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Chen, Ziyan; Falla, Deborah; Elgueta Cancino, Edith; A Deane, Janet

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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

Ziyan Chen [1], Deborah Falla [1], Edith Elgueta Cancino [1,2], Janet A Deane [1]

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For numbered affiliations see end of article.

Correspondence to
Ziyan Chen;
zxc207@student.bham.ac.uk

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.

Author affiliations
[1]Centre of Precision Rehabilitation for Spinal Pain (CPR Spine), School of Sport, Exercise and Rehabilitation Sciences, University of Birmingham, Birmingham, UK
[2]Exercise and Rehabilitation Sciences Institute, School of Physical Therapy, Faculty of Rehabilitation Sciences, Universidad Andrés Bello, Santiago, Chile

Twitter Ziyan Chen @ZiyanCh49156459, Deborah Falla @Deb_Falla, Edith Elgueta Cancino @edirroz and Janet A Deane @Dr Janet Deane

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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ORCID iDs
Ziyan Chen http://orcid.org/0000-0003-1406-8068
Deborah Falla http://orcid.org/0000-0003-1689-6190
Edith Elgueta Cancino http://orcid.org/0000-0003-4439-7305
Janet A Deane http://orcid.org/0000-0002-0710-2881

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