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Can baseline features predict a reduction in pain and disability following neck-specific exercise in people with chronic non-specific neck pain?: A systematic review and meta-analysis protocol

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ABSTRACT

Introduction Neck-specific exercises (NSEs) are commonly used for the treatment of chronic non-specific neck pain (CNSNP). However, it remains unclear whether baseline features can predict the response to neck-specific exercise (NSE) in people with CNSNP. This systematic review aims to assess whether baseline features such as age, gender, muscle activity, fatigability, endurance and fear of movement can predict pain and disability reduction following a NSE intervention.

Methods and analysis This systematic review and meta-analysis will be reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Protocols guidelines checklist. The Web of Science, PubMed, Scopus, MEDLINE, Embase and CINAHL databases; key journals; and grey literature will be searched up until June 2023, including medical subject heading terms and keywords combinations. Included studies will investigate an association between the baseline features and pain and disability outcomes following NSE in people with CNSNP. Two independent reviewers will oversee the searching, screening, data extraction and assessment of risk of bias. The risk of bias will be assessed using the Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I) and Risk-Of-Bias tool for randomised trials 2 (ROB 2). The quality of evidence will be assessed using the Grading of Recommendations Assessment, Development and Evaluation approach (GRADE). Using standardised forms, details regarding study characteristics, baseline features (predictive factors), intervention, primary outcome and effect size (OR and 95% CI of each predictive factor and p value) will be extracted from included studies. Meta-analyses will be considered, if the studies are sufficiently homogeneous and if three or more studies investigate the same or comparable factors that predict the same response (pain intensity or disability). In the event that less than three studies investigated the same factors, a narrative synthesis will be conducted.

Ethics and dissemination Ethical approval will not be required as this review will be based on published studies. The results of this study will be submitted to a peer-reviewed journal and presented at conferences.

PROSPERO registration number CRD42023408332.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This systematic review examines whether baseline features can predict a reduction in pain and disability following neck-specific exercise in people with chronic non-specific neck pain.
⇒ By including randomised controlled trials (RCTs), non-RCTs and secondary analyses, this systematic review will result in the highest level of evidence for informed decision-making.
⇒ Robust quality assessment criteria will be used to appraise and evaluate the existing literature.
⇒ Potential limitations are likely to be study heterogeneity and a low number of studies, which may prevent meta-analysis from being performed.

INTRODUCTION

More than 80% of individuals experience neck pain and associated disability during their lifetime, with 30%–50% of the general adult population reporting neck pain annually.[1 2] For many people, neck pain is a complex biopsychosocial disorder with associated psychological and clinical features (physical impairments).[3] Neck pain is associated with decreased health-related quality of life, decreased work productivity, daily activity limitations and increased healthcare utilisation.[3] Although most cases of neck pain are generally acute and resolve spontaneously regardless of treatment, some patients go on to develop chronic non-specific neck pain (CNSNP), defined as persistent pain

of 12 weeks or more with no identifiable underlying pathology.[4 5]

People with CNSNP commonly present with clinical features including reduced neck muscle strength, flexors endurance and force steadiness,[6–9] in addition to changes in the quantity and quality of neck movement.[10] Several studies have also documented specific changes in muscle behaviour, including reduced activation of deep neck flexor and extensor muscles,[11–14] reduced directional specificity of neck muscle activation,[15] increased neck muscle co-contraction,[16 17] delayed onset time[18] and increased postural sway to external perturbations.[19] Besides, changes in motor control,[20] changes in neck muscle morphology, including atrophy and fatty infiltration[21 22] and changes in muscle fatigability have also been described.[23]

Clinical practice guidelines recommendations for CNSNP management suggest that there is strong evidence to support exercise for pain relief.[24] Specifically, neck-specific exercises (NSEs), targeting the muscles in the neck region, are specifically recommended for the management of CNSNP, although based on weak evidence.[25] A wide range of NSEs have been described, including strengthening and/or endurance exercises for the neck muscles,[26 27] specific motor control training targeting the deep neck flexors,[28] craniocervical flexion training based on the craniocervical flexion test (CCFT),[29] neck proprioception training[29] and isometric neck exercises.[30]

Several studies have shown that neck-specific exercise (NSE) can revert some of the neuromuscular disturbances described in people with CNSNP,[11 31–33] improving neuromuscular coordination,[31] muscle activation[11] and performance.[32] For example, NSE significantly increases the activity of the deep neck flexors and decreases sternocleidomastoid and anterior scalene activity during performance of the CCFT.[11] NSE also positively influences joint position error in rotation (left and right) and extension.[34] In addition, the endurance time of deep flexor muscle is significantly increased following NSE.[35] Two systematic reviews have also demonstrated that NSEs are effective in reducing pain intensity and disability for patients with CNSNP.[36 37]

Clinical practice guidelines recommend evaluating motor control and strength impairments and subclassifying patients accordingly.[24 38–40] Since patients may have different treatment responses due to different baseline features, it may mean that they are more responsive to particular forms of exercise. Bahat *et al* investigated the association between response to NSE and gender and age in people with CNSNP and found that women were more likely to have poorer responses than men.[41] Another study indicated that duration of pain was the strongest predictor of reduction in disability scores following the McKenzie exercises.[42] While Daher *et al* revealed three significant physiological features (symptom duration, neck flexor endurance and absence of referred pain) that may be important predictors of the therapeutic success rate of NSE when combined with aerobic exercise.[43] However, we do not know which baseline features (demographic, clinical, physiological) are the most predictive of a reduction in pain and disability in people with CNSNP. Therefore, further analysis of whether these baseline features are predictive of positive pain and disability outcomes is warranted and could become an important part of personalising patient care in the future.[41] The main objective of this systematic review will be to synthesise the current literature to determine whether baseline features can predict pain and disability reduction following a NSE intervention in people with CNSNP.

METHODS

This systematic review and meta-analysis will be reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Protocols guidelines checklist (see online supplemental file 1).[44] The participants, interventions, comparators, outcomes and study design (PICOS) framework has been used to inform the eligibility criteria of studies.[45]

Inclusion criteria

Population

Studies will be included if they investigate participants (age between 18 and 55 years) experiencing CNSNP≥3 months, defined as pain perceived anywhere in the posterior region of the cervical spine, from the superior nuchal line to the first thoracic spinous process, with or without radiation to the head, trunk and upper limbs.[46] Studies that include people with specific causes of neck pain and a specific pathoanatomical diagnosis (eg, nerve root compression, trauma, malignancy, infection), inflammatory arthritis (eg, rheumatoid arthritis, spondyloarthritis) or neurological diseases (eg, multiple sclerosis) will be excluded.[47]

Intervention

All physical exercises targeting the muscles in the neck region will be classified as NSEs, such as strengthening and/or endurance exercises for the neck muscles,[26 27] specific motor control training targeting the deep neck flexors,[28] craniocervical flexion training based on CCFT,[29] neck proprioception training[29] and isometric neck exercise.[30] Exercises that do not meet the definition of NSE, such as mental exercises and respiratory exercises, will be excluded from the study.

Comparators

In this systematic review, there will be no comparators. Randomised controlled trials (RCTs) and non-RCTs will be included when at least one group is treated with NSEs.

Exposure and outcome measures

This systematic review aims to investigate the baseline features of people with CNSNP in association with their response to NSE.

The baseline features such as the following will be examined and included in this study:

1. Demographic features: age, gender, body mass index, craniovertebral angle, duration of symptom, education level, income level and occupation.
2. Clinical features: muscle activity, fatigability/endurance, range of motion, strength, joint position sense, motor control (eg, CCFT), tenderness (palpation), pain intensity (measured by Visual Analogue Scale[43] and Numerical Rating Scale[48]) and disability (measured using the Neck Disability Index[43 48] and the Patient Specific Function Scale[15]).
3. Psychosocial features: including quality of life (measured using the 36-Item Short Form Survey[15]), anxiety and depression (measured using the Hospital Anxiety and Depression Scale[49]), fear avoidance (measured using Fear-Avoidance Beliefs Questionnaire[15]), and kinesiophobia (measured using the Tampa Scale of Kinesiophobia[50]).

All included studies must include measures of pain intensity and/or disability as outcomes.

Study design

The study shall include RCTs and non-RCTs (eg, cohort studies) including secondary analyses. Included studies will have investigated whether baseline features predict response to NSE in people with CNSNP. The studies will identify baseline features and report a statistical association (or lack of association) with an outcome (disability and pain intensity). Only published, peer-reviewed articles will be considered in this study.

Exclusion criteria

Exclusion criteria are as follows: (1) studies that do not include NSEs; (2) studies that do not pertain to people with CNSNP; (3) studies that do not clarify the baseline features of participants; (4) studies where pain intensity and disability outcomes were not measured; (5) studies that do not investigate baseline features to predict responses to NSE interventions; (6) manuscripts that are published in a language other than English and Chinese.

Information sources

Comprehensive searches of the following databases will be completed by the lead reviewer (ZC), from inception to June 2023: MEDLINE (OVID Interface), Embase (OVID Interface), Web of Science (All Databases), Scopus, CINAHL (EBSCO interface) and PubMed. Handsearching through checking reference lists and grey literature searching through the main sources, including British National bibliography for report literature and open Grey, will also be conducted. Authors' lists of eligible articles will be explored.

Search strategy

Following discussion and in agreement with all authors and a health sciences librarian, the search strategy was derived, including medical subject heading (MeSH) terms and keywords combinations. Keywords and their synonyms were identified and entered into databases using the Boolean terms AND/OR. The search process was streamlined by piloting the search strategy with MEDLINE (OVID Interface), confirming MeSH terms and checking relevant article search terms. The same strategy will be adapted for use with other databases (see online supplemental file 2).

Data management

Comprehensive searches on the afore-mentioned databases will be carried out by the first author (ZC). Articles resulting from the search process will be downloaded to EndNote (V.9 or later) software (Clarivate Analytics) and duplicates identified and deleted.

Study selection

Two reviewers (ZC and EEC) will independently screen titles and abstracts against the predetermined inclusion and exclusion criteria. Studies will be categorised into include, exclude or undecided, and for articles meeting the inclusion criteria or where uncertainty exists, full articles will be downloaded. Any disagreements will be first discussed by two reviewers (ZC and EEC), and where consensus is not reached, an independent reviewer will be consulted (JD). Once the above procedure has been completed and full texts have been collated, the screening process will be repeated. Information on and reasons for excluding studies will then be reported.

Data items

Table 1 summarises the relevant data to be extracted from the included studies. The data extraction form will initially be piloted to ensure relevant data is being extracted and amendments made as appropriate prior to final data extraction. This will be completed independently by both reviewers (ZC and EEC) to maintain autonomy.

Risk of bias

RCTs and non-RCTs are likely to be included in this systematic review. The Cochrane risk-of-bias tool for randomised trials (ROB 2) will be used to assess the risk of bias in RCTs.[51] The risk-of-bias tool for non-randomised studies of interventions (ROBINS-I) will be used to assess risk of bias for non-randomised studies.[52] Each study will be independently assessed by the two reviewers (ZC and EEC) using the appropriate tool and risk-of-bias judgements recorded for the study overall. Where a consensus cannot be found, a third author (JD) will be consulted. Cohen's kappa coefficient will be calculated to explore agreement between the two reviewers.

Data synthesis

Meta-analyses will be considered if three or more sufficiently homogeneous studies investigated the same or comparable baseline features that predicted the same response (change in pain intensity and/or disability). Statistical heterogeneity will be assessed using the I^2 statistics. Due to the heterogeneity of predictive baseline features, the random effects model will likely be used for meta-analysis. We will report on mean effect size and heterogeneity of effect size on meta-analysis.[53 54]

Table 1 Overview of data items to be extracted from included studies

Content	Data items
General study information	Authors Title Year
Study characteristics	Study design Sample size (both groups)
Baseline features/ predictive factors	1. Demographic features: age, gender, body mass index, craniovertebral angle, duration of symptom, education level, income level and occupation. 2. Clinical features: muscle activity, fatigability/endurance, range of motion, strength, joint position sense, motor control (eg, craniocervical flexion test), tenderness (palpation), pain intensity (measured by Visual Analogue Scale[43] and Numerical Rating Scale[48]) and disability (measured using the Neck Disability Index[43 48] and the Patient Specific Function Scale[15]). 3. Psychosocial features: quality of life (measured using the 36-Item Short Form Survey[15]), anxiety and depression (Hospital Anxiety and Depression Scale[49]), fear avoidance (measured using Fear-Avoidance Beliefs Questionnaire[15]) and kinesiophobia (measured using the Tampa Scale of Kinesiophobia[50]).
Intervention	Neck-specific exercises procedure (eg, strength, endurance and motor control exercises targeting at neck) Intervention period
Primary outcome	Pain intensity Disability
Effect size	OR, 95% CI OR of each predictive feature and p value from included studies

When less than three studies investigate the same or comparable baseline features that predict the same response (change in pain intensity or disability), a narrative synthesis will be conducted taking into account classifying predictive baseline features. We will extract and report the number of people, predictive baseline features, OR, 95% CI OR of each predictive features and p values from included studies. Associations between predictive baseline features and outcomes will be defined as a significant association between predictive baseline features and outcomes ($p \leq 0.05$) or an insignificant association between predictive baseline features and outcomes ($p > 0.05$). We will classify the extracted predictive baseline features and a synthesised analysis will be performed for the same classification of predictive features. The remaining predictors that are not classified will be described separately.

Metabias

To eliminate any chance of publication bias, grey literature and conference papers will be searched.

Confidence in cumulative evidence

In order to evaluate the quality of evidence, the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach will be used.[55] The GRADE approach supports reporting on both the size of the effect and certainty of evidence.[56] Reporting will use statements recommended by the GRADE working group.[57] The size of effect will be reported using four categories: large effect; moderate effect; small important effect; and trivial, small unimportant effect or no effect. Similarly, the four categories for certainty of evidence will be high, moderate, low and very low. The quality of evidence will be assessed for each of the individual primary outcome measures included in the PICOS.[58] As per guidelines around assessing certainty of evidence, the initial assessment will begin by classifying the study design. If relevant studies are RCTs, the body of evidence begins as high certainty, whereas for non-randomised studies, the body of evidence will be considered as low certainty.[59] Ratings can then be lowered or raised based on further assessment of eight further domains. Risk of bias, inconsistency, indirectness, imprecision and publication bias are reasons for lowering quality of evidence. Conversely, large effect size, dose–response gradient and plausible confounding biases that underestimate the effect size are reasons to upgrade the certainty of evidence.[60]

Patient and public involvement

The research question in this study forms part of a larger discussion within our patient and public involvement meetings. Patients and the public will not participate in the data collection and analysis of the review. However, the results and findings of the study will be shared with this group and at other public engagement events.

Clinical implications

Neck pain is a highly prevalent condition, leading to enormous personal, social and financial costs.[61] Previous studies have confirmed that NSE is effective for reducing pain intensity and disability in people with CNSNP.[31 37] It is possible, however, that NSE could be more effective for specific groups of people with CNSNP. This systematic review aims to confirm if baseline features are associated with reduced pain and disability following NSE interventions in order to target management, optimise outcomes and ensure that the right patient receives the appropriate care.

ETHICS AND DISSEMINATION

This study will not require ethics since no patient data will be collected. The results of this review will be submitted for publication in a peer-reviewed journal and presented at conferences.

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Contributors EEC, JD and DF were supervisors. ZC, EEC, DF and JD contributed to the systematic review topic. ZC drafted the protocol with guidance and feedback from EEC, DF and JD. EEC, DF and JD reviewed the manuscript and commented on the protocol. EEC acted as a second reviewer. All authors have approved and contributed to the final manuscript.

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REFERENCES

1 Hogg-Johnson S, van der Velde G, Carroll LJ, *et al*. The burden and determinants of neck pain in the general population: results of the bone and joint decade 2000-2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther* 2009;32:S46–60.
2 Cassidy JD, Carroll LJ, Côté P. The Saskatchewan health and back pain survey. The prevalence of neck pain and related disability in Saskatchewan adults. *Spine (Phila Pa 1976)* 1998;23:1860–6;
3 Côté P, Wong JJ, Sutton D, *et al*. Management of neck pain and associated disorders: A clinical practice guideline from the Ontario protocol for traffic injury management (OPTIMA) collaboration. *Eur Spine J* 2016;25:2000–22.
4 Viikari-Juntura E, Martikainen R, Luukkonen R, *et al*. Longitudinal study on work related and individual risk factors affecting radiating neck pain. *Occup Environ Med* 2001;58:345–52.
5 Martimbianco ALC, Porfírio GJ, Pacheco RL, *et al*. Transcutaneous electrical nerve stimulation (TENS) for chronic neck pain. *Cochrane Database Syst Rev* 2019;12:CD011927.
6 Miranda IF, Wagner Neto ES, Dhein W, *et al*. Individuals with chronic neck pain have lower neck strength than healthy controls: A systematic review with meta-analysis. *J Manipulative Physiol Ther* 2019;42:608–22.
7 Guru K, Praveen N, Selvamani K. Isometric endurance of neck muscles and muscles for Scapular positioning in individuals with and without postural neck pain. *IJAHSP* 2013;11.
8 Muceli S, Farina D, Kirkesola G, *et al*. Reduced force steadiness in women with neck pain and the effect of short term vibration. *J Electromyogr Kinesiol* 2011;21:283–90.
9 Arvanitidis M, Falla D, Sanderson A, *et al*. Does pain influence force steadiness? A protocol for a systematic review. *BMJ Open* 2021;11:e042525.
10 Kapreli E, Vourazanis E, Strimpakos N. Neck pain causes respiratory dysfunction. *Med Hypotheses* 2008;70:1009–13.
11 Jull GA, Falla D, Vicenzino B, *et al*. The effect of therapeutic exercise on activation of the deep Cervical Flexor muscles in people with chronic neck pain. *Man Ther* 2009;14:696–701.
12 Jull GA, O'Leary SP, Falla DL. Clinical assessment of the deep Cervical Flexor muscles: the Craniocervical flexion test. *J Manipulative Physiol Ther* 2008;31:525–33.
13 Schomacher J, Falla D. Function and structure of the deep Cervical Extensor muscles in patients with neck pain. *Man Ther* 2013;18:360–6.
14 Falla DL, Jull GA, Hodges PW. Patients with neck pain demonstrate reduced electromyographic activity of the deep Cervical Flexor muscles during performance of the Craniocervical flexion test. *Spine (Phila Pa 1976)* 2004;29:2108–14.
15 Falla D, Lindstrøm R, Rechter L, *et al*. Effectiveness of an 8-week exercise programme on pain and specificity of neck muscle activity in patients with chronic neck pain: a randomized controlled study. *Eur J Pain* 2013;17:1517–28.
16 Cheng C-H, Cheng H-YK, Chen CP-C, *et al*. Altered Co-contraction of Cervical muscles in young adults with chronic neck pain during voluntary neck motions. *J Phys Ther Sci* 2014;26:587–90.
17 Lindstrøm R, Schomacher J, Farina D, *et al*. Association between neck muscle Coactivation, pain, and strength in women with neck pain. *Man Ther* 2011;16:80–6.
18 Hsu W-L, Chen CP, Nikkhoo M, *et al*. Fatigue changes neck muscle control and deteriorates postural stability during arm movement perturbations in patients with chronic neck pain. *Spine J* 2020;20:530–7.
19 Juul-Kristensen B, Clausen B, Ris I, *et al*. Increased neck muscle activity and impaired balance among females with whiplash-related chronic neck pain: a cross-sectional study. *J Rehabil Med* 2013;45:376–84.
20 Tsang SMH, So BCL, Lau RWL, *et al*. Effects of combining Ergonomic interventions and motor control exercises on muscle activity and Kinematics in people with work-related neck-shoulder pain. *Eur J Appl Physiol* 2018;118:751–65.
21 Elliott JM, Courtney DM, Rademaker A, *et al*. The rapid and progressive degeneration of the Cervical Multifidus in whiplash: an MRI study of fatty infiltration. *Spine (Phila Pa 1976)* 2015;40:E694–700.
22 De Pauw R, Coppieters I, Kregel J, *et al*. Does muscle morphology change in chronic neck pain patients? - A systematic review. *Man Ther* 2016;22:42–9.
23 Falla D. Unravelling the complexity of muscle impairment in chronic neck pain. *Man Ther* 2004;9:125–33.
24 Childs JD, Cleland JA, Elliott JM, *et al*. Neck pain: clinical practice guidelines linked to the International classification of functioning, disability, and health from the orthopedic section of the American physical therapy Association. *J Orthop Sports Phys Ther* 2008;38:A1–34.
25 Price J, Rushton A, Tyros V, *et al*. Expert consensus on the important chronic non-specific neck pain motor control and segmental exercise and dosage variables: an international E-Delphi study. *PLoS ONE* 2021;16:e0253523.
26 O'Leary S, Jull G, Kim M, *et al*. Training mode-dependent changes in motor performance in neck pain. *Arch Phys Med Rehabil* 2012;93:1225–33.
27 Chiu TTW, Lam T-H, Hedley AJ. A randomized controlled trial on the efficacy of exercise for patients with chronic neck pain. *Spine (Phila Pa 1976)* 2005;30:E1–7.
28 Khosrokiani Z, Letafatkar A, Sokhanguei Y. Long-term effect of direction-movement control training on female patients with chronic neck pain. *J Bodyw Mov Ther* 2018;22:217–24.
29 Gallego Izquierdo T, Pecos-Martin D, Lluch Girbés E, *et al*. Comparison of Cranio-Cervical flexion training versus Cervical Proprioception training in patients with chronic neck pain: a randomized controlled clinical trial. *J Rehabil Med* 2016;48:48–55.

30 Chung S, Jeong YG. Effects of the Craniocervical flexion and Isometric neck exercise compared in patients with chronic neck pain: A randomized controlled trial. *Physiother Theory Pract* 2018;34:916–25.
31 Blomgren J, Strandell E, Jull G, *et al*. Effects of deep Cervical Flexor training on impaired physiological functions associated with chronic neck pain: a systematic review. *BMC Musculoskelet Disord* 2018;19:415.
32 Lluch E, Schomacher J, Gizzi L, *et al*. Immediate effects of active Cranio-Cervical flexion exercise versus passive Mobilisation of the upper Cervical spine on pain and performance on the Cranio-Cervical flexion test. *Man Ther* 2014;19:25–31.
33 Jull GFD, Treleaven J, O'Leary S. *Management of neck pain disorders*. London: Elsevier, 2018.
34 Jull G, Falla D, Treleaven J, *et al*. Retraining Cervical joint position sense: the effect of two exercise regimes. *J Orthop Res* 2007;25:404–12.
35 Ghaderi F, Jafarabadi MA, Javanshir K. The clinical and EMG assessment of the effects of stabilization exercise on nonspecific chronic neck pain: A randomized controlled trial. *J Back Musculoskelet Rehabil* 2017;30:211–9.
36 Tsiringakis G, Dimitriadis Z, Triantafylloy E, *et al*. Motor control training of deep neck Flexors with pressure Biofeedback improves pain and disability in patients with neck pain: A systematic review and meta-analysis. *Musculoskelet Sci Pract* 2020;50:S2468-7812(20)30086-2.
37 Villanueva-Ruiz I, Falla D, Lascurain-Aguirrebeña I. Effectiveness of specific neck exercise for nonspecific neck pain; usefulness of strategies for patient selection and tailored exercise—A systematic review with meta-analysis. *Phys Ther* 2022;102:pzab259.
38 Blanpied PR, Gross AR, Elliott JM, *et al*. Neck pain: revision 2017. *J Orthop Sports Phys Ther* 2017;47:A1–83.
39 Bier JD, Scholten-Peeters WGM, Staal JB, *et al*. Clinical practice guideline for physical therapy assessment and treatment in patients with nonspecific neck pain. *Phys Ther* 2018;98:162–71.
40 Monticone M, Iovine R, de Sena G, *et al*. The Italian society of physical and rehabilitation medicine (SIMFER) recommendations for neck pain. *G Ital Med Lav Ergon* 2013;35:36–50.
41 Sarig Bahat H, Hadar D, Treleaven J. Predictors for positive response to home Kinematic training in chronic neck pain. *J Manipulative Physiol Ther* 2020;43:779–90.
42 May S, Gardiner E, Young S, *et al*. Predictor variables for a positive long-term functional outcome in patients with acute and chronic neck and back pain treated with a McKenzie approach: A secondary analysis. *J Man Manip Ther* 2008;16:155–60.
43 Daher A, Carel RS, Dar G. Neck pain clinical prediction rule to prescribe combined aerobic and neck-specific exercises: secondary analysis of a randomized controlled trial. *Phys Ther* 2022;102:pzab269.
44 Moher D, Shamseer L, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015;4:1.
45 Shamseer L, Moher D, Clarke M, *et al*. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. *BMJ* 2015;350:g7647.
46 Misailidou V, Malliou P, Beneka A, *et al*. Assessment of patients with neck pain: a review of definitions, selection criteria, and measurement tools. *J Chiropr Med* 2010;9:49–59.
47 Domingues L, Cruz EB, Pimentel-Santos FM, *et al*. Prognostic factors for recovery and non-recovery in patients with non-specific neck pain: a protocol for a systematic literature review. *BMJ Open* 2018;8:e023356.
48 Pool JJM, Ostelo RWJG, Knol D, *et al*. Are psychological factors Prognostic indicators of outcome in patients with sub-acute neck pain *Man Ther* 2010;15:111–6.
49 Blozik E, Laptinskaya D, Herrmann-Lingen C, *et al*. Depression and anxiety as major determinants of neck pain: a cross-sectional study in general practice. *BMC Musculoskelet Disord* 2009;10:13.
50 Asiri F, Reddy RS, Tedla JS, *et al*. Kinesiophobia and its correlations with pain, Proprioception, and functional performance among individuals with chronic neck pain. *PLoS One* 2021;16:e0254262.
51 Farrah K, Young K, Tunis MC, *et al*. Risk of bias tools in systematic reviews of health interventions: an analysis of PROSPERO-registered protocols. *Syst Rev* 2019;8:280.
52 Sterne JA, Hernán MA, Reeves BC, *et al*. n.d. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ*:i4919.
53 Borenstein M, Hedges LV, Higgins JPT, *et al*. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods* 2010;1:97–111.
54 Borenstein M, Higgins JPT, Hedges LV, *et al*. Basics of meta-analysis: I(2) is not an absolute measure of heterogeneity. *Res Synth Methods* 2017;8:5–18.
55 Guyatt G, Oxman AD, Akl EA, *et al*. GRADE guidelines: 1. introduction-GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011;64:383–94.
56 Matthews D, Elgueta Cancino E, Falla D, *et al*. Exploring pain interference with motor skill learning in humans: a protocol for a systematic review. *BMJ Open* 2021;11:e045841.
57 Santesso N, Glenton C, Dahm P, *et al*. GRADE guidelines 26: informative statements to communicate the findings of systematic reviews of interventions. *J Clin Epidemiol* 2020;119:126–35.
58 Guyatt G, Oxman AD, Sultan S, *et al*. GRADE guidelines: 11. making an overall rating of confidence in effect estimates for a single outcome and for all outcomes. *J Clin Epidemiol* 2013;66:151–7.
59 Schünemann HJ, Cuello C, Akl EA, *et al*. GRADE guidelines: 18. How ROBINS-I and other tools to assess risk of bias in Nonrandomized studies should be used to rate the certainty of a body of evidence. *J Clin Epidemiol* 2019;111:105–14.
60 Balshem H, Helfand M, Schünemann HJ, *et al*. GRADE guidelines: 3. rating the quality of evidence. *J Clin Epidemiol* 2011;64:401–6.
61 GBD 2015 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 310 diseases and injuries, 1990-2015: a systematic analysis for the global burden of disease study 2015. *Lancet* 2016;388:1545–602.

Supplementary file 1:

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item	Page Number
ADMINISTRATIVE INFORMATION			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	N/A
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	1
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	5
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	N/A
Support:			
Sources	5a	Indicate sources of financial or other support for the review	5
Sponsor	5b	Provide name for the review funder and/or sponsor	N/A
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	N/A
INTRODUCTION			
Rationale	6	Describe the rationale for the review in the context of what is already known	1,2
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	2
METHODS			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	2,3
Information	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other	3

sources		grey literature sources) with planned dates of coverage	
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	3 Supplementary File 2
Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	3
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility, and inclusion in meta-analysis)	3
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	3
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	3 Table 1
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	2,3 Table 1
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	3
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ)	3,4
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	4
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	4

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.

Supplementary file 2: Search strategy

Search strategy in Ovid MEDLINE(R) ALL

1 Neck Pain/
2 neck pain.mp.
3 cervical pain.mp.
4 1 or 2 or 3
5 Exercise Test/ or Exercise Therapy/ or Exercise/ or exercis*.mp.
6 train*.mp.
7 therap*.mp.
8 intervention.mp.
9 Rehabilitation/ or rehabilitation.mp.
10 Muscle Weakness/ or Muscle Strength/ or muscle*.mp. or Muscle, Skeletal/
11 cervical extensor*.mp.
12 cervical flexor*.mp.
13 craniocervical flexor*.mp.
14 craniocervical extensor*.mp.
15 neck flexor*.mp.
16 neck extensor*,.mp.
17 craniocervical flexion test.mp.
18 Proprioception/ or propriocept*.mp.
19 motor control.mp.
20 strength*.mp.
21 Endurance Training/ or endurance.mp.
22 neck-specific*.mp.
23 stabili*.mp.
24 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25 predict*.mp.
26 factor*.mp.
27 Association/ or associat*.mp.
28 25 or 26 or 27
29 Radiculopathy/ or radiculopath*.mp.
30 cervicogenic headache.mp.
31 Whiplash Injuries/ or whiplash.mp.
32 temporomandibular joint disorder.mp. or Temporomandibular Joint Disorders/
33 29 or 30 or 31 or 32
34 Disability Evaluation/ or disability evaluation*.mp.
35 recovery of function.mp. or "Recovery of Function"/
36 pain measurement*.mp. or Pain Measurement/
37 physical functional performance*.mp. or Physical Functional Performance/
38 34 or 35 or 36 or 37
39 4 and 24 and 28 and 38
40 39 not 33

41 limit 40 to (("adolescent (13 to 18 years)" or "adult (19 to 44 years)" or "middle age (45 to 64 years)") and (chinese or english))

Search strategy in Embase

1 Neck Pain/
2 neck pain.mp.
3 cervical pain.mp.
4 1 or 2 or 3
5 Exercise Test/ or Exercise Therapy/ or Exercise/ or exercis*.mp.
6 train*.mp.
7 therap*.mp.
8 intervention.mp.
9 Rehabilitation/ or rehabilitation.mp.
10 Muscle Weakness/ or Muscle Strength/ or muscle*.mp. or Muscle, Skeletal/
11 cervical extensor*.mp.
12 cervical flexor*.mp.
13 craniocervical flexor*.mp.
14 craniocervical extensor*.mp.
15 neck flexor*.mp.
16 neck extensor*,.mp.
17 craniocervical flexion test.mp.
18 Proprioception/ or propriocept*.mp.
19 motor control.mp.
20 strength*.mp.
21 Endurance Training/ or endurance.mp.
22 neck-specific*.mp.
23 stabili*.mp.
24 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23
25 predict*.mp.
26 factor*.mp.
27 Association/ or associat*.mp.
28 25 or 26 or 27
29 Radiculopathy/ or radiculopath*.mp.
30 cervicogenic headache.mp.
31 Whiplash Injuries/ or whiplash.mp.
32 temporomandibular joint disorder.mp. or Temporomandibular Joint Disorders/
33 29 or 30 or 31 or 32
34 Disability Evaluation/ or disability evaluation*.mp.
35 recovery of function.mp. or "Recovery of Function"/
36 pain measurement*.mp. or Pain Measurement/
37 physical functional performance*.mp. or Physical Functional Performance/
38 34 or 35 or 36 or 37
39 4 and 24 and 28 and 38

40 39 not 33
41 limit 40 to ((chinese or english) and adult <18 to 64 years>)

Search strategy in Web of science
1 "neck pain" (Topic) or "cervical pain" (Topic)
2 exercise* (Topic) or train* (Topic) or therap* (Topic) or intervention (Topic) or rehabilitation (Topic) or muscle* (Topic) or "cervical flexor*" (Topic) or "cervical extensor*" (Topic) or "craniocervical flexor*" (Topic) or "craniocervical extensor*" (Topic) or "neck flexor*" (Topic) or "neck extensor*" (Topic) or "craniocervical flexion test" (Topic) or propriocept* (Topic) or "motor control" (Topic) or strength* (Topic) or endurance (Topic) or "neck-specific*" (Topic) or stabili* (Topic)
3 predict* (Topic) or factor* (Topic) or associat* (Topic)
4 "disability evaluation*" (Topic) or "recovery of function" (Topic) or associat* (Topic) or "pain measurement*" (Topic) or "physical functional performance*" (Topic)
5 #1 AND #2 AND #3 AND #4
6 radiculopath* (Topic) or "cervicogenic headache" (Topic) or whiplash (Topic) or "temporomandibular joint disorder" (Topic)
7 #5 NOT #6 and English or Chinese (Languages) and Adult (Search within topic)

Search strategy in PubMed
(((((("neck pain") OR ("cervical pain")) AND ((((((((((((((((((exercise*) OR (train*)) OR (therap*)) OR (intervention)) OR (rehabilitation)) OR (muscle*)) OR ("cervical flexor*")) OR ("cervical extensor*")) OR ("craniocervical flexor*")) OR ("craniocervical extensor*")) OR ("neck flexor*")) OR ("neck extensor*")) OR ("craniocervical flexion test")) OR (propriocept*)) OR ("motor control")) OR (strength*)) OR (endurance)) OR ("neck-specific*")) OR (stabili*))) AND (((predict*) OR (factor*)) OR (associat*))) AND ((((("disability evaluation*") OR ("recovery of function")) OR ("pain measurement*")) OR ("physical functional performance*"))) NOT ((((radiculopath*) OR ("cervicogenic headache")) OR (whiplash)) OR ("temporomandibular joint disorder")) Filters: Chinese, English, Adult: 19-44 years, Middle Aged: 45-64 years

Search strategy in Scopus
(((TITLE-ABS-KEY (exercise*) OR TITLE-ABS-KEY (train*) OR TITLE-ABS-KEY (therap*) OR TITLE-ABS-KEY (intervention) OR TITLE-ABS-KEY (rehabilitation) OR TITLE-ABS-KEY (muscle*) OR TITLE-ABS-KEY ("cervical flexor*") OR TITLE-ABS-KEY ("cervical extensor*") OR TITLE-ABS-KEY ("craniocervical flexor*") OR TITLE-ABS-KEY ("craniocervical extensor*") OR TITLE-ABS-KEY ("neck flexor*") OR TITLE-ABS-KEY ("neck extensor*") OR TITLE-ABS-KEY ("craniocervical flexion test") OR TITLE-ABS-KEY (propriocept*) OR TITLE-ABS-KEY ("motor control") OR TITLE-ABS-KEY (strength*) OR TITLE-ABS-KEY (endurance) OR TITLE-ABS-KEY ("neck-specific*") OR TITLE-ABS-KEY (stabili*))) AND ((TITLE-ABS-KEY ("neck pain") OR TITLE-ABS-KEY ("cervical pain"))) AND ((TITLE-ABS-KEY (predict*) OR TITLE-ABS-KEY (factor*) OR TITLE-ABS-KEY (associat*))) AND ((TITLE-ABS-KEY ("disability

evaluation*") OR TITLE-ABS-KEY ("recovery of function") OR TITLE-ABS-KEY ("pain measurement*") OR TITLE-ABS-KEY ("physical functional performance*")))) AND NOT ((TITLE-ABS-KEY ("radiculopath*") OR TITLE-ABS-KEY ("cervicogenic headache") OR TITLE-ABS-KEY (whiplash) OR TITLE-ABS-KEY ("temporomandibular joint disorder"))) AND (LIMIT-TO (LANGUAGE , "Chinese") OR LIMIT-TO (LANGUAGE , "English")) AND (LIMIT-TO (EXACTKEYWORD , "Adult"))

Search strategy in CINAHL Plus

1 TX "neck pain" OR TX "cervical pain"
2 TX exercise* OR TX train* OR TX therap* OR TX intervention OR TX rehabilitation OR TX muscle* OR TX "cervical flexor*" OR TX "cervical extensor*" OR TX "craniocervical flexor*" OR TX "craniocervical extensor*" OR TX "neck flexor*" OR TX "neck extensor*" OR TX "craniocervical flexion test" OR TX propriocept* OR TX "motor control" OR TX strength* OR TX endurance OR TX endurance OR TX stabili*
3 TX predict* OR TX factor* OR TX associat*
4 TX "disability evaluation*" OR TX "recovery of function" OR TX "pain measurement*" OR TX "physical functional performance*"
5 S1 AND S2 AND S3 AND S4
6 TX radiculopath* OR TX "cervicogenic headache" OR TX whiplash OR TX "temporomandibular joint disorder"
7 TX S5 NOT TX S6
8 TX S5 NOT TX S6 limit 7 to (("adolescent (13 to 18 years)" or "adult (19 to 44 years)" or "middle age (45 to 64 years)") and (chinese or english))