolone, but the difference was neither statistically nor clinically significant."	Details sparse. Short follow up time. Small population. Low statistical power (7%).
Manchikanti 2012a Pain Physician pg E59-E70 RCT/ Double-blind/Active Control No mention of sponsorship or COI.	N/A	N = 60 with cervical central spinal stenosis, >30 years old with history of chronic function-limiting neck pain and upper extremity pain for at least 6 months, mean age 49.9±8.5 Group I, and 49.7±8.9 Group II.	Group 1: 5mL of 0.5% lidocaine (N = 30) vs Group 2: 4 mL of 0.5% lidocaine mixed with 1 mL or 6 mg of nonparticulate betamethasone (N = 30). Post treatment assessment at 3, 6, and 12 months.	Significant pain relief was seen in both groups with 73% of Group 1 participants and 70% of Group 2 participants reporting > 50% reduction in Numeric Rating Score (NRS) from baseline. Group 1 and Group 2: baseline NRS 7.9 + 0.8 and 8.0 + 0.9, (p = 0.862) respectively; 12 month NRS 3.6 + 1.1 and 3.8 + 1.2, (p = 0.434) respectively.	"This randomized, double-blind, controlled trial of cervical interlaminar epidural injections shows a 71.5% rate of effectiveness in pain reduction and functional-limiting neck pain and upper extremity pain secondary to central spinal stenosis."	Excluded as only ½ of the trial. Baseline differences in weight between groups (196 vs 170.7) as well as pain duration in months (115.2vs 94.3). Comparable efficacy, no placebo group, 98 patients randomized with 60 in evaluation.

Manchikanti 2012b Pain Physician pg 13-26 Randomized/Double-blind/Active Control No mention of sponsorship or COI.	N/A	N = 56 with cervical post surgery syndrome; >18 years of age; chronic function-limiting neck and upper extremity pain of >6 months duration.	Group 1: 5 mL of 0.5% lidocaine (n = 28) vs Group 2: 4mL of 0.5% lidocaine mixed with 1mL or 6 mg of nonparticulate betamethasone (n = 28). Post treatment assessment at 3, 6, and 12 months.	Significant pain relief was seen in both groups with 71% of Group 1 participants and 68% of Group 2 participants reporting > 50% reduction in Numeric Rating Score (NRS) from baseline. Group 1 and Group 2: baseline NRS 8.0 + 1.23 and 7.8 + 0.9, (p = 0.534) r; 12 month NRS 3.6 + 1.1 and 3.8 + 1.4, (p = 0.465) respectively.	"The assessment of the preliminary results of this randomized, controlled, double-blind trial of cervical interlamar epidural injection in chronic function-limiting neck pain and upper extremity pain in cervical postsurgery syndrome demonstrated significant pain relief in over 72% of patients with improvement in functional status, requiring 4 procedures per year and providing almost 40 weeks of relief during a 52-week period in appropriately selected patients."	Incomplete trial.
Manchikanti 2012d	N/A	See Manchikanti 2012b				Same study data and results of Manchikanti, 2012b.

FACET JOINT HYALURONIC ACID INJECTIONS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Park 2012 RCT No mention of sponsorship or COI.	3.0	N = 400 with myofascial pain syndrome (MPS) in cervical region for longer than 6 months.	Therapeutic cervical facet joint (CFJ) injections (mixture of 0.5ml 1% lidocaine, 5mg triamcinolone, and 187.5 IR hyaluronidase) on the bilateral C5/C6 and C6/C7 (group I, n = 200) vs. no therapeutic CFJ injections (group N, n = 200) for 1 year.	Cervical ROM (CROM): increased in group I, p<0.05. NRS: reduced in group I, p<0.05. Combined tension-type headache: decreased incidence in Group I, p<0.05	"Therapeutic CFJ injections showed increased CROM, increased mean reduction in NRS, and decreased incidence of combined tension-type headache for long-standing MPS with referral pain patterns of CFJ syndrome across all age groups."	Lack of study details for randomization, allocation, concealment, compliance to intervention, blinding.
Hinderaker 1995 RCT	2.0	N = 82 patients suffering from neck pain for more than 3 months, with or	Short-acting local anaesthetic (lignocaine 2%) vs. long-acting anaesthetic	No differences were found between location of the axis and response to diagnostic blocks.	"Previous false-positive assertions appear to be due to insufficient attention to the precision and reproducibility of the	Controls not randomized, were "last patients to enter" study. Different areas injected based on clinical presentation. No mention of co-interventions. No

Sponsored by a grant from the Motor Accident Authority of New South Wales. No mention of COI.		without headache, following and attributed to a motor vehicle accident.	(bupivacaine 0.5%) for first block. For last 68 entering program, normal saline was injected as additional control.		techniques used to determine IARs."	baseline characteristics given, however patients received both lidocaine and bupivacaine, dosages not mentioned.

DISCECTOMY, MICRODISCECTOMY, SEQUESTRECTOMY, ENDOSCOPIC DECOMPRESSION

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Disc replacement vs. ACDF						
Vaccaro 2013 RCT No mention of sponsorship or COI.	3.5	N = 380 with symptomatic cervical disc disease.	SECURE-C artificial disc group randomized and 89 nonrandomized patients intended to be treated with SECURE-C (n = 151) vs Anterior cervical discectomy and fusion or ACDF (n = 140). Follow-up at 6 weeks, 3 months, 6 months, 12 months, and 24 months.	Both groups demonstrated an improvement in NDI scores from preoperative scores. At the 24 month follow up, 91.4% of the randomized SECURE-C group demonstrated at least 25 % improvement in NDI compared to 87.1% in the ACDF group. 81.2% of the SECURE-C group demonstrated VAS neck pain improvement at 24 months compared to 72.2% of ACDF.	"The current prospective, randomized clinical trial reveals that the selectively constrained SECURE-C Cervical Artificial Disc is as safe and effective as the standard of care, an ACDF, and at 24 months is statistically superior in terms of overall success."	Details sparse.
Anderson 2008 RCT Sponsored by Corporate/Industry funds. One or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party directly or indirectly to subject of	3.5	N = 463 with symptomatic single level cervical degenerative disease	Intervention group or Bryan Disc of 2 titanium shells + 2 titanium retaining wires + polycarbonate polyurethane nucleus + 2 titanium plugs (n = 242) vs Control group or arthrodesis with structural allograft + titanium alloy plate + screw construct (N=221). Follow up at 1.5, 3, 6, 12, and 24 months after surgery.	Cervical neck/arm symptoms / thoracolumbar pain / headaches / pseudoarthrosis; (5 and 11 vs. 6 and 22, total 16 vs. 28, (p=0.0003)) / (1 and 9 vs. 2 and 6, total 10 vs. 8) / (1 and 2 vs. 2 and 1, total 3 vs. 3) / (0 and 0 vs. 0 and 6, total 0 vs. 6), at early ≤6 weeks and late>6 weeks. Overall, adverse events occurred in the investigational group 33.9% vs. 29.0%.	"This prospective randomized study demonstrated small difference in adverse medical events between the Bryan Cervical Disc arthroplasty and arthrodesis groups."	Lack of methods details limits conclusions. This may be reposted elsewhere, since this is a secondary analysis.

manuscript: *e.g.*, honoraria, gifts, consultancies.						
Bartels 2006 RCT in progress	3.5	In progress	Anterior cervical discectomy vs. ACD with fusion vs. ACD with arthroplasty with Bryan disc	In progress	In progress	Trial reported in progress. Per initial report will not control well for co-interventions, however, eventual quality score appears likely to be at least moderate.
Riina 2008 RCT Sponsored by Medtronic Sofamor Danek. No COI.	3.0	N = 19 with C3–C4 to C6–C7 disc involvement at only a single level and not improvement after 6 weeks of nonoperative treatment or progressive signs of spine or nerve root compression, and NDI score of 30 of greater.	ACDF (control) group received the Atlantis anterior plate, manufactured by Medtronic Sofamor Danek, a titanium alloy implant fixed to vertebral bodies with either fixed- or variable-angle cancellous screws (n = 9) vs. Artificial cervical disc (investigational) group received Prestige ST cervical disc prosthesis, manufactured by Medtronic Sofamor Danek, a dynamic stainless steel device inserted into intervertebral disc space (n = 10). Follow up at 6, 12 and 24 months.	Before surgery, mean (SD) neck pain score was higher for investigational group compared to the control group: 74.8 (19.4) vs. 71.6 (26.0). Two years after surgery, mean (SD) neck pain score dropped for both groups investigational vs. control: 17.9 (24.1) vs. 17.4 (22.1). Before surgery, mean (SD) NDI was lower for the investigational group compared to the control group: 65.6 (11.7) vs. 60.2 (11.7). Two years after surgery, mean (SD) NDI dropped for both groups investigational vs. control: 18.9 (16.8) vs. 22.3 (13.5).	"We found that neurologic function and neck pain were better addressed with the artificial cervical disc, but arm pain was better addressed with ACDF. Patients in both groups improved over their initial complaints. The disc performed at least as well as ACDF, according to our single-center results. Both groups were successful, according to the criteria set forth in the study to determine overall success."	Taken from a non-published RCT. Small sample size methodological details sparse

Delamarter 2013 Prospective RCT Sponsored by Synthes grant. No mention of COI.	2.5	N = 209 with single-level cervical disc disease causing debilitating radiculopathy from a single vertebral segment between C3 and C7, and unresponsive to non-operative treatment for at least 6 weeks, plus neck disability index score of 15/50 (30%) or more.	Total disc replacement or TDR ProDisc-C ball-and-socket principle and composed of 3 components, 3 endplates, caudal endplate (n = 103) vs Anterior cervical discectomy and fusion or ACDF, allograft bone spacers used, local bone also packed around or within allograft, with no other bone substitution, plus fixed-angle place was placed over graft and secured with 4 screws (n = 106). Follow-up for 5 years.	Five-year follow-up rates were 72.7% or 72/99 for the ProDisc-C group and 63.5% or 61/96 for the ACDF group. ProDisc-C had a statistically significantly higher probability of no secondary surgery at the index/ adjacent levels than patients who underwent ACDF or 97.1% and 85.5%, (p = 0.0079) respectively.	"Five-year follow-up of a Prospective randomized clinical trial revealed 5-fold difference in reoperation rates when comparing patients who underwent ACDF (14.5%) with patients who underwent TDR (2.9%)."	At five years post procedure, the reoperation rates significantly (5 times lower) lower in TDR vs. ACDF patients (2.9% vs. 14.5%). Suggest use of TDR slowing adjacent disk disease post procedure vs. ACDF. High dropout rate at 5 years follow-up.
Abd-Alrahman 1999 RCT No mention of sponsorship or COI.	2.5	N = 90 with 1 or 2 level cervical disc disease; excluded PLL ossification	ACD vs. ACDF with bicortical iliac crest graft. Smith Robinson approach.	Odom's excellent or good results in overall 84.4% (ACD 36/40=90% vs. ACDF 40/50=80%, NS). Kyphosis greater in ACD (p = 0.02) (Ed., data given to not appear significant).	"The technique is still in need of more refinement of disc excision and graft harvesting and shaping, as well as more adequately controlled studies. Until that, ACD has to be limited to those patients with a soft single disc without spondylosis.	Many baseline differences, different sizes of groups (50 vs. 40) suggest randomization failure or not truly randomized. Most variables appear to bias against fusion. Conclusion regarding which patients for discectomy not directly tested. Data suggest no difference but potential bias against fusion in baseline data.
Zigler 2013 Prospective RCT Sponsored by Synthes. COI, relevant financial activities outside the submitted work: consultancy, patents,	2.0	N = 209 with symptomatic cervical disc disease with radiculopathy from 1 vertebral level between C3-C7.	ProDisc-C disc replacement group (n = 103) vs Anterior cervical discectomy and fusion (ACDF; n = 106).	Both groups showed statistically significant improvement in NDI scores from baseline (p<0.0001). No significant difference between groups. At 5 year follow-up, ProDisc-C group showed a significantly larger percentage of improvement of VAS neck pain intensity and frequency compared to ACDF group ((p = 0.0122) and (p = 0.0263) respectively).	"Five-year results show that TDR with ProDisc-C is a safe and effective treatment of single-level symptomatic cervical disc disease. Clinical outcomes were comparable with ACDF."	Methodological details sparse. Very little description of methods used.

royalties, board membership, expert testimony, stock/stock options, support for travel.						
Upadhyaya 2012 RCT No sponsorship or COI.	NA	N = 1213 with symptomatic, single-level cervical disc disease, between the C-3 and C-7 levels who presented with intractable radiculopathy or myelopathy or both.	Artificial cervical disc defined as follows; revision or adjustment or modifies the original implant; removal or removal of one or more components; supplemental fixation or additional spinal devices; reoperation or any surgical procedure that does not remove, modify, or add any component, and discs evaluated include; Prestige ST, Bryan, and ProDisc-C artificial discs (n = 621) vs Anterior cervical discectomy and fusion or ACDF (n = 592). Follow-up for 12 months.	In this 3 randomized trials; NDIs in both groups reduced effectively at the 1-year follow-up compared with preoperative indices. Neck and arm pain scores at the 24-months pain frequency trended toward significance favoring arthroplasty and neck pain intensity, but did not reach significance, with WMD of -3.736 and -1.979. 8 patients or 3.6% in the ACDF group and 7 patients or 2.9% in the arthroplasty group required surgery for adjacent-level disease at the final 24 months follow-up.	"The currently available 2-year data suggest that cervical arthroplasty is a safe and effective alternative to ACDF to treat patients with single-level cervical disc disease meeting the FDA inclusion and exclusion criteria."	Meta-analysis, cannot be scored
Coric 2013 RCT No mention of sponsorship. Dr. Coric was Principal Investigator for the Bryan Disc and Kineflex|C IDE studies, is a consultant for	N/A	N=74 patients with 1-level symptomatic cervical disc disease with medically refractory radiculopathy.	Cervical total disc replacement (TDR) (n = 41) vs Anterior cervical discectomy and fusion (ACDF; n = 33). Follow-up was 6 years (72 months) with a range from 48 to 108 months.	A total of 63 patients (86.3) with a minimum of 4 years of follow-up data were available for analysis. In both TDR and ACDF groups, mean NDI scores improved significantly 6 weeks after surgery and continued to improve through 48 weeks. (p <0.001). TDR had a higher range of motion (8.6°) than the preoperative mean (8.2°). Conversely, the postoperative mean for range of motion in ACDF (.2°) was	"Both cervical TDR and ACDF groups showed excellent clinical outcomes that were maintained over an average of 6 years of long-term follow-up. Both cervical TDR and ACDF are viable options for the treatment of single-level cervical radiculopathy."	Pooled results from 2 studies.

Medtronic, and is a consultant for and stock owner of SpinalMotion.				significantly reduced compared to preoperative mean (7.6°).		
Titanium vs. PEEK						
Chen 2013 RCT No sponsorship or COI.	3.5	N = 60 with symptoms of cervical myelopathy and/or radiculopathy, disc herniation or degeneration, cervical pathology in 3 consecutive levels, and non-response to conservative treatment for 6 weeks.	Titanium box cage SynCage C (Synthes, Oberdorf, Switzerland; n = 29) vs. PEEK box cage (Depuy Spine, Raynham, MA, USA; n = 31). Follow up range from 86 to 116 months (mean: 99.7 months).	JOA scores significantly increased from 9.6 ± 1.4 to 12.8 ± 1.8 in the titanium group ($p<0.05$), from 9.8 ± 1.4 to 14.2 ± 1.8 in the PEEK group ($p<0.05$), respectively. The corresponding NDI scores significantly decreased from 36.2 ± 3.7 to 21.6 ± 2.6 in the titanium group ($P<0.05$), from 35.4 ± 3.6 to 15.2 ± 2.3 in the PEEK group ($P<0.05$), respectively.	"[I]n addition, without anterior cervical plate augmentation, stand-alone PEEK cages provided good maintenance of intervertebral height and cervical lordosis, as well as better clinical outcomes compared with titanium cages in the long-term follow-up. These advantages were added in the treatment of multilevel CSM."	Randomization and group allocation are not detailed in the study. PEEK group outperformed Titanium group for disability scores and clinical outcome.
Kast 2009 No sponsorship or COI.	2.5	N = 52 with planned ACDF for radiculopathy or cervical myelopathy.	Group 1: Solis cage (Stryker Company, Kalamazoo, USA), ring-shaped with 2mm thickness (n = 26) vs. Group 2: Shell cage (AMT Company, Nonnweiler, Germany), trapezoid-shaped with a thickness of about 1 to 4 mm (n = 26). Follow up at 3 and at 6 months.	At 3 months follow-up, the mean segmental height in the Solis group was lower than presurgery, but not in the Shell group. There was significantly more kyphosis in the Solis group at last follow-up ($p= 0.032$). Subsidence occurred statistically significantly more in group1 (42%) than in group2 (15%) at last follow-up ($p=0.014$).	"In the current study, there was a significant difference in subsidence and segmental kyphosis between both treatment groups. Furthermore, there is a significant correlation between some radiological and clinical results. Although there was no significant difference in short-term clinical results between the two treatment groups, the aim should be to preserve the determined segmental height and lordosis. Therefore, we recommend using cages with a large-enough contact surface area, increased at the anterior lower aspect of the implant."	Methodological details sparse

ACDF vs. PCM						
Phillips 2013 Prospective RCT Sponsored by NuVasive, Inc. COI, board membership, consultancy, consulting fee or honorarium, royalties, stock/stock options, grants, fees for participation in review activities, payment for lectures, patents, etc.	3.5	N=416 with single-level radiculopathy and/or myelopathy.	Porous Coated Motion (PCM) cervical disc group (N = 224) vs. Anterior cervical discectomy and fusion (ACDF; N=192). Follow up immediately post-op 1.5-, 3-, 6-, 12-, and 24-month.	In both groups, mean Neck Disability Index (NDI) improved significantly from baseline at all time points (p <0.001). Mean NDI score at 24 months was significantly lower in the PCM group (21.8) compared to the ACDF group (25.5) (p=0.029). Overall success was achieved in 75.1% of PCM and 64.9% in the ACDF group.	"Overall, it was found that cervical disc arthroplasty with the PCM Cervical Disc is safe and effective for the treatment of symptomatic single-level cervical spondylosis. Compared with instrumented anterior cervical fusion, equivalent or better clinical outcomes were achieved while preserving cervical motion.	Details sparse.
McAfee 2010 RCT No mention of sponsorship or COI.	N/A	N = 251 1-level anterior cervical reconstructions was undertaken to compare the incidence of dysphagia between cervical disk replacement and conventional anterior cervical fusion and instrumentation.	Anterior cervical diskectomy and fusion or ACDF control group (n = 100) vs Porous-coated motion or PCM arthroplasty group (n = 151). Follow-up for 24 months.	Confounding variables for control and the arthroplasty group were not significantly different between groups. The PCT treatment indicated significantly lower incidence of dysphagia at 3 and 12 months postoperatively compared with ACDF controls ($p < 0.05$), and an increase in dysphagia severity at either the 6-week or 3-month follow up visit was reported in 35 (42%) PCM and 29 (64%) ACDF subjects.	"In a prospective randomized clinical study the incidence of postoperative dysphagia and the long-term resolution of the dysphagia was greatly improved in the PCM group compared with the instrumented ACDF control group."	
Plating vs. without plating						
Grob 2001 RCT No mention of sponsorship or COI.	3.5	N = 54 with 1 or 2 segments from degenerative conditions	ACDF with vs. without anterior interlocking cervical spine plate.	Permanent pain in 4 plated vs. 8 non-plated. Intensity of pain decreased pre/post: plated 8.7/3.8 vs. non-plated 8.4/4.4. No differences in pain VAS, medication, sensory deficits, motor weakness; 3 retained pathological weaknesses in 3 non-plated vs. 0 plated. Solid fusions in 27/35 plated vs. 28/37 non-plated. Pseudarthrosis in 1 plated vs. 3 non-plated.	"[T]he overall data do not suggest better results with plating in mono- or bisegmental anterior spine fusions. Indications for additional internal fixation are restricted to special conditions with increased instability, insufficient bone quality or inappropriate graft placing."	Sparse details. Data suggest minimal differences between groups. Somewhat more fusion in the plated group.

Rigid vs. Dynamic Plating						
Pitzen 2009 RCT No sponsorship. One or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to subject of this manuscript.	3.5	N=132 with A fractures, symptomatic degenerative disease in 1-2 levels, or traumatic discoligamentous injuries.	Study group underwent a routine anterior cervical discectomy with tricortical iliac crest autograft fusion including a dynamic plate with screws locked in ap–position (ABC, Aesculap AG & Co. KG; n = 69) vs. Control group, received a rigid plate (CSLP, Synthes, Switzerland) following the insertion of a tricortical iliac crest autograft. (n = 63). Follow up at discharge, 3, 6 and 24 months.	Mean segmental mobility in study group 1.7mm at time of discharge, 1.4 mm after 3 months, 0.8mm after 6 months, and 0.4mm after 2 years. As for control group, measurements were 1.0, 1.8, 1.6, and 0.5mm, respectively ((p = 0.024), after 6 months, and (p> 0.05) at discharge, 3 months, and 2 years). Mean loss of lordosis for study group was 1.3° at discharge, 2.4° after 3 months, 3.4° after 6 months, and 4.3° after 2 years. As for control group, these values were 0.9°, 1.0°, 1.7°, and 0.7°, respectively ((p = 0.017) at here months, (p = 0.032) at 6 months, and (p = 0.003) at 2 year follow up. Mean NDI for patients in study group is 37% before surgery, 24% after 3 months, 21% after 6 months, and21% at 2-year follow-up. As for control group, results are 38%, 26%, 25%, and 21% (p <0.05).	"[D]ynamic cervical plate designs provide less implant complications (no patient) compared with rigid plate designs (4 patients). Speed of fusion was faster in the presence of a dynamic plate. However, loss of segmental lordosis is significantly higher if dynamic plates are used, which did not result in differences regarding clinical outcome between dynamic and constrained plates after 2 years. Thus, dynamic plates should be considered to be the preferred treatment option because of the lower risk for implant failure-related revision surgery."	Methodological details sparse. Dynamic may be more efficacious at 3,6,12 months but no difference at 2 years.
Stulik 2007 No sponsorship. COI, study monitored by employee of Aesculap, Germany. Pitzen consultant to Aesculap, Germany	3.5	N = 132 with degenerative disc disease between ages of 21-80	Dynamic plate with screws locked in ap–position (ABC, Aesculap AG & Co. KG; n = 69) vs. Rigid plate (CSLP, Synthes, Switzerland; n = 63).	Mean segmental mobility in study group was 1.7mm at time of discharge, 1.4mm after 3 months, 0.8 mm after 6 months, and 0.4 mm after 2 years. As for the control group, measurements were 1.0, 1.8, 1.6, and 0.5 mm, respectively ((p = 0.02), after 6 months, and (p = 0.124) at discharge, and (p = 0.452) at 3 months, and 2 years). Study group demonstrated less implant complications compared with the control group (p = 0.0375).	"Dynamic plate designs provided a faster fusion of the cervical spine compared with rigid plate designs after prior spinal surgery. Moreover, the rate of implant complications is lower within the group of patients receiving a dynamic plate. These interim results refer to a follow-up period of 6 months after prior spinal surgery with no statistically significant differences observed after shorter time intervals."	This article and Pitzen 2009 (above) are the same (have same results). Methodological details sparse. Statistical difference between groups at 6 months, favoring the dynamic groups
Surgery vs. nonsurgical						

Peolsson 2013 RCT Sponsored by the Medical Research Council of Southeast Sweden. No mention of COI.	3.5	Same population as Engquist 2013	Same treatments as Engquist 2013	Both groups improved for neck muscle endurance (NME) flexion (p = 0.01), extension (p = 0.006), manual dexterity (p = 0.0001-0.03), and right handgrip strength (p = 0.01). Neither group improved for neck active ROM, left-handgrip strength, and arm elevation (p> 0.13). No significant differences between groups for any outcomes (p = 0.17-0.92).	"Compared with a structured physiotherapy program alone, ACDF followed by physiotherapy did not result in additional improvements in neck active range of motion, neck muscle endurance, or hand-related function in patients with radiculopathy."	Study only looked at physical function outcomes but is the same as Engquist 2013 No difference between groups. Methodological details sparse.
ACDF vs. disc replacement						
Porchet 2004 RCT Sponsored by Medtronic Sofamor Danek. COI, Metcalf is employee of Medtronic Sofamor Danek.	3.0	N = 55 with cervical degenerative disc disease (DDD) with intractable radiculopathy or myelopathy, unresponsive to conservative treatment for 6 weeks. Mean age ACDA 44.3 years, ACDF 43.2 years.	Anterior cervical discectomy and arthroplasty (ACDA) with Prestige II disc (N=27) vs. ACDF with iliac crest autograft (n = 28). Follow-up at 6 weeks and 3, 6, 12, and 24 months postsurgery.	Adverse events: 17 in ACDA vs. 19 in ACDF, (p>0.05). NS between groups for radiologic outcomes, neck pain frequency and intensity, and SF-36. Neck disability index and arm pain frequency and intensity: improvement seen in treatment groups up to 24 months (p<0.05).	"The preliminary results from this limited number of patients indicate that the Prestige II disc is potentially a viable alternative to fusion for primary cervical disc disease; however, further clinical studies with larger sample sizes will be required to show statistical equivalence."	Methodological details sparse.
Post-Operative						
Abbott 2013 RCT No sponsorship or COI.	3.0	N = 33 with cervical root compression with corresponding pain distribution for more than 3 months, a primary diagnosis of cervical spondylosis, disc herniation, or degenerative disc disease, and selected for ACDF.	Postoperative neck movement restriction (n = 16) vs. Rigid cervical collar during day time over a 6-week period (n = 17). Follow up at 6 weeks, 3, 6, 12, and 24 months post-surgery.	Both groups improved in all outcome measures and intermittently showed statistically significant improvements from baseline to 2 years follow up (p < 0.05). Mean (SD) difference from baseline of NDI in cervical collar group vs. non cervical collar group compared to 2 years follow up: −7.94 (2.7) vs. −9.93 (1.1), (p = 0.584). Mean (SD) difference from baseline of neck pain in cervical collar group vs. non cervical collar group compared to two years follow up: −3.19 (0.3) vs. −2.73(0.3); (p=0.093).	"This pilot study suggests that short-term cervical collar use post ACDF with interbody cage may help certain patients cope with initial post-operative pain and disability. Larger data collections are required to investigate health-related quality of life and fusion rates in patients with and without rigid collar use post ACDF surgery."	Pilot study. Small population sample. Small sample size (N=33). High dropout in both groups. Few statistically significant differences.
Other						

Martins 1976 RCT No mention of sponsorship or COI	3.5	N = 51 symptomatic cervical disc disease refractory to conservative management	Anterior cervical discectomy vs. radical discectomy and foraminotomy. Cervical collars for 6 wks.	Bone bridged at 1 year in 7/11 discectomy vs. 12/12 Cloward group, p = 0.04). Alignment better after Cloward than discectomy.	"Anterior cervical discectomy with and without interbody bone graft are equally safe and effective operations for the relief of recalcitrant symptoms of cervical disc disease at one or two levels between C-4 and C-7."	Sparse details. Dropout high at 1 year.
McGuire 1994 RCT No mention of sponsorship or COI.	3.5	N = 46 cervical radiculopathy patients	Vertebral body autograft (n = 6 points) vs. modified Smith-Robinson technique (n = 40 points).	Only 1 patient had resolution of neck pain in experimental group. Outcome good in 3/6 (50%) and poor in 2 vs. excellent to good in 36/40 and poor in 3.	"We do not recommend vertebral body autograft over the modified Smith-Robinson technique for anterior cervical fusion following discectomy."	Sparse details. Very small numbers in experimental group. Suggests iliac crest autograft superior.
Coric 2006 RCT No mention of sponsorship or COI.	3.5	N = 33 single-level cervical DDD with radiculopathy or myelopathy	Bryan cervical disc (n = 17) vs. ACDF (spinal fusion, n = 16)	NDI Baseline/ 12 month scores: Disc (42/9) vs. ACDF (47/24) (interpretation of graphic results). Similar results for Neck pain scores and arm scores also appeared to favor disc replacement. (Statistical testing not noted.)	"The preliminary results of disc replacement according to this study are promising but the authors note that more long term follow-up is needed as this is a relatively new procedure and long term wear of the disc prosthesis has yet to be established."	Sparse details. Suggests disc replacement may be superior to fusion.
Hacker 2005 RCT No mention of sponsorship. No COI.	3.5	N = 46 symptomatic radiculopathy and/or myelopathy C3-C7	Microdiscectomy with Bryan cervical disc vs. ACDF with plating.	12 month results excellent in 17/22 Bryan vs. 15/24 fusion.	"Although extended follow-up data and larger patient populations are needed, the results of this study indicate that arthroplasty is a viable alternative to cervical fusion."	Sparse details. Part of study results reported above (Hacker, Sasso, Heller)
Hacker Spine 2000 RCT No sponsorship. COI, Griffith is employed by Sulzer Spine-Tech. COI category: 17.	3.5	N = 488 radicular symptoms and 1 or 2 adjacent levels C3-C7	ACDF vs. fusion with Bagby and Kuslich cervical fusion cage (BAK/C) vs. hydroxyapatite-coated BAK/C.	Excellent/good results (6/12/24 months): cage groups 71.3/75.7/ 78.4% vs. 83/72.9/80% controls. No differences in 3 groups in improvements in radicular symptoms with 1 level. 2-level cases radicular improvements BAK/C (63.9/71.4/62.5%) vs. HA-BAK/C (72.2/78.1/ 89.5%) vs. ACDF (78.9/78.9/90.0%). Degeneration of another disk in 2.2 vs. 1.2 vs. 1.4%.	"[O]utcomes after a cervical fusion procedure with a threaded cage are the same as those of a conventional uninstrumented bone-only anterior discectomy and fusion with a low risk of complications and rare need for autogenous bone graft harvest."	Details sparse. Some baseline differences. 390 one and 98 2-level procedures, but were not randomized on it. High dropout rate at 2 years. Data suggest does not reduce risk of adjacent disease.
Cho 2005 RCT	3.5	N = 100 degenerative cervical spondylosis C2-C7, all with at	Discectomy and fusion with interbody poly-etheretherketone (PEEK) containing either biphasic	Fusion rates for first 6 months (each month): group A (57, 67, 77, 82, 92, 100%) vs. Group B (81, 86, 95, 95, 100, and 100%). Fusion rate lower first 6 months in Group B. Spinal	"The clinical outcome was satisfactory in both groups. The cage containing triosite lead to shorter hospital stay, a reduction in blood loss, and	Somewhat more 2-level disease in Group B, presumably biases in favor of Group A. Shorter hospital stay in A (4.4±2.4 vs. 7.0±3.8, p =

Sponsored by a grant from CMUH (China Medical University Hospital). No mention of COI.		least 3 months of conservative treatment; nearly all radiculopathy, myelopathy or both	calcium phosphate ceramic (Triosite, Group A) or autogenous iliac bone graft. (Group B). 1-year follow-up.	curve correction, neuroforamen enlargement, neurological recovery did not differ between groups. JOA recovery rate in 86.5% Group A vs. 83.5% Group B, p = 0.22.	shorter operative time for iliac grafting and did not result in donor site complications. Based on our own results, the cage containing triosite is a good substitute in treating cervical spondylotic fusion."	0.001). Data suggest autograft superior to biphasic calcium phosphate ceramic for fusion, but inferior for EBL, operative time and donor site pain. Data suggest slower fusion with calcium phosphate ceramic, but no differences in clinical outcomes.
Hacker J Neurosurg 2000 RCT No mention of sponsorship. No COI.	3.5	N = 54 radiculopathy with/out myelopathy. 1 or 2 adjacent levels C4-C7 treated	ACF with iliac crest autograft vs. BAK/C and HA-BAK/C	SF-36 scores similar. Fusion rates comparable.	"[T]he use of an interbody fusion cage avoided donor site morbidity and placement of autograft achieved a high rate of good or excellent results."	Unclear, but suggests subset of above study.
Nabhan Eur Spine J 2007 RCT No mention of sponsorship or COI.	3.0	N = 25 cervical disc herniation	Disc vs. ACDF (Solis)	VAS arm pain (pre-op/3 weeks/12 weeks/24 weeks): Disc (7.6±1.4/1.5±0.4/1.6±0.3/1.4±0.2) vs. ACDF (7.2±1.7/1.7±0.4/1.7±0.3/1.7±0.3). Neck pain also not significant.	"Cervical spine disc prosthesis preserves cervical spine segmental motion within the first 6 months after surgery. The clinical results are the same when compared to the early results following ACDF."	Total study population reported in Nabhan J Long Term Eff Med Implants 2007. Data suggest disc replacement not superior for pain relief.
Hwang 2004 RCT No mention of sponsorship or COI.	2.5	N = 56 cervical DDD (neck pain, cervical radiculopathy and myelopathy) undergoing 3 or 4 level discectomies	Interbody titanium cage-augmented anterior cervical discectomy and fusion vs. interbody titanium cage-augmented ACD. All rigid collars for 4 to 8 weeks post-op.	VAS pain scores improved in each group, but not different between groups. Spine stability at 1 year, but not different between groups.	"Interbody cage-based fusion with or without plate fixation in the three- and four-level cervical discectomies achieved good stability and neurological outcomes; however, there was a lower complication rate in the patients in whom supplemental plate fixation was not performed."	Sparse details. Unclear if RCT. Appears to be comparative clinical trial, as group sizes differ and some baseline differences. Variable follow-up periods from 13-28 months.
Sasso 2011 RCT Sponsored by corporate/ industry funds (organization not mentioned). COI, one or more of the author(s) has/have	2.5	N = 48 with cervical radiculopathy or myelopathy refractory.	Control group single-level anterior cervical discectomy and fusion with allograft and place (n = 26) vs. Single-level cervical artheroplasty with Bryan Cervical Disc Prosthesis (n = 22).	At 24 moth overall lordosis was not different that from the preoperative, p = 0.12 vs. Bryan group, p = 0.38. No statistical significance in functional spinal unit (p=0.38); disc angle at the treatment level and change at the immediately adjacent level (p>0.45). NDI for fusion patients vs. those where treatment level was C5/6, p = 0.021.	"Global cervical sagittal alignment was statistically not different between groups at all time points."	Lack of study details. Allocation unclear. No blinding, no data or co-intervention control, completions rates. Data suggest similar outcomes in alignment and ROM.

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An 1995 Pseudo-randomization RCT No mention of sponsorship or COI.	2.0	N = 77 ACD with fusion patients	Iliac crest autograft vs. freeze-dried allografts. All in rigid Philadelphia collar for 6 wks.	Rate of non-union 46.2% allograft vs. 26.3% autograft.	"[T]he allograft-demineralized bone matrix construct gives a higher rate of graft collapse and pseudarthrosis when compared with autograft in a prospective series, although the differences were not statistically significant."	Randomization by every other. Compliance with assignment unclear.
Campbell 2008 Possibly non-randomized comparative clinical trial Sponsored by institutional funds (institution not specified). COI, one or more of the author(s) has/have received or will receive benefits for personal or professional use from commercial party related directly or indirectly to subject of this manuscript.	N/A	N = 257 single-level decompressions	ACDF with plating.	No differences in NDI or working status.	"[U]se of a cervical brace does not improve the fusion rate or the clinical outcomes of patients undergoing single-level anterior cervical fusion with plating."	Appears to be non-randomized observation arm from Mummaneni 2007 above. Without randomization, low quality study.

DECOMPRESSIVE SURGERY FOR SPINAL STENOSIS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Cervical Corpectomy with Preserved Posterior Vertebral Wall vs. Conventional Corpectomy						
Lian 2010 RCT No sponsorship or COI.	3.5	N = 105 with myelopathy in physical examination and the spinal cord comparison was seen in MRI at three or four disc levels. Average age was 60.2 years.	Noncontiguous anterior decompression and fusion (NADF group) (n = 55) vs Contiguous corpectomies and fusion (CCF group) (n =50). All wore cervical collar. Follow-up for 24 to 48 months.	VAS mean±SD: pre-op NADF 50.1±13.7 vs. CCF 49.3±13.3, NS; 6 months NADF 8.2±5.9 vs. CCF 13.3+7.1 (p <0.05); final follow-up NADF 9.5±5.8 vs. CCF 14.3±8.1 (p <0.05). Loss of cervical lordosis mean±SD (degrees): 6 months NADF 0.8±0.9 vs. CFF 2.0±1.0 (p <0.001); final follow-up NADF 1.4±1.3 vs. CFF 4.0±1.4, (p <0.001). Loss of height of fusion segments mean±SD (mm): 6 months NADF 0.8±0.5 vs. CFF 1.9±0.7 (p <0.001); final follow-up NADF 1.0±0.6 vs. CFF 3.1±0.9 (p <0.001).	"In conclusions, in the patients with MCSM, without developmental stenosis and continuous or combined ossification of posterior longitudinal ligaments, NADF and CCF showed an identical effect of decompression."	Quasi-randomization (consecutive admissions) lack of method details on blinding. Data suggest no difference in scoring decompression. Significant differences in clinical measures were most likely clinically significant.
Young 1980 RCT No mention of sponsorship or COI.	N/A	N = 29 with mean age of 58.3 years. All participants had a diagnosed malignant tumor of CNS origin.	Group 1 (n = 16) decompressive laminectomy followed by megavoltage radiotherapy (RT) with total dose of 3000 rads given in 10 divided doses over approximately 14 days immediately post-op vs. Group 2 (n = 13) received RT alone. 400 rads/day for 3 days. Then 1800 rads in 7 doses over 14 days. Also received 21mg dexamethasone followed by 4mg every 6 hours until conclusion of RT.	Differences between groups are not statistically different either immediately following treatment or at 4 months. Pain relief – Group 1 and Group 2 had 88% and 92% significant pain before treatment respectively. Following treatment Group 1 had a net improvement of 38% and Group 2 had a net improvement of 46% based off narcotic analgesics use.	"No significant difference was found in the effectiveness of the two treatment methods in regard to pain relief, improved ambulation, or improved sphincter function."	Study lacks sufficient population. A 24% mortality rate occurred in Group 2. Randomization was ineffective. Lack of control for confounding factors.
ACDF vs. Laminoplasty						
Liu 2011 Non-RCT	N/A	N = 52 with plate cage benezech or	Anterior cervical discectomy and fusion or ACDF	Functional results: Japanese Orthopedic Association or JOA score significantly improved in both groups	"Both ACDF with the PCB system and laminoplasty are effective therapies for	

No sponsorship or COI.		PCB implant system or laminoplasty.	group used the plate cage benezech or PCB system operation technique (n = 25) vs Laminoplasty open-door principles decompression usually extended from C3 to C7 (n = 27). Follow-up 25.4 and 24.5 months; specifically, at 3 months, 6 months, 1 year, 2 years, and at latest follow-up assessment.	after surgery at ($p<0.001$), averaging 13.20±2.72 for the ACDF group and 13.67±2.70 for the laminoplasty group, whereas, the JOA score after the operation was similar for the 2 groups, at ($p > 0.05$). Radiographic evaluation: the cervical alignment was 21.92 ± 13.46 degrees before operation and 21.02 ± 13.82 degrees after operation, not significantly changed after the surgery, ($p > 0.05$).	multilevel cervical spondylotic myelopathy."	

SPINAL FUSION

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
ACDF vs. Conservative Treatment						
Peolsson 2013 RCT Sponsored by the Medical Research Council of Southeast Sweden. No mention of COI.	3.5	Same population as Engquist 2013	Same treatments as Engquist 2013	Both groups improved for neck muscle endurance (NME) flexion ($p = 0.01$), extension ($p = 0.006$), manual dexterity ($p = 0.0001$-0.03), and right handgrip strength ($p = 0.01$). Neither group improved for neck active ROM, left-handgrip strength, and arm elevation ($p > 0.13$). No significant differences between groups for any outcomes ($p = 0.17$-0.92).	"Compared with a structured physiotherapy program alone, ACDF followed by physiotherapy did not result in additional improvements in neck active range of motion, neck muscle endurance, or hand-related function in patients with radiculopathy."	Study evaluated physical function outcomes but is the same as Engquist 2013. No difference between groups. Methodological details sparse.
Total Disc Replacement vs. ACDF						

Vaccaro 2013 RCT No mention of sponsorship or COI.	3.5	N = 380 with symptomatic cervical disc disease.	SECURE-C artificial disc group randomized and 89 nonrandomized patients intended to be treated with SECURE-C (n = 151) vs Anterior cervical discectomy and fusion or ACDF (n = 140). Follow-up time at 6 weeks, 3 months, 6 months, 12 months, and 24 months.	Both groups demonstrated an improvement in NDI scores from preoperative scores. At the 24 month follow up, 91.4% of the randomized SECURE-C group demonstrated at least 25 % improvement in NDI compared to 87.1% in ACDF group. 81.2% of SECURE-C group demonstrated VAS neck pain improvement at 24 months compared to 72.2% of ACDF.	"The current prospective, randomized clinical trial reveals that the selectively constrained SECURE-C Cervical Artificial Disc is as safe and effective as the standard of care, an ACDF, and at 24 months is statistically superior in terms of overall success."	Details sparse.
Riina 2008 RCT Sponsored by Medtronic Sofamor Danek. No COI.	3.0	N= 19 with C3–C4 to C6–C7 disc involvement at only a single level and not improvement after 6 weeks of nonoperative treatment or progressive signs of spine or nerve root compression, and NDI score of 30 of greater.	ACDF (control) group received Atlantis anterior plate, manufactured by Medtronic Sofamor Danek, which is a titanium alloy implant that is fixed to vertebral bodies with either fixed- or variable-angle cancellous screws (n = 9) vs. Artificial cervical disc (investigational) group received the Prestige ST cervical disc prosthesis, manufactured by Medtronic Sofamor Danek, which is a dynamic stainless steel device that is inserted into intervertebral disc space (n = 10). Follow up at 6, 12 and 24 months.	Before surgery, mean (SD) neck pain score higher for investigational group compared to control group: 74.8 (19.4) vs. 71.6 (26.0). Two years after surgery, mean (SD) neck pain score dropped for both groups investigational vs. control: 17.9 (24.1) vs. 17.4 (22.1). Before surgery, mean (SD) NDI was lower for the investigational group compared to the control group: 65.6 (11.7) vs. 60.2 (11.7). Two years after surgery, mean (SD) NDI dropped for both groups investigational vs. control: 18.9 (16.8) vs. 22.3 (13.5).	"We found that neurologic function and neck pain were better addressed with the artificial cervical disc, but arm pain was better addressed with ACDF. Patients in both groups improved over their initial complaints. The disc performed at least as well as ACDF, according to our single-center results. Both groups were successful, according to the criteria set forth in the study to determine overall success."	Small sample size methodological details sparse

Porchet 2004 RCT Sponsored by Medtronic Sofamor Danek. COI, Metcalf is employee of Medtronic Sofamor Danek.	3.0	N = 55 with cervical degenerative disc disease (DDD) with intractable radiculopathy or myelopathy, unresponsive to conservative treatment for 6 weeks. Mean age ACDA 44.3 years, ACDF 43.2 years.	Anterior cervical discectomy and arthroplasty (ACDA) with Prestige II disc (n = 27) vs. ACDF with iliac crest autograft (n = 28). Follow-up at 6 weeks and 3, 6, 12, and 24 months postsurgery.	Adverse events: 17 in ACDA vs. 19 in ACDF, (p >0.05). NS between groups for radiologic outcomes, neck pain frequency and intensity, and SF-36. Neck disability index and arm pain frequency and intensity: improvement seen in treatment groups up to 24 months (p<0.05).	"The preliminary results from this limited number of patients indicate that the Prestige II disc is potentially a viable alternative to fusion for primary cervical disc disease; however, further clinical studies with larger sample sizes will be required to show statistical equivalence."	Methodological details sparse.
Delamarter 2013 RCT Sponsored by Synthes grant. No mention of COI.	2.5	N = 209 with single-level cervical disc disease causing debilitating radiculopathy from a single vertebral segment between C3 and C7, and unresponsive to non-operative treatment for at least 6 weeks, plus neck disability index score of 15/50 (30%) or more.	Total disc replacement or TDR ProDisc-C ball-and-socket principle and is composed of 3 components, 3 endplates, caudal endplate (n = 103) vs Anterior cervical discectomy and fusion or ACDF, allograft bone spacers were used, local bone also packed around or within allograft, with no other bone substitution, plus fixed-angle place was placed over the graft and secured with 4 screws (n = 106). Follow-up for 5 years.	Five-year follow-up rates were 72.7% or 72/99 for the ProDisc-C group and 63.5% or 61/96 for the ACDF group. ProDisc-C had a statistically significantly higher probability of no secondary surgery at the index/ adjacent levels than patients who underwent ACDF or 97.1% and 85.5%, (p = 0.0079) respectively.	"Five-year follow-up of a Prospective randomized clinical trial revealed 5-fold difference in reoperation rates when comparing patients who underwent ACDF (14.5%) with patients who underwent TDR (2.9%)."	At five years post procedure, the reoperation rates significantly (5 times lower) lower in TDR vs. ACDF patients (2.9% vs. 14.5%). Suggest use of TDR slowing adjacent disk disease post procedure vs. ACDF. High dropout rate at 5 years follow-up.
McAfee 2010 RCT No mention of sponsorship or COI.	NA	N = 251 1-level anterior cervical reconstructions was undertaken to compare the incidence of dysphagia between cervical disk replacement and conventional anterior cervical fusion and instrumentation.	Anterior cervical diskectomy and fusion or ACDF control group (n = 100) vs Porous-coated motion or PCM arthroplasty group (n = 151). Follow-up for 24 months.	Confounding variables for the control and the arthroplasty group were not significantly different between groups. PCT treatment indicated significantly lower incidence of dysphagia at 3 and 12 months postoperatively compared with ACDF controls (p < 0.05), and an increase in dysphagia severity at either the 6-week or 3-month follow up visit was reported in 35 (42%) PCM and 29 (64%) ACDF subjects.	"In a prospective randomized clinical study the incidence of postoperative dysphagia and the long-term resolution of the dysphagia was greatly improved in the PCM group compared with the instrumented ACDF control group."	Secondary analysis.

Qureshi 2013 Cost-effectiveness analysis No sponsorship or COI.	N/A	For treatment of single-level cervical disc disease with associated radiculopathy.	Cervical disc replacement vs. anterior cervical discectomy and fusion.	Effectiveness expressed in units of quality-adjusted life years QALYs that cervical disc replacement resulted in generation of 3.94 QALYs compared to ACDF in 1.92. QALYs gained at a lower cost to society if both strategies survived for 20 years or $3042 / QALY for CDR vs $8760 / QALY for ACDF group.	"Cervical disc replacement has the potential to advance the treatment of symptomatic cervical disc disease unresponsive to appropriate conservative management."	
Upadhyaya 2012 RCT No sponsorship or COI.	N/A	N = 1213 with symptomatic, single-level cervical disc disease, between the C-3 and C-7 levels who presented with intractable radiculopathy or myelopathy or both.	Artificial cervical disc defined as follows; revision or adjustment or modifies original implant; removal or removal of one or more components; supplemental fixation or additional spinal devices; reoperation or any surgical procedure that does not remove, modify or add any component, and discs evaluated include; Prestige ST, Bryan, and ProDisc-C artificial discs (n = 621) vs. Anterior cervical discectomy and fusion or ACDF (n = 592). Follow-up for 12 months.	NDIs in both groups reduced effectively at 1-year follow-up compared with preoperative indices. Neck and arm pain scores at 24-months pain frequency trended toward significance favoring arthroplasty and neck pain intensity, but did not reach significance, with WMD of -3.736 and -1.979. 8 patients or 3.6% in ACDF group and 7 patients or 2.9% in arthroplasty group required surgery for adjacent-level disease at the final 24 months follow-up.	"The currently available 2-year data suggest that cervical arthroplasty is a safe and effective alternative to ACDF to treat patients with single-level cervical disc disease meeting the FDA inclusion and exclusion criteria."	Meta-analysis, cannot be scored.
Anterior Decompression and Fusion vs. Corpectomy						
Lian 2010 RCT No sponsorship or COI.	3.5	N = 105 with myelopathy in physical examination and the spinal cord comparison was seen in MRI at three or four disc levels. Average age was 60.2 years.	Noncontiguous anterior decompression and fusion (NADF group) (n = 55) vs. Contiguous corpectomies and fusion (CCF group) (n = 50). All patients wore cervical collar. Follow-up for 24 to 48 months.	VAS mean±SD: pre-op NADF 50.1±13.7 vs. CCF 49.3±13.3, NS; 6 months NADF 8.2±5.9 vs. CCF 13.3+7.1 ($p<0.05$); final follow-up NADF 9.5±5.8 vs. CCF 14.3±8.1 ($p<0.05$). Loss of cervical lordosis mean±SD (degrees): 6 months NADF 0.8±0.9 vs. CFF 2.0±1.0 ($p <0.001$); final follow-up NADF 1.4±1.3 vs. CFF 4.0±1.4, ($p <0.001$). Loss of height of fusion segments mean±SD (mm): 6 months NADF 0.8±0.5 vs. CFF 1.9±0.7 ($p <0.001$); final follow-up	"In conclusions, in the patients with MCSM, without developmental stenosis and continuous or combined ossification of posterior longitudinal ligaments, NADF and CCF showed an identical effect of decompression."	Quasi-randomization (consecutive admissions) lack of method details on blinding. Data suggest no difference in scoring decompression. Significant differences in clinical measures were most likely clinically significant.

				NADF 1.0±0.6 vs. CFF 3.1±0.9 (p <0.001).		
ACDF with Steroid vs. Without Steroid						
Lee 2011 RCT No sponsorship or COI.	3.0	N = 50 that underwent anterior cervical discectomy and anterior cervical discectomy and fusion or ACDF involving 1 or 2 segments for treatment of radiculopathy or myelopathy.	Steroid group ACDF as general procedure and continued with meticulous hemostasis and saline irrigation of 200mL (n = 25) vs. Control group received operation without steroid, same method as steroid group and only ground collagen fragments applied before wound closure to exclude possible effect of collagen sponge (N = 25). Follow-up 22 months.	Mean age, sex, number of fusion segments, and follow-up period not statistically significant, (p <0.05). Radiographic results and clinical outcomes: prevertebral soft tissue swelling or PSTS not significantly different between groups at C3, 4, 5, 6 and 7; at 4 days significant difference found between groups at C3/C4/C5/C6 and C7 with 44.5 or 73.7%/46.8 or 85.5%/77.5 or 92.7% and 73.9 or 82.9% and 82.8 or 83.9%. No significant difference found pre-operatively between groups in white blood cells or WBC count and C-reactive protein or CRP with 6729.6:7061.5/mm 3 at (p = 0.421 and 0.13):0.19 mg/dL at (p = 0.306), respectively.	"Using the retropharyngeal local steroid, we significantly reduced PSTS and odynophagia following ACDF without additional complication."	Sparse methodological details. Small follow-up time period. Steriod may be beneficial immediately post surgery to decrease PSTS.
ACDF vs. Laminoplasty						
Liu 2011 Non-RCT No sponsorship or COI.	N/A	N = 52 with plate cage benezech or PCB implant system or laminoplasty.	Anterior cervical discectomy and fusion or ACDF group used the plate cage benezech or PCB system operation technique (n = 25) vs Laminoplasty was open-door principles decompression usually extended from C3 to C7 (n = 27). Follow-up 25.4 months and 24.5 months; specifically, at 3 months, 6 months, 1 year, 2 years, and at latest follow-up assessment.	Functional results: Japanese Orthopedic Association or JOA score significantly improved in both groups after surgery at (p <0.001), averaging 13.20±2.72 for ACDF group and 13.67±2.70 for laminoplasty group, whereas JOA score after operation was similar for the 2 groups at (p >0.05). Radiographic evaluation: cervical alignment was 21.92±13.46° before operation and 21.02±13.82° after operation, not significantly changed after surgery, (p >0.05).	"Both ACDF with the PCB system and laminoplasty are effective therapies for multilevel cervical spondylotic myelopathy."	
Comparisons between Autograft, Allograft, Xenograft						

Anderson 2008 RCT Sponsored by Corporate/Industry funds. COI, one or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party directly or indirectly to the subject of the manuscript: *e.g.*, honoraria, gifts, consultancies.	3.5	N = 463 with symptomatic single level cervical degenerative disease disease.	Intervention group or Bryan Disc of 2 titanium shells + 2 titanium retaining wires + polycarbonate polyurethane nucleus + 2 titanium plugs (N = 242) vs. Control group or arthrodesis with structural allograft + titanium alloy plate + screw construct (n = 221).	Cervical neck/arm symptoms/ thoracolumbar pain / headaches / pseudoarthrosis; (5 and 11 vs. 6 and 22, total 16 vs. 28, (p = 0.0003)) / (1 and 9 vs. 2 and 6, total 10 vs. 8) / (1 and 2 vs. 2 and 1, total 3 vs. 3) / (0 and 0 vs. 0 and 6, total 0 vs. 6), at early ≤6 weeks and late>6 weeks. Overall, adverse events occurred in investigational group 33.9% vs. 29.0%.	"This prospective randomized study demonstrated small difference in adverse medical events between the Bryan Cervical Disc arthroplasty and arthrodesis groups."	Lack of study details limits conclusions.
Autograft vs. Cage						
Hermansen 2013 RCT Sponsored by Swedish Research Council, the Medical Research Council of Southeast Sweden (FORSS), and also from the County Council of Östergötland. No mention of COI.	2.5	N = 103 with radiculopathy of degenerative origin with or without neck pain lasting 6 months or more.	Cloward procedure or CP performed using bicortical iliac autograft harvested with aid of Cloward dowel cutter through 5-cm skin incision (n = 46) vs Cervical Intervertebral Fusion Cage Procedure or CIFC with additional of carbon fiber cage to support segment (n = 49). Follow-up at least 10 years; 8 refused surgery, 23 dropped out or lost to follow up.	Outcome, a change from preoperative values to outcome at 10-13 years of follow-up or CRI; in neck related pain / neck-specific disability: 57% / 25% respectively. No significant differences in background variables values of neck-related pain, between those with and without CRI pain or for neck disability index or NDI, except for pre-op values between CRI pain or not, (p = 0.003).	"Preoperative predictive factors of good outcome 10–13 years after ACDF included initial high neck-related pain intensity, nonsmoking status at the time of surgery, and male sex."	Sparse methodology in this clinical article along with a high dropout rate since study designed for long term (10-13 year) follow-up. It appears that good post surgical outcomes are associated with non-smoking, being a male vs. female and reported a high pain intensity at the onset of the study.
Plate vs. No Plate						
Sasso 2011 RCT No mention of sponsorship. COI, one or	2.5	N = 582 at least 21 years old with radiculopathy or myelopathy from single-level cervical disc disease	Arthroplasty with an artificial disc (Bryan Cervical Disc, n = 242) v. fusion with anterior cervical plate stabilization and bone allograft (n =	Overall success at 48 months: arthroplasty (85.1%) v. fusion (72.4%), (p = 0.004). Neck Disability Index success: arthroplasty (90.6%) v. fusion (79.0), (p = 0.003). Arm pain:	"The forty-eight-month follow-up data in the present report showed consistent, sustained significantly superior outcomes for cervical spine arthroplasty compared with cervical spine fusion."	Lack of study details. Allocation unclear, no blinding. No data on co-interventions in control, completion

more of authors received payments or services, either directly or indirectly (i.e., via his or her institution), from a third party in support of an aspect of this work.		secondary to disc herniation or focal osteophytests not responding to at least 6 weeks of conservative treatment,	221). Follow-up 48 months post-surgery.	small significant differences seen between groups at 12 and 48 months in favor of the arthroplasty group. Neck pain: improvement significantly greater in arthroplasty group at all times. SF-36 summary scores: significantly better in arthroplasty group at 48 months, (p = 0.007).		rate. Data suggest similar outcomes in alignment and ROM.
Luszczyk 2013 RCT No sponsorship. No mention of COI.	N/A	N = 573 who underwent a single-level ACDF with allograft and locked plate fixation.	Solid fusion assessed by independent observers using lateral, neutral, and flexion/extension radiographs (n = 142 smokers/ 382 non-smokers) vs Pseudarthrosis was diagnosed when lucency was visualized between graft and vertebral endplate or when motion detected at operative segment (n = 14 smokers/35 non-smokers). Minimum follow-up of 24 months required.	To evaluate impact of smoking on outcome of radiographic fusion; in 156 patients who were smokers, 142 had a solid union, resulting in fusion rate of 91.0%, similarly 91.6% was obtained in the group of patients who did not smoke.	"The authors found no statistically significant difference in fusion status between smokers and nonsmokers who underwent a single-level ACDF with allograft and a locked anterior cervical plate."	Article does not show a difference in fusion status between smokers and non-smokers, although length of time of smoking status and amount and types were not distinguished.
Comparisons between Different Plates						
Pitzen 2009 RCT No sponsorship. COI, one or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to	3.5	N=132 with A fractures, symptomatic degenerative disease in 1-2 levels, or traumatic discoligamentous injuries.	Study group underwent routine anterior cervical discectomy with tricortical iliac crest autograft fusion including a dynamic plate with screws locked in ap–position (ABC, Aesculap AG & Co. KG; n = 69) vs. Control group, received a rigid plate (CSLP, Synthes, Switzerland) following insertion of tricortical iliac crest autograft. (n = 63). Follow-up at discharge, 3, 6 and 24 months.	Mean segmental mobility (Figure 3) in the study group was 1.7mm at discharge, 1.4mm after 3 months, 0.8 mm after 6 months, and 0.4 mm after 2 years. Control group measurements were 1.0, 1.8, 1.6, and 0.5 mm, respectively (p = 0.024), after 6 months, and (p> 0.05) at discharge, 3 months, and 2 years). Mean loss of lordosis for study group was 1.3° at discharge, 2.4° after 3 months, 3.4° after 6 months, and 4.3° after 2 years. As for control group, these values were 0.9°, 1.0°, 1.7°, and 0.7°,	"[D]ynamic cervical plate designs provide less implant complications (no patient) compared with rigid plate designs (4 patients). Speed of fusion was faster in the presence of a dynamic plate. However, loss of segmental lordosis is significantly higher if dynamic plates are used, which did not result in differences regarding clinical outcome between dynamic and constrained plates after 2 years. Thus, dynamic plates should be considered to be the preferred treatment option because of the	Methodological details sparse Dynamic may be more efficacious at 3,6,12 months but no difference at 2 years.

the subject of this manuscript.				respectively (p = 0.017) at 3 months, (p = 0.032) at 6 months, and (p = 0.003) at 2 year follow up. Mean NDI for study group is 37% before surgery, 24% after 3 months, 21% after 6 months, and21%a t 2-year follow-up. As for control group, results are 38%, 26%, 25%, and 21% (p <0.05)	lower risk for implant failure-related revision surgery."	
Stulik 2007 RCT No sponsorship. COI, study monitored by employee of Aesculap, Germany. Pitzen consultant to Aesculap, Germany	3.5	N = 132 with degenerative disc disease between the ages of 21-80	Dynamic plate with screws locked in ap–position (ABC, Aesculap AG & Co. KG; n = 69) vs. Rigid plate (CSLP, Synthes, Switzerland; n = 63).	Mean segmental mobility in study group 1.7mm at discharge, 1.4mm after 3 months, 0.8mm after 6 months, and 0.4mm after 2 years. Control group measurements were 1.0, 1.8, 1.6, and 0.5mm, respectively (p = 0.02), after 6 months, and (p = 0.124) at discharge, and (p = 0.452) at 3 months, and 2 years). Study group demonstrated less implant complications vs. control group (p = 0.0375).	"Dynamic plate designs provided a faster fusion of the cervical spine compared with rigid plate designs after prior spinal surgery. Moreover, the rate of implant complications is lower within the group of patients receiving a dynamic plate. These interim results refer to a follow-up period of 6 months after prior spinal surgery with no statistically significant differences observed after shorter time intervals"	This article and Pitzen 2009 are the same (have same results). Methodological details sparse. Statistical difference between groups at 6 months, favoring the dynamic groups
Comparisons between Different Cages						
Chen 2013 RCT No sponsorship or COI.	3.5	N= 60 with symptoms of cervical myelopathy and/or radiculopathy, disc herniation or degeneration, cervical pathology in 3 consecutive levels, and non-response to conservative treatment for 6 weeks.	Titanium box cage SynCage C (Synthes, Oberdorf, Switzerland (n = 29) vs. PEEK box cage (Depuy Spine, Raynham, MA, USA; n = 31). Follow up range from 86 to 116 months (mean: 99.7 months).	JOA scores significantly increased from 9.6±1.4 to 12.8±1.8 in titanium group (p <0.05), from 9.8±1.4 to 14.2±1.8 in PEEK group (p <0.05), respectively. Corresponding NDI scores significantly decreased from 36.2±3.7 to 21.6±2.6 in titanium group (p <0.05) from 35.4±3.6 to 15.2±2.3 in PEEK group (p <0.05), respectively.	"[I]n addition, without anterior cervical plate augmentation, stand-alone PEEK cages provided good maintenance of intervertebral height and cervical lordosis, as well as better clinical outcomes compared with titanium cages in the long-term follow-up. These advantages were added in the treatment of multilevel CSM."	PEEK group outperformed Titanium group for disability scores and clinical outcomes.
Kast 2009 RCT No sponsorship or COI.	2.5	N = 52 with planned ACDF for radiculopathy or cervical myelopathy.	Group 1: Solis cage (Stryker Company, Kalamazoo, USA), ring-shaped with 2mm thickness (n = 26) vs. Group 2: Shell cage (AMT Company, Nonnweiler, Germany), trapezoid-shaped with thickness of 1-4 mm (n = 26). Follow-up at 3 and 6 months.	At 3 months follow-up, the mean segmental height in the Solis group was lower than presurgery, but not in the Shell group. Significantly more kyphosis in the Solis group at last follow-up (p= 0.032). Subsidence occurred statistically significantly more in group1 (42%) than in group2	"In the current study, there was a significant difference in subsidence and segmental kyphosis between both treatment groups. Furthermore, there is a significant correlation between some radiological and clinical results. Although there was no significant difference in short-term clinical results between the two treatment groups, the aim	Methodological details sparse.

				(15%) at last follow-up (p=0.014).	should be to preserve the determined segmental height and lordosis. Therefore, we recommend using cages with a large-enough contact surface area, increased at the anterior lower aspect of the implant."	
ACDF vs. Posterior Fixation for Unilateral Facet Injury						
Kwon 2007 RCT No mention of sponsorship or COI.	3.5	N = 42 unilateral facet fracture, dislocation or fracture/dislocation with subluxation <25% AP diameter C3-T1. Age 17 years and older.	ACDF with iliac crest autograft and cervical spine locking plate (n = 20) vs. posterior fixation with synthes and/or interspinous and/or oblique wiring (n = 22). Follow-up at 6 weeks and 3, 6, and 12 months post-op.	Hospitalization time ACDF 2.75d vs. 3.5 day (p = 0.096). Pain postop days 1/2: ACDF (2.6±0.5/2.1±0.5) vs. Posterior (3.6±0.5/3.0±0.4), (p = 0.15). Fusion at 1 year in 100% ACDF vs. 86% posterior group (NS).	"[B]oth the anterior and posterior fixation approaches appear to be valid treatment options. Although statistical significance was not reached in the primary outcome measure, some secondary outcome measures favored anterior fixation and others favored posterior treatment for unilateral facet injuries."	Relatively small sample size and likely underpowered. No clear preference between 2 approaches in data. Allocation unclear, baseline comparisons sparse without table, lack blinding. Each intervention had multiple types of surgical techniques. Data suggest no significant differences between approaches.
Postoperative						
Abbott 2013 No sponsorship or COI.	3.0	N= 33 with cervical root compression with corresponding pain distribution for more than 3 months, a primary diagnosis of cervical spondylosis, disc herniation, or degenerative disc disease, and selected for ACDF.	Postoperative neck movement restriction (n = 16) vs. Rigid cervical collar during day time over a 6-week period (n = 17). Follow up at 6 weeks, 3, 6, 12, and 24 months post-surgery.	Both groups improved in all outcome measures and intermittently showed statistically significant improvements from baseline to 2 years follow up ($p < 0.05$). Mean (SD) difference from baseline of NDI in cervical collar group vs. non cervical collar group compared to 2 years follow up: −7.94 (2.7) vs. −9.93 (1.1), (p = 0.584). Mean (SD) difference from baseline of neck pain in cervical collar group vs. non cervical collar group compared to two years follow up: −3.19 (0.3) vs. −2.73(0.3); (p=0.093).	"This pilot study suggests that short-term cervical collar use post ACDF with interbody cage may help certain patients cope with initial post-operative pain and disability. Larger data collections are required to investigate health-related quality of life and fusion rates in patients with and without rigid collar use post ACDF surgery."	Pilot study. Small population sample. Small sample size (N=33) High dropout in both groups Few statistically significant differences.

DISC REPLACEMENT

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Disc Replacement vs. Fusion						
Peng-Fei 2008 RCT No mention of sponsorship or COI.	3.5	N = 24 with intervertebral disk hernia of C5-6. Average age 42 years.	Artificial cervical disc replacement (n = 17) vs. Interbody fusion (n = 7). Average follow-up time 17 months.	Groups compared with t-test, (p> 0.05). No significant statistical difference between groups.	"In the follow-up of 14 months, the artificial cervical intervertebral disc replacement did not show any statistical advantage compared with interbody fusion with bone graft."	Lack of study details. Randomization, allocation not explained. No blinding. No baseline comparison presented, Data suggest no differences between clinical measures of fusion or prosthesis.
Anderson 2008 RCT Sponsored by corporate Industry funds received in support of this work. COI, one or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party directly or indirectly to the subject of the manuscript: *e.g.*, honoraria, gifts, consultancies	3.5	N = 463 with symptomatic single level cervical degenerative disease disease.	Intervention group or Bryan Disc of 2 titanium shells + 2 titanium retaining wires + polycarbonate polyurethane nucleus + 2 titanium plugs (n = 242) vs. Control group or arthrodesis with structural allograft + titanium alloy plate + screw construct (n = 221).	Cervical neck/arm symptoms/ thoracolumbar pain/headaches/ pseudoarthrosis; (5 and 11 vs. 6 and 22, total 16 vs. 28, (p=0.0003)) / (1 and 9 vs. 2 and 6, total 10 vs. 8)/(1 and 2 vs. 2 and 1, total 3 vs. 3) / (0 and 0 vs. 0 and 6, total 0 vs. 6), at early ≤6 weeks and late>6 weeks. Overall, adverse events occurred in investigational group 33.9% vs. 29.0%.	"This prospective randomized study demonstrated small difference in adverse medical events between the Bryan Cervical Disc arthroplasty and arthrodesis groups."	Lack of methods details limits conclusions. This may be reposted elsewhere, since this is a secondary analysis.
Peng 2009 RCT	3.5	N = 166 with single-level ProDisc-C arthroplasty. Mean age 42.7 years.	Total disc arthroplasty or TDR (n = 102) vs. Anterior cervical	Clinical trial outcomes for mean disc height at TRD level / flexion-extension ROM/NDI/VAS neck and arm pain: (3.7±0.2mm and 5.5±0.2mm)/(8.4º±0.7º and	"Patient with greater disc collapse benefit more in ROM from a TDR."	While minimal difference in range of motion in patients with disc height less than 4mm no

No mention of sponsorship or COI.			discectomy and fusion or ACDF (n = 64). Only those who received TDR single level analyzed. For 25 months.	9.6º±0.84º, plus overall delata ROM 1.24º±0.9º, (p = 0.03)), at post and pre-op time points/(overall mean improvement 30.5±4.2, (p <0.001))/ (4.3±0.7, (p <0.001) and 3.9±0.7, (p <0.001)). Follow-up with periodic clinical outcomes; no access to clinical outcomes.		functional clinical outcome differences at 2 years. Concerns about need for more procedures after cervical total disc replacement in 7% - 15% of patients.
Phillips 2013 RCT Sponsored by NuVasive, Inc. COI, relevant financial activities outside the submitted work.	3.5	N = 416 with single-level radiculopathy and/or myelopathy. Age range 18-65 years.	Porous Coated Motion (PCM) cervical disc group (n = 224) vs. Anterior cervical discectomy and fusion (ACDF) (n = 192). Follow-up at 1.5, 3, 6, 12, and 24 months.	In both groups, mean Neck Disability Index (NDI) improved significantly from baseline at all time points (p <0.001). Mean NDI score at 24 months was significantly lower in PCM group (21.8) compared to ACDF group (25.5) (p = 0.029). Overall success was achieved in 75.1% of PCM and 64.9% in ACDF group.	"Overall, it was found that cervical disc arthroplasty with the PCM Cervical Disc is safe and effective for the treatment of symptomatic single-level cervical spondylosis. Compared with instrumented anterior cervical fusion, equivalent or better clinical outcomes were achieved while preserving cervical motion.	Details sparse.
Vaccaro 2013 RCT No mention of sponsorship or COI.	3.5	N = 380 with symptomatic cervical disc disease. Age range 18-60 years.	SECURE-C artificial disc group randomized and 89 non-randomized patients intended to be treated with SECURE-C) (n = 151) vs. Anterior cervical discectomy and fusion (ACDF) (n = 140). Follow-up immediate post-op and 6 weeks, and 3, 6, 12, and 24 months.	Both groups demonstrated an improvement in NDI scores from preoperative scores. At the 24 month follow up, 91.4% of the randomized SECURE-C group demonstrated at least 25 % improvement in NDI compared to 87.1% in the ACDF group. 81.2% of the SECURE-C group demonstrated VAS neck pain improvement at 24 months compared to 72.2% of ACDF.	"The current prospective, randomized clinical trial reveals that the selectively constrained SECURE-C Cervical Artificial Disc is as safe and effective as the standard of care, an ACDF, and at 24 months is statistically superior in terms of overall success."	Details sparse.
Porchet 2004 RCT Sponsored by Medtronic Sofamor Danek. COI, Metcalf is employee of	3.0	N = 55 with cervical degenerative disc disease (DDD) with intractable radiculopathy or myelopathy, unresponsive to conservative treatment for 6	Anterior cervical discectomy and arthroplasty (ACDA) with Prestige II disc (n = 27) vs. ACDF with iliac crest autograft (n = 28).	Adverse events: 17 in ACDA vs. 19 in ACDF, (p>0.05). NS between groups for radiologic outcomes, neck pain frequency and intensity, and SF-36. Neck disability index and arm pain frequency and intensity: improvement seen in treatment groups up to 24 months (p<0.05).	"The preliminary results from this limited number of patients indicate that the Prestige II disc is potentially a viable alternative to fusion for primary cervical disc disease; however, further clinical studies with larger sample sizes will be required to show statistical equivalence."	Methodological details sparse.

Medtronic Sofamor Danek.		weeks. Mean age ACDA 44.3 years, ACDF 43.2 years.	Follow-up at 6 weeks and 3, 6, 12, 24 months postsurgery.			
Park 2011 RCT No sponsorship. COI, one or more of the author(s) has/have received or will receive benefits for personal or professional use from commercial party related directly or indirectly to the subject of this manuscript: *e.g.*, royalties, stocks, stock options, decision-making position.	2.5	N = 454 with cervical radiculopathy or myelopathy, at 23 sites. Mean age TDR45.9±9.1, fusion 44.0±8.5 years.	Single-level total disc replacement or TDR (n = 272) vs. Anterior cervical discectomy and fusion or ACDF (n = 182). Evaluated outcomes before surgery, 3,6 and 12 months.	Mean flexation/ extension rotation; (8.0º± 4.5º, 4.7º±3.0º, & 6.2º±4.0º, before surgery, at 6 weeks, and 12 months respectively vs. (p <0.001) at all postoperative time points, to a rotation of 1.0º±1.1º, at 12 months). At 12 months, superior adjacent-level rotation for both groups, (p <0.001), disc angle and disc height for both groups (p <0.00).	"Computerized analysis of in vivo kinematics of the PCM TDR demonstrates its ability to increase and maintain lordotic alignment, disc height, and functional spinal motion at the operated level and 1 level above and below."	Lack of study details limits conclusions.
Delamarter 2013 Prospective RCT Sponsored by Synthes grant. No mention of COI.	2.5	N = 209 with single-level cervical disc disease causing debilitating radiculopathy from single vertebral segment between C3 and C7, and unresponsive to non-operative treatment for at least 6 weeks, plus neck disability index score of 15/50 (30%) or more.	Total disc replacement or TDR ProDisc-C ball-and-socket principle and composed of 3 components, 3 endplates, caudal endplate (n = 103) vs Anterior cervical discectomy and fusion or ACDF, allograft bone spacers used, local bone also packed around or within allograft, with no other bone	Five-year follow-up rates were 72.7% or 72/99 for ProDisc-C group and 63.5% or 61/96 for the ACDF group. ProDisc-C had Statistically significantly higher probability of no secondary surgery at index/adjacent levels than patients who underwent ACDF or 97.1% and 85.5%, (p = 0.0079) respectively.	"Five-year follow-up of a prospective randomized clinical trial revealed 5-fold difference in reoperation rates when comparing patients who underwent ACDF (14.5%) with patients who underwent TDR (2.9%)."	At five years post procedure, the reoperation rates significantly (5 times lower) lower in TDR vs. ACDF patints (2.9% vs. 14.5%). Suggest use of TDR slowing adjacent disk disease post procedure vs. ACDF. High dropate rate at 5 years follow-up.

			substitution, plus fixed-angle place was placed over graft and secured with 4 screws (n = 106). Follow-up for 5 years.			
Zigler 2013 Prospective RCT Sponsored by Synthes. COI, relevant fi nancial activities outside the submitted work: consultancy, patents, royalties, board membership, expert testimony, stock/stock options, support for travel.	2.0	N = 209 with symptomatic cervical disc disease with radiculopathy from 1 vertebral level between C3-C7. Mean age ProDisc-C 42.1±8.4 years, ACDF 43.5±7.1.	ProDisc-C disc replacement group (n = 103) vs. Anterior cervical discectomy and fusion (ACDF) (n = 106). Follow-up at 6 weeks, and 3, 6, 12, and 18 months, and annually up for 5 years post surgery.	Both groups showed statistically significant improvement in NDI scores from baseline (p <0.0001). No significant difference between groups. At 5 year follow up ProDisc-C group showed a significantly larger percentage of improvement of VAS neck pain intensity and frequency compared to the ACDF group (p = 0.0122 and p = 0.0263 respectively).	"Five-year results show that TDR with ProDisc-C is a safe and effective treatment of single-level symptomatic cervical disc disease. Clinical outcomes were comparable with ACDF."	Methodological details sparse. Very little description of methods used.
Anakwenze 2009 RCT Sponsored by corporate/industr y funds were received in support of this work. COI, one or more of the author(s)has/hav e received or will be received benefits for personal or professional use from a	NA	N = 180 with 1-level disease treated surgically at C3-4, C4-5, C5-6, and C6-7. Age range 18-60 years.	TDR-C or total disc replacement (n = 89) vs. ACDF or Anterior cervical discectomy and fusion (n = 91). Follow-up for 24 months.	Total level lordosis C2-C6 increased in TDR-C by 3.1º (p = 0.001) vs. ACDF by 3.8º (p <0.001). Loss of lordosis was greater in TDR-C vs. ACDF,0.39º (p = 0.05).	"In both TDR-C and ACDF, lordosis increased at the device-level, cranial adjacent level, and in total cervical lordosis, while lordosis decreased at the caudal adjacent level."	Secondary analysis of ProDisc-C trial. Clinical relevance of results are unknown.

commercial party related directly or indirectly to the subject of this manuscript: *e.g.*, honoraria, gifts, consultancies.						
Burkus 2010 RCT Sponsored by Medtronic Spinal and Biologics. COI, all the authors are consultants and clinical investigators for Medtronic Spinal and Biologics. Dr. Traynelis reports he is also a consultant for United Healthcare. In addition, Drs. Traynelis, Burkus, and Haid report holding Medtronic patents. Dr. Mummaneni reports receiving grant support and Dr. Traynelis financial support for a fellowship program from Medtronic Spinal and Biologics. Dr. Mummaneni is	NA	N = 541 with symptomatic degenerative cervical disc disease. Age range 22-73 years.	Investigational group received cervical disc prosthesis, Prestige disc (N = 272) vs. Control group underwent interbody fusion using allograft with plate fixation (n = 261). Follow-up for 5 years.	NDI / Neck Pain / Arm Pain / SF-36; (36.3 and 38.4 vs. 31.3 and 34.1) / (53.8 and 56 vs. 49.2 and 52.4) / (47.1 and 52.5 vs. 45.0 and 47.7) / (13.6 and 14.7 vs. 11.1 and 12.9) scores improvement at 36, 60 months. Neurological Success / Radiographical Outcomes subsidence rates; (91.6%, 92.8%, 95.0% vs. 83.6%, 83.2%, 88.9%) / (2.6% (of 190 patients), 2.8% (of141 patients), 2.8 (of 71 patients) vs. 4.9% (164), 0.9% (116), 1.4% (71) at 24, 36, 60 months. No difference found for implant removal and adjacent-level surgery between the groups.	"Cervical disc arthroplasty has the potential for preserving motion at the operated level while providing biomechanical stability and global neck mobility and may result in a reduction in adjacent segment degeneration."	Secondary analysis. Data presented included only 50% of original sample.

also a consultant for and receives other financial support from DePuy Spine.						
Jawahar 2010 RCT No mention of sponsorship. COI, PDN (royalties, BioMet, Osprey Biomedical, LDR Spine; stock ownership, including options and warrants, Amedica, K2M, Paradigm Spine, Spineology; speaking and teaching arrangements, K2M, NuVasive; scientific advisory board, K2M, SpineMark, Spinal Motion, Vertebral Technologies).	NA	N = 93 with established symptomatic one or two-level cervical disc disease who failed to responded to conservative treatment. Age information not reported.	TDA or total disc arthroplasty (n = 59) vs. ACDF or Anterior cervical discectomy and fusion (N=34). Mean follow-up 36.4 months.	VAS and NDI/VAS; (p = 0.693), similar for both groups)/(61.6±4.1 vs. 61.7±3.5).	"Total disc arthroplasty demonstrates equivalence of safety and efficacy when compared with anterior cervical fusion in the management of symptomatic DDD of the cervical spine."	Data presented is analysis from 3 RCTs for 3 separate types of artificial disc replacements vs. pooled fusion results. Methods for each trial not described, limiting ability to make conclusions.
Coric 2010 RCT No mention of sponsorship. COI, Dr. Coric is a consultant for Depuy Spine and Spinal Motion.	NA	N = 98 with 1-and-2 level cervical disc disease producing radiculopathy or/and myelopathy. Age range 18-70 years.	Cervical arthroplasty including Bryan, Kineflex/C and Discover cervical disc (N = 57) vs. ACDF or Anterior cervical discectomy and fusion with plate or artificial disc	NDI scores improvement / NPI/VAS / Angular Motion; (94%, 89%, and 91% vs. 81%, 87, and 85%) / (27.8, 26.9, and 26.7 vs. 31.9, 29.8, and 31.6), at 6, 12, and 24 months / (combined arthroplasty group 0.91 vs. 7.8 reduction in ACDF group). All groups showed significant improvement from pre-op to minimum 2-year follow-up, (p <0.0001).	"Patients treated with the artificial discs showed significantly better clinical results, maintained motion at the treated level, and trended toward less adjacent-level disease."	Data is pooled analysis of 3 separate trials from one investigational site that is included in large trials for the Bryan Disc, Kineflex/C disco, and the discover disc.

			placement (N = 41). Follow-up for 2-6 years.			
Garrido 2010 RCT No mention of sponsorship or COI.	NA	N = 47 with single level cervical spine disease (C3-7) manifesting as radiculopathy or myelopathy and failed nonoperative treatment for at least 6 weeks. Mean age Bryan cervical disc 40.0 years. Mean age fusion 43.3 years.	Cervical arthroplasty group with Bryan disc arm-milling jig 2 concave surfaces that accept titanium alloy metal, long term fixation (N = 21) vs. Arthrodesis high-speed burr appropriately sized Cornerstone SR fibural allograft ACDF group or Anterior cervical discectomy and fusion (N=26). Evaluated outcomes at preoperatively, 6, 12 weeks + 6, 12, 24, 36, 48 months.	Preoperatively Neck Disability Index / Neck Pain Scores / Arm Pain Score / SF-36 PCS & MCS; (51.1 vs. 51.5 ACDF group) / (76.2 vs. 80.6, at 6 weeks 32.3 vs. 39.2) / (78.8 vs. 77.1, at 6 weeks 16.3 vs. 22.8) /(33.1 vs. 31.4 and 43.2 vs. 46.3, at 6 weeks 26% Bryan vs. 33% ACDF & 52.4 vs. 47.2). Postoperatively NDI at 6 weeks / 48 months; (22.2 vs. 26.4 in ACDF group). At 4 years, 24% improvement in SF-36 MCS in Bryan group vs. 13% in ACDF group.	"At 48 months, cervical arthroplasty with the Bryan cervical disc prosthesis continues to compare favorably to ACDF at our institution."	Single site report of a multicentre trial.
Park 2010 RCT Sponsored by Corporate/Industry and Foundation funds were received in support of this work. COI, one or more of the author(s) has/have received or will receive benefits for personal or professional use	NA	N = 164 with single-level ProDisc-C arthroplasty were evaluated radiographically using Medical Metrics. Age information not reported.	CDR or cervical disc replacement at C6/7 (N = 44) vs. CDR at C5/6 (N = 96) vs. CDR at C4/5 (N = 18) vs. CDR at C3/4 (N = 6). For 24 months.	At 24 months delta sagittal and lateral ROM; C4/5 lost sagittal ROM (-2.5º) compared with the other levels C3/4 (0.9º), C4/5 (1.8º), C5/6 (1.6º), and no difference in delta lateral ROM between segments C3/4, C4/5, C5/6, and C6/7.	"CDR is becoming more feasible and generally accepted alternative to ACDF for degenerative cervical disc disease."	Post hoc analysis of single level disc replacement with Pro-Disc C

from commercial party related directly or indirectly to the subject of this manuscript: *e.g.*, honoraria, gifts, consultancies, royalties, stocks, stock options, decision making position.						
Coric 2013 RCT No mention of sponsorship. COI, Dr. Coric was a Principal Investigator for the Bryan Disc and Kineflex|C IDE studies, is a consultant for Medtronic, and is a consultant for and stock owner of Spinal Motion.	N/A	N = 74 with 1-level symptomatic cervical disc disease with medically refractory radiculopathy.	Cervical total disc replacement (TDR) (N = 41) vs. Anterior cervical discectomy and fusion (ACDF) (N = 33).	A total of 63 patients (86.3) with a minimum of 4 years of follow-up data were available for analysis. In both TDR and ACDF groups, mean NDI scores improved significantly 6 weeks after surgery and continued to improve through 48 weeks. (p <0.001). TDR had a higher range of motion (8.6°) than the preoperative mean (8.2°). Conversely, the postoperative mean for range of motion in ACDF (.2°) was significantly reduced compared to the preoperative mean (7.6°).	"Both cervical TDR and ACDF groups showed excellent clinical outcomes that were maintained over an average of 6 years of long-term follow-up. Both cervical TDR and ACDF are viable options for the treatment of single-level cervical radiculopathy."	Pooled results from 2 studies.
Upadhyaya 2012 RCT No sponsorship or COI.	NA	N = 1213 with symptomatic, single-level cervical disc disease, between the C-3 and C-7 levels who presented with intractable radiculopathy or myelopathy or both.	Artificial cervical disc defined as follows; revision or adjustment or modifies original implant; removal or removal of 1 or more components; supplemental fixation or additional spinal devices; reoperation or	In this 3 randomized trials; NDIs in both groups reduced effectively at the 1-year follow-up compared with preoperative indices. Neck and arm pain scores at the 24-months pain frequency trended toward significance favoring arthroplasty and neck pain intensity, but did not reach significance, with WMD of -3.736 and -1.979. 8 patients or 3.6% in the ACDF group and 7 patients or 2.9% in the arthroplasty group required surgery for adjacent-level disease at the final 24 months follow-up.	"The currently available 2-year data suggest that cervical arthroplasty is a safe and effective alternative to ACDF to treat patients with single-level cervical disc disease meeting the FDA inclusion and exclusion criteria."	

			any surgical procedure that does not remove, modify, or add any component, and discs evaluated include; Prestige ST, Bryan, and ProDisc-C artificial discs (N = 621) vs Anterior cervical discectomy and fusion or ACDF (N = 592). Follow-up for 12 months.			
Phase I vs. Phase II						
Goffin 2010 RCT No mention of sponsorship or COI.	N/A	N = 98 with surgical treatment at any 1 level or 2 adjacent levels of the cervical spine from C3-4 to C6-7 adjacent levels of the cervical spine from C3-4-C6-7 for disc herniation w/radiculopathy &/or myelopathy, spodilotic radiculopathy. Age at least 21 years old.	Phase I; 1-Level surgery (N = 44) and 2-Level (N = 10) vs. Phase II; 1-Level Implantation (N = 48). Follow-up for 10 years.	NDI / Neck and arm pain / Radiographic outcome / Adverse Events and Second Surgery; (19.8 vs. 20.3) / (2.2 vs. 2.0), at 4, 6 years / (mean angular values for combined 1 and 2 level patients were constant and similar over time) /(success rate was 93.9% at >7 years following surgery and 60% of adverse events occurred 2 years after the study surgery including 15% of these were continuous of earlier reports.	"The favorable clinical and angular motion outcomes of the Bryan Cervical Disc Prosthesis that were previously observed at 1- and 2-years follow-up after cervical disc replacement appear to continue at 4- and 6-year's follow-up."	A follow up study for complications of original article stating that the original post operation complications from 1 and 2 years. Post operations present at 4-6 years as well.

KYPHOPLASTY

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Chen 2011 Randomized Prospective Study	2.0	N = 46 with osteopathic vertebral compression fractures	Unilateral Group (N = 24) vs. Bilateral Group (N = 25)	Unilateral Group VAS score decreased from 7.8+2.1 to 2.7+1.9 ($p<0.05$). Bilateral Group VAS score decreased from 7.9+1.9 to 2.3+2.2 ($p<0.05$).	"Both unilateral and bilateral kyphoplasty results in significant pain relief."	Lack of study details. No comparison of kyphoplasty with other treatments or sham limits conclusions of efficacy.

WORK REHABILITATION PROGRAMS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Bültmann 2009 RCT Sponsored by grants from the Danish National Labor Market Authority, Vejle County, and the Danish Chiropractic Research Fund. COI, Kilsgaard now director of KIA*pro* (work rehab program).	3.0	N = 119 absent from work for 4-12 weeks with a reimbursement request indicating low back pain or musculoskeletal disorder (MSD) as the main cause of sick leave. Mean age 43.7±11.3 years.	Coordinated and Tailored Work Rehabilitation (CTWR): 2 components – work disability screening and formulation and implementation of a coordinated, tailored and action-oriented work rehabilitation plan developed by an interdisciplinary team using feedback-guided approach beginning after 4-12 weeks of sick leave for ≤ 3 months (N=68) vs. Control: conventional case management (CCM) – provided by the municipality (N=51). Follow-up at 3, 6, and 12 months.	Mean±SD cumulative sickness absence hours: 6-12 months CTWR 190.4±312.1 vs. CCM 411.7±423.1 (p=0.009); 0-6 months CTWR 465.9±319.3 vs. CCM 585.6±322.6 (p=0.034); 0-12 months CTWR 656.6±565.2 vs. CCM 997.3±668.8 (p = 0.006). Mean improvement±SD pain intensity last month: 3 months CTWR -2.91±2.6 vs. CCM -1.27±2.6, mean difference 1.64 (95% CI 0.47, 2.81).	"[T]he findings of this pragmatic randomized trial provide suggestive evidence that CTWR employed by an interdisciplinary team is effective compared to conventional case management in workers absent from work due to MSDs."	A pragmatic economic RCT. Some baseline differences between groups which could impact outcome. CTWR vs. CCM showed potential for less lost productivity due to sick time.

PARTICIPATORY ERGONOMICS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Mahmud 2011 Cluster RCT No mention of sponsorship or COI.	3.5	N = 179 computer workers (3h/day) with incidence of musculoskeletal symptoms of neck/shoulder	Experimental Group: received office ergonomic training, 3 units, and same leaflet as group 2 (N = 43) vs. Control Group: no	Mean Score (SD) for Workstation habits: baseline vs. 2-weeks: intervention: keyboard: 3.9(2.2) vs. 5.4(1.6), (p = 0.005); mouse: 0.8(0.8) vs. 1.2(0.8), (p = 0.042); chair: 3.8(1.4) vs. 5.7(1.3), (p < 0.0001); desk: 1.5(0.6) vs. 1.8(0.4), (p = 0.033); control: desk: 1.4(0.6) vs. 1.7(0.4), (p = 0.025). Percentage (95% CI) for self-	"Consistent reductions were observed for all musculoskeletal disorders at the follow-up time point, although the difference was not statistically significant for the upper back. The improvements in the musculoskeletal disorders did not translate into fewer days lost	Statistically significant results on upper limb symptoms but no difference for low back symptoms.

			training, 3 units; a leaflet of an ergonomic office diagram, tips on how to take a break, reduce workload, stretching exercises. (N = 55). Both groups: received office ergonomic training, 1full day, 2 sessions; first session: NIOSH trainers led lectures on office ergonomics, relationship between ergonomics and development of musculoskeletal disorders (MSD's), ergonomic improvements, and stretching exercises; second session: trainers visited workstations and provided assistance (group 1 only). Follow-up: baseline, 2 weeks, 6-months	reported MSD's: difference between 6 month of intervention vs. control: neck: -42.2 (-60.00 to -24.4), ($p < 0.001$); right shoulder: -26.2 (-45.1 to -7.2), ($p = 0.017$); right upper limb: -19.9 (-39.45 to -0.35), ($p = 0.049$); left upper limb: -29.6 (-46.31 to 12.89), ($p = 0.002$); lower back: -21.9 (-38.8 to -4.9), ($p = 0.031$); right lower limb: -25.8 (-40.33 top -11.27), ($p = 0.002$); left lower limb: -28.1 (-41.99 to -14.21), ($p = 0.001$).	from work or improved psychological well-being."	
Esmaeilzadeh 2014 RCT	3.5	N = 81 computer workers with work related upper extremity musculoskeletal symptoms (WUEMSS).	Ergonomic Intervention Group (IG): 2 90-minute comprehensive ergonomic training,	Mean (SD) for Within and Between groups: Postural abnormality: IC vs. CG: -0.5 (0.5) vs. 0.2(0.9), ($p<0.001$) (decreased in IG). Improper equipment location: -0.4(0.6) vs. 0.2(0.9), ($p = 0.003$) (decreased in IG). Intensity of Symptoms: -0.3(0.5) vs. 0.1(0.4),	"Ergonomic intervention programs may be effective in reducing ergonomic risk factors among computer workers and consequently in the secondary prevention of WUEMSDs."	Methodological details sparse.

Sponsored by Istanbul Faculty of Medicine. No COI.			brochure, workstation evaluation (N = 40) vs. Control Group (CG): one page leaflet (N = 41). Outcome Measures: Upper Extremity Function Scale (UEFS), Health Related Quality of Life/ Short Form-36 (SF-36). Follow-up: baseline, 6-month.	(p<0.001) (decreased in IG). Duration of Symptoms: -0.1(0.4) vs. 0.1(0.5), (p = 0.002) (decreased in IG). Frequency of Symptoms: -0.1(0.4) vs. 0.1(0.7), (p = 0.001) (decrease in IG). Functional status (UEFS): -0.0(0.5) vs. 0.3(1.1), (p = 0.011) (decrease in IG)		
Driessen 2011 Cluster RCT No mention of sponsorship or COI	3.0	N = 3047 with no sick leave period longer than 4 weeks due to low back or neck pain.	Participatory Ergonomics or PE group attended 6 h working group meeting under the guidance of trained ergonomist (n = 1472) vs. Control group, no PE intervention (n = 1575). Both groups watched 3 45 second educational films (twisting of the low back, neck position) showing LBP and neck pain risk factors+ergonomic solutions.	Psychosocial risk factors / Exposure to physical risk factors; (decision latitude & authority or, 0.29 points; 95% CI 0.07-0.52, & 0.16 points; 95% CI 0.04-0.28 improved significantly for the intervention vs. no difference for the control group) / (exposure to risk LBP factor reduced for the intervention or, 0.52, 95% CI 0.27-1.01, (p = 0.05) vs. no difference in the control group).	"The results of this cluster RCT showed that after 6 months, exposure to the psychosocial risk factors decision latitude and decision authority significantly improved among workers in the intervention group."	A European study where demographics only described with no table. A pragmatic study with high dropout rate which could not prove that the (PE) intervention prevented low back pain or neck pain.
Gerr 2005 RCT	3.0	N = 362 with incidence of musculoskeletal symptoms of	Group A, alternative intervention + head tilt angle ≤ 3º + armrest +	33.3 % in the alternative intervention group vs. 31% in the conventional group vs. 30.03% in the comparison group developed incident neck or shoulder symptoms.	"This study provides evidence that two specific workplace postural interventions are unlikely to reduce the risk of upper extremity	Allocation unclear, compliance less than 80%, loss to follow-up high at 6-months. Data suggest no differences

Sponsored by US National Institute for Occupational Safety and Health. No COI.		neck/shoulder and hand/arm.	other (n = 122) vs. B, conventional intervention + eye height level + head rotation less than 15º + other (n = 125) vs. C, no intervention (n= 115).		musculoskeletal symptoms among computer users."	in symptom development, prevalence between the interventions. Prevalence rates of approximately 20% across groups.
Feuerstein 2004 RCT Sponsored by Office Ergonomics Research Committee. No COI.	2.5	N = 70 with upper extremity symptoms; pain aching, burning, tingling in fingers, hands, shoulders, neck in past 12 months, worked on computer 3-4 hours per day.	"Ergo-stress" intervention group, ergonomic modification + job stress management education and training during 2 70-minute meetings (n= 34) vs. "Ergo-only" control group, ergonomic modification only (n= 36).	VAS pain score and DASH severity score / upper extremity function / ergonomic change; (($p < 0.01$, $p < 0.01$, $p = 0.60$, and $p < 0.01$, $p < 0.31$, $p = 0.22$) for VAS and DASH on significance effect for time, between groups, and by time interaction, respectively)/(($p = 0.69$, $p = 0.06$, $p = 0.76$), for group, time, and interaction of group by time, respectively) /(($p < 0.01$, $p < 0.029$, $p = 0.44$), for upper extremity risk indicated, between groups, and group by time interaction, respectively).	"Findings indicate that additional two-session job stress management component did not significantly enhance the short- or long-term improvements brought about by the ergonomic intervention alone."	Lack of details for randomization allocation. No compliance data presented. Author states assessors were blinded, but they did not appear to be blinded to assessments of outcome measures. High loss to follow-up due to nature of employees studied. Data suggest no difference between interventions (2-session stress management). Lack of control limits conclusion on efficacy of ergonomic intervention.
Rempel 2007 RCT Sponsored by a grant from the Centers for Disease Control/ National Institutes for Occupational Safety and Health. No COI.	2.5	N = 277 sewing machine operators, mean age 38.1 (8.5) for control intervention, mean 37.2 (9.2) for flat seat intervention, and mean 36.5 (10.7) for curved seat intervention	Control group; miscellaneous items (foot rest, storage box) (N = 105) vs. Flat seat intervention and miscellaneous items (N = 100) vs. Curved seat intervention and miscellaneous items (N = 72). Follow-up: baseline, 1, 2, 3, and 4 month	“Participants in the curved chair intervention group with baseline pain score ≤ 2 had slightly more pain improvement than those with a baseline pain score >2 (-0.37 (-51,-0.24) and -0.31 (-0.45, -0.16, respectively.”	“These findings demonstrate that an adjustable height task chair with a curved seat pan can reduce neck and shoulder pain severity among sewing machine operators.”	Methodological details sparse.

Bohr 2002 RCT Sponsored by Office Ergonomics Research Committee. No COI.	2.0	N= 102 using computers at least five hours per week day.	Participatory education intervention group involved in active learning sessions including discussions + problem solving exercises to aid in applying ergonomic concept (n = 38) vs. Traditional education intervention group participated in a one-hour education session that consisted of lectures + informational handouts + basic task analysis + recognition of problems + general wellness information (n = 39).	Pain discomfort composite score at baseline and at the 3th follow-up for the upper body; 6.69 and 4.41 vs. 6.87 and 4.86.	"In summary, the present study provided no evidence that participatory methods were more effective than traditional methods for office ergonomics education."	Data suggest no differences in participatory and traditional office ergonomics. Lack of study details limits conclusions.
Veiersted 2008 RCT Sponsored by the Norwegian Fund for Post-Graduate Training in Physiotherapy and the Swedish Council for Work Life and Social Research, the Medical faculty of Lund University and the County	2.0	N = 38 hairdressers between 20 and 45 years of age, working more than 30 hours per week and reporting less than two weeks sick leave due to neck or shoulder pain for the prior 12 months	Intervention I, given only pamphlet of 5 recommendations which showed a few illustrations (N = 18) vs. Intervention II, given pamphlet and visited for longer period of time for a personal follow-up, demonstration and discussion of	"The hairdressing tasks showed significantly more arm elevation and higher angular velocity compared to the auxiliary tasks on all measured items listed. The prevalence of neck complaints in the Intervention II group was reduced from 37% before intervention to 21% after, and the reported shoulder complaints was reduced from 21% before to 11% after the intervention (none statistically significant)."	"In conclusion, hairdressers worked with their arms elevated 60° or more, for approximately 13% of the total working time and 16% of the specific hairdressing tasks. A small intervention on working technique resulted in a reduction from 4.0% to 2.5% of hairdressing time with highly elevated right upper arm (above 90°)."	Block randomized. Methodological details sparse.

Councils of Southern Sweden. No mention of COI.			each recommendation (N = 20) EMG: upper trapezius muscle activity Inclinometers: postures and movements of upper arm			
Lundblad 1999 RCT Sponsored by Swedish Council for Work Life Research and the Work Life Fund. No mention of COI.	2.0	N = 58 female workers with neck and shoulder complaints, mean age 33±9 years	Group-Based Physiotherapy (P-T), knowledge about how to cope with pain, muscle tension, and complaints; learn stabilizing exercises; achieve awareness about body posture; exercises: strength, coordination, endurance, flexibility/smoothness and rhythm; 50 minutes twice a week (N = 15) Vs. Feldenkrais Intervention (F-group), increase body awareness, coordination and control; emphasizes learning based on experience of individual; individual: Functional integration (FI), group: Awareness Through Movement	Percent of period prevalence for complaint of neck: previous seven days: P-T vs. F-group vs. C-group: 26.7 vs. 65.0 vs. 30.4, (p = 0.03) in favor of the F-group; complaint of shoulder: 40.0 vs. 75.0 vs. 39.1, (p = 0.04). Improvements in neck-shoulder index: F-group vs. C-group: 13/20 vs. 7/23, p = 0.023 in favor of F-group. Absolute changes for neck index: F-group vs. C-group: 0.45±1.32 vs. -0.35±1.07, (p = 0.034); neck-shoulder index: 1.25±2.75 vs. -0.43±2.00, (p = 0.025), both in favor of the F-group. Cortical Control: after intervention: F-group vs. C-group: 34.9±4.3 vs. 30.4±5.3, (p <0.05), in favor of F-group.	"The present study showed significant positive changes in complaints after the Feldenkrais intervention but not after the physiotherapy intervention. Possible mechanisms behind the effects in the F-group are discussed."	Methodological details sparse.

			(ATM) ; 50 minutes per week, individually 4 times, groups 12 times (N = 20) vs. Control Regime (C-group), no intervention (N = 23). Follow up: 5 months before intervention, 1 year after intervention; 16 week intervention			
Mekhora 2000 RCT Sponsored by Thai government. No mention of COI.	1.5	N = 80 volunteers with tension neck syndrome (TNS), age range 19 to 55, average age: 29 (SD = 5.8)	Early Intervention (G1): ergonomic intervention for computer workstation (N = 40) vs. Delayed Intervention (G2): unadjusted workstation, intervention: 3 months later (N = 40). Both groups: 2 pre-tests of discomfort rating measure; post-test was administered 8 times for 6 months. Follow-up: 26 week intervention	Mean Visual Analogue Discomfort Scale (VADS) in centimeters: Discomfort pre vs. post: Upper Back: G1: 2.5 vs. 1.0, (p = 0.0202) for pre-test. No significant results for G2.	"[T]herefore, it is recommended that all computer users, with or without symptoms of TNS or other musculoskeletal disorders, should use ergonomic recommendations to structure their workplace to gain the benefits of discomfort reduction."	Details sparse
Voerman 2008 RCT Sponsored by EC within the RTD	1.5	N = 38 elderly (over 45 years) female computer workers, working 16h/week, with persistent	Ergonomic Counseling (EC): 4 week intervention, diary of activities and	Visual Analogue Scale (VAS): After intervention: 4 weeks of intervention vs VAS(?): (p = 0.000); EQ5D-VAS: (p = 0.03); MPI_1: (p = 0.030); 3-month follow-up: VAS baseline: (p = 0.000) Pain Disability Index (PDI):	"Subjects with high levels of initial discomfort and disability and specific psychological patient profiles benefit most from	Methodological details sparse.

action QRLT and AFA Insurance, Sweden. No mention of COI.		complaints of pain in neck/shoulder area for at least 30 days.	discomfort scores, therapist visits, ergonomic workplace investigation (N = 20) vs. Myofeedback training (Mfb/EC): 2channel ambulant feedback system for training of muscular relaxation (N = 18). Psychological factors: Fear Avoidance Beliefs Questionnaire (FABQ), Multidimensional Pain Inventory (MPI), Coping Strategies Questionnaire (CSQ). Follow-up: baseline, 4 weeks, 3-month.	After intervention: 4 weeks of intervention vs PDI(?): (p = 0.000); MPI_1: 0.000; CSQ 'catastrophizing': (p = 0.010); VAS baseline: (p = 0.020); CSQ 'ignoring sensations': (p = 0.050) 3-month follow-up: PDI baseline: (p = 0.000); CSQ 'ignoring sensations': (p = 0.029) **Confused at how to report the results**	interventions. Myofeedback training contributes a specific quality to those who ignore pain sensations."	

BEHAVIORAL INTERVENTIONS

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Andersson 2012 RCT No mention of sponsorship or COI.	3.5	N = 21 with age over 65 years, chronic back and/or neck pain with no radiation to arms or legs, pain duration >6 months.	Waitlist condition (N = 10) vs Treatment consisting of applied relaxation, plus problem solving, assertiveness,	Between group treatment effect size, d = 1.0, with respect to perceived ability to function despite the discomfort of pain. PAIRS (Pain and Chronic pain in older adults 241 Impairment Relationship Scale) / QOLI (The Quality of Life Inventory); treatment credibility was correlated with both	"The study provides some preliminary support for the use of group-based CBT with a focus on applied relaxation for older adults with chronic pain."	Small sample size (N=21) Methodological details sparse.

			communication strategies, sleep management, and relapse prevention or treatment group was based on Cognitive Behavioral Therapy (CBT) protocols 2 hour sessions, with 15 minutes break (N = 11). Follow-up for 6 weekly group sessions.	PAIRS / QOLI outcomes; r = 0.76 / r = - 0.67 at (p = 0.01 / 0.03).		
Dunne 2012 RCT No COI. No mention of sponsorship.	3.5	N = 26 with Whiplash-associated disorders (WAD) and post-traumatic stress disorder (PTSD)	Trauma-focused cognitive-behavioral therapy (TF-CBT) (N = 13) vs. waitlist control (N = 13). Follow-up at 6 months.	Significantly more people could not be classified as having PTSD in treatment group than in placebo group (61.5%, 8/13 vs. 7.7% 1/13, P = 0.004). No differences seen between groups in amount of depression or alcohol use. Greater reductions in treatment group than waitlist group for the NDI percentage score (P = 0.006) and for NRS negative affect ratings (P = 0.01).	"This study provides support for the effectiveness of TF-CBT to target PTSD symptoms within chronic WAD. The finding that treatment of PTSD resulted in improvements in neck disability and quality of life and changes in cold pain thresholds highlights the complex and interrelating mechanisms that underlie both WAD and PTSD."	Two participants dropped out of the treatment group. Lack of details for randomization, allocation, control for cointerventions, no blinding described. Control group not followed. Same duration as intervention.
Bergström 2012 RCT No mention of COI. Sponsored by AFA Insurance.	3.5	N = 194 with chronic neck or back pain.	Cognitive behavioral therapy group (CBT) consisting of scheduled activities for 13-14 hours per week and homework assignments given at each session (N = 44) vs. Behavioral-oriented physical therapy (PT) consisting of an	BM group had less sickness absence at the 10 year follow-up than the CG and the BM group showed a reduction in the average sickness absence per quarter after rehabilitation (P = 0.021, -12.9, CI: -23.9 to -2.0) compared to CG. The BM program was the most favorable for older patients with high sickness absence prior to interventions.	"In terms of long-term follow-up of sickness absence, the multidisciplinary program appears to be most beneficial for DYS and AC patients. In contrast, the CBT and PT interventions failed to benefit any patient group."	There were 34 drop outs. Data suggest no differences in long term absenteeism between interventions. Lack of details for baseline comparisons (no analysis provided), lack of blinding, high drop pit rate limits conclusions.

			individually tailored training program, about 20 hours per week (N = 54) vs. Behavioral medicine rehabilitation (BM) consisting of PT and CBT programs combined (N = 50) vs. control group (CG) consisting of normal routines of health care. Last follow-up at 10 years.			
Jungquist 2010 RCT Sponsored by NINR. No mention of COI.	3.0	N = 28 with chronic non-malignant pain located in the spinal region, neck and back, and insomnia reported as originating after, and/or aggravated by, the pain condition.	CBT-I included 2.5 day seminar, viewed videotaped CBT-I sessions, weekly supervision (60-120 minutes per week) for the duration of the study by experienced therapist (N = 19) vs Allocated intervention included self-monitoring/waiting-list control condition (N = 9).	42% in CBT-I group and 11% in control group achieved normal sleep (remission). There was no difference on the sleep diary measures / pain severity scale of the MPI / PDI; (p = 0.6669 / 0.2645 / 0.0656). No significant differences were not seen on the Back Depression Scale.	"[T]he sleep continuity results of this study provide further evidence that CBT-I can be effectively applied to patients with chronic pain."	1º outcome was insomnia small (N=28).
Dworkin 1994 RCT Sponsored by NIDR Program Project grant.	2.5	N = 185 with temporomandibular disorders (TMD) with signs and symptoms in masticatory and related muscles of the head and neck.	Cognitive-behavioral intervention delivered, 2 hour session spaced 1 week apart (N = 95) vs Usual Treatment or UT	Baseline comparison of the CB and UT groups revealed no significant differences between the groups. Significant time x group interaction for characteristic pain, F = 5.79, (p = 0.017). 86.4% patients in the CB group and 70.1% in the UT group reported improvement in their TMD condition compared to the baseline.	"The present study supports the utility of a brief group CB intervention, placed before conventional clinical treatment for TMD began, to ameliorate the report of TMD pain."	Methodological details sparse.

No mention of COI.			group, anti-inflammatory medications, jaw motion exercise, cold/hot heat packs (N = 90). 3- and 12-month follow-ups.			
Gale 2002 RCT No mention of sponsorship or COI.	2.5	N = 68 with chronic head and neck pain.	Nerve block group used were occipital, supraorbital, paravertebral and spinal accessory blocks (N = 34) vs Cognitive Therapy utilizing Caudill's protocol (N = 34). 7 week follow-up.	At the end of trial, VAS pain scores were similar in both groups. No statistically significant differences between the two treatments.	"The protocol of measuring relief at the end of a treatment week appears to obscure the maximal effects that can be associated with an acute intervention by nerve blocks for pain."	Methodological details sparse High dropout in cognitive arm may invalidate all results dropout ~85% in that arm.
Soderlund 2001 RCT Sponsored by the Swedish Foundation for Health Care Sciences and Allergy Research. No mention of COI.	2.5	N = 33 with chronic neck pain after a whiplash injury.	Comparison group was given oral or written information and were expected to enhance muscular stabilization of neck and shoulder mobility with stretching and coordination of head movements, and exercise to maintain body posture and arm muscle strength (N = 17) vs Experimental group included learning of basic physical and psychological	At 3 months, patient's perceived ability to perform daily activities differed significantly between groups, $x = 10.27$, $df = 3$, ($p < 0.05$) in favor of the experimental group. There was significantly positive effects for the merged experimental and comparison group over time regarding disability, $F = 6.41$ and ($p<0.01$), pain intensity $F = 4.35$ and ($p < 0.05$), head posture $F = 7.77$ and ($p<0.001$), and neck range of motion in flexion/extension lambda = 0.61 and ($p<0.01$).	"In conclusion cognitive behavioural components can be useful in physiotherapy treatment for patients with chronic WAD, but their contributions are not yet fully understood."	Methodological details sparse

			skills, application and generalization of basic skills in everyday activities, plus functional behavioral (N = 16). Follow-up time for 3 months.			
Glossop 1982 RCT No mention of sponsorship or COI.	2.0	N = 29 with neck and back pain.	Category I, teaching of exercise together with booklet, after 2 weeks to fill out check list whether the patients had understood the exercise and instructions, plus memory test and on a five-point scale rating neck and back pain, from "much better" to "much worse" (N = 11) vs Category II, teaching of exercise, but booklet not given, plus the same procedure as described in Category I (N = 16) vs Category III, given booklet and told to read and carry out exercise, plus the same process as described in Category I (N =	There was a positive relationship between outcome and compliance, no statistics provided. Average pain score in each category, neck pain for Categories I, II, and III; 6.0, 4.4, and 5.2, and for the back pain: 5.0, 2.8, and 4.7. Total for both neck/back average pain; 5.6, 3.5 and 4.9.	"The results of the compliance study, although based on upon small numbers, are interesting and important in the light of current practice."	Methodological details sparse

			12). Follow-up at 2 weeks.			
Kamwendo 1991 RCT Sponsored by the Swedish Work Environment Fund and the Orebro Medical center Research Committee. No mention of COI.	2.0	N = 79 females with pain in either neck or shoulder region during the previous year.	Group A, 4-hour traditional neck school conducted by a physiotherapist, twice weekly (N = 25) vs Group B, traditional neck school, plus measures to enhance compliance, plus interview with psychologist with regard to work organization, plus additional 2 hours per individual allowed (N = 28) vs Group C, assessed at pre, post and follow-up periods, but no intervention was offered until after completion of their follow-up assessments (N = 26). Follow-up after 3 months.	No significant changes were found only for group B, less fatigue and pain experienced at the afternoon and when leaving work. Pain pre-post significantly improved at noon / afternoon / and on leaving work in group A; (p = 0.01 / 0.02 / and 0.05) compared to group B; in the afternoon / on leaving work; (p = 0.04 / 0.02). No significant changes in pain for group C. Pre-follow-up pain improvement in group B at noon / afternoon / and on leaving work; (p = 0.04 / 0.04 / and 0.05).	"In summary, despite good compliance, there was little indication that neck school had any effect of clinical importance on muscular discomfort."	Methodological details sparse.
Horneij 2001 RCT Sponsored by the AMF-trygghetsforaakring. No mention of COI.	2.0	N = 282 with reported neck, shoulder and back pain. Female home-care personnel (nursing aides and assistant nurses).	Individually designed physical training programme or IT group adapted 20 minute exercise and created individual goals, plus diary was kept every time training was perceived hard	At baseline, no significant differences for any demographic or outcome variable, SM group was more satisfied than IT group and control group, (p = 0.02 and 0.03), respectively. No significant differences were shown between the groups at the follow-us concerning the neck and shoulder. Perception of neck, shoulder pain during the previous 6 months, and no chance since 12-month follow-up, p - statistics not provided.	"The positive outcome within the intervention groups generally seemed to decrease after 12 months, though compared with baseline, improvements were still seen at the 18-month follow-up."	Methodological details sparse

			(N = 90) vs Work-place stress management or SM group consisted of 12 groups, each group met 7 times over 7 weeks meetings covering theory and practice for 1.5 hours each time (N = 93) vs Control group or Non-Intervention Group was requested to live as usual (N = 99). Follow-up for 12 and 18 months.			
Jensen 1995 RCT Sponsored by The Board for Research in Health and Care in the Northern region of Sweden and Folksam research. No mention of COI.	1.5	N = 66 with chronic neck and shoulder pain without objective neurological signs, age 20-55 years.	Treatment A; improving physical fitness (strength and endurance), health behaviors and develop plans for return to work (N = 37) vs Treatment B; multimodal cognitive-behavioral intervention (MMCBT) administrated by psychologist for 2 hours (N = 29). 6-month after treatment follow-up.	There were no significant differences between the groups in sick-leave at either the six-month or twelve month assessment; F = 0.05, (p = 0.822) and F = 0.28, (p = 0.596), respectively. Total cost per patient in treatment design A was SEK 1,100 and for treatment design B 3,710.	"In conclusion, the results in this study suggest that both versions of the MMCBT model are effective in improving the health of neck/shoulder pain patients (as assessed by the outcome variables), with the psychologist administrated group therapy setting having the significantly best effect in decreasing a helpless coping style."	Methodological details sparse. No difference in treatment groups.
Manca 2007 RCT	N/A	N = 315 with back or neck pain that was considered to be non-systemic in	McKenzie arm using physiotherapist conducted a	On average, patients in both treatment arms showed continued improvement at 6 weeks, 6 and 12 months. Mean costs and incremental mean QALYs	"Results suggest that the additional cost associated with the McKenzie treatment when compared with the Solution Finding Approach may be	Cost analysis of original data

Sponsored by the Arthritis Research Campaign. No COI.		origin for more than 2 weeks, to assess the cost effectiveness analysis.	biomechanical assessment using repeated movements of the spine (N = 161) vs Solution Finding arm Based on cognitive behavioral principles, which included an interview, a brief physical examination, explanation about the condition, reassurance and goal setting (N = 154). At 6 and 12 months follow-up.	gives an ICER of £1220 (-24.4/-0.020). The mean difference in QALYs for the complete case analysis was -0.023 (95% CI -0.066 to 0.019), leading to an ICER or £1061. The incremental mean QALYs over 12 months was larger compared with the base case and complete case analysis at -0.034 (95% CI -0.064 to -0.004), giving an ICER of £718—the likelihood of Solution Finding being cost effective.	worth paying, given the additional benefit the approach seems more likely to provide."	
Lindell 2010 RCT Sponsored by grants from the Stockholm County Social Insurance Agency, Stockholm County Council, Ministry of Health and Social Affairs, Vårdal Foundation, Cardionics, Pharmacia (now part of Pfizer) and Grunenthal Sweden AB. No COI.	N/A	N = 125 males with non-specific spinal pain (NSP), comprising back and/or neck pain, full-time sick-listed 6 weeks-2 years. Up to 59 years of age.	Cognitive-behavioural rehab program at rehab center, plus baseline questionnaire (N = 63) vs Traditional primary care, plus baseline questionnaire (N = 62). Follow-up at 24 months.	Back- and neck-pain domination was seen in 38 or 30.6% and 86 or 69.4% patients, respectively. Stable return-to-work gradually increased and was 47.5% at 24 months, and at full-time was 74.1%.	"In primary-care patients with non-acute NSP, the strong predictors of stable return-to-work were 2 socioeconomic variables, Low total prior sick-listing and Young age, and 1 subjective variable, High self-prediction."	Reassessment of RCT as a prospective cohort?
Manca 2006 RCT	N/A	N = 268 with neck pain of musculoskeletal	Usual physiotherapy group treated	QALYs and EQ-5D questionnaires at baseline and at 12-months; 0.001 or 95 % CI, -0.028 to 0.030 in favor of	"Usual physiotherapy may not be good value for money for the average individual in this trial but could be a	Cost effectiveness analysis of prior published RCT

Sponsored by the Northern and Yorkshire R&D Executive and Trent Region NHS Executive. No mention of COI.		origin lasting at least 12 weeks.	same as usual by physiotherapists according to their individual judgment (N = 129) vs brief intervention based on cognitive-behavioral principles and encouraged to return to daily activities as soon as possible through self-management by application of cognitive-behavioral principles (N = 139). Follow-up for 12 months after randomization.	usual physiotherapy, and after adjusting for baseline difference in EQ-5D score between the trial arms, and NPQ score of 0.686 or 95% CI, -0.255 to 1.665 was in favor of usual physiotherapy. Cost – usual physiotherapy was associated with higher cost compared to brief intervention higher private expenditures.	cost-effective strategy for those who are indifferent toward which treatment they receive."	
May 2008 Secondary analysis RCT No mention of sponsorship or COI.	N/A	N = 161 with back pain and neck pain	McKenzie treatment method with a cognitive behavioral approach known as Solution-Finding Approach (N = unknown) vs Finding Approach or SFA further randomized to receive The Back Book or The Neck Book as appropriate or no booklet (N = unknown). Follow-up for 6 and 12 months.	There were 21 or 20.6% treatment successes according to the liberal definition, and 16 or 15.7% cases according to the strict definition.	"In this study, duration of pain was the strongest predictor of success, although back pain and centralization had some predictive ability."	Secondary analysis of RCT from 2006 (REF#27) not original report.

FEAR AVOIDANCE BELIEF TRAINING

Author/Year Study Type Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Derebery 2009 RCT No sponsorship or COI.	2.5	N = 187 with first-time neck pain; mean age 38.9(11.9) for group 1, 38.1(10.5) for group 2, and 37.9(12.3)	Group 1, intervention group, "The Neck Book" (N = 57) vs. Group 2, educational control group, "Neck Owner's Manual" (N = 64) Vs. Group 3, no educational/reading materials (N = 66). Follow-up baseline, 2 weeks, 3 and 6 months.	Mean ± SD for not reading booklet: 2 weeks: group 1 (educational booklet) vs. group 2 (control booklet): 12.3±7 vs. 9.4±6, (p = 0.006). "The subjects who had completed reading the booklet reported higher NPDS scores compared with the subjects who did not complete the booklet; 45.0 vs. 36.4, (p = 0.039).	"This study demonstrates that the educational booklets studied were not associated with improved outcomes in patients with neck pain receiving workers' compensation. Whether these results would apply to a nonworkers' compensation population requires further study. The loss of many patients to follow-up also makes any other firm conclusions more difficult to determine."	Methodological details sparse.

MULTIDISCIPLINARY REHABILITATION

Author/Year StudyType Conflict of Interest (COI)	Score (0-11)	Sample Size	Comparison Group	Results	Conclusion	Comments
Jensen 1995 RCT Sponsored by the Board for Research in Health and Care and Folksam research. No mention of COI.	1.5	N = 66 with neck and shoulder pain without objective neurological signs; age 20-55 years	Treatment A, improve physical fitness (strength and endurance), health behavior, return to work plans, psychologist acted as a coach for patients (meetings for 1 hour3, 30 minutes for additional meetings), 5 hours total per patient (N = 37) vs. Treatment B, cognitive behavioral intervention guided by psychologist; coping	Mean ± SD for VAS pain intensity: treatment A vs. treatment B: 6 month follow up: 48.5±23.2 vs. 45.2±13.5, (p = 0.05), f = 3.91; disability: 25.6±11.2 vs. 26.2±9.1, (p = 0.50), f = 6.14; anxiety: 25.2±13.8 vs. 15.7±17.0, (p = 0.01), f = 4.89; 8.9±5.5 vs. 8.4±5.3, (p = 0.001), f = 9.59; helplessness: 42.0±6.9 vs. 39.2±5.8, (p = 0.001), f = 15.96. Long term results found a significant difference between the treatments in proportion of improved/deteriorated subjects was found in depression, (p = 0.02).	"It is concluded that in terms of input of clinical psychology, the treatment setting with the 'coaching' technique proved to be the most cost-effective use of the psychologist in the two treatment settings investigated."	Methodological details sparse. No difference in treatment groups.

			techniques, problem solving and goal setting, 3 hours a week, plus 20 minutes, 5 times during follow-up, total time of 16 hours and 40 minutes per patient (N = 29). Follow-up: baseline, post treatment, and 6 months.			

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