Future Research Identification: Comparative Effectiveness of Nonsurgical Treatment for Cervical Disc and Neck Pain

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ABSTRACT

Neck pain is a common, bothersome, and potentially debilitating problem. Approximately 37% of adults worldwide experience neck pain in a given year. Conditions that can cause neck pain include cervical strain, internal disc disruption syndrome, cervical facet-mediated pain, cervical "whiplash" syndrome, and myofascial pain. Conditions that can cause neck pain associated with radiculopathy (neurological symptoms in the upper extremity) include cervical disc disease and spondylotic myelopathy. Management options for acute or chronic neck pain include: surgery; pharmacotherapy; nonpharmacologic, noninvasive management; and injections. At the request of the Patient-Centered Outcomes Research Institute (PCORI), we developed a stakeholder-informed research agenda designed to inform decision making in the classification and treatment of cervical disc and neck pain disorders. We solicited the input of a small group of stakeholders through a teleconference-based group discussion and email communications. This group of stakeholders assisted us in identifying future research gaps and developing recommendations for targeted future funding by PCORI. Our diverse group of relevant stakeholders prioritized comparative effectiveness research exploring: 1) classification of cervical disc and neck pain disorders; 2) the effectiveness and safety of nonsurgical options for neck pain; 3) the effectiveness of assessment instruments for persons with neck pain; and 4) identifying predictors of chronic pain, opioid dependence, or other undesirable outcomes. We then formulated specific research questions and performed database searches to identify recently published and ongoing studies relevant to one or more of the prioritized research areas.

INTRODUCTION

Neck pain is a common, bothersome, and potentially debilitating problem. Most neck pain results from problems affecting the structures of the cervical spine, which include the 7 cervical vertebrae, the pads between them (intervertebral discs), and the other joints between the vertebrae. Neck pain can also result from other nonspinal disorders such as fibromyalgia or injury to the soft tissue organs in the neck, which will not be addressed in this report. There are many different ways of classifying neck pain, but no one system is universally used or accepted. Examples include nonspecific neck pain vs. neck pain from a known (or presumed) etiology; acute vs. chronic neck pain; neck pain with vs. without accompanying neurological symptoms in the shoulder, arm, or hand ("radiculopathy"); and classification by disease or clinical characteristic, such as cervical degenerative disc diseases, cervical facet syndrome, cervical spine sprain or strain injury (including "whiplash"), or arthritis. In this report, we focus primarily on axial neck pain (i.e., pain that is located primarily in the midline of the back of the neck) with or without radiculopathy. Conditions that can cause axial neck pain include cervical strain, internal disc disruption syndrome, cervical facet-mediated pain, cervical "whiplash" syndrome, and myofascial pain.[1] Conditions that can cause radiculopathy include cervical disc disease and spondylotic myelopathy.[1]

The incidence of new neck pain has been estimated to be 146 to 179 per 1000 person-years, and the incidence of diagnosed disc herniation with radiculopathy is 0.055 per 1000 person years.[2] A large systematic review estimated the point prevalence of neck pain among adults worldwide to be 8%, and the one-year prevalence to be 37%.[3] The 12-month prevalence of activity-limiting neck pain for adults is 1.7% (limited ability to work); 2.4% (limited social activities); and 11.5% (limited activities overall).[2] Neck pain prevalence peaks in middle age and

is higher among women than men. Although some studies have demonstrated an association between neck pain prevalence and employment/lower education, most show no association between neck pain and socioeconomic status.[2] Neck pain is associated with significantly decreased quality of life as demonstrated by validated scales, and depressive symptoms are much more common among sufferers of neck pain than the general population.[4] Neck pain negatively affects productivity and functional capacity.[4,5] Although there are substantial impact of neck pain on patient-centered outcomes, common causes for neck pain are unlikely to result in mortality.

Clinical evaluation of neck pain typically consists of a history and physical exam that evaluate "red-flag" symptoms that might necessitate further radiographic evaluation. Red-flag symptoms include trauma, symptoms of spinal cord compromise (pain/weakness/sensory loss in arms/legs, incontinence of bowel/bladder), fever or other signs of infection, history of cancer, severe pain with tenderness palpable over the spine, or prior neck surgery. Radiographic evaluation is indicated with red-flag symptoms, advanced age, or persistent pain. X-rays are relatively insensitive though may show vertebral fractures, evidence of significant spinal misalignment, loss of disc height suggestive of disc herniation, or facet joint arthritis. CT and MRI are more sensitive for disc herniation, spinal cord compression, infection, and malignancy.[6] Of note, the extent to which radiographic findings correlate with clinical neck pain is highly variable; patients with severe cervical spine degeneration may have minimal symptoms, while others with normal radiographic findings may report severe pain.[2,7]

The goals of treatment for neck pain are generally to reduce pain and muscle spasm, to reestablish normal cervical alignment, and to improve functionality. Most cases of neck pain improve within a few weeks with conservative management. Options for addressing neck pain depend greatly on its cause and chronicity. Only a minority of people with neck pain seek

healthcare; seeking care is likely determined by multiple factors, including perceived pain severity, speed of onset, presence of trauma at onset, previous experience, costs, and availability of care.[8] When neck pain causes chronic symptoms, it becomes necessary to consider the full range of management options.

Management options include: surgery; pharmacotherapy; nonpharmacologic, noninvasive management; and injections. It is unclear whether surgical treatments like cervical fusion and cervical arthroplasty improve long-term outcomes for neck pain (with or without radicular symptoms) compared with nonoperative approaches. Preferred pharmacotherapy options include acetaminophen and nonsteroidal anti-inflammatory drugs, but muscle relaxants and narcotics are frequently prescribed. Nonpharmacologic, noninvasive management options include physical therapy, exercise therapy, massage therapy, manual therapy (spinal manipulation), transcutaneous electrical nerve stimulation, acupuncture, electromagnetic therapy, yoga or Tai Chi Qigong, meditation and relaxation, low-level laser therapy, and psychological/behavioral interventions such as cognitive behavioral therapy. Injection options include epidural corticosteroid injections, cervical facet joint injections, radiofrequency neurotomy, cervical medial branch blocks, trigger point injections, and botulinum toxin injections.

There are many areas of uncertainty relating to the diagnosis, classification, prognosis, treatment, and management of cervical disc and neck pain. Uncertainties include: limitations associated with the different approaches to classifying neck pain; the comparative effectiveness and safety of a wide variety of different nonsurgical treatment options; the potential for assessment instruments for neck pain to inform decision making; and prognostic indicators that could potentially decrease the risk of developing chronic pain or other undesirable outcomes. Given the key role of appropriate classification and treatment of cervical disc and neck pain

disorders in enhancing patient-centered outcomes and the need to address remaining areas of uncertainty, the Patient-Centered Outcomes Research Institute (PCORI) tasked the Duke Evidence Synthesis Group (ESG) with identifying potential comparative effectiveness research gaps in this area that would: 1) incorporate the perspectives of relevant stakeholders; and 2) have a high likelihood of impacting practice within the next 3-5 years.

METHODS

Overview of Approach

Our approach to identifying future research gaps and developing recommendations for targeted future funding by PCORI involved appraisal of recent systematic reviews to identify important evidence gaps, transformation of evidence gaps into potential research questions, engagement of a select group of stakeholders to identify additional gaps and help refine the research questions, and scans of recently published and ongoing studies relevant to the list of identified research questions. Note that for this project we did not produce an initial broad list of research questions or not perform a prioritization exercise of the identified gaps but instead worked with the stakeholders to have them identify a select set of research questions for discussion by the PCORI Advisory Panel.

Selection and Engagement of Stakeholders

We engaged a small group of stakeholders (Table 1). We solicited stakeholder input during this project through a teleconference-based group discussion and email communications.

Table 1. Stakeholder organizations and perspectives

Organization	Stakeholder Perspective	Purpose
North American Spine Society	Professional societies/researchers	The North American Spine Society is a global multidisciplinary medical society that utilizes education, research and advocacy to foster the

Organization	Stakeholder Perspective	Purpose
		highest quality, ethical, value- and evidence-based spine care for patients.
National Business Group on Health	Purchaser/Employer	Non-profit organization devoted exclusively to representing large employers' perspective on national health policy issues and providing practical solutions to our members' most important health care problems.
American Physical Therapy Association	Professional societies/researchers	The American Physical Therapy Association (APTA) represents more than 90,000 physical therapists, physical therapist assistants, and students of physical therapy. APTA seeks to improve the health and quality of life of individuals in society by advancing physical therapist practice, education, and research, and by increasing the awareness and understanding of physical therapy's role in the nation's health care system.
International Association for the Study of Pain	Professional societies/researchers	The International Association for the Study of Pain brings together scientists, clinicians, health-care providers, and policymakers to stimulate and support the study of pain and to translate that knowledge into improved pain relief worldwide.

Identification of Evidence Gaps

We identified and appraised recent published systematic reviews, clinical practice guidelines, and future research needs documents (including a topic brief developed for PCORI by the Duke Evidence Synthesis Group in April 2014) to develop an initial list of evidence gaps targeting 3-5 comparative effectiveness research questions. We distributed these questions to our stakeholders and asked them to review, modify, and add to the list. Stakeholders participated in a teleconference discussion of the questions and provided additional feedback via email. Our team reviewed this stakeholder input and produced a revised list of questions reflecting gaps in the evidence. We circulated this revised list to the stakeholder team for review to ensure that our edits reflected their proposed additions.

Horizon Scan of Studies Potentially Relevant to Identified Research Questions

We performed 2 database searches to identify recently published and ongoing studies relevant to the identified research questions. We searched PubMed to identify recent relevant

studies published during the past 2 years and ClinicalTrials.gov for ongoing and recently completed studies. For the search of ClinicalTrials.gov, we used the keywords “neck pain” OR “cervical disc disease” OR “intervertebral disc degeneration” and focused on ongoing Phase 3 or 4 studies. Appendix A provides the exact search strategy used for PubMed.

Members of our team reviewed the identified titles and abstracts. Articles were included if they met all of the following criteria: presented original data or secondary analysis of data from a randomized controlled trial (RCT), prospective or retrospective observational study, or relevant modeling study; included data related to neck pain treatment; and had a stated objective that could be categorized according to our identified list of research gaps.

For the ClinicalTrials.gov search, a member of the ESG team reviewed all study abstracts identified by the search and coded them as potentially relevant to one or more of the identified research gaps. We then abstracted study type (such as observational or RCT), recruitment status, and sample size.

RESULTS

Expansion of Evidence Gaps Through Stakeholder Engagement

We solicited participation of small group of targeted stakeholders who provided input related to neck pain treatment through participation on the teleconference and/or email feedback (Appendix B). These stakeholders represented the perspectives described in Table 1. Central themes from the stakeholders included the following:

- Nonspecific neck pain is not sufficiently useful as a clinical topic because many different etiologies contribute to neck pain. The recommendation was made to specify a more specific diagnosis or clinical characteristics (e.g., neck pain due to

"whiplash" or hyperextension injury, or cervical disk injury/disease, or axial neck pain with directional preference, etc.).

- Proper diagnosis and classification is important, with the recognition that many different classification systems are currently in use.
- Axial neck pain with and without radiculopathy usually represent different clinical entities.
- Treatment options should be a function of specific etiology.
- There is a paucity of comparative effectiveness research that evaluates some of the many therapeutic options in current practice. The suggestion was made that head-to-head RCTs would be useful.
- There was interest in the question of patient preferences for therapeutic options, but in the absence of adequate effectiveness data from RCTs, stakeholders felt that studying patient preferences directly might not be especially helpful.
- There is an interest in CER that includes persons of working age (as opposed to solely Medicare populations) and outcomes that would be of interest to large employers.
- Outcomes of interest include commonly used standardized questionnaires such as the Neck Disability Scale. Functional outcomes are of interest to stakeholders.

Following the stakeholder teleconference and email discussion we finalized our research questions. We did not do a prioritization exercise for this group of questions:

1. Does the presence of centralization vs. noncentralization or directional preference vs. no directional preference predict response to therapy for axial neck pain without radiculopathy?

2. Within specific patient populations of interest, what is the comparative effectiveness and safety of available nonsurgical treatments (prescription oral pharmacotherapy, over-the-counter oral pharmacotherapy, injections, or nonpharmacologic treatments) either alone or in combination for short-term symptomatic improvement of neck pain? Patient populations of interest include: (1) patients with axial neck pain with radiculopathy, and (2) patients with axial next pain without radiculopathy.
3. What is the comparative effectiveness of existing assessment instruments for persons with neck pain with or without radiculopathy for the purpose of prognosis or assessing the effectiveness of therapeutic interventions?
4. Are there patient characteristics, biopsychosocial and economic factors, physical examination and imaging findings that predict which patients with new onset axial neck pain are at risk for developing chronic pain, opioid dependence, or other undesirable outcomes?

Horizon Scan of Studies Potentially Relevant to Identified Research Questions

Our PubMed search identified 1,365 articles. Of these, 211 met our inclusion criteria and included 50 systematic reviews, 87 RCTs, 32 cohort studies, 0 case–control studies, and 14 other studies. Sample sizes ranged from 3 to 23,794. Thirty five studies either were placebo-controlled or used standard of care as the comparison, 101 studies were active comparator studies, and 13 studies had no comparator. Two studies, one of which was a systematic review, were applicable to the research question about centralization or directional preference as predictors of response to treatment; 152 were applicable to the comparative effectiveness of nonsurgical treatment options question; 4 were applicable to question about the effectiveness of existing assessment instruments for the purpose of prognosis or assessing the effectiveness of interventions; and 28

were applicable to question about predictors for developing chronic pain, opioid dependence, or other undesirable outcomes. Our search of ClinicalTrials.gov yielded 87 studies; of these, we identified 4 protocols as potentially relevant to the second research question. Sample sizes ranged from 52 to 160 patients.

The Tables in Appendix C detail key characteristics of the included PubMed and ClinicalTrials.gov articles separately for each of the identified future research needs.

DISCUSSION

Neck pain is a prevalent condition that is responsible for a great deal of lost productivity, suffering, and health care resource utilization in the United States. Although there are a variety of ways of classifying cervical disk and neck pain disorders and there are many different treatment options, ongoing uncertainty about classification, prognosis, and treatment of neck pain a high-yield area for PCORI involvement. We have worked with a group of relevant stakeholders to identify possible research questions for targeted PCORI funding initiatives.

A central theme of our stakeholder discussions was that appropriate classification of neck pain disorders is essential to informing decision making and preventing undesirable outcomes. There was general consensus among our stakeholders that the physical exam findings from the examination procedures known as directional preference and centralization show promise for informing clinical decisions and guiding patient management, but that the evidence supporting this assessment and classification system is insufficient. There was also a general consensus that the term “nonspecific neck pain” is too vague, and the clinical entities it encompasses are too heterogeneous, to be useful, despite its relatively widespread use in the published literature. Our stakeholders recommended that future studies on neck pain clearly specify the nature or etiology

of neck pain, and that neck pain with radiculopathy be classified separately from neck pain without radiculopathy. Finally, our stakeholders agreed that there is a paucity of comparative effectiveness research to inform the selection of one or more of the many surgical and nonsurgical treatment options available to patients.

Our stakeholders' assessment and recommendations align with those proposed by a task force that articulated a series of evidence gaps and research priorities relating to neck pain in a 2008 publication.[9] Research priorities recommended by that task force included: 1) Understanding the actual course of neck pain and determinants of that course; 2) investigations of modifiable risk and prognostic factors in neck pain; 3) understanding the role of work-related exposures in risk or prognosis of neck pain; and 4) how physical, psychological, and societal factors interact in both the risk of neck pain and recovery from neck pain.

Identified Research Questions

Classification of Cervical Disc and Neck Pain Disorders

Our stakeholders felt that the physical exam findings from the examination procedures known as directional preference and centralization show promise for informing clinical decisions and guiding patient management, but that the evidence supporting these procedures for purposes of classification and treatment-related decision making is insufficient. Our literature search identified a systematic review published in 2012 that included 62 studies, and that concluded: "Findings of centralization or directional preference at baseline would appear to be useful indicators of management strategies and prognosis, and therefore warrant further investigation."[10] There was a general consensus among our stakeholders that new CER on this topic would provide useful information to improve clinical decision making.

Comparing the Effectiveness and Safety of Nonsurgical Options for Neck Pain

Surgery is not indicated for the vast majority of neck pain cases. A systematic review published in 2008 concluded that manual therapy, supervised exercise interventions, low-level laser therapy, and perhaps acupuncture are more effective than no treatment, sham, or alternative interventions, but that none of the active treatments was clearly superior to any other in either the short- or long-term.[12] Another systematic review concluded that cervical facet joint injections and radiofrequency neurotomy for neck pain without radiculopathy are not supported by current evidence, and there is there is limited evidence available for cervical medial branch blocks, trigger point injections, or botulinum toxin injections.[13] And compared to low back pain, there is relatively little CER for pharmacologic treatments for neck pain.

Our literature search identified 152 potentially studies, 45 of which are systematic reviews. This relatively large amount of evidence reflects the large number and wide variety of treatment options for neck pain, as well as a high proportion of clinical trials with small sample sizes. Of the 86 trials that compared two or more interventions for neck pain, 60 (70%) included fewer than 100 subjects. A similar proportion (75%) of the 4 studies identified via the ClinicalTrials.gov website have sample sizes smaller than 100. This body of evidence is also limited by the large variability in how neck pain was classified. Our stakeholders felt that direct comparisons of different nonsurgical treatment approaches for well-defined neck pain disorders would be of great value for informing clinical decision making, especially if measured outcomes included impact on pain, function, and work loss or return to work or degree and longevity of disability or impairment, and if patient populations and neck pain conditions were clearly described.

Assessing the Effectiveness of Instruments for Persons with Neck Pain

There is a relatively large number of instruments that can be used to assess the severity of neck pain and related symptoms and functional impairment, but our stakeholders felt that new CER to assess the ability of existing instruments to assess the effectiveness of therapeutic intervention or to help with prognosis among patients with neck pain is needed. Our stakeholders' perspective is similar to that of the authors of the single systematic review that we identified. The authors of that review, published in 2012, concluded: "Our findings imply that studies of high methodological quality are needed to properly assess the measurement properties of the currently available questionnaires. Until high quality studies are available, we recommend using these questionnaires with caution. There is no need for the development of new neck-specific questionnaires until the current questionnaires have been adequately assessed."[14] We believe that evidence derived from new CER on this topic could be rapidly implanted in practice and could improve patient-centered outcomes.

Identifying Predictors of Chronic Pain, Opioid Dependence, or Other Undesirable Outcomes

Given the many different etiologies than can cause neck pain the large number of possible treatment options, we believe (and our stakeholders agreed) that new CER that identified predictors of response to treatment or the development of undesirable outcomes would inform patient and clinic decision making and could lead to significantly improved outcomes among persons with neck pain. Our search identified 28 studies that reported on the natural history of several different kinds of neck pain syndromes or long-term outcomes associated with specific

treatments, but none of these studies was designed to identify potential predictors for developing chronic pain or opioid dependence.

Limitations

While we worked with our stakeholders to identify the most pertinent evidence gaps and research questions pertaining to the classification, prognosis, or treatment of cervical disc and neck pain disorders, the identified list may not reflect the full range of possible future research needs relating to this topic. Although our small stakeholder group comprised key stakeholders in the topic area it is possible that a different group of stakeholders might highlight future research needs differently. Because patients did not contribute to this identification exercise, PCORI may wish to elicit patient perspectives on these research questions in order to assure all perspectives are adequately considered. Finally, because a comprehensive systematic review has not been performed for any of the identified evidence gaps, we cannot determine with certainty the degree to which identified future research needs have already been addressed.

CONCLUSIONS

Based on input from our stakeholder group, key research gaps pertaining to cervical disc and neck pain include the comparative effectiveness of: 1) the presence of centralization vs. noncentralization or directional preference vs. no directional preference as predictors of response to therapy for axial neck pain without radiculopathy; 2) available nonsurgical treatments (prescription oral pharmacotherapy, over-the-counter oral pharmacotherapy, injections, or nonpharmacologic treatments) either alone or in combination for short-term symptomatic improvement of neck pain; 3) existing assessment instruments for persons with neck pain with or

without radiculopathy for the purpose of prognosis or assessing the effectiveness of therapeutic interventions; 4) patient characteristics, biopsychosocial and economic factors, physical examination and imaging findings for predicting which patients with new onset axial neck pain are at risk for developing chronic pain, opioid dependence, or other undesirable outcomes.

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Appendix A. Pub Med Search Strategy

Search date: September 21, 2015

Set #	Terms	Results
#1	“Neck Pain”[MeSH] OR (“Cervical Vertebrae”[MeSH] AND “pain”[tiab]) OR (“Intervertebral Disc Degeneration”[MeSH] AND “cervical”[tiab]) OR “cervical disc disease”[tiab] OR “neck pain”[tiab]	11486
#2	(randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR randomly[tiab] OR trial[tiab] OR Clinical trial[pt] OR “clinical trial”[tiab] OR “clinical trials ”[tiab] OR "comparative study"[Publication Type] OR "comparative study"[tiab] OR systematic[subset] OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[tiab] OR "meta-analyses"[tiab]) OR ("evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tiab] OR “evaluation studies”[tiab] OR "intervention studies"[MeSH Terms] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "case-control studies"[MeSH Terms] OR "case-control"[tiab] OR "cohort studies"[MeSH Terms] OR cohort[tiab] OR "longitudinal studies"[MeSH Terms] OR "longitudinal”[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "retrospective studies"[MeSH Terms] OR "retrospective"[tiab]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh])	4286623
#4	#1 AND #2	4945
	Limit: English	4637
	Dates: 2012/01/01 – present	1365

Appendix B. Participating Stakeholders

Shari Davidson
Vice President, National Business Group on Health

Matthew R. D'Uva
Executive Director, International Association for the Study of Pain

Justin Moore, PT, DPT
Executive Vice President of Public Affairs, American Physical Therapy Association

Serge Perrot, MD, PhD
Vice President, Société Française d'Etude et de Traitement de la Douleur (SFETD**)**
France Chapter of International Association for the Study of Pain (IASP)

Heidi Prather, DO
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Appendix C. Supplementary Tables

Appendix Table B-1. Published and ongoing studies potentially relevant to Research Question 1 *[Does the presence of centralization vs. noncentralization or directional preference vs. no directional preference predict response to therapy for axial neck pain without radiculopathy?]*

Study	N	Objective/Conclusion
Systematic Reviews		
May, 2012[1]	62 studies	OBJECTIVE: The aim of this study was to systematically review the literature relating to centralization and directional preference, and specifically report on prevalence, prognostic validity, reliability, loading strategies, and diagnostic implications. CONCLUSION: Centralization and directional preference appear to be useful treatment effect modifiers in 7 out of 8 studies. Levels of reliability were very variable (kappa 0.15-0.9) in 5 studies. Findings of centralization or directional preference at baseline would appear to be useful indicators of management strategies and prognosis, and therefore warrant further investigation.
RCTs		
None	–	–
Cohorts		
Patroncini, 2014[2]	45 patients	OBJECTIVE: The aim of this study was to determine the inter-tester reliability of movement control impairment [MCI] tests on the cervical spine. CONCLUSION: The physiotherapists were able reliably rate the majority the tests in this series of motor control tasks. There have been studies performed describing the assessment and treatment of movement control impairment problems and low back pain. However, no study has involved the assessment of the cervical dysfunction subgroup. This study presents a reliable test battery, for clinical use, to perform more specific examination of this subgroup.
Case-Control Studies		
None	–	–
Other		
None	–	–
Ongoing Studies (ClinicalTrials.gov)		
None	–	–

Abbreviations not defined above: N=number of studies/patients; RCTs=randomized controlled trials

Appendix Table B-2. Published and ongoing studies potentially relevant to Research Question 2 [*Within specific patient populations of interest, what is the comparative effectiveness and safety of available nonsurgical treatments (prescription oral pharmacotherapy, over-the-counter oral pharmacotherapy, injections, or nonpharmacologic treatments) either alone or in combination for short-term symptomatic improvement of neck pain? Patient populations of interest include: (1) patients with axial neck pain with radiculopathy, and (2) patients with axial next pain without radiculopathy. Outcomes of interest should include intervention's impact on pain, function, and work loss/return to work/degree and longevity of disability or impairment.]*

Study	N	Objective/Conclusions
Systematic Reviews		
Wei, 2015[3]	8 studies	OBJECTIVE: This overview aims to summarize the characteristics and evaluate critically the evidence from systematic reviews. CONCLUSIONS: Current systematic reviews showed potential advantages to CAM for CR. Due to the frequently poor methodological quality of primary studies, the conclusions should be treated with caution for clinical practice.
Shearer, 2015[4]	19 studies	OBJECTIVE: To update findings of the NPTF and evaluate the effectiveness of psychological interventions for the management of neck pain and associated disorders (NAD) or whiplash-associated disorders (WAD). CONCLUSIONS: The limited evidence of effectiveness for psychological interventions may be due to several factors: interventions that are ineffective, poorly conceptualized or poorly implemented. Further methodologically rigorous research is needed.
Manchikanti, 2015[5]	26 studies (21 RCTs, 5 observational studies)	OBJECTIVE: To evaluate and update the clinical utility of therapeutic lumbar, cervical, and thoracic facet joint interventions in managing chronic spinal pain. CONCLUSIONs: Based on the present assessment for the management of spinal facet joint pain, the evidence for long-term improvement is Level II for lumbar and cervical radiofrequency neurotomy, and therapeutic facet joint nerve blocks in the cervical, thoracic, and lumbar spine.
Monticone, 2015[6]	10 studies	OBJECTIVE: To assess the effects of cognitive-behavioural therapy (CBT) on Neck Pain (NP). CONCLUSIONS: CBT was shown to induce changes on pain and disability for chronic NP only when compared to no treatment. On subacute NP, benefit was found on pain relief but not on disability when comparing CBT to other interventions. However, none of these effects were clinically meaningful. Due to the low quality of the evidence, our conclusions might change over time while new data are available.
Monticone, 2015[7]	10 studies	OBJECTIVE: To assess the effects of CBT among individuals with subacute and chronic NP. Specifically, the following comparisons were investigated: (1) cognitive-behavioural therapy versus placebo, no treatment, or waiting list controls; (2) cognitive-behavioural therapy versus other types of interventions; (3) cognitive-behavioural therapy in addition to another intervention (e.g. physiotherapy) versus the other intervention alone.

Study	N	Objective/Conclusions
		CONCLUSIONS: With regard to chronic neck pain, CBT was found to be statistically significantly more effective for short-term pain reduction only when compared to no treatment, but these effects could not be considered clinically meaningful. Further research is recommended to investigate the long-term benefits and risks of CBT including for the different subgroups of subjects with NP.
Cheng, 2015[8]	6 studies	OBJECTIVE: Nonspecific neck pain is a common musculoskeletal disease. Therapeutic exercise has been shown to improve pain and disability in short-term and midterm follow-ups. This study performed a literature review of the long-term effects of therapeutic exercise on subjects with nonspecific chronic neck pain. CONCLUSIONS: The results of the six high-quality studies suggest that long-term exercise have long-term benefits for patients with nonspecific neck pain in terms of body function and structure.
Marchado, 2015[9]	13 studies	OBJECTIVE: To investigate the efficacy and safety of paracetamol (acetaminophen) in the management of spinal pain and osteoarthritis of the hip or knee. CONCLUSIONS: Paracetamol is ineffective in the treatment of low back pain and provides minimal short term benefit for people with osteoarthritis. These results support the reconsideration of recommendations to use paracetamol for patients with low back pain and osteoarthritis of the hip or knee in clinical practice guidelines.
Wong, 2015[10]	14 studies	OBJECTIVE: To evaluate the effectiveness of non-steroidal anti-inflammatory drugs (NSAIDs) for the management of neck pain and associated disorders (NAD), whiplash-associated disorders, and non-specific low back pain (LBP) with or without radiculopathy. CONCLUSIONS: For NAD, oral NSAIDs may be more effective than placebo. Oral NSAIDs are more effective than placebo for persistent LBP, but not for recent-onset LBP. Different oral NSAIDs lead to similar outcomes for neck pain and LBP.
Cagnie, 2015[11]	15 studies	OBJECTIVE: The aim of this review was to describe the effects of ischemic compression and dry needling on trigger points in the upper trapezius muscle in patients with neck pain and compare these two interventions with other therapeutic interventions aiming to inactivate trigger points. CONCLUSIONS: On the basis of this systematic review, ischemic compression and dry needling can both be recommended in the treatment of neck pain patients with trigger points in the upper trapezius muscle. Additional research with high-quality study designs are needed to develop more conclusive evidence.
Yuan, 2015[12]	75 studies	OBJECTIVE: The objective of the present study was to review and analyze the existing data about pain and disability in TCM treatments for NP and LBP. CONCLUSIONS: Acupuncture, acupressure, and cupping could be efficacious in treating the pain and disability associated with CNP or CLBP in the immediate term. Gua sha, tai chi, qigong, and Chinese manipulation showed fair

Study	N	Objective/Conclusions
		effects, but we were unable to draw any definite conclusions, and further research is still needed. The efficacy of tuina and moxibustion is unknown because no direct evidence was obtained. These TCM modalities are relatively safe.
Zhu, 2015[13]	3 studies	OBJECTIVE: To access the effectiveness and safety of cervical spine manipulation for cervical radiculopathy. CONCLUSIONS: There was moderate level evidence to support the immediate effectiveness of cervical spine manipulation in treating people with cervical radiculopathy. The safety of cervical manipulation cannot be taken as an exact conclusion so far.
Manchikanti, 2015[14]	7 studies	OBJECTIVE: To determine the long-term efficacy of cervical interlaminar and transforaminal epidural injections in the treatment of cervical disc herniation, spinal stenosis, discogenic pain without facet joint pain, and post surgery syndrome. CONCLUSIONS: This systematic review with qualitative best evidence synthesis shows Level II evidence for the efficacy of cervical interlaminar epidural injections with local anesthetic with or without steroids, based on at least one high-quality relevant randomized control trial in each category for disc herniation, discogenic pain without facet joint pain, central spinal stenosis, and post surgery syndrome.
Gross, 2015[15]	27 studies	OBJECTIVE: To assess the effectiveness of exercises to improve pain, disability, function, patient satisfaction, quality of life and global perceived effect in adults with neck pain. CONCLUSIONS: No high quality evidence was found, indicating that there is still uncertainty about the effectiveness of exercise for neck pain.
Liu, 2015[16]	20 studies	OBJECTIVE: To evaluate current evidence of the effectiveness of dry needling of myofascial trigger points (MTrPs) associated with neck and shoulder pain. CONCLUSIONS: Dry needling can be recommended for relieving MTrP pain in neck and shoulders in the short and medium term, but wet needling is found to be more effective than dry needling in relieving MTrP pain in neck and shoulders in the medium term.
McCaskey, 2014[17]	1380 studies	OBJECTIVE: The aim of this systematic review was to summarise and analyse the existing data on the effects of PrT on pain alleviation and functional restoration in patients with chronic (>/= 3 months) neck- or back pain. CONCLUSIONS: There are few relevant good quality studies on proprioceptive exercises. A descriptive summary of the evidence suggests that there is no consistent benefit in adding PrT to neck- and low back pain rehabilitation and functional restoration.
Young, 2014[18]	14 studies	OBJECTIVE: The purpose of this systematic review was to evaluate the current literature regarding the effectiveness of thoracic manipulation versus mobilization in patients with mechanical neck pain. CONCLUSIONS: Current limitations in the body of research, specifically regarding the use of thoracic

Study	N	Objective/Conclusions
		mobilization, limit the recommendation of its use compared to thoracic manipulation for patients with mechanical neck pain. There is, however, a significant amount of evidence, although of varied quality, for the short-term benefits of thoracic manipulation in treating patients with this condition.
Sutton, 2014[19]	14 studies	OBJECTIVE: To update findings of the Bone and Joint Decade 2000-2010 Task Force on Neck Pain and Its Associated Disorders and evaluate the effectiveness of multimodal care for the management of patients with WAD or NAD. CONCLUSIONS: Multimodal care can benefit patients with WAD and NAD with early or persistent symptoms. The evidence does not indicate that one multimodal care package is superior to another. Clinicians should avoid high utilization of care for patients with WAD and NAD.
Yu, 2014[20]	6 studies	OBJECTIVE: To update the findings of the Bone and Joint Decade 2000 to 2010 Task Force on Neck Pain and Its Associated Disorders and evaluate the effectiveness of structured patient education for the management of patients with whiplash-associated disorders (WAD) or neck pain and associated disorders (NAD). CONCLUSIONS: Results suggest that structured patient education alone cannot be expected to yield large benefits in clinical effectiveness compared with other conservative interventions for patients with WAD or NAD. Moreover, structured patient education may be of benefit during the recovery of patients with WAD when used as an adjunct therapy to physiotherapy or emergency room care. These benefits are small and short lived.
Cheng, 2014[21]	15 studies	OBJECTIVE: To systematically evaluate the evidence of whether massage therapy (MT) is effective for neck pain. Conclusions. CONCLUSIONS: There was no valid evidence of MT on improving dysfunction. With regard to follow-up effects, there was not enough evidence of MT for neck pain. Conclusions. This systematic review found moderate evidence of MT on improving pain in patients with neck pain compared with inactive therapies and limited evidence compared with traditional Chinese medicine. There were no valid lines of evidence of MT on improving dysfunction. High quality RCTs are urgently needed to confirm these results and continue to compare MT with other active therapies for neck pain.
Southerst, 2014[22]	10 studies	OBJECTIVE: To update the findings of the NPTF on the effectiveness of exercise for the management of neck pain and WAD grades I to III. CONCLUSIONS: We found evidence that supervised qigong, Iyengar yoga, and combined programs including strengthening, range of motion, and flexibility are effective for the management of persistent neck pain. We did not find evidence that one supervised exercise program is superior to another.

Study	N	Objective/Conclusions
Schroeder, 2013[23]	7 studies	OBJECTIVE: To compare manipulation or mobilization of the cervical spine to physical therapy or exercise for symptom improvement in patients with neck pain. CONCLUSIONS: This systematic review is limited by the variability of treatment interventions and lack of standardized outcomes to assess treatment benefit.
Bicket, 2013[24]	43 studies	OBJECTIVE: This study of epidural steroid "control" injections aimed to determine whether epidural nonsteroid injections constitute a treatment or true placebo in comparison with nonepidural injections for back and neck pain treatment. CONCLUSION: Epidural nonsteroid injections may provide improved benefit compared with nonepidural injections on some measures, though few, low-quality studies directly compared controlled treatments, and only short-term outcomes."
Gross, 2013[25]	12 studies	OBJECTIVE: To determine the effectiveness of physician-delivered injections on pain, function/disability, quality of life, global perceived effect and patient satisfaction for adults with mechanical neck disorders. CONCLUSIONS: Current evidence does not confirm the effectiveness of IM-lidocaine injection for chronic mechanical neck pain nor anaesthetic nerve block for cervicogenic headache. There is moderate evidence of no benefit for steroid blocks vs controls for mechanical neck pain.
Peloso, 2013[26]	26 studies (47 RCTs)	OBJECTIVE: To conduct an overview (review-of-reviews) on pharmacological interventions for neck pain. CONCLUSIONS: While in general there is a lack of evidence for most pharmacological interventions, current evidence is against botulinum toxin-A for chronic neck pain or subacute/chronic whiplash; against medial branch block with steroids for chronic facet joint pain; but in favour of the muscle relaxant eperison hydrochloride for chronic neck pain.
Gross, 2013[27]	17 studies	OBJECTIVE: This systematic review update evaluated low level laser therapy (LLLT) for adults with neck pain. CONCLUSIONS: We found diverse evidence using LLLT for neck pain. LLLT may be beneficial for chronic neck pain/function/QoL. Larger long-term dosage trials are needed.
Gross, 2013[28]	30 studies (75 RCTs)	OBJECTIVE: To conduct an overview on psychological interventions, orthoses, patient education, ergonomics, and 1(0)/2(0) neck pain prevention for adults with acute-chronic neck pain. CONCLUSIONS: Moderate evidence exists for quantifying beneficial and non-beneficial effects of a limited number of interventions for acute WAD and chronic neck pain. Larger trials with more rigorous controls need to target promising interventions.
Kroeling, 2013[29]	20 studies	OBJECTIVE: This systematic review assessed the short, intermediate and long-term effects of electrotherapy on pain, function, disability, patient satisfaction, global

Study	N	Objective/Conclusions
		perceived effect, and quality of life in adults with neck pain with and without radiculopathy or cervicogenic headache. CONCLUSIONS: We cannot make any definite statements on the efficacy and clinical usefulness of electrotherapy modalities for neck pain.
Rhee, 2013[30]	5 studies	OBJECTIVE: To conduct a systematic review investigating the evidence of (1) efficacy, effectiveness, and safety of nonoperative treatment of patients with cervical myelopathy; (2) whether the severity of myelopathy affects outcomes of nonoperative treatment; and (3) whether specific activities or minor injuries are associated with neurological deterioration in patients with myelopathy or asymptomatic stenosis being treated nonoperatively. CONCLUSIONS: There is a paucity of evidence for nonoperative treatment of cervical myelopathy, and further studies are needed to determine its role more definitively.
Kadhim-Saleh, 2013[31]	8 studies	OBJECTIVE: The aim of this study is to determine the efficacy of low-level laser therapy (LLLT) in reducing acute and chronic neck pain as measured by the visual analog scale (VAS). CONCLUSIONS: This systematic review provides inconclusive evidence because of significant between-study heterogeneity and potential risk of bias. The benefit seen in the use of LLLT, although statistically significant, does not constitute the threshold of minimally important clinical difference.
Bertozzi, 2013[32]	7 studies	OBJECTIVE: The purpose of this study was to conduct a current review of randomized controlled trials concerning the effect of TE on pain and disability among people with CNSNP, perform a meta-analysis, and summarize current understanding. CONCLUSIONS: Only one study investigated the effect of TE on pain and disability at follow-up longer than 6 months after intervention.
Kong, 2013[33]	12 studies	OBJECTIVE: To evaluate the effectiveness of massage therapy (MT) for neck and shoulder pain. CONCLUSIONS: MT may provide immediate effects for neck and shoulder pain. However, MT does not show better effects on pain than other active therapies. No evidence suggests that MT is effective in functional status.
Thoomes, 2013[34]	11 studies	OBJECTIVE: The aim of this systematic review is to assess the effectiveness of conservative treatments for patients with cervical radiculopathy, a term used to describe neck pain associated with pain radiating into the arm. CONCLUSIONS: On the basis of low-level to very low-level evidence, no 1 intervention seems to be superior or consistently more effective than other interventions.
Huisman, 2013[35]	10 studies	OBJECTIVE: The aim of this systematic review was to determine the efficacy of thoracic spine manipulation (TSM) in reducing pain and disability in patients diagnosed with non-specific neck pain. CONCLUSIONS: There is insufficient evidence that TSM is more effective in reducing pain and disability than control treatments in patients with non-specific neck pain.

Study	N	Objective/Conclusions
Vincent 2013[36]	27 studies	OBJECTIVE: To evaluate the effectiveness of manual therapies in the treatment of nonspecific neck pain. CONCLUSIONS: Manual therapies contribute usefully to the management of nonspecific neck pain. The level of evidence is moderate for short-term effects of upper thoracic manipulation in acute neck pain, limited for long-term effects of neck manipulation, and limited for all techniques and follow-up durations in chronic neck pain.
Falco, 2012[37]	10 studies	OBJECTIVE: To determine and update the clinical utility of therapeutic cervical facet joint interventions in the management of chronic neck pain. CONCLUSIONS: The indicated evidence for cervical radiofrequency neurotomy is fair. The indicated evidence for cervical medial branch blocks is fair. The indicated evidence for cervical intraarticular injections with local anesthetic and steroids is limited.
Van Middelkoop, 2013[38]	9 studies	OBJECTIVE: Are surgical interventions to the cervical spine effective when compared to conservative care for patients with neck pain? CONCLUSIONS: Most studies on surgical techniques comparing these to conservative care showed a high risk of bias. The benefit of surgery over conservative care is not clearly demonstrated.
Patel, 2012[39]	15 studies	OBJECTIVE: To assess the effects of massage on pain, function, patient satisfaction, global perceived effect, adverse effects and cost of care in adults with neck pain versus any comparison at immediate post-treatment to long-term follow-up. CONCLUSIONS: No recommendations for practice can be made at this time because the effectiveness of massage for neck pain remains uncertain. Additionally, future research is needed in order to assess the long-term effects of treatment and treatments provided on more than one occasion.
Kay, 2012[40]	21 studies	OBJECTIVE: To improve pain, disability, function, patient satisfaction, quality of life and global perceived effect in adults with neck pain. CONCLUSIONS: Low to moderate quality evidence supports the use of specific cervical and scapular stretching and strengthening exercise for chronic neck pain immediately post treatment and intermediate term
Fourney, 2012[41]	5 studies	OBJECTIVE: To critically review and summarize evidence on the treatment of cervical adjacent segment pathology (ASP). CONCLUSIONS: Insufficient. Strength of Statement: Strong. Recommendation no.1: Despite the importance of this topic, a dearth of literature was found. We recommend further studies on this topic.
Diwan, 2012[42]	34 studies	OBJECTIVE: To evaluate the effect of cervical interlaminar epidural injections in managing various types of chronic neck and upper extremity pain emanating as a result of cervical spine pathology. CONCLUSION: The evidence is good for radiculitis secondary to disc herniation with local anesthetics and steroids, fair with local anesthetic only; whereas, it is fair for

Study	N	Objective/Conclusions
		local anesthetics with or without steroids, for axial or discogenic pain, pain of central spinal stenosis, and pain of post surgery syndrome.
Posadzki, 2012[43]	4 studies	OBJECTIVE: This article is aimed at critically evaluating the evidence from systematic reviews (SRs) of spinal manipulation in patients with pain. CONCLUSIONS: Collectively, these data fail to demonstrate that spinal manipulation is an effective intervention for pain management.
Lin, 2012[44]	4 studies	OBJECTIVE: To assess whether Chinese manipulation improves pain, function/disability and global perceived effect in adults with acute/subacute/chronic neck pain. CONCLUSIONS: Very low-quality evidence showed that Chinese manipulation alone was superior to Chinese traditional massage in immediate post-intervention pain relief (mean difference: -2.02; 95%
Driessen, 2012[45]	5 studies	OBJECTIVE: The aim of this systematic review was to investigate the cost-effectiveness of conservative treatments for non-specific neck pain. CONCLUSIONS: At present, the limited number of studies and the heterogeneity between studies warrant no definite conclusions on the cost-effectiveness of conservative treatments for non-specific neck pain.
Gross, 2012[46]	15 studies	OBJECTIVE: To assess the short- to long-term effects of therapeutic patient education (TPE) strategies on pain, function, disability, quality of life, global perceived effect, patient satisfaction, knowledge transfer, or behaviour change in adults with neck pain associated with whiplash or non-specific and specific mechanical neck pain with or without radiculopathy or cervicogenic headache. CONCLUSIONS: With the exception of one trial, this review has not shown effectiveness for educational interventions, including advice to activate, advice on stress-coping skills, workplace ergonomics and self-care strategies. Future research should be founded on sound adult learning theory and learning skill acquisition.
Gebremariam, 2012[47]	11 studies	OBJECTIVE: To assess the effectiveness of interventions for treating cervical disc herniation. CONCLUSIONS: No evidence for effectiveness of conservative treatment compared with surgery was found. More high-quality RCTs using validated outcome measures (including adjacent level disease) are needed.
RCTs		
Thompson, 2015[48]	57 patients	OBJECTIVE: To determine whether adding a physiotherapist-led cognitive-behavioural intervention to an exercise programme improved outcome in patients with chronic neck pain (CNP).
Kim, 2015[49]	24 patients	OBJECTIVE: To compare the influences of the active release technique (ART) and joint mobilization (JM) on the visual analog scale (VAS) pain score, pressure pain threshold (PPT), and neck range of motion (ROM) of patients with chronic neck pain.
Haller, 2015[50]	54 patients	OBJECTIVE: With growing evidence for Craniosacral Therapy (CST) effectiveness for pain management, the

Study	N	Objective/Conclusions
		question about CST efficacy remained unclear. This study therefore aimed at investigating CST in comparison to sham treatment in chronic non-specific neck pain patients.
Celenay, 2015[51]	60 patients	OBJECTIVE: This study was planned to assess and compare the effectiveness of cervical and scapulothoracic stabilization exercise treatment with and without connective tissue massage (CTM) on pain, anxiety, and the quality of life in patients with chronic mechanical neck pain (MNP)
Brage, 2015[52]	20 patients	OBJECTIVE: To evaluate the effect of training and pain education vs pain education alone, on neck pain, neck muscle activity and postural sway in patients with chronic neck pain
Yun, 2015[53]	20 patients	OBJECTIVE: This study aimed to investigate the effects of neurac training on pain, function, balance, fatigability, and quality of life.
Griswold, 2015[54]	20 patients	OBJECTIVE: Neck pain is routinely managed using manual therapy (MT) to the cervical and thoracic spines. While both mobilizations and manipulations to these areas have been shown to reduce neck pain, increase cervical range of motion, and reduce disability, the most effective option remains elusive. The purpose of this preliminary trial was to compare the pragmatic use of cervical and thoracic mobilizations vs. manipulation for mechanical neck pain.
Cook, 2015[55]	179 patients	OBJECTIVE: The aim was to determine the optimal dose of massage for neck pain.
Marchand, 2015[56]	413 patients	OBJECTIVE: The aim of the present study was to evaluate changes in pain and disability at the 12-month follow-up of patients with neck and back pain treated with a work-focused intervention compared to patients treated with standard interventions, and the influence of improvement fear avoidance beliefs during the interventions on pain, disability and return to work at 12-month follow-up.
Beltran-Alacreu, 2015[57]	45 patients	OBJECTIVE: The aim of this study was to determine the effectiveness of a multimodal treatment in the short and medium term for disability in nonspecific chronic neck pain.
Lauche, 2015[58]	72 patients	OBJECTIVE: To test the efficacy of the Alexander Technique, local heat and guided imagery on pain and quality of life in patients with chronic non-specific neck pain.
Javanshir, 2015[59]	60 patients	OBJECTIVE: The effect of different exercise programs on cervical flexor muscles dimensions in patients with chronic neck pain is yet to be demonstrated. The purpose of this study was to assess the effect of two exercise programs; craniocervical flexion (CCF) and cervical flexion (CF), on flexor muscles dimensions in patients with chronic neck pain.
Tunwattanapong, 2015[60]	96 patients	OBJECTIVE: To determine the effectiveness of neck and shoulder stretching exercises for relief neck pain among office workers.
Puntumetakul, 2015[61]	48 patients	OBJECTIVE: This study investigated the acute effects of single-level and multiple-level thoracic manipulations on chronic mechanical neck pain (CMNP)
Pecos-Martin, 2015[62]	72 patients	OBJECTIVE: To evaluate the effect of dry needling into a myofascial trigger point (MTrP) in the lower trapezius muscle of patients with mechanical idiopathic neck pain.

Study	N	Objective/Conclusions
Jeitler, 2015[63]	89 patients	OBJECTIVE: We aimed to evaluate the effectiveness of an 8-week meditation program (jyoti meditation) in patients with chronic neck pain by means of a randomized clinical trial.
Field, 2014[64]	48 patients	OBJECTIVE: In the present study an attempt was made to enhance the effects of weekly massage therapy by having the participants massage themselves daily. And in addition to self-reports on pain, range of motion (ROM) and the associated ROM pain were assessed before and after the first massage session and pre-post the last session one month later.
Wilke, 2014[65]	19 patients	OBJECTIVE: This trial aimed to evaluate the short-term effectiveness of acupuncture plus stretching to reduce pain and improve range of motion in patients afflicted by cervical myofascial pain syndrome.
Langevin, 2015[66]	36 patients	OBJECTIVE: To compare a rehabilitation program thought to increase the size of the intervertebral foramen (IVF) of the affected nerve root to a rehabilitation program that doesn't include any specific techniques thought to increase the size of the IVF in patients presenting with cervical radiculopathy (CR).
Akhter, 2014[67]	62 patients	To evaluate the role of manual therapy with exercise regime versus exercise regime alone in the management of non-specific chronic neck pain.
Creighton, 2014[68]	30 patients	The purpose of this clinical trial was to describe two translatory non-thrust mobilization techniques and evaluate OBJECTIVE: their effect on cervical pain, motion restriction, and whether any adverse effects were reported when applied to the C7 segment.
Zheng, 2014[69]	169 patients	OBJECTIVE: To compare ultrasound-guided miniscalpel-needle (UG-MSN) release versus ultrasound-guided dry needling (UG-DN) for chronic neck pain.
Lluch, 2014[70]	23 patients	OBJECTIVE: The purpose of this study was to investigate the effect of active vs passive scapular correction on pain and pressure pain threshold at the most symptomatic cervical segment in patients with chronic neck pain.
Llamas-Ramos, 2014[71]	94 patients	OBJECTIVE: To compare the effects of trigger point (TrP) dry needling (DN) and TrP manual therapy (MT) on pain, function, pressure pain sensitivity, and cervical range of motion in subjects with chronic mechanical neck pain.
Ganesh, 2015[72]	60 patients	OBJECTIVE: While studies have looked into the effects of Maitland mobilization on symptom relief, to date, no work has specifically looked at the effects of Mulligan mobilization. The objective of this work was to compare the effectiveness of Maitland and Mulligan's mobilization and exercises on pain response, range of motion (ROM) and functional ability in patients with mechanical neck pain.
Khan, 2014[73]	68 patients	OBJECTIVE: To evaluate the effectiveness of isometric exercises as compared to general exercises in chronic non-specific neck pain.
Moustafa, 2014[74]	216 patients	OBJECTIVE: The purpose of this study was to investigate the immediate and long-term effects of a 1-year multimodal program with the addition of 2 different traction approaches on the pain, function, disability, and nerve root function in

Study	N	Objective/Conclusions
		patients with discogenic cervical radiculopathy (CR). This study also attempted to identify the optimal traction angle based on the maximum recovery of the peak-to-peak amplitude of the flexor carpi radialis (FCR) H-reflex.
Ou, 2014[75]	60 patients	OBJECTIVE: To assess the efficacy of aromatic essential oils on neck pain.
Rudolfsson, 2014[76]	108 patients	OBJECTIVE: To evaluate the effect of neck coordination exercise on sensorimotor function in women with neck pain compared with best-available treatment and sham treatment.
Bakar, 2014[77]	45 patients	OBJECTIVE: The purpose of this study was to evaluate the short-term effects of classic massage (CM) and connective tissue massage (CTM) on pressure pain threshold and muscle relaxation response in women with chronic neck pain.
Amorim, 2014[78]	30 patients	OBJECTIVE: The purpose of this study was to assess the effectiveness of global postural reeducation (GPR) relative to segmental exercises (SE) in the treatment of scapular dyskinesis (SD) associated with neck pain.
Sarig, 2015[79]	32 patients	OBJECTIVE: The objective of this study was to investigate the effect of kinematic training (KT) with and without the use of an interactive VR device.
Ruiz-Molinero, 2014[80]	54 patients	OBJECTIVE: To determine if ultrasound (US) is effective in reducing pain and mobility limitation in the treatment of traumatic cervical sprain, we performed an experimental study.
Rolving, 2014[81]	83 patients	OBJECTIVE: To compare the effect of two different exercise programs on pain, strength and fear-avoidance belief.
Salom-Moreno, 2014[82]	52 patients	OBJECTIVE: The purpose of this study was to compare the effects of thoracic thrust manipulation vs thoracic non-thrust mobilization in patients with bilateral chronic mechanical neck pain on pressure pain sensitivity and neck pain intensity.
Casanova-Mendez, 2014[83]	60 patients	OBJECTIVE: Comparative short-term effects of two thoracic spinal manipulation techniques in subjects with chronic mechanical neck pain: a randomized controlled trial
Sherman, 2014[84]	228 patients	OBJECTIVE: This trial was designed to evaluate the optimal dose of massage for individuals with chronic neck pain.
Manchikanti, 2014[85]	120 patients	OBJECTIVE: To assess the effectiveness of cervical interlaminar epidural injections of local anesthetic with or without steroids for the management of axial or discogenic pain in patients without disc herniation, radiculitis, or facet joint pain.
Mejuto-Vazquez, 2014[86]	17 patients	OBJECTIVE: To determine the effects of trigger point dry needling (TrPDN) on neck pain, widespread pressure pain sensitivity, and cervical range of motion in patients with acute mechanical neck pain and active trigger points in the upper trapezius muscle.
Izquierdo, 2014[87]	51 patients	OBJECTIVE: Our purpose was to compare the effectiveness of three manual therapy techniques: high velocity, low amplitude (HVLA), mobilization (Mob) and

Study	N	Objective/Conclusions
		sustained natural apophyseal glide (SNAG) in patients with chronic neck pain (CNP).
Snodgrass, 2014[88]	64 patients	OBJECTIVE: To determine if force magnitude during posterior-to-anterior mobilization affects immediate and short-term outcomes in patients with chronic, nonspecific neck pain.
Fritz, 2014[89]	86 patients	OBJECTIVE: To examine the effectiveness of cervical traction in addition to exercise for specific subgroups of patients with neck pain.
Karlsson, 2014[90]	57 patients	OBJECTIVE: Different types of exercises can help manage chronic neck pain. Supervised exercise interventions are widely used, but these protocols require substantial resources. The aim of this trial, which focused on adherence, was to evaluate two home exercise interventions.
Durmus, 2014[91]	61 patients	OBJECTIVE: The aim of this trial was to investigate and compare the effects of phonophoresis (PP), placebo PP and exercise therapies on pain, disability, sleep quality, and depression in the patients with chronic neck pain (CNP).
Borisut, 2013[92]	100 patients	OBJECTIVE: To compare muscle activities and pain levels of females with chronic neck pain receiving different exercise programs.
Suvarnnato, 2013[93]	39 patients	OBJECTIVE: To investigate effects of thoracic manipulation versus mobilization on chronic neck pain.
Maiers, 2014[94]	241 patients	OBJECTIVE: To assess the relative effectiveness of spinal manipulative therapy and supervised rehabilitative exercise, both in combination with and compared to home exercise (HE) alone for neck pain in individuals ages 65 years or older.
Andrade, 2014[95]	149 patients	OBJECTIVE: The purpose of this study was to determine the efficacy of microwave diathermy to treat nonspecific chronic neck pain.
Cho, 2014[96]	45 patients	OBJECTIVE: To investigate the feasibility and sample size required for a full-scale randomised controlled trial of the effectiveness of acupuncture with non-steroidal anti-inflammatory drugs (NSAIDs) for chronic neck pain compared with acupuncture or NSAID treatment alone.
Predel, 2013[97]	72 patients	OBJECTIVE: The aim of this study was to assess the efficacy and safety of DDEA 1.16% gel compared with placebo gel in acute NP.
Lauche, 2013[98]	61 patients	OBJECTIVE: This study aimed to test the efficacy of 12 weeks of a partner-delivered home-based cupping massage, compared to the same period of progressive muscle relaxation in patients with chronic non-specific neck pain.
Jull, 2013[99]	101 patients	OBJECTIVE: This randomized, single-blind, controlled trial tested whether multidisciplinary individualized treatments for patients with acute whiplash (<4 weeks postinjury) could reduce the incidence of chronicity at 6 mo by 50% compared to usual care.
Falla, 2013[100]	46 patients	OBJECTIVE: A randomized controlled trial was conducted on 46 women with chronic neck pain to investigate the immediate effectiveness of an 8-week exercise programme on pain and directional specificity of neck muscle activity.

Study	N	Objective/Conclusions
Andersen, 2013[101]	118 patients	OBJECTIVE: The purpose of this study is to evaluate the effectiveness of specific strength training in women with severe neck pain and to analyze the dose-response relationship between training adherence and pain reduction.
Klein, 2013[102]	61 patients	OBJECTIVE: We aimed to investigate whether a single strain-counterstrain intervention is more effective than a sham intervention in improving restricted cervical range of motion in patients with neck pain.
Cramer, 2013[103]	51 patients	OBJECTIVE: The aim of this study was to evaluate the effect of Iyengar yoga compared with exercise on chronic nonspecific neck pain.
Masaracchio, 2013[104]	64 patients	OBJECTIVE: To investigate the short-term effects of thoracic spine thrust manipulation combined with cervical spine nonthrust manipulation (experimental group) versus cervical spine nonthrust manipulation alone (comparison group) in individuals with mechanical neck pain.
Paoloni, 2013[105]	220 patients	OBJECTIVE: To determine if a Patient Oriented approach may be more beneficial for CMNP patients when compared to a Prescription Oriented one.
Saavedra-Hernandez, 2013[106]	82 patients	OBJECTIVE: To compare the effects of an isolated application of cervical spine thrust joint manipulation vs. the application of cervical, cervico-thoracic junction and thoracic manipulation on neck pain, disability and cervical range of motion in chronic neck pain.
Michalsen, 2012[107]	77 patients	OBJECTIVE: We aimed to evaluate the effectiveness of Iyengar yoga in chronic neck pain by means of a randomized clinical trial.
McLean, 2013[108]	151 patients	OBJECTIVE: This study investigated the effectiveness of a group neck and upper limb exercise programme (GET) compared with usual physiotherapy (UP) for patients with non-specific neck pain.
Hohmann, 2012[109]	40 patients	OBJECTIVE: The objective was to investigate whether a treatment with a needle stimulation pad (NSP) changes perceived pain and/or sensory thresholds in patients with chronic neck (NP) and lower back pain (BP).
Sherman, 2012[110]	228 patients	OBJECTIVE: This study is designed to address these gaps in our knowledge by determining, for persons with chronic neck pain: 1) the optimal combination of number of treatments per week and length of individual treatment session, and 2) the optimal number of weeks of treatment.
Kim, 2012[111]	40 patients	OBJECTIVE: This was a randomized controlled pilot trial to evaluate the effectiveness of cupping therapy for neck pain in video display terminal (VDT) workers
Lauche, 2012[112]	18 patients	OBJECTIVE: This study aimed to measure the effects of Gua Sha therapy on the pain ratings and pressure pain thresholds of patients with chronic neck pain (CNP) and chronic low back pain (CLBP).
La Touche, 2013[113]	32 patients	OBJECTIVE: The aims were to investigate the effects of anterior-posterior upper cervical mobilization (APUCM) on pain modulation in craniofacial and cervical regions and its influence on the sympathetic nervous system.
Schabrun, 2012[114]	23 patients	OBJECTIVE: This trial was conducted to assess the effectiveness of interactive neurostimulation (INS) therapy

Study	N	Objective/Conclusions
		on the treatment of pain associated with myofascial trigger points (MTPs) in adults with mechanical neck pain.
Manchikanti, 2012[115]	120 patients	OBJECTIVE: To evaluate the effectiveness of cervical interlaminar epidural injections of local anesthetic with or without steroids in the management of chronic neck pain and upper extremity pain in patients with disc herniation and radiculitis.
Manchikanti, 2012[116]	120 patients	OBJECTIVE: A randomized, double-blind, active, controlled trial was conducted to evaluate the effectiveness of cervical interlaminar epidural injections of local anesthetic with or without steroids for the management of chronic neck pain with or without upper extremity pain in patients without disc herniation, radiculitis, or facet joint pain.
Andersen, 2012[117]	447 patients	OBJECTIVE: This study investigates how one weekly hour of strength training for the neck and shoulder muscles is most effectively distributed.
Park, 2012[118]	400 patients	OBJECTIVE: This study aimed to investigate the effects of therapeutic CFJ injections on patients with long-standing cervical MPS with referral pain patterns of CFJ syndrome.
Topolska, 2012[119]	60 patients	OBJECTIVE: The aim of this study was to evaluate the effectiveness and impact of therapeutic massage on the range of motion in patients with neck pain.
Jee, 2013[120]	120 patients	OBJECTIVE: To compare the short-term effects and advantages of ultrasound-guided selective nerve root block with fluoroscopy-guided transforaminal epidural block for radicular pain in the lower cervical spine through assessment of pain relief, functional improvement, and safety.
Saavedra-Hernandez, 2012[121]	80 patients	OBJECTIVE: To compare the effectiveness of cervical spine thrust manipulation to that of Kinesio Taping applied to the neck in individuals with mechanical neck pain, using self-reported pain and disability and cervical range of motion as measures.
Salo, 2012[122]	101 patients	OBJECTIVE: To evaluate whether long-term neck and upper body exercises conducted in economical community-based outpatient clinic and home-based settings could improve health-related quality of life (HRQoL) for individuals affected by chronic neck pain.
Manchikanti, 2012[123]	60 patients	OBJECTIVE: Emerging evidence for cervical interlaminar epidurals for various conditions in the cervical spine is positive; however, the effect of fluoroscopic epidural injections in cervical spinal stenosis has not been studied.
Manchikanti, 2012[124]	56 patients	OBJECTIVE: To evaluate the effectiveness of cervical interlaminar epidural injections of local anesthetic with or without steroids in providing effective and long-lasting relief in the management of chronic neck pain and upper extremity pain in patients with cervical postsurgery syndrome, and to evaluate the differences between local anesthetic with or without steroids.
Bronfort, 2012[125]	272 patients	OBJECTIVE: To determine the relative efficacy of spinal manipulation therapy (SMT), medication, and home exercise with advice (HEA) for acute and subacute neck pain in both the short and long term.

Study	N	Objective/Conclusions
Lauche, 2012[126]	50 patients	OBJECTIVE: In this pilot study, we investigated the effect of traditional cupping therapy on chronic nonspecific neck pain (CNP) and mechanical sensory thresholds.
Evans, 2012[127]	270 patients	OBJECTIVE: To evaluate the relative effectiveness of high-dose supervised exercise with and without spinal manipulation and low-dose home exercise for chronic neck pain.
Dunning, 2012[128]	107 patients	OBJECTIVE: This aim of this study was to determine the effect of different conservative treatment methods on pain intensity, disability, quality of life, and mood in patients with cervical spondylosis during a 6-month period.
Cohort Studies		
Maiers, 2015[129]	241 patients	OBJECTIVE: This paper provides a detailed report of AE experienced by elderly participants in a randomized comparative effectiveness trial of SMT and exercise for chronic NP.
Cohen, 2014[130]	169 patients	OBJECTIVE: Cervical radicular pain is a major cause of disability. No studies have been published comparing different types of nonsurgical therapy.
Carlesso, 2013[131]	20 patients	OBJECTIVE: To pilot and determine the feasibility of estimating adverse events in patients with neck pain treated with cervical manipulation/mobilization by Canadian orthopaedic manual physiotherapists (OMPTs) using an online data-collection system to provide estimates for a future larger multi-centre international study.
Schwerla, 2013[132]	42 patients	OBJECTIVE: The objective of this study was to investigate whether a series of osteopathic treatments of patients with LWS may improve their symptoms.
Matijevic-Mikelic, 2012[133]	100 patients	OBJECTIVE: The aim of this study was to investigate the effectiveness of the therapeutic ultrasound on the psycho-physiological functioning in patients who presented with neck pain.
Walk, 2012[134]	246 patients	OBJECTIVE: The goal of this retrospective review was to determine the safety and efficacy of CT-guided transforaminal epidural injections by using a posterior approach.
Clinical Guideline		
Graham, 2013[135]	103 studies	OBJECTIVE: To systematically review existing literature to establish the evidence-base for recommendations on physical modalities for acute to chronic neck pain.
Case Control Studies		
None	--	--
Other		
Skillgate, 2015[136]	600 patients	OBJECTIVE: This study protocol describes a randomized controlled trial aiming to determine the effect of massage and/or exercise therapy on subacute and long-lasting neck pain over the course of 1 year.
Ritchie, 2015[137]	100 patients	OBJECTIVE: This study (StressModEx) will target individuals in the acute stage of injury and address the stress responses associated with the accident or injury (event-related distress) with the aim of improving both physical and mental health outcomes.
Langenfeld, 2015[138]	54 patients	OBJECTIVE: The objective of this study is to compare the short- and long-term effects of manual versus mechanically

Study	N	Objective/Conclusions
		assisted manipulations of the thoracic spine for neck pain patients.
Calamita, 2015[139]	12 patients	OBJECTIVE: The aim of the proposed study is to evaluate the immediate effect of acupuncture on pain, cervical range of motion and electromyographic activity of the upper trapezius muscle in patients with nonspecific neck pain.
Sun, 2014[140]	36 patients	OBJECTIVE: This pilot study was designed to evaluate the feasibility and efficacy of acupuncture at the Houxi (SI3) acupoint for treatment of acute neck pain.
Blodt, 2014[141]	220 patients	OBJECTIVE: The aim of these two pragmatic randomized studies is to evaluate whether an additional app-delivered relaxation is more effective in the reduction of chronic LBP or NP than usual care alone.
Takakurl, 2014[142]	400 patients	OBJECTIVE: Herein, we describe a protocol of an ongoing, single-centre, randomised, placebo-controlled trial which aims to assess whether, in functional neck/shoulder stiffness, acupuncture treatment with skin piercing has a specific effect over two types of placebo: skin-touching plus ritual or ritual alone.
Seo, 2014[143]	60 patients	OBJECTIVE: This pilot study will provide the clinical evidence to evaluate the feasibility and refine the protocol for a full-scale RCT on combined treatment of bee venom acupuncture (BVA) and non-steroidal anti-inflammatory drugs (NSAIDs) in patients with CNP.
Sun, 2013[144]	NR	OBJECTIVE: Electroacupuncture at Jing-jiaji points for neck pain caused by cervical spondylosis: a study protocol for a randomized controlled pilot trial.
Cui, 2013[145]	240 patients	OBJECTIVE: The purpose of the present study is to examine the efficacy and safety of Qishe Pill, a compound traditional Chinese herbal medicine, for neck pain in patients with cervical radiculopathy.
MacPherson, 2013[146]	500 patients	OBJECTIVE: We propose to evaluate the effect of Alexander Technique lessons and acupuncture in a rigorously conducted pragmatic trial with an embedded qualitative study.
Que, 2013[147]	456 patients	OBJECTIVE: The primary aim of this trial is to assess the efficacy and safety of active acupuncture compared with sham acupuncture intervention for neck pain caused by cervical spondylosis.
Liang, 2012[148]	945 patients	OBJECTIVE: We present a randomized controlled trial protocol evaluating the use of acupuncture for CS neck pain, comparing the effects of the optimized acupuncture therapy in real practice compared with sham and shallow acupuncture.
Langevin, 2012[149]	36 patients	OBJECTIVE: The primary objective of this randomised clinical trial is to compare, in terms of pain and disability, a rehabilitation program targeting the opening of intervertebral foramen to a conventional rehabilitation program, for patients presenting acute or subacute cervical radiculopathies.
Ongoing Studies (ClinicalTrials.gov)		
Use of ThermaCare Heat Wraps and	90 patients	Ongoing (estimated completion March 2015). OBJECTIVE: To see if the use of heat at home between physical therapy

Study	N	Objective/Conclusions
Ibuprofen as an Adjunct to Physical Therapy for Neck Pain (NCT02327338)		sessions results in better therapy outcomes in people with acute neck pain.
C7-T1 Epidural Steroid Injections Versus Targeted Injection Via Cervical Epidural Catheter for Treatment of Cervical Radicular Pain (NCT02095197)	140 patients	Ongoing (estimated completion March 2016). OBJECTIVE: The investigators hypothesize that this technique results in superior pain control, decreased medication use, improved function and fewer repeat injections. This data could improve patient safety and affect the evolving treatment guidelines for cervical epidural injections.
Lidocaine Injection Versus Sham Needling in Treating Whiplash Associated Disorder (NCT02060734)	52 patients	Ongoing (estimated completion September 2016). OBJECTIVE: To determine the efficacy of lidocaine injection of trigger points versus subcutaneous injection in patients with subacute whiplash associated disorder following injury.
Surgery Prevention by Transforaminal Injection of Epidural Steroids for Cervical Radicular Pain (NCT02226159)	60 patients	Ongoing (estimated completion 2/1/2017). OBJECTIVE: The purpose of this study is to determine the effectiveness of cervical transforaminal epidural steroid injections in decreasing the need for an operation in patients with cervical radicular pain, otherwise considered to be operative candidates.

Abbreviations not defined above: CAM=Complementary/Alternative Medicine; CR=cervical radiculopathy; CBT=Cognitive Behavior Therapy; CLBP=Chronic Lower Back Pain; CMNP=chronic mechanical neck pain; NPTF=Task Force on Neck Pain; TCM=Traditional Chinese Medicine; NP=neck pain; LBP=lower back pain; WAD=whiplash-associated disorders; NAD=neck pain and associated disorders; CNP=chronic neck pain; CLBP=chronic lower back pain; PrT=Proprioceptive training; QOL=Quality of Life; TE=therapeutic exercise; CNSNP=chronic nonspecific neck pain; MT=massage therapy; SR=systematic review; VR=virtual reality; DDEA=diclofenac diethylamine; CFJ=cervical facet joint; MPS=myofascial pain syndrome; AE=adverse events; SMT=spinal manipulative therapy; CT-guided=cervical transforaminal; CS=cervical spondylosis; N=number of studies/patients; RCTs=randomized controlled trials

Appendix Table B-3. Published and ongoing studies potentially relevant to Research Question 3 *[What is the comparative effectiveness of existing assessment instruments for persons with neck pain with or without radiculopathy for the purpose of prognosis or assessing the effectiveness of therapeutic interventions?]*

Study	N	Objective
Systematic Reviews		
Schellingerhout, 2012[150]	8 studies	OBJECTIVE: To critically appraise and compare the measurement properties of the original versions of neck-specific questionnaires. CONCLUSIONS: Our findings imply that studies of high methodological quality are needed to properly assess the measurement properties of the currently available questionnaires. Until high quality studies are available, we recommend using these questionnaires with caution. There is no need for the development of new neck-specific questionnaires until the current questionnaires have been adequately assessed.
RCTs		
Sundseth, 2015[151]	136 patients	OBJECTIVE: The purpose of this study was to evaluate whether the NDI score correlated with other assessments of quality of life and mental health in a specific group of patients with single-level cervical disc disease and corresponding radiculopathy.
Cohort Studies		
Walton, 2015[152]	198 patients	OBJECTIVE: The purpose of this paper was to explore the utility of the BIPQ for evaluating and classifying uncomplicated mechanical neck pain in the rehabilitation setting.
Wibault, 2014[153]	201 patients	OBJECTIVE: The purpose of this study was to assess how physical impairments, psychosocial factors, and life style habits were associated with neck disability based on the Neck Disability Index (NDI), in patients with cervical radiculopathy scheduled for surgery.
Case-Control Studies		
None	–	–
Other		
None	–	–
Ongoing Studies (ClinicalTrials.gov)		
None	--	--

Abbreviations not defined above: BIPQ= The Brief Illness Perceptions Questionnaire; N=number of studies/patients; NR=not reported; RCTs=randomized controlled trials

Appendix Table B-4. Published and ongoing studies potentially relevant to Research Question 4 *[Are there patient characteristics, biopsychosocial and economic factors, physical examination and imaging findings that predict which patients with new onset axial neck pain are at risk for developing chronic pain, opioid dependence, or other undesirable outcomes?]*

Study	N	Objective
Systematic Reviews		
Walton, 2013[154]	13 studies	OBJECTIVE: As part of the International Consensus on Neck (ICON) project, we sought to establish the general state of knowledge in the area through a structured, systematic review of systematic reviews. CONCLUSIONS: Despite the presence of multiple SR and this overview, there is insufficient evidence to make firm conclusions on many potential prognostic variables.
Rhee, 2013[30]	5 studies	OBJECTIVE: To conduct a systematic review investigating the evidence of (1) efficacy, effectiveness, and safety of nonoperative treatment of patients with cervical myelopathy; (2) whether the severity of myelopathy affects outcomes of nonoperative treatment; and (3) whether specific activities or minor injuries are associated with neurological deterioration in patients with myelopathy or asymptomatic stenosis being treated nonoperatively. CONCLUSIONS: There is a paucity of evidence for nonoperative treatment of cervical myelopathy, and further studies are needed to determine its role more definitively.
Walton, 2013[155]	4 studies	OBJECTIVE: To update a previous review and meta-analysis on risk factors for persistent problems following whiplash secondary to a motor vehicle accident.
Mayer, 2012[156]	21 studies	OBJECTIVE: In comparison, this review summarizes existing evidence from longitudinal studies only. CONCLUSIONS: This analysis of longitudinal studies allowed for new evidence with regard to four cause-effect chains between physical exposures at work and the development of shoulder, neck and neck/shoulder complaints. As outcome variables varied greatly among the included studies, harmonization in studies on musculoskeletal research is desirable.
RCTs		
None	--	--
Cohort Studies		
Cook, 2015[157]	3137 patients	OBJECTIVE: The aim of the present study was to identify predictive characteristics related to patients with neck impairments who have a high risk of a poor prognosis (lowest functional recovery compared to visit utilization) as well as those who are at low risk of a poor prognosis (highest functional recovery compared to visit utilization).
De Pauw, 2015[158]	437 patients	OBJECTIVE: This study was conducted to identify possible prognostic factors to predict drop-out and favorable outcome in patients following a multimodal treatment program at an outpatient rehabilitation clinic.
Aili, 2015[159]	2286 patients	OBJECTIVE: This study aims to study the association between self-reported sleep quality and sickness absence 5 years later, among individuals stratified by presence of lower back pain (LBP) and neck and shoulder pain (NSP).

Study	N	Objective
Smith, 2015[160]	53 patients	OBJECTIVE: Physical and psychological symptoms of individuals with chronic whiplash-associated disorders (WAD) are modulated by successful treatment with cervical radiofrequency neurotomy (cRFN). However, not all individuals respond to cRFN, and it is unknown which clinical features predict successful response to cRFN.
Paksaichol, 2015[161]	559 patients	OBJECTIVE: The etiology of nonspecific neck pain is widely accepted to be multifactorial. Each risk factor has not only direct effects on neck pain but may also exert effects indirectly through other risk factors. This study aimed to test this hypothesized model in office workers.
Kovacs, 2014[162]	422 patients	OBJECTIVE: To assess whether sleep quality (SQ) at baseline is associated with improvement in pain and disability at three months.
Trippolini, 2014[163]	267 patients	OBJECTIVE: To determine whether functional capacity evaluation (FCE) tests predict future work capacity (WC) of patients with whiplash-associated disorders (WADs) grades I and II who did not regain full WC 6 to 12 weeks after injury.
Paksaichol, 2014[164]	559 patients	OBJECTIVE: The purpose of this study was to develop a neck pain risk score for office workers (NROW) to identify office workers at risk for developing nonspecific neck pain with disability.
Gehrt, 2015[165]	740 patients	OBJECTIVE: To examine (1) whether the patients' perceptions of their symptoms immediately after the accident and at 3-month follow-up predict working ability and neck pain at 12-month follow-up and (2) the possible changes in patients' illness perceptions during the follow-up period.
Christensen, 2014[166]	1250 patients	OBJECTIVE: The current study estimated the impact of psychological and social work factors over time on neck pain.
Lee, 2014[167]	96 patients	OBJECTIVE: We compared anatomic differences in the neck and trunk area of young adult patients with chronic NP and control subjects without NP to identify risk factors and predictors.
Wibault, 2014[153]	201 patients	OBJECTIVE: The purpose of this study was to assess how physical impairments, psychosocial factors, and life style habits were associated with neck disability based on the Neck Disability Index (NDI), in patients with cervical radiculopathy scheduled for surgery.
Walton, 2014[168]	50 patients	OBJECTIVE: To investigate the short-term trajectory of recovery from mechanical neck pain, and predictors of trajectory.
Ritchie, 2013[169]	NR	OBJECTIVE: The purpose of this study was to assess the plausibility of developing a clinical prediction rule following whiplash injury.
Vasseljen, 2013[170]	219 patients	OBJECTIVE: In this prospective cohort study we aimed to describe the natural course of acute neck and low back pain in a general population of Norway.
Rasmussen-Barr, 2013[171]	1730 patients	OBJECTIVE: The study sought to examine the gender-specific effects of physical activity level and body mass index on recovery from persistent neck pain (PNP) among citizens of working age in Stockholm, Sweden.

Study	N	Objective
Kasch, 2013[172]	688 patients	OBJECTIVE: An initial stratification of acute whiplash patients into seven risk-strata in relation to 1-year work disability as primary outcome is presented.
Bohman, 2012[173]	680 patients	OBJECTIVE: Therefore, we aimed to develop a prediction model for the recovery of WAD in a cohort of patients who consulted physical therapists within six weeks after the injury
Saavedra-Hernandez, 2012[174]	97 patients	OBJECTIVE: This study examined the relationship of pain, physical impairment, and pain-related fear to disability in individuals with chronic mechanical neck pain.
Dagfinrud, 2013[175]	81 patients	OBJECTIVE: The purpose of this study was to compare the predictive ability of the standardised screening tool Orebro Musculoskeletal Pain Questionnaire (OMPQ) and the clinicians' prognostic assessment in identifying patients with low back pain (LBP) and neck pain at risk for persistent pain and disability at eight weeks follow-up.
Skillgate, 2012[176]	23,794 patients	OBJECTIVE: Our objective was to report on the prevalence and incidence of, as well as the rate of recovery from, bothersome neck pain in men and women of different ages in the general population
Kaaria, 2012[177]	5277 patients	OBJECTIVE: To study the associations of sociodemographic factors, working conditions, lifestyle and previous pain in the spine with new onset chronic neck pain (NP).
Salo, 2012[178]	220 patients	OBJECTIVE: To study whether neck muscle strength or cervical spine mobility values could serve as predictors for future neck pain among originally pain-free working-age subjects during a long period.
Kristman, 2012[179]	22,952 patients	OBJECTIVE: To determine whether radiating spinal pain from the low back, mid back, and neck is associated with future use of health-related benefits and their duration as compared with those with nonradiating spinal pain.
Case-Control Studies		
None	–	–
Other		
None	–	–
Ongoing Studies (ClinicalTrials.gov)		
None	–	–

Abbreviations not defined above: SR=systematic review; NP=neck pain; WAD=whiplash-associated disorders; N=number of studies/patients; NR=not reported; RCTs=randomized controlled trials

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