

Comparative effectiveness of physical exercise interventions for chronic non-specific neck pain: a systematic review with network meta-analysis of 40 randomised controlled trials

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ABSTRACT

Objective To compare the effectiveness of different physical exercise interventions for chronic non-specific neck pain.

Design Systematic review and network meta-analysis.

Data sources Electronic databases: AMED, CINAHL, Cochrane Central Register of Controlled Trials, Embase, MEDLINE, Physiotherapy Evidence Database, PsycINFO, Scopus and SPORTDiscus.

Eligibility criteria Randomised controlled trials (RCTs) describing the effects of any physical exercise intervention in adults with chronic non-specific neck pain.

Results The search returned 6549 records, 40 studies were included. Two networks of pairwise comparisons were constructed, one for pain intensity (n=38 RCTs, n=3151 participants) and one for disability (n=29 RCTs, n=2336 participants), and direct and indirect evidence was obtained. Compared with no treatment, three exercise interventions were found to be effective for pain and disability: motor control (Hedges' *g*, pain −1.32, 95% CI: −1.99 to −0.65; disability −0.87, 95% CI: −1.45 to −0.29), yoga/Pilates/Tai Chi/Qigong (pain −1.25, 95% CI: −1.85 to −0.65; disability −1.16, 95% CI: −1.75 to −0.57) and strengthening (pain −1.21, 95% CI: −1.63 to −0.78; disability −0.75, 95% CI: −1.28 to −0.22). Other interventions, including range of motion (pain −0.98 CI: −2.51 to 0.56), balance (pain −0.38, 95% CI: −2.10 to 1.33) and multimodal (three or more exercises types combined) (pain −0.08, 95% CI: −1.70 to 1.53) exercises showed uncertain or negligible effects. The quality of evidence was very low according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) criteria.

Conclusion There is not one superior type of physical exercise for people with chronic non-specific neck pain. Rather, there is very low quality evidence that motor control, yoga/Pilates/Tai Chi/Qigong and strengthening exercises are equally effective. These findings may assist clinicians to select exercises for people with chronic non-specific neck pain.

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INTRODUCTION

Neck and back pain are the leading cause of years-lived-with-disability,¹ and neck pain is responsible for a substantial burden to society.² Up to 70% of the global population experiences neck pain at

least once in their lives,^{3,4} of which 50% to 85% is expected to become recurring within 1 to 5 years after the initial onset.⁴ This leads to neck pain being a global burdensome problem,⁵ contributing to a rapidly increasing trend in spinal pain-related healthcare expenditures.⁵

Different types of physical exercise, including strengthening, range of motion, motor control, stretching and proprioceptive training, are recommended in clinical guidelines⁶ and are commonly used as a management strategy in the first-line treatment of neck pain.⁷ However, review articles investigating the effectiveness of different physical exercise interventions for people with chronic neck pain report modest effect sizes at best, on pain intensity and pain-related disability.^{8–12} Together with the patient, clinicians are therefore required to choose the type of exercise they prefer or expect to most effectively improve clinical outcomes.

While randomised controlled trials (RCTs), systematic reviews and meta-analyses allow for pairwise comparisons of two types of exercise, they are not suitable to compare the effectiveness of all types of physical exercise. Furthermore, as study interventions often incorporate different types of exercise, it is difficult to draw conclusions regarding the effectiveness of separate types of physical exercise. Investigating the effectiveness of these exercise interventions in separate pairwise meta-analyses is not possible, as insufficient data are available to address each type of physical exercise.

In order to investigate the relative effectiveness of different physical exercise interventions, network meta-analysis (NMA)^{13,14} enables for the interpretation of an entire body of evidence,¹⁵ even though some interventions may not have been directly compared with others.¹⁶ By using direct and indirect evidence from a network of pairwise RCTs, the effectiveness of interventions can be estimated.¹⁷ This approach was recently used to investigate the effectiveness of pharmacological management for depression¹⁸ and physical exercise for chronic low back pain.¹⁹ By generating a hierarchy of interventions, these NMAs were able to provide valuable information for clinical decision-making.

While evidence indicates that exercise therapy has modest effects on pain and disability in individuals with chronic neck pain, there are currently no treatment options that demonstrate medium or large effect sizes.¹² Meta-analyses generally

provide ambiguous evidence with modest effect sizes for exercise therapy versus 'no treatment', whereas NMA can add valuable information by combining evidence from both direct and indirect comparisons. In this NMA, we aimed to systematically investigate the effectiveness of different types of physical exercise interventions in people with chronic non-specific neck pain. The primary research question is: What is the effectiveness of different types of physical exercise on neck pain intensity and pain-related disability? The secondary research question is: What is the effectiveness of different durations, frequencies and intensities of physical exercise interventions on neck pain intensity and pain-related disability?

METHODS

Protocol and registration

This network meta-analysis is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and PRISMA extension for NMA (PRISMA-NMA).^{20,21} This study was prospectively registered on PROSPERO and a detailed protocol was published elsewhere.²²

Information sources

We searched nine electronic databases: AMED, CINAHL, Cochrane Central Register of Controlled Trials, Embase, MEDLINE, Physiotherapy Evidence Database, PsycINFO, Scopus and SPORTDiscus. The database search was conducted on 12 March 2019.

Search strategy

We developed a search strategy with a medical librarian consisting of three parts, including terms for (1) physical exercise, (2) chronic neck pain and (3) RCTs. The neck pain search terms were consistent with those recommended by the Cochrane Back and Neck review group.²³ Initially the search strategy was developed for the MEDLINE database (online supplemental file A), subsequently we adjusted this strategy to the requirements of the other databases. The electronic searches were complemented with manual searches for prospectively identified systematic reviews and meta-analyses.

Eligibility criteria

We included RCTs describing the effects of any physical exercise intervention in adults (age ≥ 18 years) with chronic non-specific neck pain (symptoms persisting for ≥ 12 weeks). Neck pain was defined as pain between the occiput and the first thoracic vertebra as primary complaint. Other terms for non-specific neck pain that may be used are idiopathic neck pain, non-traumatic neck pain, insidious onset neck pain, mechanical neck pain and work-related neck pain. As comparator, we included any physical exercise intervention, or a control group, sham group, placebo group or no-treatment group. We excluded studies if they included participants younger than 18 years, non-human participants, participants with traumatic neck pain (eg, whiplash associated disorder) or participants with specific pathology (eg, cancer). Studies reporting primary complaints other than neck pain, such as post-concussion syndrome, headache and migraine, were excluded. Full-text papers published in the English language were included, and no date limits were applied.

Study selection

Two reviewers (RMJdZ and KC) independently screened titles and abstracts to identify potentially eligible studies. For each identified study, two reviewers independently reviewed the

full-text papers. In either stage, a third reviewer (MS) resolved any disagreements on study inclusion as necessary. Inter-rater agreement was calculated using Cohen's kappa coefficient (k). Where studies were reported in multiple papers, only the paper reporting the most complete analysis of effectiveness was included (ie, reports of subgroups or secondary analyses were discarded).

Data extraction

Two reviewers extracted and recorded data from the included studies using a standardised extraction table agreed on by all authors.

Extracted data comprised: study characteristics (author and year), participant characteristics (sample size, age and sex), type of exercise intervention, duration, frequency and intensity and timing of follow-up assessment. Means and SDs for primary outcome measures at baseline and the follow-up time point closest to the end of the treatment period were extracted. Data were converted where necessary as described in our protocol.²² Where studies reported more than two physical exercise interventions which independently could be included in this NMA, data from all study arms were extracted.

Primary outcomes

The primary outcome measures were pain intensity (eg, Visual Analogue Scale (VAS), Numeric Rating Scale (NRS)) and pain-related disability (eg, Neck Disability Index (NDI), Northwick Park Neck Pain Questionnaire (NPNPQ), Neck Pain and Disability scale (NPAD)), measured at the time point after, and closest to, the end of the treatment.

Categorisation of studies

We identified 10 categories of physical exercise interventions through an iterative process of reviewing relevant RCTs.²² The definitions of these physical exercise interventions are provided in [table 1](#).

Risk of bias assessment

Methodological quality of the included studies was assessed independently by two reviewers using the PEDro (Physiotherapy Evidence Database) scale, which is a validated tool²⁴ for assessing the risk of bias of RCTs and commonly used to assess physiotherapeutic interventions. A third reviewer was available to resolve disagreements as required. Inter-rater agreement was calculated using Cohen's kappa coefficient (k). All studies were included in the systematic review, however only those with a summary score ≥ 5 (cut-off for moderate-quality evidence) were included in the statistical analysis.²⁵

GRADE assessment

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess study limitations, indirectness and transitivity, statistical heterogeneity and inconsistency, imprecision and publication bias.²⁶ Considering the certainty of evidence across paired comparisons might differ, the GRADE approach was used for each pairwise comparison, in line with the GRADE framework which has been adapted for NMA.^{27,28} As all studies included in this NMA were RCTs, consistent with the Cochrane Handbook we assumed the highest quality rating for each comparison.²⁹ Based on the assessment of each of the above-mentioned factors, the certainty of evidence was downgraded to moderate, low or very low quality where appropriate.

Table 1 Definitions of physical exercise interventions and non-exercise comparators

Type	Definition
<i>Intervention</i>	
Strengthening	Exercises to increase the power or endurance of cervical musculature, without a specific focus on deep cervical flexors.
Stretching	Static or isometric exercises focussed on muscle lengthening, optionally includes passively added (over)pressure.
Motor control	Exercises to increase the control and coordination of deep cervical musculature, specifically flexors. Most commonly achieved with the craniocervical flexion action.
Proprioception	Exercises to increase the proprioceptive and kinesthetic control of head, neck and eye movements. Examples of proprioceptive training include cervical joint repositioning and gaze direction exercises. While craniocervical flexion exercises also have a proprioceptive component, their primary aim is to improve control of the craniocervical flexion movement and the deep cervical muscles. ⁶⁵ For this reason we opted to keep these as distinct exercise types.
Balance	Exercises aimed at improving postural balance.
Prescribed physical activity	General exercises such as walking, cycling, rowing, aimed at improving overall physical activity.
Yoga/Pilates/Tai Chi/Qigong	Exercises following traditional principles with a physical component.
Range of motion	Exercises aimed at improving range of motion, performed actively without a stretching (static, overpressure) component.
Strengthening+motor control	A combination of strengthening and motor control exercises as described above.
Strengthening+stretching	A combination of strengthening and stretching exercises as described above.
Prescribed physical activity+strengthening	A combination of prescribed physical activity and strengthening exercises as described above.
Multimodal	A combination of three or more of the above-mentioned exercise types.
<i>Control</i>	
No treatment/information/sham	No active treatment, no prescribed physical exercise, no physical/manual therapy. Control interventions may include: information, general advice to stay active (without specific exercise instructions), limited pain education, sham.

Methods of analysis

The characteristics of the included trials (details of the physical exercise intervention, outcomes) were summarised and tabulated.

The available evidence was summarised visually to depict the comparative relationships between the different exercise interventions and no treatment. A network diagram was created for each outcome (pain, disability), in which nodes represent a class of intervention (as categorised in the inclusion criteria). The effect of pairwise comparisons of two interventions are shown as edges interconnecting the nodes, where the thickness of the edge lines represents the weight of pairwise comparisons. The number of studies contributing to each pairwise comparison are also shown on each edge.

NMA assumptions

The presence of inconsistency was assessed from indirect and direct evidence using node-splitting.^{30–31} Disagreement was tested statistically and reported using z-scores and p values.

To assess transitivity, we made the assumption that all physical exercise interventions included in the NMA are in-principle jointly randomisable and we inspected the distribution of measures that could potentially modify effects (age and sex) across the comparisons in the network.

Model heterogeneity was quantified using I^2 . Forest plots were visually examined to identify any obvious inconsistency between direct and indirect treatment effects (loop consistency); further Cochrane's Q statistic was calculated (Q_{total}) and decomposed to describe within-design heterogeneity (Q_{within}), and between-design ($Q_{between}$) inconsistency. Comparison-adjusted funnel plots were used to visually inspect and assess for small study effects, and assess potential publication bias.³²

Statistical models

Two frequentist NMAs were conducted: one for pain intensity and one for pain-related disability. Pairwise effect sizes were calculated by including all evidence available in the network.³³ Effect measures for treatments that have not been compared in a pairwise RCT were compared indirectly by contrasting effect sizes of comparisons with a common comparator.^{15 34 35} Because previous systematic reviews of exercise for neck pain

have shown varying effects, a random effects (*DerSimonian and Laird*³⁶) model was used to generate pooled standardised effect sizes. Corrected effect sizes (*Hedges' g*) were used to allow for the inclusion of smaller studies. While Cohen's d and Hedges' g are similar, we used Hedges' g as it has better performance over Cohen's d with inclusion of small samples.³⁷ Network forest plots, interval plots, league tables and P-scores were used to present the ranking of mixed (direct and indirect) effect sizes and 95% CIs for all combinations of treatments in the network. For a frequentist analysis, the P-score may be interpreted in a comparable way to the SUCRA.³⁸ Contribution matrices were used to demonstrate the influence of individual comparisons, and the influence of direct and indirect evidence on the overall summary of effects.

Statistical package R³⁹ was used for all statistical analyses. The netmeta R-package (V.1.2.0, <https://cran.r-project.org/web/packages/netmeta/netmeta.pdf>) was used to conduct the NMA. The netmeta package function forest.netmeta was used to create a visual network of nodes and connections.

Patient and public involvement

There was no patient or public involvement in this review.

RESULTS

Study selection

The search strategy returned 6549 records, and the flow of studies through the review is presented in [figure 1](#). Records were excluded based on the included participants (not chronic non-specific neck pain), the intervention or comparator (not a physical exercise intervention) or the study design (not an RCT). Ineligible studies were excluded for not reporting pain intensity or neck disability outcomes, not reporting follow-up assessment for either pain intensity or neck disability, or for reporting physical exercise interventions that were delivered in addition to other treatments (such as manual therapy or electrophysical agents). Forty RCTs were included in this network meta-analysis. The inter-rater agreement for the title and abstract screening was $\kappa=0.992$ (for chance-corrected, weighted kappa $\kappa_w=0.916$), and for the full-text screening $\kappa=0.886$ ($\kappa_w=0.772$).

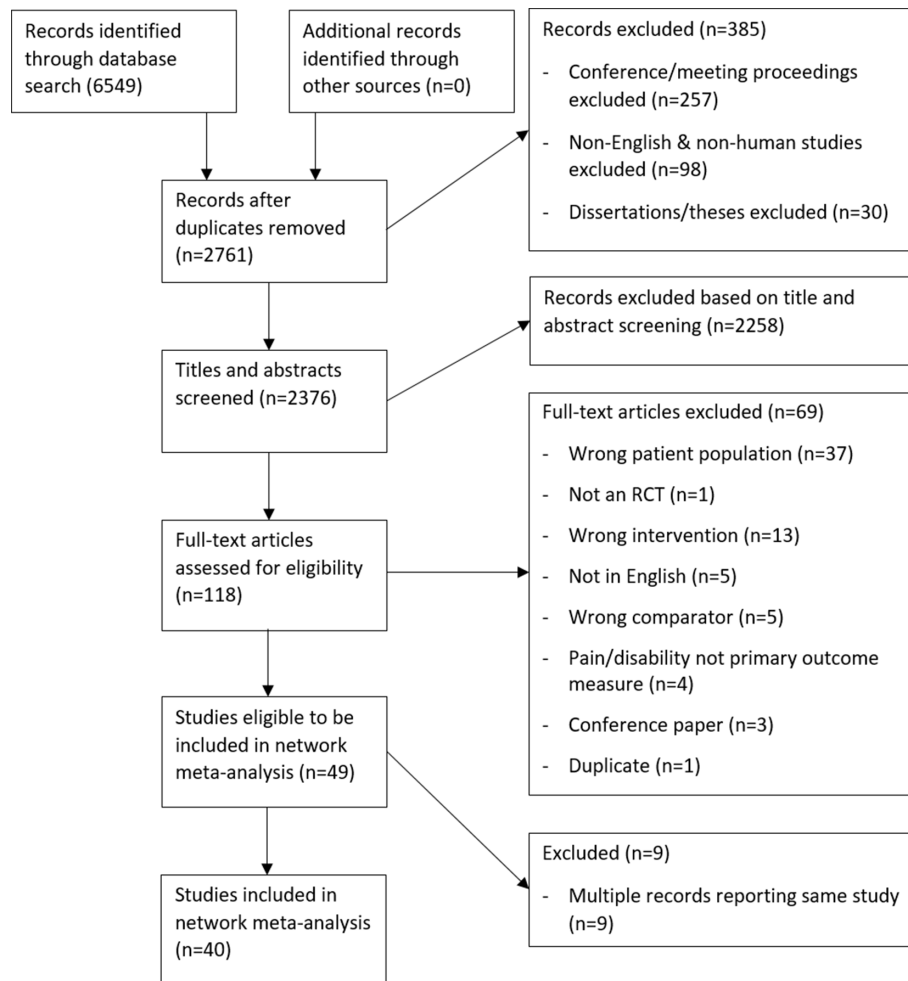


Figure 1 Flow of studies through the review. RCT, randomised controlled trial.

Outcomes of several trials were reported in multiple articles, which we identified by authors, study dates, number of participants, demographics, and baseline characteristics. For the purpose of this NMA, only one of these articles was cited, however relevant data from all publications of the same trial were combined to extract the most complete data. This was the case for the following publications: Falla *et al.* (2008) was cited for three articles,^{40–42} Lansinger *et al.* (2007) was cited for two articles,^{43 44} and Ylinen *et al.* (2003) was cited for seven studies.^{45–51}

Risk of bias assessment

Inter-rater agreement for the risk of bias assessment was $\kappa=0.964$ ($\kappa_w=0.919$). Overall, the risk of bias within individual studies assessed using the PEDro scale ranged between 5/11 and 9/11 (table 2). One of the included studies⁵² was found to be of poor methodological quality (PEDro score=4) and was therefore not included in the statistical part of the network meta-analysis.²⁹ Due to the nature of included interventions being exercise and clinician-delivered, most studies were unable to blind participants. One study⁵³ indicated subjects were unaware of the different intervention groups within the trial, however, as subjects were aware they received an exercise intervention, this was marked as high risk consistent with the assessment of other studies.

Study characteristics

Study characteristics for all 40 included studies are presented in table 3. Ambiguity around the sample (possible inclusion of traumatic neck pain when only ‘non-specific neck pain’ was reported) was resolved through contacting the original authors. Studies including a mixed sample (participants with non-traumatic and traumatic neck pain) were included if the proportion of traumatic neck pain was $\leq 25\%$. Details on participant allocation into treatment arms is provided in online supplemental files B and C. Pain intensity was reported in 38 studies (97%), 22 studies assessed pain intensity using VAS and 16 used NRS. Disability was reported in 29 studies (72%), assessed by NDI (n=24), NPNPQ (n=3) and NPAD (n=2).

The following sections (ie, presentation of network structure, summary of network geometry, synthesis of results) are reported separately for each of the two networks (ie, pain intensity and pain-related disability). Table 4 provides a summary of study characteristics, heterogeneity and inconsistency, as well as treatment rankings.

Pain intensity

Presentation of network structure

Thirty-eight studies were included in the NMA for pain intensity (figure 2A), including a total of 3151 participants with chronic non-specific neck pain. The NMA demonstrated the following ranking of P-scores for the interventions: strengthening and

Table 2 Risk of bias assessment using the Physiotherapy Evidence Database (PEDro) scale

Author (year)	1	2	3	4	5	6	7	8	9	10	11	PEDro sum score
Alpayci and Ilter 2017 ⁶⁶	Low	Low	High	Low	High	High	Low	High	High	Low	Low	6
Andersen <i>et al</i> 2013 ⁵⁴	Low	Low	Low	Low	High	High	High	Low	Low	Low	Low	8
Andersen <i>et al</i> 2014 ⁶⁷	Low	Low	High	Low	High	High	Low	High	Low	Low	High	7
Andersen <i>et al</i> 2012 ⁶⁸	Low	Low	High	Low	High	High	High	Low	Low	Low	Low	7
Andersen <i>et al</i> 2008 ⁶⁹	Low	Low	High	Low	High	High	High	Low	Low	Low	Low	7
Beinert 2013 ⁷⁰	Low	Low	High	High	High	High	Low	Low	Low	High	Low	6
Bobos <i>et al</i> 2016 ⁷¹	Low	Low	Low	Low	High	High	High	Low	Low	High	High	6
Caputo <i>et al</i> 2017 ⁷²	Low	Low	Low	Low	High	High	Low	High	Low	Low	Low	8
Chiu <i>et al</i> 2005 ⁷³	Low	Low	Low	Low	High	High	Low	High	Low	Low	Low	8
Cramer <i>et al</i> 2013 ⁷⁴	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
de Araujo <i>et al</i> 2018 ⁷⁵	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Dellve <i>et al</i> 2011 ⁷⁶	Low	Low	Low	Low	High	High	High	High	High	Low	Low	6
Dunleavy <i>et al</i> 2016 ⁷⁷	Low	Low	High	Low	High	High	High	High	High	Low	Low	5
Duray <i>et al</i> 2018	Low	High	High	Low	High	High	High	High	High	Low	Low	4
Evans <i>et al</i> 2012 ⁷⁸	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Falla <i>et al</i> 2008 ⁴⁰	Low	Low	High	Low	High	High	Low	Low	Low	Low	Low	8
Falla <i>et al</i> 2006 ⁴¹	Low	Low	High	Low	High	High	Low	Low	High	Low	Low	7
Falla <i>et al</i> 2007 ⁴²	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	8
Falla <i>et al</i> 2013 ⁷⁹	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	8
Gallego Izquierdo <i>et al</i> 2016 ⁸⁰	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Ghaderi <i>et al</i> 2017 ⁸¹	Low	Low	High	Low	High	High	High	Low	High	Low	Low	6
Griffiths <i>et al</i> 2009 ⁵³	Low	Low	High	Low	High	High	Low	Low	Low	Low	Low	7
Häkkinen <i>et al</i> 2008 ⁸²	Low	Low	High	Low	High	High	Low	Low	Low	Low	Low	8
Hoving <i>et al</i> 2012 ⁸³	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	8
Javanshir <i>et al</i> 2015 ⁸⁴	Low	Low	High	Low	High	High	Low	Low	Low	Low	Low	8
Jordan <i>et al</i> 2011 ⁸⁵	Low	Low	Low	Low	High	High	High	Low	Low	Low	Low	8
Jull <i>et al</i> 2009 ⁶⁵	Low	Low	Low	Low	High	High	Low	Low	High	Low	Low	8
Jull <i>et al</i> 2002 ⁸⁶	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Karlsson <i>et al</i> 2014 ⁸⁷	Low	Low	High	Low	High	High	High	High	High	Low	Low	5
Khosrokiani <i>et al</i> 2018 ⁸⁸	Low	Low	High	Low	High	High	High	Low	High	Low	Low	6
Kjellman 2002 ⁸⁹	Low	Low	Low	Low	High	High	High	Low	High	Low	Low	7
Lange <i>et al</i> 2013 ⁹⁰	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Lansinger <i>et al</i> 2013	Low	Low	Low	Low	High	High	High	Low	Low	Low	Low	8
Lansinger <i>et al</i> 2007 ⁴⁴	Low	Low	Low	Low	High	High	High	Low	Low	Low	Low	8
Lauche <i>et al</i> 2016 ⁹¹	Low	Low	Low	Low	High	High	Low	High	Low	Low	Low	8
Li <i>et al</i> 2017 ⁹²	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Michalsen <i>et al</i> 2012 ⁹³	Low	Low	Low	Low	High	High	Low	High	Low	Low	Low	7
Nikander <i>et al</i> 2006 ⁴⁵	Low	Low	High	Low	High	High	High	Low	High	Low	High	5
O'Leary <i>et al</i> 2012 ⁹⁴	Low	Low	High	Low	High	High	Low	Low	Low	Low	Low	8
Ravi <i>et al</i> 2016 ⁹⁵	Low	Low	High	Low	High	High	High	Low	High	Low	Low	6
Rendant <i>et al</i> 2011 ⁹⁶	Low	Low	Low	Low	High	High	High	Low	Low	Low	Low	8
Tunwattanapong <i>et al</i> 2016 ⁹⁷	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Viljanen <i>et al</i> 2003 ⁹⁸	Low	Low	Low	Low	High	High	Low	Low	Low	Low	Low	9
Ylinen <i>et al</i> 2003 ⁵¹	Low	Low	High	Low	High	High	Low	Low	Low	Low	Low	8

Criteria: (1) Eligibility criteria specified; (2) Subjects randomly allocated to groups; (3) Concealed allocation; (4) Groups were similar at baseline; (5) Blinding of all subjects; (6) Blinding of all therapists; (7) Blinding of all assessors; (8) Measures obtained from more than 85% of subjects allocated to groups; (9) Subjects received treatment or control condition as allocated, or intention-to-treat analysis; (10) Between-group statistical comparisons reported for at least one outcome; (11) Both point measures and measures of variability were reported. high, high risk of bias; low, low risk of bias, sum score is sum of 'low' count per reference.

motor control ($p=0.705$), proprioceptive ($p=0.704$), strengthening and stretching ($p=0.686$), motor control ($p=0.664$), yoga/Pilates/Tai Chi/Qigong ($p=0.627$), stretching ($p=0.600$), strengthening ($p=0.592$), range of motion ($p=0.485$), prescribed physical activity ($p=0.379$), balance ($p=0.282$) and multimodal ($p=0.186$) exercise training. The P-score indicates the likelihood that an intervention is more effective than the other interventions in the network.³⁸

Summary of network geometry

As illustrated in figure 2, most evidence of the pain intensity network comes from pairwise comparison that have been

reported by several studies, for example yoga/Pilates/Tai Chi/Qigong exercises versus no treatment and strengthening exercises versus no treatment. It is important to note that pairwise comparisons in the network were not only between different exercise interventions and no treatment, but also between two separate exercise interventions, for example, strengthening versus motor control exercises and yoga/Pilates/Tai Chi/Qigong exercises versus prescribed physical activity. The network plot further demonstrates that several multi-arm studies with more than two exercise interventions were included, indicated by the coloured areas between multiple nodes.

Table 3 Overview of included studies (n=40)

Author (year)	Total sample size, neck pain definition	Sex (n female)	Age mean (SD)	Intervention duration	Timing of follow-up assessment	Pain, disability outcome	Intervention details
Alpayci and Ilter 2017 ⁶⁶	65, NTNP	53 F	STRE: 33 (9), NOTR: 33 (10)	3 months	3 months	VAS	Daily exercises (3×30s)
Andersen <i>et al</i> 2013 ⁵⁴	118, NSNSP	118 F	STRE: 36 (9), NOTR: 35 (9)	20 weeks	20 weeks	VAS	3×1 hour session per week
Andersen <i>et al</i> 2014 ⁶⁷	47, NSNSP	37 F	STRE: 44 (13), NOTR: 45 (11)	10 weeks	10 weeks	VAS	3×20min session
Andersen <i>et al</i> 2012 ⁶⁸	158, NSNSP	?	STRE: 46 (10), NOTR: 46 (10)	20 weeks	20 weeks	VAS	1 hour per week
Andersen <i>et al</i> 2008 ⁶⁹	42, NTNP	42 F	STRE: 44(9), PRES: 45(9), NOTR: 42 (8)	10 weeks	10 weeks	VAS	3×20min session
Beinert 2013 ⁷⁰	34, SCNP	?	TOTAL: 23 (3)	5 weeks	5 weeks	NRS	three sessions per week, at least 15 min
Bobos <i>et al</i> 2016 ⁷¹	67, INP	47 F	MOTO: 38 (13), STRE: 40 (13), NOTR: 39 (13)	7 weeks	7 weeks	NRS, NDI	two sessions, 30 to 40 min
Caputo <i>et al</i> 2017 ⁷²	35, WRNP	27 F	STRE: 43 (41-45), STRT: 42 (38.5-44)	7 weeks	7 weeks	VAS, NDI	45 min, 2 sessions per week
Chiu <i>et al</i> 2005 ⁷³	145, NTNP	100 F	STRE+MOTO: 43 (10), NOTR: 44 (10)	6 weeks	6 weeks	NRS, NPNPQ	two sessions per week
Cramer <i>et al</i> 2013 ⁷⁴	51, NSNP	63 F	YOGAP: 46 (11), STRE+STRT: 50 (10)	9 weeks	9 weeks	VAS, NDI	one session a week, 10 min at home daily
de Araujo <i>et al</i> 2018 ⁷⁵	64, MNP	14 F	YOGAP: 49 (12), NOTR: 49 (12)	12 weeks	90 days	NPS, NDI	two sessions per week, 1 hour
Dellve <i>et al</i> 2011 ⁷⁶	60, NP	60 F	STRE:<44: n=7, 45-54: n=9,>54: n=7, NOTR:<44: n=6, 45-54: n=10,>54: n=4	1 month	1 month	NRS	6 days per week
Dunleavy <i>et al</i> 2016 ⁷⁷	56, MNP	49 F	TOTAL: 56 (9)	12 weeks	12 weeks	NRS, NDI	one session per week
Duray <i>et al.</i> 2018	40, NSNP	32 F	PROP: 44 (7), NOTR: 46 (6)	3 weeks	3 weeks	NPI, NDI	three times per day, sets of 10
Evans <i>et al</i> 2012 ⁷⁸	270, NSNP	194 F	STRE: 49 (10), PRES: 46 (10)	12 weeks	12 weeks	NRS, NDI	twenty 1 hour sessions
Falla <i>et al</i> 2008 ⁴⁰	37, NP	37 F	MOTO: 38 (10), STRE: 38 (10)	6 weeks	7 weeks	VAS, NDI	one 30 min session per week, 10 to 20 min training daily
Falla <i>et al</i> 2013 ⁷⁹	46, NTNP	46 F	STRE+MOTO: 39 (9), NOTR: 39 (9)	8 weeks	8 weeks	NRS, NDI	one 30 min session per week, 10 to 20 min training daily
Gallego Izquierdo <i>et al</i> 2016 ⁸⁰	28, NSNP	18 F	MOTO: 28 (6), PROP: 30 (7)	2 months	2 months	VAS, NDI	six sessions+20 min per day
Ghaderi <i>et al</i> 2017 ⁸¹	40, NTNP	?	MOTO: 36 (3), NOTR: 36 (3)	10 weeks	10 weeks	VAS, NDI	10 sessions
Griffiths <i>et al</i> 2009 ⁵³	74, MNP	46 F	NOTR: 52 (14), MOTO: 51 (14)	6 weeks	6 weeks	NPAD	four 30 min sessions+exercises 5-10 times daily
Hakkinen <i>et al</i> 2008 ⁸²	101, NSNP	91 F	STRT: 40 (10), STRE+STRT: 41 (9)	12 months	12 months	VAS, NDI	weekly session for 6 weeks, thereafter bimonthly
Hoving <i>et al</i> 2012 ⁸³	123, NSNP	77 F	MULTI: 46 (12), CON 46 (11)	6 weeks	6 weeks	NRS, NDI	weekly session
Javanshir <i>et al</i> 2015 ⁸⁴	60, NTNP	40 F	MOTO: 37 (4), STRE: 36 (5)	6 weeks	6 weeks	VAS, NDI	weekly session, 30 min
Jordan <i>et al</i> 2011 ⁸⁵	123, NP	108 F	TOTAL: 46 (11)	6 months	6 months	VAS, NPAD	18 sessions
Jull <i>et al</i> 2009 ⁸⁵	46, NP	46 F	MOTO: 40 (12), STRE: 37 (10)	6 weeks	6 weeks	NRS, NDI	one session per week, twice a day home practice
Jull <i>et al</i> 2002 ⁸⁶	100, NP	80 F	STRE+MOTO: 37 (2), NOTR: 37 (2)	6 weeks	6 weeks	VAS, NPNPQ	8 to 12 sessions over 6 weeks, 30 min per session
Karlsson <i>et al</i> 2014 ⁸⁷	57, NSP	57 F	STRE: 46 (IQR: 40,50), STRT: 42 (IQR 33,47)	12 months	12 months	NRS, NDI	first 8 weeks supervised, then independent
Khosrokiani <i>et al</i> 2018 ⁸⁸	30, NSNP	30 F	MOTO: 36 (6) NOTR: 38 (6)	6 months	6 months	VAS, NDI	30 min/day, 3 days/week
Kjellman 2002 ⁸⁹	49, NP	35 F	PRES: 47 (9), NOTR: 43 (12)	8 weeks	8 weeks	VAS, NDI	two sessions per week
Lange <i>et al</i> 2013 ⁹⁰	55, NSP	?	STRE+MOTO: 31 (range 29-36), NOTR: 34 (range 30-36)	24 weeks	24 weeks	NRS	three times 20 min per week
Lansinger <i>et al</i> 2007 ⁴⁴	139, NSNP	86 F	YOGAP: 45 (12), STRE: 43 (1)	3 months	3 months	VAS, NDI	1 to 2 times per week, 1 hour
Lauche <i>et al</i> 2016 ⁹¹	114, INP	91 F	YOGAP: 52 (11) PRES: 47 (12), NOTR: 49 (12)	12 weeks	12 weeks	VAS, NDI	approximately 1 hour session, every week
Li <i>et al</i> 2017 ⁹²	109, NTNP	109 F	STRE: 35 (9), NOTR: 34 (8)	6 weeks	6 weeks	VAS, NDI	three training sessions per week
Michalsen <i>et al</i> 2012 ⁹³	77, NTNP	67 F	YOGAP: 48 (11), PRES: 48 (12)	9 weeks	9 weeks	VAS, NDI	90 min session once per week
O'Leary <i>et al</i> 2012 ⁹⁴	60, NP	35 F	STRE: 38 (13), MOTO: 38 (13), ROM: 38 (13)	10 week	10 weeks	VAS, NDI	eight supervised sessions, exercises twice daily at home
Ravi <i>et al</i> 2016 ⁹⁵	50, NSNP	32 F	TOTAL: 30 (11)	4 weeks	4 weeks	NRS, NDI	unclear
Rendant <i>et al</i> 2011 ⁹⁶	65, NTNP	53 F	PRES: 33 (9), NOTR: 33 (10)	3 months	3 months	NRS	3×30s per day
Tunwattanapong <i>et al</i> 2016 ⁹⁷	96, NP	77 F	STRT: 34 (9), NOTR: 37 (9)	4 weeks	4 weeks	NRS, NPNPQ	two sessions per day, 5 days per week, 10 to 15 min
Viljanen <i>et al</i> 2003 ⁹⁸	393, NSNP	393 F	STRE: 45 (7), NOTR: 44 (7)	12 weeks	12 weeks	NRS	three times per week, 30 min
Ylinen <i>et al</i> 2003 ⁵¹	179, NSNP	179 F	STRE: 46 (6), NOTR: 46 (5)	12 months	12 months	VAS, NDI	Institutional, supervised, and independent training

?, unknown. Neck pain definitions used; Exercise interventions: MOTO, motor control; F, female; INP, idiopathic neck pain; MNP, mechanical neck pain; NOT, no treatment; NP, neck pain; NSNP, non-specific neck pain; NSNSP, non-specific neck and shoulder pain; NSP, neck and shoulder pain; NTNP, non-traumatic neck pain; PRES, prescribed physical activity; PROP, proprioceptive; SCNP, subclinical neck pain; STRE, strengthening; STRE+MOTO, strengthening and motor control; STRE+STRT, strengthening and stretching; STRT, stretching; TOTAL, age characteristics for total sample, when group characteristics were not available; WRNP, work-related neck pain; YOGAP, yoga/Pilates/Tai Chi/Qigong.

Table 4 Summary of study characteristics, heterogeneity and inconsistency, and treatment rankings

	Network	
	Pain intensity	Pain-related disability
Number of studies	38	29
Number of treatments	12	11
Number of pairwise comparisons	50	37
Number of designs	21	19
Heterogeneity I^2	0.91 (0.89 to 0.93)	0.88 (0.83 to 0.91)
Tests for inconsistency		
Q_{total}	<0.0001	<0.0001
Q_{within}	<0.0001	0.0005
$Q_{between}$	<0.0001	<0.0001
P-scores		
Strength+motor	0.705	0.479
Proprioceptive	0.704	0.485
Strength+stretch	0.686	0.602
Motor control	0.664	0.739
YPTCQ	0.627	0.888
Stretch	0.600	0.622
Strength	0.592	0.656
ROM	0.485	0.388
Prescribed PA	0.379	0.156
Balance	0.282	N/A
Combined	0.186	0.286
No treatment	0.090	0.200

PA, physical activity; ROM, range of motion; YPTCQ, yoga/Pilates/Tai Chi/Qigong.

Synthesis of results

A ranked forest plot of the intervention effects demonstrates that, compared with no treatment, combined strengthening and stretching had the largest Hedges' g effect size (-1.53 , 95% CI: -3.47 to 0.41 ; only indirect evidence, GRADE=very low). Several other interventions demonstrated similar effect sizes: proprioceptive (-1.47 , 95% CI: -2.76 to -0.18 , only indirect evidence, GRADE=very low), combined strengthening and motor control (-1.44 , 95% CI: -2.42 to -0.47 ; direct evidence: $n=4$, GRADE=moderate), motor control (-1.32 , 95% CI: -1.99 to -0.65 ; direct evidence: $n=3$, GRADE=very low to moderate), yoga/Pilates/Tai Chi/Qigong (-1.25 , 95% CI: -1.85

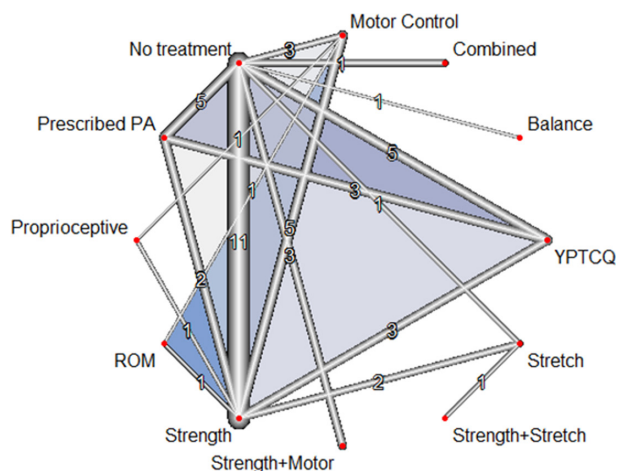


Figure 2 Network constructed for pain intensity. The number of studies contributing to each comparison is shown as label on each edge. PA, physical activity; ROM, range of motion; YPTCQ, yoga/Pilates/Tai Chi/Qigong.

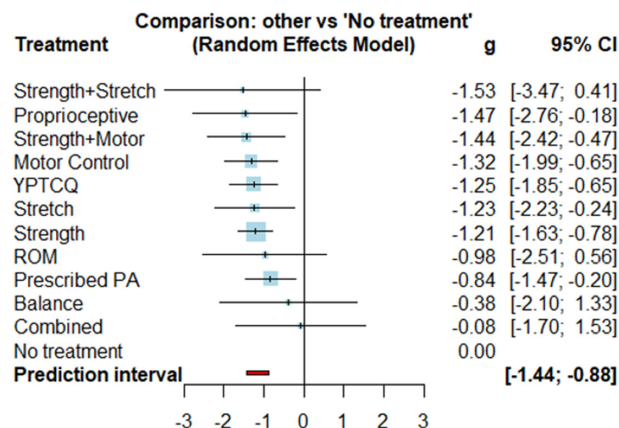


Figure 3 Forest plot for pain intensity, ranked by treatment effectiveness. PA, physical activity; ROM, range of motion; YPTCQ, yoga/Pilates/Tai Chi/Qigong.

to -0.65 ; direct evidence: $n=5$, GRADE=low to moderate), stretching (-1.23 , 95% CI: -2.23 to -0.24 ; direct evidence: $n=1$, GRADE=very low to low) and strengthening (-1.21 , 95% CI: -1.63 to -0.78 ; direct evidence: $n=9$, GRADE=low to moderate) exercises (figure 3). Motor control, yoga/Pilates/Tai Chi/Qigong and strengthening exercises had the narrowest CIs providing some certainty in the results for these exercise types. In contrast the wide CIs of strengthening and stretching, proprioceptive, prescribed physical activity (-0.84 , 95% CI: -1.47 to -0.20 ; direct evidence: $n=5$, GRADE=very low to low), balance (-0.38 , 95% CI: -2.10 to 1.33 ; direct evidence: $n=1$, GRADE=very low), multimodal (-0.08 , 95% CI: -1.70 to 1.53 ; direct evidence: $n=1$, GRADE=very low) and range of movement (-0.98 , 95% CI: -2.51 to 0.56 ; no direct studies, GRADE=very low) exercises indicates greater uncertainty in the effects of these exercise types. The effect sizes for balance and combined exercises approaches were small with wide CIs. All comparative effects for all interventions in the pain intensity network are presented in a league table (table 5).

Pain-related disability

Presentation of network structure

The NMA for pain-related disability included 28 studies and a total of 2336 participants with chronic non-specific neck pain (figure 4). The NMA demonstrated the following ranking of P-scores for the interventions: yoga/Pilates/Tai Chi/Qigong ($p=0.888$), motor control ($p=0.739$), strengthening ($p=0.656$), stretching ($p=0.622$), strengthening and stretching ($p=0.602$), proprioceptive ($p=0.485$), strengthening and motor control ($p=0.479$), range of motion ($p=0.488$) and multimodal ($p=0.286$). Notably, prescribed physical activity ($p=0.156$) was ranked below 'no treatment'.

Summary of network geometry

The network geometry for the disability network, as illustrated in figure 4, is very similar to the network for pain intensity since most studies reported both pain intensity and disability outcome measures. While most evidence in the network comes from pairwise comparison, also in this network several multi-arm studies were included. Notably, similar to the pain intensity network, several pairwise comparisons were included between separate exercise interventions (that were not 'no treatment'), for example, strengthening versus motor control exercises and

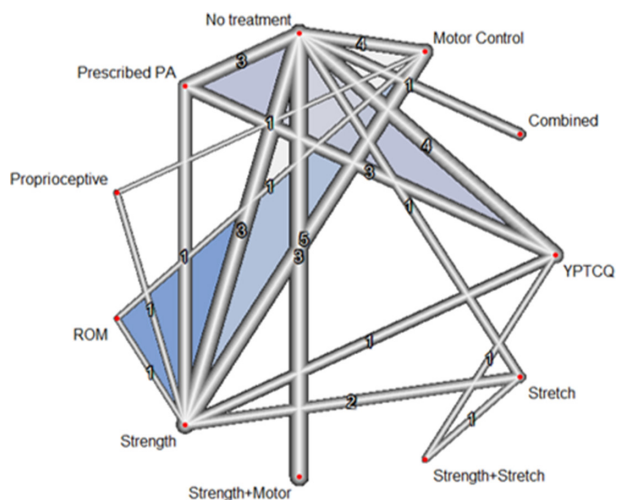


Figure 4 Network constructed for pain-related disability. The number of studies contributing to each comparison is shown as label on each edge. PA, physical activity; ROM, range of motion; YPTCQ, yoga/Pilates/Tai Chi/Qigong.

yoga/Pilates/Tai Chi/Qigong exercises versus prescribed physical activity.

Synthesis of results

A ranked forest plot of the intervention effects demonstrates that, compared with no treatment, yoga/Pilates/Tai Chi/Qigong exercise training had the largest Hedges' *g* effect size (-1.16 , 95% CI: -1.75 to -0.57 ; direct evidence: $n=4$, GRADE=very low to moderate). Several other interventions demonstrated similar effect sizes: motor control (-0.87 , 95% CI: -1.45 to -0.29 ; direct evidence: $n=4$, GRADE=very low to low), strengthening (-0.75 , 95% CI: -1.28 to -0.22 ; direct evidence: $n=3$, GRADE=very low) and stretching (-0.70 , 95% CI: -1.52 to -0.11 ; direct evidence: $n=1$, GRADE=very low) exercises (figure 5). Yoga/Pilates/Tai Chi/Qigong, motor control and strengthening exercises had the narrowest CIs providing some certainty in the results for these exercise types. In contrast, the wide CIs of strengthening and stretching (-0.69 , 95% CI: -1.83 to 0.46 only indirect evidence, GRADE=very low), proprioceptive (-0.47 , 95% CI: -1.62 to 0.67 ; only indirect evidence, GRADE=very low), combined strengthening and motor control (-0.45 , 95% CI: -1.25 to 0.35 ; direct evidence:

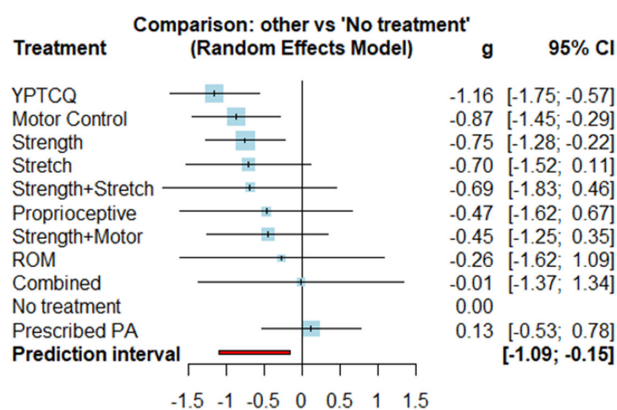


Figure 5 Forest plot for pain-related disability, ranked by treatment effectiveness. PA, physical activity; ROM, range of motion; YPTCQ, yoga/Pilates/Tai Chi/Qigong.

$n=3$, GRADE=very low), range of movement (-0.26 , 95% CI: -1.62 to 1.09 ; only indirect evidence, GRADE=very low), multimodal (-0.01 , 95% CI: -1.37 to 1.34 ; direct evidence: $n=1$, GRADE=very low) and prescribed physical activity (0.13 , 95% CI: -0.53 to 0.78 ; direct evidence: $n=3$, GRADE=very low) exercises indicates greater uncertainty in the effects of these exercise types. The effect sizes for balance and combined exercises approaches were small with wide CIs. All comparative effects for all interventions in the disability network are presented in a league table (table 6).

Of the included studies, one study with a high risk of bias (Duray *et al*⁵²) was not included in the NMA. This study investigated the effects of proprioceptive exercises versus 'no treatment' in 40 individuals. While both groups significantly improved in terms of both pain intensity and pain-related disability, the proprioceptive exercise group had a significantly greater improvement. This is consistent with the results of the pain intensity NMA. The effect on disability is less consistent in this NMA, reflected by a wide CI that crosses '0'.

Exploration for inconsistency

Node splitting for both the pain intensity and disability outcome networks showed no statistically significant inconsistency between direct and indirect estimates (refer to online supplemental file F for the p values for inconsistency). Forest plots (online supplemental files H and I) demonstrate direct, indirect and network estimates for both the pain and disability network.

GRADE assessment

The GRADE approach was used to assess study limitations, indirectness and transitivity, inconsistency, imprecision and publication bias. Table 7 presents a summary of the certainty of evidence for the two networks (all details on the GRADE assessment for all pairwise comparisons are provided in online supplemental files D and E). Reasons for downgrading were imprecision, severe imprecision and risk of bias. Funnel plots were visually inspected and the p value for the Egger test was considered in order to assess the symmetry of both networks (online supplemental files F and G). The funnel plot for the pain intensity network was considerably asymmetrical, and the p value for its Egger test ($p=0.0006$) indicated statistically significant asymmetry. This mean that there is a potential existence of publication bias, which was not the case for the disability network's funnel plot.

DISCUSSION

This is the first study using NMA to investigate the comparative effectiveness of different physical exercise interventions for people with chronic non-specific neck pain. While none of the interventions was superior, three types of exercise (ie, motor control, yoga/Pilates/Tai Chi/Qigong and strengthening) were found to be most effective in improving both pain intensity and disability, when compared with no treatment. According to the GRADE criteria, the quality of the evidence was very low, indicating that the findings should be interpreted with caution. 'No treatment' was least effective followed by combined exercise approaches, range of movement exercise and prescribed physical activity (for disability).

Summary of findings

Two networks were constructed investigating the effects of physical exercise interventions on pain intensity ($n=38$ RCTs, $n=3151$ subjects) and on pain-related disability ($n=29$ RCTs, $n=2336$ subjects). In terms of improving pain intensity, several

Table 6 League table reporting the comparative effects for all interventions for the pain-related disability network

Combined	Motor Control	No treatment	Prescribed PA	Proprioceptive	ROM	Strength	Strength+motor	Strength+stretch	Stretch	YPTCQ
-0.85										
-2.33 to 0.62										
0.01	0.87									
1.34 to -1.37	0.29 to 1.45									
0.14	0.99	0.13								
-1.37 to 1.65	0.18 to 1.81	-0.53 to 0.78								
-0.46	0.4	-0.47	-0.6							
-2.23 to 1.32	-0.68 to 1.47	-1.62 to 0.67	-1.86 to 0.67							
-0.25	0.6	-0.26	-0.39	0.21						
-2.17 to 1.67	-0.69 to 1.89	-1.62 to 1.09	-1.85 to 1.07	-1.43 to 1.84	ROM					
-0.73	0.12	-0.75	-0.87	-0.28	-0.48					
-2.19 to 0.72	-0.41 to 0.65	-1.28 to -0.22	-1.61 to -0.14	-1.35 to 0.79	-1.77 to 0.81	Strength				
-0.44	0.41	-0.45	-0.58	0.02	-0.19	0.29				
-2.02 to 1.14	-0.58 to 1.40	-1.25 to 0.35	-1.61 to 0.46	-1.38 to 1.41	-1.76 to 1.38	-0.66 to 1.25	Strength+motor			
-0.67	0.18	-0.69	-0.81	-0.22	-0.42	0.06	-0.23			
-2.45 to 1.10	-1.04 to 1.40	-1.83 to 0.46	-2.05 to 0.42	-1.77 to 1.34	-2.14 to 1.29	-1.10 to 1.22	-1.63 to 1.16			
-0.69	0.16	-0.7	-0.83	-0.23	-0.44	0.04	-0.25			
-2.28 to 0.90	-0.73 to 1.06	-1.52 to 0.11	-1.81 to 0.15	-1.54 to 1.07	-1.93 to 1.05	-0.74 to 0.83	-1.39 to 0.90	Strength+stretch		
-1.14	-0.29	-1.16	-1.28	-0.68	-0.89	-0.41	-0.7	-0.02		
-2.62 to 0.34	-1.06 to 0.48	-1.75 to -0.57	-1.98 to -0.59	-1.92 to 0.55	-2.32 to 0.54	-1.09 to 0.28	-1.70 to 0.29	-1.12 to 1.08	Stretch	
								-0.47	-0.45	
								-1.57 to 0.64	-1.36 to 0.46	

Mean effect sizes (Hedges' g) with 95% CIs between separate physical exercise interventions as per the network meta-analysis model investigating the effectiveness on pain-related disability. Negative values favour the row-defined intervention, whereas positive values favour the column-defined intervention. Bold denotes statistical significance at $p < 0.05$.

PA, physical activity; ROM, range of motion; YPTCQ, yoga/Pilates/Tai Chi/Qigong

Table 7 Summary of certainty of evidence (GRADE approach) for network meta-analysis in studies examining the effects of physical exercise in individuals with chronic non-specific neck pain, for pain intensity and pain-related disability.

Outcome	Certainty of evidence	Reason for downgrade
Pain intensity	Very low	Imprecision, risk of bias
Pain-related disability	Very low	Imprecision, risk of bias

GRADE, Grading of Recommendations Assessment, Development and Evaluation.

exercise interventions showed similar effect sizes. However, the effects of some of these interventions (combined strengthening and stretching, proprioceptive exercise) had wide CIs and were based on only a few studies and small sample sizes. In contrast, motor control, strengthening and yoga/Pilates/Tai Chi/Qigong exercise showed similar large effect sizes with more narrow CIs and a greater number of studies and participants. These exercise types would seem to be promising approaches for neck pain. Similar results were found for improving pain-related disability. For other exercise types, including physical activity, range of motion, balance, strengthening and stretching combined, and multimodal exercises, effects were small with wide CIs indicating inconsistency and uncertainty in the interpretation of findings.

We were not able to address the secondary research question because insufficient data were available within separate nodes to allow for an investigation of the differential effects of different exercise durations, intensities and frequencies. Therefore, we cannot provide guidance on the dose-response relationship between exercise therapy and treatment effectiveness. Clinicians can refer to [table 3](#) for details around the parameters of the exercise interventions.

Clinical implications of findings

The results of the NMA indicate that there is not one superior type of exercise that should be prescribed for chronic neck pain. However, three interventions (ie, motor control, yoga/Pilates/Tai Chi/Qigong and strengthening) showed large effect sizes, narrow CIs and a relatively large number of studies and participant numbers for both pain and disability outcomes. Using the recommended method in the Cochrane handbook²⁹ and SD of 2.0 for VAS pain intensity⁵⁴ and 13% for the NDI,⁵⁵ the effect sizes can be re-expressed in the units of measurement of these commonly used tools. Compared with no treatment, motor control exercises would reduce pain intensity by 2.6 points, yoga/Pilates/Tai Chi/Qigong by 2.5 points and strengthening exercises by 2.4 points, all clinically relevant effects (usually defined by a 2.0 point change on a VAS).⁵⁶ For disability and using the NDI as the example, motor control exercises would improve disability by 11%, yoga/Pilates/Tai Chi/Qigong by 15% and strengthening exercises by 9.8%, close to or exceeding a clinically relevant difference of 10% on the NDI.⁵⁷ These results indicate that these three exercise approaches are the most promising and could be clinically useful in the management of chronic neck pain. As such, a clinician could choose any of these three physical exercise interventions with the highest confidence of improving patient-reported outcomes. Until further high-quality evidence becomes available, the selection of motor control, yoga/Pilates/Tai Chi/Qigong or strengthening exercises may be aligned with clinician and/or patient personal preference.

Although the majority of the exercise interventions showed positive effects on pain intensity, most of these are associated with wide CIs. In particular, the CIs for combined strengthening and stretching, range of motion, balance and multimodal

exercises cross '0', indicating the effectiveness of these interventions is uncertain. A similar pattern of results was found for disability outcomes; aside from motor control, yoga/Pilates/Tai Chi/Qigong and strengthening exercises, the effects of all other exercise types had wide CIs that cross '0' indicating uncertainty of treatment effectiveness. Small effect sizes and wide CIs for range of motion, multimodal and prescribed physical activity indicate that these interventions may not be effective in improving pain-related disability. Range of motion, balance and multimodal exercises are commonly recommended in clinical guidelines for the management of neck pain.⁶ Based on the results of the NMA, these recommendations should be revisited in the development of future clinical guidelines.

It should be noted that some of the evidence was obtained from a small number of pairwise comparisons with small sample sizes. This may have led to some unlikely results, for example, strengthening and stretching as separate interventions were effective in improving pain and disability (compared with 'no treatment': nine direct comparisons for strengthening and one for stretching), but when combined (no direct comparison) appeared to lose their effectiveness. Similarly, the finding that prescribed physical activity did not improve disability is surprising, but perhaps also reflects imprecision due to the small number of studies (online supplemental file E). We found that the signs (ie, positive or negative) of some effect estimates point in opposite directions, which is unsurprising in cases where the estimates are close to zero or where precision is low because of lack of data. In the evaluation of precision, we did therefore not focus on sign alone.

Other network meta-analyses

No other NMA investigating the effectiveness of different interventions for chronic neck pain is available for comparison, though some other groups have published protocols indicating they are conducting similar work.^{58 59} These NMAs are substantially different to the current NMA, however, as they (1) include any intervention, not only exercise, for neck pain, (2) do not differentiate between the numerous different types of exercise and (3) do not only include non-specific neck pain, but also traumatic neck pain.

In contrast to the two above-mentioned NMAs, our NMA only included physical exercise interventions. By focussing on these exercise interventions, we were able to differentiate between specific, separate types of physical exercise. This can provide more nuanced information for clinicians who prescribe therapeutic exercise. International guidelines for the treatment of neck pain state that different types of exercise should be incorporated for the best treatment effects.⁶⁰ These include strengthening and motor control exercises, and the current NMA demonstrates that these types of exercise are expected to exert similar effects.

Including different types of chronic neck pain in one NMA affects the transitivity assumption of NMA, as all interventions should be joint randomisable across all participants.²⁶ From a clinical point of view, there may be differences in the therapeutic exercise prescription between individuals with chronic non-specific neck pain and those with chronic traumatic neck pain, for example, whiplash associated disorder.⁶ Through a preliminary literature search we identified that it was not possible to conduct separate NMAs for non-specific neck pain and traumatic neck pain due to an insufficient number of RCTs for traumatic neck pain. For this reason, we have included only chronic non-specific neck pain, a group that is more common than any other

type of neck pain.⁶¹ While not all potential effect modifiers were investigated, we compared the descriptive statistics of the participant characteristics across the included studies. Based on this investigation, we made the assumption of joint randomisability.

Two recent NMAs investigated the effectiveness of exercise interventions¹⁹ and exercise and education⁶² in individuals with chronic non-specific low back pain. The findings of the current NMA are similar to these two NMAs, both concluding that several types of exercise are equally effective. Owen and colleagues¹⁹ found that Pilates, aerobic, stabilisation/motor control, multi-modal, resistance and 'other' exercise training were effective in improving pain. Stabilisation and motor control, resistance, water-based, Pilates, yoga, multimodal, aerobic and 'other' exercises were most effective in improving disability. While slightly different exercise nodes were identified compared with the two aforementioned NMAs, results of our NMA on neck pain were broadly similar to those conducted in low back pain.

Limitations

An inherent limitation of NMA is deriving indirect evidence from a limited number of direct pairwise comparisons. For the pain intensity NMA, 19 direct pairwise comparisons were available between the 10 nodes of the network, from which indirect evidence for a total of 63 pairwise comparisons was derived. For the pain-related disability NMA, 18 direct comparisons were available between the 10 nodes, from which 59 indirect comparisons were derived. Despite NMA allowing for combining direct and indirect evidence, some of the results may be derived from small sample studies further affecting the certainty of evidence. In the current study, this is apparent from the forest plots for both NMAs, demonstrating uncertainty in the point measure as well as large CIs for many of the exercise interventions. Although these limitations are inevitable, the proportion of indirect evidence and the precision of the effects have been taken in consideration in the GRADE assessment. From this assessment, we determined that the certainty of evidence for both networks is very low. Furthermore, the inconsistency measure was not statistically significant, indicating that evidence from direct and indirect comparisons is not different. While PEDro is commonly used to assess methodological quality, compared with the Cochrane Risk of Bias 2 tool it may underestimate risk of bias of included studies.⁶³

Measures of treatment effectiveness for pain intensity and pain-related disability were extracted from the included studies at the follow-up time point closest to the completion of the treatment period. From the data provided in table 3 it is apparent that treatments of varying durations, ranging from 1 to 12 months, were included in the analyses.

Our grading of the evidence quality as very low is consistent with a recent Cochrane review investigating therapeutic exercise for neck disorders, which found that no high quality evidence was available.⁶⁴ Reasons for downgrading the quality of evidence included in our NMA were substantial risk of bias and imprecision. Although imprecision may be caused by variance in treatment outcomes, that is, some patients will respond well to a treatment, and others do not, the quality of evidence appears to be primarily limited by small sample sizes, few studies for some comparisons and (for future studies preventable) flaws in study designs. Performing more small-sized RCTs, and systematic reviews and meta-analyses of existing literature, will inevitably show similar low quality evidence for modest effects of exercise. Therefore, it appears to be more beneficial to conduct

well-designed, large trials investigating the comparative effective of different types of physical exercise for people with neck pain.

Compared with the forest plot for pain intensity (figure 3), visual inspection of the forest plot for pain-related disability (figure 5) reveals that the CIs are considerably wider. A possible reason for this is that the tools used for the assessment of pain-related disability (ie, NDI, NPAD and NPNPI) are multifactorial questionnaires and comprise of different aspects of disability. Rather than only assessing one aspect in the pain intensity NMA, the pain-related disability NMA assesses effectiveness on aspects such as pain interference, physical function, psychological function and social status. While this is inherent to these types of tools, it is worth noting that it is likely that combining pairwise comparisons with a high level of uncertainty have led to wide CIs in the NMA.

Although we acknowledge there are differences between yoga, Pilates, Tai Chi and Qigong exercises, for the purpose of this NMA we combined these regimes into one exercise 'type' (node). Considering these are all whole-body, non-specific exercise regimes (ie, the exercises do not specifically target cervical function), they did not suit combining with any of the other types of exercise. It was not possible to separate these interventions into four separate nodes due to the low number of studies. Although it is possible that they may have different effects on pain intensity and pain-related disability, the forest plots would suggest otherwise. The 95% CIs were small, indicating precision in the outcome measure and consistent results across the exercise regimes within this group.

Lastly, due to a variety of mixed strengthening regimes, we were not able to separate out strengthening exercises. While Gross *et al*⁶⁴ reported upper limb and cervical exercises separately, both interventions included also scapulothoracic and shoulder stabilisation exercises. Since clinically there is often no clear distinction between just cervical exercises and exercises for the cervical, scapulothoracic and shoulder girdle regions, exercises commonly target multiple areas. While this reflects common clinical practice, it does not allow for further investigation of the effectiveness of isolated strengthening exercises.

Conclusion

The findings of this NMA indicate that there is not one superior type of exercise for people with chronic non-specific neck pain. Rather, compared with 'no treatment' some exercise types have positive effects on pain intensity and pain-related disability, including motor control, yoga/Pilates/Tai Chi/Qigong and strengthening exercises. Other types of physical exercise

What is already known, what are the new findings?

- ▶ Exercise therapy is commonly prescribed for people with chronic non-specific neck pain.
- ▶ The most effective exercise type for people with neck pain is not known.
- ▶ Motor control, yoga/Pilates/Tai Chi/Qigong and strengthening exercises were found to have large effects on pain and disability. There was no one form of exercise that was superior to others.
- ▶ Some interventions (range of motion, balance and multimodal exercises) had uncertain or negligible effects.
- ▶ The certainty of evidence for physical exercise interventions to manage chronic non-specific neck pain was graded as very low.

were less consistently effective, and some interventions (range of motion, balance and multimodal exercises) were found to be not effective. Comparing all interventions against each other did not identify which types of exercise were superior to others. These novel findings may assist clinicians to choose an appropriate exercise intervention for individuals with chronic non-specific neck pain, while recognising that the certainty of evidence included in the two NMAs is very low.

Twitter Rutger MJ de Zoete @DrRdeZoete and Michele Sterling @MicheleSterlin7

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Supplementary files

Supplementary file A: Search Strategy for all databases

MEDLINE, AMED, CINAHL, and SPORTDiscus:

(exercis* OR exertion OR "physical fitness" OR sport* OR pliability OR "physical endurance" OR "physical therapy" OR rehabilitation OR exertion* OR resistance OR run* OR jog* OR treadmill* OR swim* OR bicycl* OR walk* OR muscle strength* OR (physical W3 (fitness OR therapy)) OR (physical* W2 endur*) OR ((strength* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR endurance OR weight*) N3 train*) OR (cycle* OR cycling) OR (row OR rows OR rowing) OR (skate* OR skating)) AND (("Neck Pain" OR "Neck Injuries" OR neckache OR "neck ache" OR cervicodynia OR cervicalgia) OR ((injur* OR pain* OR ach* OR sore OR stiff* OR discomfort OR "chronic pain") N3 (neck OR cervical OR cervico*))) AND (Randomi?ed OR randomly OR RCT OR "placebo controlled")

EMBASE:

(exercis* OR exertion OR "physical fitness" OR sport* OR pliability OR "physical endurance" OR "physical therapy" OR rehabilitation OR exertion* OR resistance OR run* OR jog* OR treadmill* OR swim* OR bicycl* OR walk* OR "muscle strength*" OR (physical adj3 (fitness OR therapy)) OR (physical* adj2 endur*) OR ((strength* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR endurance OR weight*) adj3 train*) OR (cycle* OR cycling) OR (row OR rows OR rowing) OR (skate* OR skating)) AND (Neck Pain OR Neck Injuries OR neckache OR neck ache OR cervicodynia OR cervicalgia OR ((injur* OR pain* OR ach* OR sore OR stiff* OR discomfort OR chronic pain) adj3 (neck OR cervical OR cervico*))) AND (Randomi?ed OR randomly OR RCT OR "placebo controlled")

PsycINFO:

(exercis* OR exertion OR physical fitness OR sport* OR pliability OR physical endurance OR physical therapy OR rehabilitation OR exertion* OR resistance OR run* OR jog* OR treadmill* OR swim* OR bicycl* OR walk* OR muscle strength* OR (physical near/3 (fitness OR therapy)) OR (physical* near/2 endur*) OR ((strength* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR endurance OR weight*) near/3 train*) OR (cycle* OR cycling) OR (row OR rows OR rowing) OR (skate* OR skating)) AND (Neck Pain OR Neck Injuries OR neckache OR neck ache OR cervicodynia OR cervicalgia OR ((injur* OR pain* OR ach* OR sore OR stiff* OR discomfort OR chronic pain) near/3 (neck OR cervical OR cervico*))) AND (Randomi?ed OR randomly OR RCT OR placebo controlled)

Cochrane Central Register of Controlled Trials:

(exercis* OR exertion OR physical fitness OR sport* OR pliability OR physical endurance OR physical therapy OR rehabilitation OR exertion* OR resistance OR run* OR jog* OR treadmill* OR swim* OR bicycl* OR walk* OR muscle strength* OR (physical NEAR/3 (fitness OR therapy)) OR (physical* NEAR/2 endur*) OR ((strength* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR endurance OR weight*) NEAR/3 train*) OR (cycle* OR cycling) OR (row OR rows OR rowing) OR (skate* OR skating)) AND ((Neck Pain OR Neck Injuries OR neckache OR neck ache OR cervicodynia OR cervicalgia) OR ((injur* OR pain* OR ach* OR sore OR stiff* OR discomfort OR chronic pain) NEAR/3 (neck OR cervical OR cervico*))) AND (Randomi?ed OR randomly OR RCT OR placebo controlled)

Scopus:

(exercis* OR exertion OR "physical fitness" OR sport* OR pliability OR "physical endurance" OR "physical therapy" OR rehabilitation OR exertion* OR resistance OR run* OR jog* OR treadmill* OR swim* OR bicycl* OR walk* OR "muscle strength") OR ((physical W/3 (fitness OR therapy)) OR (physical* W/2 endur*) OR ((strength* OR isometric* OR isotonic* OR isokinetic* OR aerobic* OR endurance OR weight*) W/3 train*) OR (cycle* OR cycling) OR (row OR rows OR rowing) OR (skate* OR skating)) AND (("Neck Pain" OR "Neck Injuries" OR neckache OR "neck ache" OR cervicodynia OR cervicalgia) OR ((injur* OR pain* OR ach* OR sore OR stiff* OR discomfort OR "chronic pain") W/3 (neck OR cervical OR cervico*))) AND (Randomi?ed OR randomly OR RCT OR "placebo controlled")

Physiotherapy Evidence Database:*Search 1:*

Abstract & title: exercise neck pain

Therapy: fitness training

Problem: pain

Body part: head or neck

Sub discipline: Musculoskeletal

Topic: chronic pain

Method: clinical trial

Search 2:

Abstract & title: exercise neck pain

Therapy: strength training

Problem: pain

Body part: head or neck

Sub discipline: Musculoskeletal

Topic: chronic pain

Method: clinical trial

Supplementary file B: Summary table of all data included in the network for pain intensity

Treatment types: 1 Strengthening, 2 Multimodal, 3 PPA+Strength, 4 Motor Control, 5 Stretching, 6 Proprioceptive, 7 No treatment, 8 Prescribed PPA, 9 Strength+Stretch, 10 Balance, 11 Yoga/Pilates/Tai Chi/Qigong, 12 Strength+Motor Control, 13 ROM

painID	study	Author year	Treatment arm 1				Treatment arm 2				Treatment arm 3				Treatment arm 4			
			treat	y	sd	n	treat	y	sd	n	treat	y	sd	n	treat	y4	sd4	n4
1	1	Alpayci 2017	1	-3.91	1.672692	34	7	-1.56	1.478276	31								
2	2	Andersen 2013	1	-26	22.89509	69	7	-12	24.37041	49								
3	3	Andersen 2014	1	-1.862	0.508	24	7	0.015	0.554	23								
4	4	Andersen 2012	1	-2.291	0.309	43	1	-3.02	0.355	40	1	-2.509	0.455	27	7	-1.164	0.364	48
5	5	Andersen 2008	1	-20	13.0767	18	8	-2	18.24829	16	7	-1	21.07131	8				
6	7	Beinert 2013	10	-1.68	1.645934	17	7	-0.83	2.585595	17								
7	8	Bobos 2016	4	-3.45	2.045558659	23	1	-1.65	2.082327399	22	7	-1	1.873932	22				
8	9	Caputo 2017	1	2.86667	2.26017	18	5	4.16667	2.592593	17								
9	11	Chiu 2005	12	-1.6	2.12838	67	7	-0.5	2.206808	78								
10	12	Cramer 2013	11	-28.6	17.10205	25	9	-12.1	22.26028	26								
11	13	deAurajo 2018	11	-5.1	1.665023	32	7	-0.28	1.905282	32								
12	14	Dellve 2011	1	-0.1	1.7	20	7	0.5	1.6	20								
13	15	Dunleavy 2016	11	-0.9	1.282012	20	11	-0.3	1.348591	19	7	-0.2	0.447338	17				
14	17	Evans 2012	1	-3.1	1.68226	89	8	-1.9	1.852026	90								
15	18	Falla 2008	4	-0.9	2.4	28	1	-1.1	2.8	29								
16	21	Falla 2013	12	-1.7	2.2	22	7	-0.3	2.1	23								
17	22	Izquierdo 2016	4	3.49667	0.955412	14	6	3.52667	1.274332	14								
18	23	Ghaderi 2017	4	-39.62	24.24067	20	7	-39	19.57217	20								
19	26	Hakkinen 2008	5	-32	25.14352	52	1	-37	24.37041	49								
20	27	Hoving 2012	2	-2.8	2.3	59	7	-2.6	2.4	64								

21	30	Javanshir 2015	4	-2.7	1.63	30	1	-2.32	1.19	30				
22	31	Jordan 2011	11	-31	17.47311	42	8	-30.1	22.94796	39	7	-12.4	23.64007	41
23	32	Jull 2009	4	-1.7	2	23	1	-1	3.3	23				
24	33	Jull 2002	12	-3.26	2.740219	52	7	-1.43	2.078461	48				
25	34	Karlsson 2014 Khosrokiani	9	-2.5	4.50575	34	5	1.33333	2.566001	23				
26	36	2018	4	-2.4	1.848351	15	7	0.73	2.604304	15				
27	38	Kjellman 2002	8	-29	24.63737	23	7	-26	21.65641	26				
28	40	Lange 2013	12	-1	0.34641	27	7	0.2	0.4	28				
29	42	Lansinger 2007	11	-13.75	17.58954	60	1	-23.25	17.86016	62				
30	43	Lauche 2016	11	-21.8	22.11357	38	8	-21	18.76619	37	7	-9.7	21.83369	39
31	44	Li 2017	1	-2.86	1.130796	38	1	-2.41	0.972163	35	7	-0.34	1.104898	36
32	46	Michalsen 2012	11	-31.3	17.47598	38	8	-7.5	21.51116	39				
33	50	OLeary 2012	1	-9	16.53028	20	4	-19.2	11.85074	20	13	-10.1	11.63228	20
34	51	Ravi 2016	1	-2.8	0.750395	25	6	-3.08	0.676683	25				
35	52	Rendant 2011 Tunwattanapong	8	-6.82	1.45	34	7	-1.56	1.478276	31				
36	59	2016	5	-2.2	1.587451	48	7	-0.6	1.56205	48				
37	60	Viljanen 2003	1	-1.9	2.463737	135	7	-1.4	2.364318	130				
38	69	Ylinen 2003	1	-39	21.07130751	60	1	-34	22	59	7	-15	21.65640783	60

Supplementary file C: Summary table of all data included in the network for disability

disabID	study	Author year	Treatment arm 1				Treatment arm 2				Treatment arm 3			
			treat	y	sd	n	treat	y	sd	n	treat	y	sd	n
1	8	Bobos 2016	4	-11.4	6.956469	23	1	-4.2	5.184963	22	7	-2.4	3.880434	22
2	9	Caputo 2017	1	-7.83333	7.379577	18	5	-9	9.281455	17				
3	11	Chiu 2005	12	-0.4	0.556776	67	7	-0.3	0.556776	78				
4	12	Cramer 2013	11	-7.8	9.901515	25	9	-3.8	13.22876	26				
5	13	deAurajo 2018	11	-9.72	6.066927	32	7	-2.19	6.442911	32				
6	15	Dunleavy 2016	11	-4.3	5.662219	20	11	-4.7	5.498101	19	7	-0.3	0.447338	17
7	17	Evans 2012	1	-10.1	10.62968	89	8	-9	9.76166	90				
8	18	Falla 2008	4	-3.7	4.7	28	1	-2.8	4	29				
9	21	Falla 2013	12	-4.1	4.8	22	7	-1	4.4	23				
10	22	Gallego Izquierdo 2016	4	-3.25	2.488614	14	6	-3.28	2.753525	14				
11	23	Ghaderi 2017	4	-16	10.97133	20	7	-15.72	13.43093	20				
12	24	Griffiths 2009	7	-6.98	20.24654	37	4	-6.83	21.39445	37				
13	26	Hakkinen 2008	5	-8	10.77579	52	1	-8	10.44446	49				
14	27	Hoving 2012	2	-6	7	59	7	-5.9	7.2	64				
15	30	Javanshir 2015	4	-18.07	10.2	30	1	-14.2	11.2	30				
16	31	Jordan 2011	11	-14	11.73065	42	8	-8	15.11241	39	7	-5.1	15.01558	41
17	32	Jull 2009	4	-5	4.2	23	1	-3.5	2.3	23				
18	33	Jull 2002	12	-11.03	15.57598	52	7	-3.72	9.976613	48				
19	34	Karlsson 2014	9	-5	5.925926	34	5	-5.83333	5.185185	23				
20	36	Khosrokiani 2018	4	-17.86	11.89003	15	7	0.26	11.6042	15				
21	38	Kjellman 2002	8	-12	16	23	7	-9	14.52584	26				
22	42	Lansinger 2007	11	0	13.18038	60	1	-4.5	10.19103	62				
23	43	Lauche 2016	11	-9.3	10.73499	38	8	-7.4	9.559812	37	7	-1.8	10.1843	39
24	44	Li 2017	1	-12.53	5.708756	38	1	-12.06	6.087988	35	7	-0.34	6.435985	36
25	46	Michalsen 2012	11	-7	4.71593	38	8	24.5	6	39				

26	50	O'Leary 2012	1	-4.9	3.724245	20	4	-4.4	2.666458	20	13	-2.9	2.98161	20
27	51	Ravi 2016	1	-8.424	7.564225	25	6	-3.64	7.022052	25				
28	59	Tunwattanapong 2016	5	-7	11.54686	48	7	-2.3	13.01576	48				
29	69	Ylinen 2003	1	-24	13	60	1	-22	14.5284	59	7	-12	15	60

Supplementary file D: Details of GRADE assessment for all pairwise comparisons within the pain intensity network

Comparison	k	Prop	direct SMD [95% CI]	Quality of	Indirect SMD [95% CI]	Quality of	NMA SMD [95% CI]	Quality	p-
				evidence		evidence		of	
Balance vs No treatment	1	1	-0.3829 [-2.1548;1.3889]	Very low‡*			-0.3829 [-2.1548;1.3889]	Very low‡	
Multimodal vs No treatment	1	1	-0.0845 [-1.7588;1.5899]	Very low‡			-0.0845 [-1.7588;1.5899]	Very low‡	
Motor control vs No treatment	3	0.47	-0.845 [-1.8703;0.1803]	Very low‡*	-1.9015 [-2.8725;-0.9305]	Moderate	-1.402 [-2.1070;-0.6970]	Moderate	0.1426
Prescribed PA vs No treatment	5	0.7	-0.9854 [-1.7704;-0.2004]	Low†	-0.5854 [-1.7850;0.6142]	Very low‡	-0.8655 [-1.5223;-0.2086]	Low†	0.5845
Strength vs No treatment	9	0.7	-1.3998 [-1.9805;-0.8190]	Low*	-1.1585 [-2.0380;-0.2790]	Low†	-1.3265 [-1.8111;-0.8419]	Moderate	0.6537
Strength+Motor vs No treatment	4	1	-1.1944 [-2.0585;-0.3304]	Moderate			-1.1944 [-2.0585;-0.3304]	Moderate	
Stretch vs No treatment	1	0.33	-1.0079 [-2.6989;0.6831]	Very low‡	-1.2142 [-2.3937;-0.0347]	Low†	-1.1467 [-2.1141;-0.1792]	Low†	0.8445
YPTCQ vs No treatment	5	0.68	-1.018 [-1.7924;-0.2436]	Low†	-1.761 [-2.8900;-0.6321]	Moderate	-1.2557 [-1.8943;-0.6171]	Moderate	0.2874
Motor control vs Strength	5	0.69	-0.4064 [-1.1820;0.3693]	Very low‡	0.6706 [-0.4942;1.8353]	Very low‡	-0.0755 [-0.7211;0.5701]	Very low‡	0.1315
Prescribed PA vs Strength	2	0.35	0.8472 [-0.3714;2.0657]	Very low‡	0.2536 [-0.6397;1.1468]	Very low‡	0.4611 [-0.2594;1.1815]	Very low‡	0.4413
Proprioceptive vs Strength	1	0.55	-0.3857 [-2.1154;1.3439]	Very low‡*	-0.0809 [-1.9976;1.8358]	Very low‡	-0.2489 [-1.5330;1.0352]	Very low‡	0.817
ROM vs Strength	1	0.78	-0.0797 [-1.8298;1.6704]	Very low‡	1.4512 [-1.8917;4.7941]	Very low‡	0.2496 [-1.3008;1.8001]	Very low‡	0.4265
Motor control vs Proprioceptive	1	0.52	0.0259 [-1.7705;1.8223]	Very low‡	0.3307 [-1.5236;2.1850]	Very low‡	0.1734 [-1.1168;1.4637]	Very low‡	0.817
Motor control vs ROM	1	0.78	-0.6593 [-2.4159;1.0972]	Very low‡	0.8604 [-2.4479;4.1687]	Very low‡	-0.3251 [-1.8765;1.2263]	Very low‡	0.4265
Strength vs Stretch	2	0.59	0.1431 [-1.0765;1.3628]	Very low‡	-0.6528 [-2.1286;0.8230]	Very low‡	-0.1799 [-1.1200;0.7603]	Very low‡	0.4152
Strength+Stretch vs Stretch	1	0.6	-0.299 [-2.0198;1.4219]	Very low‡*	0.9456 [-1.1569;3.0481]	Very low‡	0.2003 [-1.1314;1.5320]	Very low‡	0.3693
Prescribed PA vs YPTCQ	3	0.58	0.4231 [-0.5582;1.4044]	Very low‡	0.3446 [-0.8132;1.5025]	Very low‡	0.3903 [-0.3583;1.1389]	Very low‡	0.9193

Strength vs YPTCQ	2	0.33	-0.0993 [-1.3104;1.1118]	Very low‡	-0.0564 [-0.9154;0.8026]	Very low‡	-0.0708 [-0.7714;0.6299]	Very low‡	0.9549
Strength+Stretch vs YPTCQ	1	0.59	0.8163 [-0.9177;2.5503]	Very low‡	-0.4282 [-2.5199;1.6635]	Very low‡	0.3094 [-1.0255;1.6444]	Very low‡	0.3693
Proprioceptive vs No treatment	0	0			-1.5754 [-2.9206;-0.2303]	Low†	-1.5754 [-2.9206;-0.2303]	Low†	
ROM vs No treatment	0	0			-1.0769 [-2.6775;0.5237]	Very low‡	-1.0769 [-2.6775;0.5237]	Very low‡	
Strength+Stretch vs No treatment	0	0			-0.9463 [-2.3175;0.4248]	Very low‡	-0.9463 [-2.3175;0.4248]	Very low‡	
Balance vs Multimodal	0	0			-0.2984 [-2.7363;2.1394]	Very low‡	-0.2984 [-2.7363;2.1394]	Very low‡	
Balance vs Motor control	0	0			1.0191 [-0.8879;2.9260]	Very low‡	1.0191 [-0.8879;2.9260]	Very low‡	
Multimodal vs Motor control	0	0			1.3175 [-0.4992;3.1342]	Very low‡	1.3175 [-0.4992;3.1342]	Very low‡	
Balance vs Prescribed PA	0	0			0.4825 [-1.4072;2.3722]	Very low‡	0.4825 [-1.4072;2.3722]	Very low‡	
Multimodal vs Prescribed PA	0	0			0.781 [-1.0176;2.5796]	Very low‡	0.781 [-1.0176;2.5796]	Very low‡	
Motor control vs Prescribed PA	0	0			-0.5365 [-1.4474;0.3743]	Very low‡	-0.5365 [-1.4474;0.3743]	Very low‡	
Balance vs Proprioceptive	0	0			1.1925 [-1.0321;3.4171]	Very low‡	1.1925 [-1.0321;3.4171]	Very low‡	
Multimodal vs Proprioceptive	0	0			1.491 [-0.6568;3.6387]	Very low‡	1.491 [-0.6568;3.6387]	Very low‡	
Prescribed PA vs Proprioceptive	0	0			0.71 [-0.7450;2.1649]	Very low‡	0.71 [-0.7450;2.1649]	Very low‡	
Balance vs ROM	0	0			0.694 [-1.6938;3.0817]	Very low‡	0.694 [-1.6938;3.0817]	Very low‡	
Multimodal vs ROM	0	0			0.9924 [-1.3239;3.3088]	Very low‡	0.9924 [-1.3239;3.3088]	Very low‡	
Prescribed PA vs ROM	0	0			0.2114 [-1.4827;1.9056]	Very low‡	0.2114 [-1.4827;1.9056]	Very low‡	
Proprioceptive vs ROM	0	0			-0.4985 [-2.4616;1.4646]	Very low‡	-0.4985 [-2.4616;1.4646]	Very low‡	
Balance vs Strength	0	0			0.9436 [-0.8934;2.7805]	Very low‡	0.9436 [-0.8934;2.7805]	Very low‡	
Multimodal vs Strength	0	0			1.242 [-0.5010;2.9851]	Very low‡	1.242 [-0.5010;2.9851]	Very low‡	
Balance vs Strength+Motor	0	0			0.8115 [-1.1598;2.7828]	Very low‡	0.8115 [-1.1598;2.7828]	Very low‡	
Multimodal vs Strength+Motor	0	0			1.1099 [-0.7742;2.9941]	Very low‡	1.1099 [-0.7742;2.9941]	Very low‡	

Motor control vs Strength+Motor	0	0	-0.2076 [-1.3227;0.9076]	Very low‡	-0.2076 [-1.3227;0.9076]	Very low‡
Prescribed PA vs Strength+Motor	0	0	0.329 [-0.7564;1.4143]	Very low‡	0.329 [-0.7564;1.4143]	Very low‡
Proprioceptive vs						
Strength+Motor	0	0	-0.381 [-1.9798;1.2177]	Very low‡	-0.381 [-1.9798;1.2177]	Very low‡
ROM vs Strength+Motor	0	0	0.1175 [-1.7014;1.9365]	Very low‡	0.1175 [-1.7014;1.9365]	Very low‡
Strength vs Strength+Motor	0	0	-0.1321 [-1.1228;0.8586]	Very low‡	-0.1321 [-1.1228;0.8586]	Very low‡
Balance vs Strength+Stretch	0	0	0.5634 [-1.6770;2.8039]	Very low‡	0.5634 [-1.6770;2.8039]	Very low‡
Multimodal vs Strength+Stretch	0	0	0.8619 [-1.3023;3.0260]	Very low‡	0.8619 [-1.3023;3.0260]	Very low‡
Motor control vs						
Strength+Stretch	0	0	-0.4557 [-1.9489;1.0375]	Very low‡	-0.4557 [-1.9489;1.0375]	Very low‡
Prescribed PA vs Strength+Stretch	0	0	0.0809 [-1.3722;1.5340]	Very low‡	0.0809 [-1.3722;1.5340]	Very low‡
Proprioceptive vs						
Strength+Stretch	0	0	-0.6291 [-2.5011;1.2429]	Very low‡	-0.6291 [-2.5011;1.2429]	Very low‡
ROM vs Strength+Stretch	0	0	-0.1306 [-2.1941;1.9330]	Very low‡	-0.1306 [-2.1941;1.9330]	Very low‡
Strength vs Strength+Stretch	0	0	-0.3802 [-1.7568;0.9965]	Very low‡	-0.3802 [-1.7568;0.9965]	Very low‡
Strength+Motor vs						
Strength+Stretch	0	0	-0.2481 [-1.8688;1.3726]	Very low‡	-0.2481 [-1.8688;1.3726]	Very low‡
Balance vs Stretch	0	0	0.7637 [-1.2550;2.7825]	Very low‡	0.7637 [-1.2550;2.7825]	Very low‡
Multimodal vs Stretch	0	0	1.0622 [-0.8716;2.9959]	Very low‡	1.0622 [-0.8716;2.9959]	Very low‡
Motor control vs Stretch	0	0	-0.2554 [-1.3691;0.8584]	Very low‡	-0.2554 [-1.3691;0.8584]	Very low‡
Prescribed PA vs Stretch	0	0	0.2812 [-0.8345;1.3969]	Very low‡	0.2812 [-0.8345;1.3969]	Very low‡
Proprioceptive vs Stretch	0	0	-0.4288 [-2.0111;1.1536]	Very low‡	-0.4288 [-2.0111;1.1536]	Very low‡

ROM vs Stretch	0	0	0.0698 [-1.7352;1.8747]	Very low‡	0.0698 [-1.7352;1.8747]	Very low‡
Strength+Motor vs Stretch	0	0	-0.0478 [-1.3448;1.2493]	Very low‡	-0.0478 [-1.3448;1.2493]	Very low‡
Balance vs YPTCQ	0	0	0.8728 [-1.0106;2.7562]	Very low‡	0.8728 [-1.0106;2.7562]	Very low‡
Multimodal vs YPTCQ	0	0	1.1713 [-0.6207;2.9633]	Very low‡	1.1713 [-0.6207;2.9633]	Very low‡
Motor control vs YPTCQ	0	0	-0.1463 [-1.0424;0.7499]	Very low‡	-0.1463 [-1.0424;0.7499]	Very low‡
Proprioceptive vs YPTCQ	0	0	-0.3197 [-1.7652;1.1258]	Very low‡	-0.3197 [-1.7652;1.1258]	Very low‡
ROM vs YPTCQ	0	0	0.1788 [-1.5072;1.8649]	Very low‡	0.1788 [-1.5072;1.8649]	Very low‡
Strength+Motor vs YPTCQ	0	0	0.0613 [-1.0131;1.1357]	Very low‡	0.0613 [-1.0131;1.1357]	Very low‡
Stretch vs YPTCQ	0	0	0.1091 [-0.9600;1.1782]	Very low‡	0.1091 [-0.9600;1.1782]	Very low‡

k = Number of studies providing direct evidence, prop = proportion of direct evidence, NMA (SMD) = estimated treatment effect (SMD) in network meta-analysis, direct (SMD) = estimated treatment effect (SMD) derived from direct evidence, indirect (SMD) = estimated treatment effect (SMD) derived from indirect evidence, p = p-value of test for disagreement (difference between direct and indirect evidence)

Reasons for downgrading: †Imprecision (1 downgrade), ‡Severe imprecision (2 downgrades), *risk of bias (1 downgrade)

The p-value indicated that the findings between direct and indirect comparisons was not statistically significant and therefore no comparisons have been downgraded based on inconsistency

Supplementary file E: Details of GRADE assessment for all pairwise comparisons within the pain-related disability network

Comparison	k	prop	Direct SMD [95% CI]	Quality of evidence	Indirect SMD [95% CI]	Quality of evidence	NMA SMD [95% CI]	Quality of evidence	p-value
Multimodal vs No treatment	1	1	-0.014 [-1.3719; 1.3440]	Very low‡			-0.014 [-1.3719; 1.3440]	Very low‡	
Motor Control vs No treatment	4	0.63	-0.7316 [-1.4629; -0.0004]	Very low‡*	-1.095 [-2.0454; -0.1447]	Very low‡	-0.8668 [-1.4463; -0.2873]	Low†	0.5525
Motor Control vs Proprioceptive	1	0.51	0.0111 [-1.4948; 1.5170]	Very low‡	-0.8175 [-2.3492; 0.7143]	Very low‡	-0.3961 [-1.4700; 0.6777]	Very low‡	0.4496
Motor Control vs ROM	1	0.79	-0.4659 [-1.9201; 0.9882]	Very low‡	-1.103 [-3.8939; 1.6879]	Very low‡	-0.602 [-1.8916; 0.6877]	Very low‡	0.6915
Motor Control vs Strength	5	0.69	-0.4188 [-1.0595; 0.2219]	Very low‡	0.5482 [-0.4051; 1.5015]	Very low‡	-0.1179 [-0.6497; 0.4139]	Very low‡	0.0989
Prescribed PA vs No treatment	3	0.66	-0.3163 [-1.1241; 0.4914]	Very low‡	0.9814 [-0.1436; 2.1063]	Very low‡	0.1251 [-0.5310; 0.7813]	Very low‡	0.0663
Prescribed PA vs Strength	1	0.3	0.1074 [-1.2361; 1.4508]	Very low‡	1.1999 [0.3240; 2.0758]	Very low‡	0.874 [0.1403; 1.6077]	Very low‡	0.1818
Prescribed PA vs YPTCQ	3	0.68	1.702 [0.8569; 2.5471]	Moderate	0.3958 [-0.8290; 1.6207]	Very low‡	1.2807 [0.5851; 1.9764]	Moderate	0.0854
Proprioceptive vs Strength	1	0.56	0.6452 [-0.7843; 2.0747]	Very low‡*	-0.1834 [-1.7866; 1.4199]	Very low‡	0.2782 [-0.7888; 1.3452]	Very low‡	0.4496
ROM vs Strength	1	0.78	0.6212 [-0.8360; 2.0785]	Very low‡	-0.0131 [-2.7871; 2.7609]	Very low‡	0.484 [-0.8060; 1.7741]	Very low‡	0.6915
Strength vs No treatment	3	0.43	-1.0156 [-1.8203; -0.2110]	Very low‡	-0.546 [-1.2476; 0.1556]	Very low‡	-0.7489 [-1.2777; -0.2201]	Very low‡	0.3886
Strength vs Stretch	2	0.61	0.0633 [-0.9379; 1.0646]	Very low‡	-0.2153 [-1.4723; 1.0418]	Very low‡	-0.0448 [-0.8280; 0.7384]	Very low‡	0.734
Strength vs YPTCQ	1	0.25	-0.3804 [-1.7395; 0.9787]	Very low‡	0.6721 [-0.1170; 1.4612]	Very low‡	0.4067 [-0.2757; 1.0892]	Very low‡	0.1893
Strength+Motor vs No treatment	3	1	-0.4542 [-1.2547; 0.3463]	Very low‡			-0.4542 [-1.2547; 0.3463]	Very low‡	
Strength+Stretch vs Stretch	1	0.61	0.1457 [-1.2684; 1.5598]	Very low‡*	-0.1833 [-1.9355; 1.5690]	Very low‡	0.016 [-1.0845; 1.1164]	Very low‡	0.7746
Strength+Stretch vs YPTCQ	1	0.6	0.3361 [-1.0869; 1.7591]	Very low‡	0.6651 [-1.0800; 2.4101]	Very low‡	0.4675 [-0.6353; 1.5703]	Very low‡	0.7746
Stretch vs No treatment	1	0.36	-0.379 [-1.7508; 0.9929]	Very low‡	-0.8839 [-1.9041; 0.1363]	Very low‡	-0.7041 [-1.5227; 0.1146]	Very low‡	0.5627
YPTCQ vs No treatment	4	0.7	-0.8575 [-1.5609; -0.1542]	Very low‡	-1.8585 [-2.9386; -0.7784]	Moderate	-1.1556 [-1.7450; -0.5662]	Moderate	0.128
Multimodal vs Motor Control	0	0			0.8528 [-0.6236; 2.3292]	Very low‡	0.8528 [-0.6236; 2.3292]		
Multimodal vs Prescribed PA	0	0			-0.1391 [-1.6473; 1.3690]	Very low‡	-0.1391 [-1.6473; 1.3690]		
Multimodal vs Proprioceptive	0	0			0.4567 [-1.3195; 2.2328]	Very low‡	0.4567 [-1.3195; 2.2328]		
Multimodal vs ROM	0	0			0.2508 [-1.6660; 2.1677]	Very low‡	0.2508 [-1.6660; 2.1677]		
Multimodal vs Strength	0	0			0.7349 [-0.7224; 2.1922]	Very low‡	0.7349 [-0.7224; 2.1922]		

Multimodal vs Strength+Motor	0	0	0.4402 [-1.1362; 2.0165]	Very low‡	0.4402 [-1.1362; 2.0165]
Multimodal vs Strength+Stretch	0	0	0.6741 [-1.1014; 2.4496]	Very low‡	0.6741 [-1.1014; 2.4496]
Multimodal vs Stretch	0	0	0.6901 [-0.8955; 2.2757]	Very low‡	0.6901 [-0.8955; 2.2757]
Multimodal vs YPTCQ	0	0	1.1416 [-0.3387; 2.6220]	Very low‡	1.1416 [-0.3387; 2.6220]
Motor Control vs Prescribed PA	0	0	-0.9919 [-1.8069; -0.1769]	Very low‡	-0.9919 [-1.8069; -0.1769]
Motor Control vs Strength+Motor	0	0	-0.4126 [-1.4009; 0.5757]	Very low‡	-0.4126 [-1.4009; 0.5757]
Motor Control vs Strength+Stretch	0	0	-0.1787 [-1.4017; 1.0444]	Very low‡	-0.1787 [-1.4017; 1.0444]
Motor Control vs Stretch	0	0	-0.1627 [-1.0604; 0.7350]	Very low‡	-0.1627 [-1.0604; 0.7350]
Motor Control vs YPTCQ	0	0	0.2888 [-0.4775; 1.0552]	Very low‡	0.2888 [-0.4775; 1.0552]
Prescribed PA vs Proprioceptive	0	0	0.5958 [-0.6701; 1.8616]	Very low‡	0.5958 [-0.6701; 1.8616]
Prescribed PA vs ROM	0	0	0.39 [-1.0674; 1.8473]	Very low‡	0.39 [-1.0674; 1.8473]
Prescribed PA vs Strength+Motor	0	0	0.5793 [-0.4557; 1.6144]	Very low‡	0.5793 [-0.4557; 1.6144]
Prescribed PA vs Strength+Stretch	0	0	0.8133 [-0.4211; 2.0476]	Very low‡	0.8133 [-0.4211; 2.0476]
Prescribed PA vs Stretch	0	0	0.8292 [-0.1522; 1.8106]	Very low‡	0.8292 [-0.1522; 1.8106]
Proprioceptive vs No treatment	0	0	-0.4706 [-1.6155; 0.6742]	Very low‡	-0.4706 [-1.6155; 0.6742]
Proprioceptive vs ROM	0	0	-0.2058 [-1.8393; 1.4276]	Very low‡	-0.2058 [-1.8393; 1.4276]
Proprioceptive vs Strength+Motor	0	0	-0.0165 [-1.4134; 1.3805]	Very low‡	-0.0165 [-1.4134; 1.3805]
Proprioceptive vs Strength+Stretch	0	0	0.2175 [-1.3374; 1.7723]	Very low‡	0.2175 [-1.3374; 1.7723]
Proprioceptive vs Stretch	0	0	0.2334 [-1.0739; 1.5407]	Very low‡	0.2334 [-1.0739; 1.5407]
Proprioceptive vs YPTCQ	0	0	0.685 [-0.5511; 1.9210]	Very low‡	0.685 [-0.5511; 1.9210]
ROM vs No treatment	0	0	-0.2648 [-1.6177; 1.0880]	Very low‡	-0.2648 [-1.6177; 1.0880]
ROM vs Strength+Motor	0	0	0.1893 [-1.3826; 1.7613]	Very low‡	0.1893 [-1.3826; 1.7613]
ROM vs Strength+Stretch	0	0	0.4233 [-1.2913; 2.1379]	Very low‡	0.4233 [-1.2913; 2.1379]
ROM vs Stretch	0	0	0.4392 [-1.0549; 1.9333]	Very low‡	0.4392 [-1.0549; 1.9333]
ROM vs YPTCQ	0	0	0.8908 [-0.5407; 2.3222]	Very low‡	0.8908 [-0.5407; 2.3222]
Strength vs Strength+Motor	0	0	-0.2947 [-1.2541; 0.6647]	Very low‡	-0.2947 [-1.2541; 0.6647]
Strength vs Strength+Stretch	0	0	-0.0608 [-1.2178; 1.0962]	Very low‡	-0.0608 [-1.2178; 1.0962]

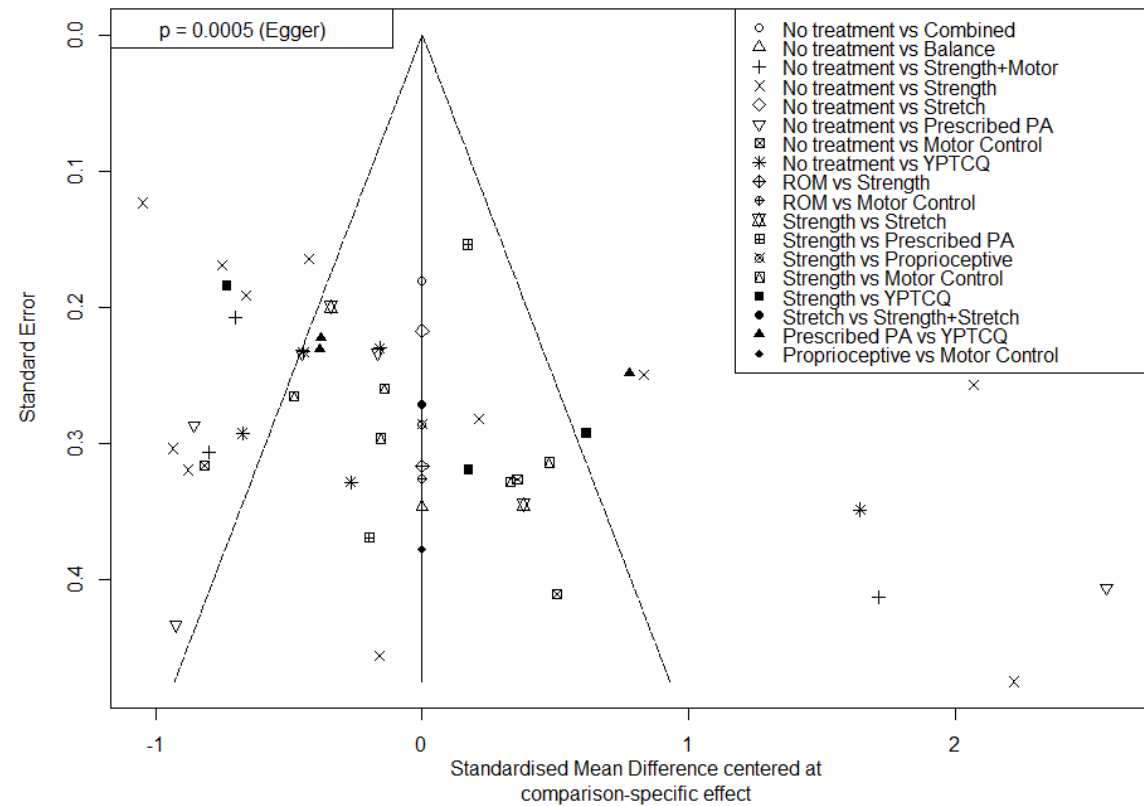
Strength+Motor vs					
Strength+Stretch	0	0	0.2339 [-1.1622; 1.6301]	Very low‡	0.2339 [-1.1622; 1.6301]
Strength+Motor vs Stretch	0	0	0.2499 [-0.8951; 1.3949]	Very low‡	0.2499 [-0.8951; 1.3949]
Strength+Motor vs YPTCQ	0	0	0.7014 [-0.2927; 1.6955]	Very low‡	0.7014 [-0.2927; 1.6955]
Strength+Stretch vs No treatment	0	0	-0.6881 [-1.8320; 0.4557]	Very low‡	-0.6881 [-1.8320; 0.4557]
Stretch vs YPTCQ	0	0	0.4515 [-0.4594; 1.3625]	Very low‡	0.4515 [-0.4594; 1.3625]

k = Number of studies providing direct evidence, prop = proportion of direct evidence, NMA (SMD) = estimated treatment effect (SMD) in network meta-analysis, direct (SMD) = estimated treatment effect (SMD) derived from direct evidence, indirect (SMD) = estimated treatment effect (SMD) derived from indirect evidence, p = p-value of test for disagreement (difference between direct and indirect evidence)

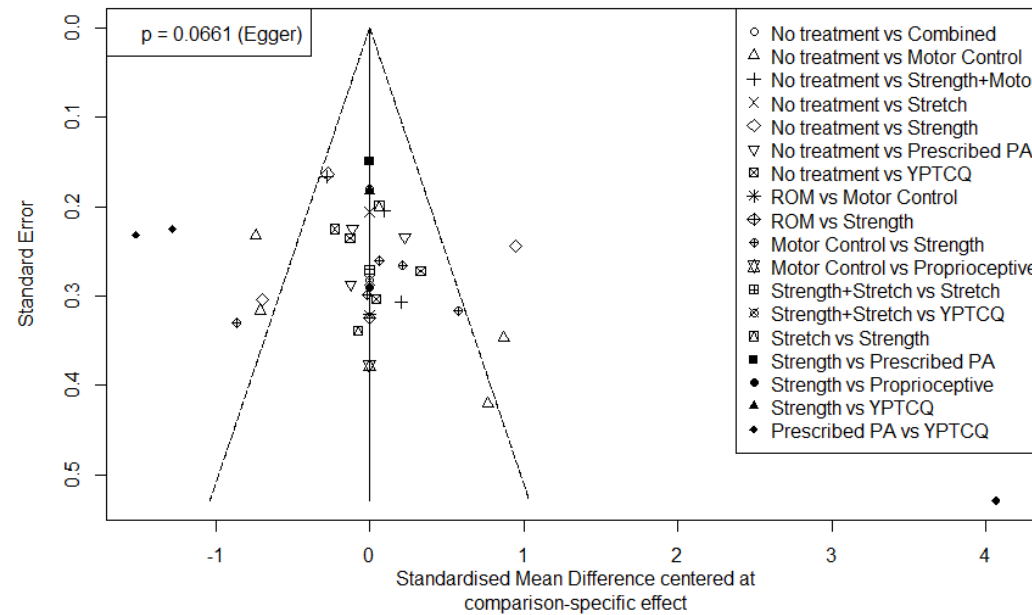
Reasons for downgrading: †Imprecision (1 downgrade), ‡Severe imprecision (2 downgrades), *risk of bias (1 downgrade)

The p-value indicated that the findings between direct and indirect comparisons was not statistically significant and therefore no comparisons have been downgraded based on inconsistency

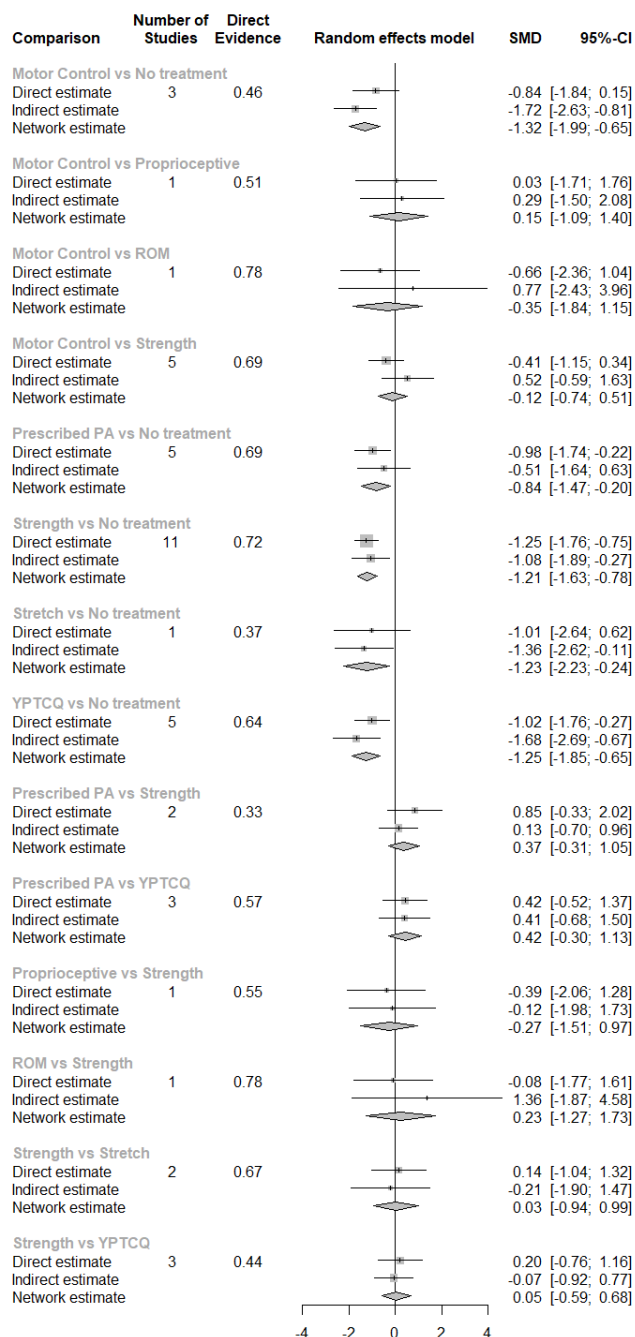
Supplementary file F: Funnel plot for the pain intensity network.



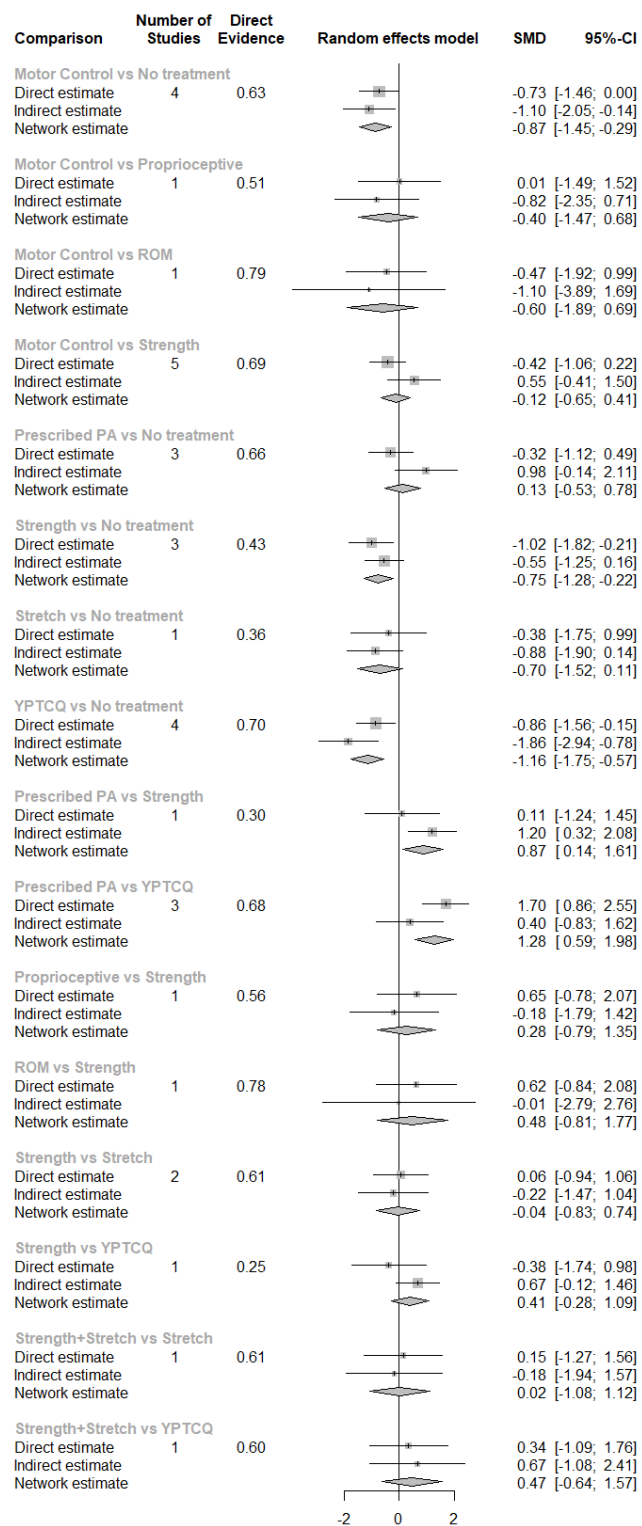
Supplementary file G: Funnel plot for the pain-related disability network.



Supplementary file H. Forest plot of direct and indirect evidence for the pain NMA.



Supplementary file I. Forest plot of direct and indirect evidence for the disability NMA.



Multiple Choice Questions:

1. Fill in the blank: The current available evidence indicates that physical exercise has effects on chronic neck pain.
 - a) Excellent
 - b) Good
 - c) Modest (correct)
 - d) Minimal

2. Whilst 'regular' systematic reviews with meta-analysis assess pairwise comparisons, network meta-analysis uses:
 - a) Direct evidence from pairwise randomised controlled trials.
 - b) Indirect evidence from pairwise randomised controlled trials.
 - c) A combination of direct and indirect evidence from randomised controlled trials. (correct)

3. The results of this NMA indicate that the following types of physical exercise have positive effects of neck pain intensity and pain-related disability:
 - a) Strengthening exercises only.
 - b) Proprioceptive exercises only.
 - c) Motor control, strengthening, and yoga/Pilates/Tai Chi/Qigong exercises (correct)
 - d) Proprioceptive, strengthening and stretching, and prescribed physical activity exercises.

4. The certainty of evidence (assessed with the GRADE approach) for randomised controlled trials investigating physical exercise interventions for individuals with chronic neck pain is:
 - a) High
 - b) Moderate
 - c) Low
 - d) Very low (correct)

5. The inconsistency measure was not statistically significant. This indicates that:
- a) Evidence from direct and indirect comparisons is not different. (correct)
 - b) Evidence from direct and indirect comparisons is different.
 - c) Results from the individual studies included in the NMA is not different.
 - d) Results from the individual studies included in the NMA is different.