

### Effects of matched vs. unmatched physical therapy interventions on pain or disability in patients with neck pain - a systematic review and meta-analysis.

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### SYSTEMATIC REVIEW

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# Effects of matched vs. unmatched physical therapy interventions on pain or disability in patients with neck pain – a systematic review and meta-analysis

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### ABSTRACT

**Background:** The interventions performed in most randomized controlled trials (RCTs) on neck pain patients are standardized, irrespective of the high heterogeneity of patients. However, clinicians tend to choose an intervention based on the patients' clinical characteristics, and thus match the treatment to the patient.

**Objectives:** To investigate the effectiveness of interventions matched to the clinical characteristics of patients with neck pain versus the same, but unmatched treatment for improving pain or disability.

**Design:** A systematic review and meta-analysis conducted following Cochrane guidelines **Methods:** Databases searches were performed from inception to September 2023. RCTs were included if the patients in the experimental group received a treatment matched to clinical presentation or to clinicians' assessment, if the patients in the control group received a similar but unmatched treatment, and if pain or disability were reported as outcome measures.

**Results:** The literature search produced 9516 records of which 27 met the inclusion criteria. Matched exercise therapy was superior to unmatched exercise for pain (SMD -0.57; 95% Cl -0.95, -0.18) and for disability (SMD -0.69; 95% Cl -1.14, -0.23) at short term, but not at intermediate-term follow-up. Matched manual treatment was not superior to unmatched manual therapy for pain or for disability at short or intermediate-term follow-up.

**Conclusions:** Results suggest that matching exercise to movement limitation, trapezius myalgia, or forward head position may lead to better outcomes in the short term, but not in the intermediate-term. Matched manual therapy was not superior to unmatched treatment either short or intermediate-term. Further research is warranted to verify if those criteria are potentially useful matching criteria.

#### **ARTICLE HISTORY**

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#### **KEYWORDS**

Neck pain; matched treatment; assessment; clinical decision making; clinical reasoning

### Introduction

Neck pain is the ninth and eleventh most common cause of disability among females and males worldwide, respectively (Vos et al., 2016). Its global annual incidence is higher in females; prevalence peaks at the 50–54 age group for females and at the 45–49 age group for males (Safiri et al., 2020). Although neck pain is generally considered to be a benign condition, 50% to 80% of people having neck pain will develop chronic or recurrent pain (Carroll et al., 2009).

Non-specific neck pain (NSNP) is defined as pain originating from the cervical spine, not related to trauma, without underlying serious pathologies or cervical radiculopathies, and constitutes the majority (90%) of those with neck pain (Verhagen, 2021). Existing European guidelines on NSNP management recommend reassurance, advice and education, non-steroidal antiinflammatory drugs (NSAIDs), paracetamol, topical medications, and exercise interventions alone or in combination with manual therapy (Corp et al., 2021). Exercise and manual therapy are the most commonly used physical therapy interventions (Verhagen, 2021); however, specific criteria for selecting a particular intervention are not given. Guidelines are based on systematic reviews of existing RCTs; however, some have criticized the value of such reviews derived as they are from trials of poor quality and clinical relevance (Jull and Moore, 2020). Furthermore, a recent Delphi study investigating the research agenda for neck pain, prioritized the need for the assessment of effectiveness of available treatments and the identification of clinical features that can be used to direct treatment decisions (Silva et al., 2019). Given the

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high heterogeneity of NSNP patients and the homogeneity of the application of interventions in most randomized controlled trials (RCTs), it could be important, in the overall judgment of trial quality, to examine whether there is a match between the intervention investigated and the patients' presentations. A recent systematic review assessed the quality and the effectiveness of 13 treatment-based classification systems that attempted any such matching (Maissan et al., 2020). They concluded that clinical implementation should not be recommended given the overall low quality and clinical relevance of such systems and the low quality of the clinical comparison trials. Therefore, it could be speculated whether any matching or assessment strategy is in vain, or if sets of clinical criteria could aid clinicians in the identification of the most effective treatment for the individual patient. However, Maissan et al. (2020) investigated mainly statistically or theoretically derived classification systems but the use of high quality RCTs is recommended when the aim is to identify clinical features able to predict the effectiveness of a specific inter-(Kelly, vention Ritchie, and Sterling, 2017). Consequently, the aim of this systematic review is to investigate the effectiveness of interventions matched with any form of clinical assessment compared with similar but unmatched interventions for improving pain and disability for people with NSNP.

### **Methods**

A systematic review was conducted following the Cochrane guidelines (Higgins et al., 2019) and reported according to the PRISMA guidelines (Page et al., 2021). The protocol was registered with PROSPERO (CRD42021297163).

### Information sources and search strategy

A comprehensive systematic literature search was performed using international databases including PubMED, MEDLINE, EMBASE, CINAHL, COCHRANE CENTRAL, psycINFO and SPORTDiscus from their inception to September 2023. For the full search strings see Appendix 1.

### **Eligibility criteria**

Studies were included if they: 1) were RCTs; 2) investigated patients with NSNP; 3) the patients in the experimental group received a treatment or a set of treatments matched to their clinical presentations, to healthcare professionals' evidence-based assessment or to patient preference; 4) patients in the control group received similar, but unmatched treatment; and 5) reported pain or disability as outcome measures.

Studies were excluded if 1) they investigated patients with serious pathology or radicular signs, headache as a primary complaint or history of trauma (whiplash); 2) patients were simply randomized to intervention without regard for matching or suitability; 3) patients in the control group received inactive/different treatment; and 4) full text articles were not available or were not written in English.

### Selection process

The studies identified during the searches were screened to remove duplicates. Following this, a three-stage screening strategy of titles, abstracts, and full-texts was then conducted against inclusion and exclusion criteria with findings recorded using Rayyan software comments section. Studies were first screened based on the title by a single reviewer (PM) to remove irrelevant studies. Abstracts and subsequently potentially relevant full-text studies were then assessed independently by two reviewers (PM, SM). Differences during the screening process were discussed between the two reviewers until consensus was reached. If no consensus was obtained a third researcher (SMc) was consulted to make a final decision.

### Data items and collection process

Data extracted from each paper included date, country, sample size, duration of symptoms, eligibility criteria, matched and unmatched interventions, number of sessions and frequency, means and standard deviations for pain and disability, short term (0–3 months), intermediate term (4–6 months), and long term (>6 months) follow-ups, and integrity of intervention in case of exercises. Data were recorded on a purposefully developed electronic sheet by one reviewer (PM) and checked by the second reviewer (SM).

### **Risk of bias assessment**

The risk of bias (RoB) of the included papers was rated by two independent assessors (PM, SM) using the Revised Cochrane Risk of Bias tool (RoB2) (Sterne et al., 2019). This tool rates each paper according to potential bias arising from five main domains: randomization process, deviation from intended intervention, missing outcome data, measurement of the outcome and selection of the reported results. Judgements of each domain and of overall risk of bias were based on an algorithm aimed to assign to each item a quality rating of low RoB, some concern or high RoB (Sterne et al., 2019). Disagreements were discussed between the two reviewers and any remaining disagreements were resolved through further discussion with a third researcher (SMc).

### Synthesis methods and data analysis

Meta-analysis was performed using the RevMan 5.4.1 (Cochrane software) for pain and disability at similar follow-up periods. We used the standardized mean difference (SMD) and 95% confidence interval (95% CI) of the change score from baseline because it has been shown to be more generalizable than the mean difference with continuous variable in meta-analyses (Takeshima et al., 2014). Forest plots of "matched" versus "unmatched" interventions were used to graphically represent the findings. The SMDs with standard deviations of the change rate for each outcome and for each paper were grouped according to the timing of the follow-ups. Where the standard deviation of the change rate was not presented it was imputed through the correlation coefficient calculated from the data of the other studies assessing the same intervention (Higgins et al., 2019). Cohen's d was used to calculate the magnitude of the effect size for each intervention, where 0.2 represents a small effect size, 0.5 a moderate effect size, and 0.8 a large effect size (Sullivan and Feinn, 2012). Effect sizes for matched and unmatched interventions were calculated with the SMD standardized with the pooled standard deviation. As considerable heterogeneity was expected around issues such as, the interventions used and study settings, random-effects meta-analyses were used throughout. The p-value and I<sup>2</sup> statistics were used to assess heterogeneity between trials (Guyatt et al., 2011). Higgins, Thompson, Deeks, and Altman (2003) suggested rating heterogeneity as follows: low if  $I^2 = 25\%$ ; moderate if  $I^2 = 50\%$ ; and high if  $I^2 = 75\%$ .

### **Quality of evidence**

The Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) framework was used to assess the levels of certainty of evidence for matched intervention for pain and disability, among the selected papers. This framework suggests rating levels of certainty as high, moderate, low or very low (Guyatt et al., 2011). Quality was rated down according to the: risks of bias (1–2 levels); inconsistency (1–2 levels); indirectness (1–2 levels); imprecision (1–2 levels); and publication bias (1–2 levels). Quality was upgraded according to large effect size (1–2 levels); dose response gradient (1 level); and in case of the effect of a plausible confounder (1 level).

### Results

### Study selection

The literature search produced 9516 records. After removing 9489 based on the title, abstract and full text, 27 studies were considered to have a matching treatment against a similar unmatched treatment. Figure 1 shows the PRISMA flow-chart of the search results and reasoning for exclusion. Of 27 studies identified, 12 were included in the manual therapy meta-analysis, 13 in the exercise meta-analysis and three could not be included in the meta-analysis because one described mixed interventions (Paoloni et al., 2012), and two described different interventions other than exercise and manual therapy (Gu, Yan, Zhang, and Li, 2019; Martín-Rodríguez, Sáez-Olmo, Pecos-Martín, and Calvo-Lobo, 2019). One study was included in both sets of the meta-analysis because it considered both exercise and manual therapy (Cleland et al., 2010). Two studies that could have been included in the metaanalyses displayed incomplete data (Kotteeswaran and Nayak, 2021; Puntumetakul et al., 2015) and the authors were contacted for additional information but no response was received.

## Studies characteristics, outcome measures and follow-up

The 27 studies identified in the review included 1613 patients and the 24 studies included in the meta-analysis had a total of 1119 patients. See Table 1 for study details. Twenty-two studies used the Visual Analogic Scale (VAS) or Numeric Pain Rating Scale (NPRS) to quantify pain perceived. Neck Disability Index was the disability questionnaire used in 15 studies. All studies assessed outcomes at short term, four studies at intermediate term, and only one at long-term follow-up.

### Matching criteria

For manual therapy, the eligibility criteria chosen to match patient clinical presentation with specific manual therapy treatment were as follows: manually assessed symptomatic level (Aquino et al., 2009; Schomacher, 2009); movement restriction (Joshi, Balthillaya, and Neelapala, 2020; Karas and Olson Hunt, 2014; Karas al., 2018; Martínez-Segura et al., et 2006; Puntumetakul et al., 2015); clinical prediction rule for thoracic manipulation (Cleland et al., 2010); clinical prediction rule for thoracic manipulation and movement restriction (Puentedura et al., 2011); central or unilateral neck pain (Kanlayanaphotporn,



Figure 1. Study flow diagram.

Chiradejnant, and Vachalathiti, 2009, 2010); and a pragmatic clinical assessment (Lagoutaris, Sullivan, Hancock, and Leaver, 2020).

For exercise therapy the eligibility criteria chosen to match patient clinical presentation with specific exercise treatment were diagnostic criteria for trapezius myalgia (Andersen et al., 2008); movement restriction (Lee and Kim, 2016; Petersen et al., 2015); clinical prediction rule for thoracic manipulation (Cleland et al., 2010); cranio-vertebral angle >50° (CVA) (Abd El-Azeim, Mahmoud, Mohamed, and El-Khateeb, 2022; Arif, Rehman, and Ikram, 2022; Im, Kim, Chung, and Hwang, 2016; Kang, Im, and Kim, 2021); abnormal joint position sense (Jull et al., 2007); mechanical diagnosis and therapy criteria (Kjellman and Öberg, 2002; Takasaki and Yamasaki, 2023); and muscle weakness (Giménez-Costa et al., 2022; Kotteeswaran and Nayak, 2021).

Other than manual therapy and exercise the eligibility criteria chosen to match patient clinical presentation with specific treatment were as follows: Chinese medicine criteria for acupuncture (Gu, Yan, Zhang, and Li, 2019); physiotherapist preference (Paoloni et al., 2012); and active trigger point criteria (Martín-Rodríguez, Sáez-Olmo, Pecos-Martín, and Calvo-Lobo, 2019). None of which could have been included in a meta-analysis.

### **Risk of bias assessment**

Overall, 10 papers were rated as having low risk of bias and 17 as having some concerns of risk of bias (Figure 2). There was some concern about RoB in four studies regarding randomization concealment of group allocation (Andersen et al., 2008; Im, Kim, Chung, and Hwang, 2016; Kotteeswaran and Nayak, 2021; Lee and Kim, 2016); and in 17 studies regarding potential selection of reported results because a published protocol was not available (Andersen et al., 2008; Aquino et al., 2009; Gu, Yan, Zhang, and Li, 2019; Im, Kim, Chung, and Hwang, 2016; Joshi, Balthillaya, and Neelapala, 2020; Jull et al., 2007; Kang, Im, and Kim, 2021; Kanlayanaphotporn, Chiradejnant, and Vachalathiti, 2009, 2010; Kjellman and Öberg, 2002; Kotteeswaran and Nayak, 2021; Lee and Kim, 2016; Martínez-Segura et al., 2006; Puentedura et al., 2011; Puntumetakul et al., 2015; Schomacher, 2009); or incomplete (Abd El-Azeim, Mahmoud, Mohamed, and El-Khateeb, 2022).

### Manual therapy matched vs unmatched – pain and disability short term

Twelve studies compared matched with unmatched manual therapy for pain and four for disability at shortterm follow-up. Matched manual treatment was not

### Table 1. Studies characteristics.

Table 1. Studies ch						
	Participants	Interventions	# of sessions	Follow-ups	Outcome	Std Mean difference (95%Cl)
MANUAL THERAPY	STUDIES					
MATCHING CRITERIA	A: MANUALLY ASSESSED SYN	APTOMATIC LEVEL				
Aquino et al. (2009)	48, age 18-65 years, chronic NSNP	Matched group: manual mobilization of symptomatic level ( $n = 24$ ) Unmatched group: manual mobilization of random level ( $n = 24$ )	1 session	Immediately post- intervention	Pain (NRS)	No statistically significant difference in pain intensity between groups.
Schomacher (2009)	126, neck pain, symptoms changing with selective neck movements	Matched group: manual mobilization of symptomatic level $(n = 59)$ Unmatched group: manual mobilization of random level (n = 67)	1 session	Immediately post- intervention	Pain (NRS)	No statistically significant difference in pain intensity between groups.
MATCHING CRITERIA	A: MANUALLY ASSESSED MO	VEMENT LIMITATION				
Joshi, Balthillaya, and Neelapala (2020)	42, neck pain, 18–60 years, cervico-thoracic movement dysfunction	Matched group: manual mobilization of C7-T1 ( $n = 21$ ) Unmatched group: manipulation T3-T6 ( $n = 21$ )	1 session	Immediately post- intervention	Pain (NRS)	No statistically significant difference in pain intensity between groups
Karas and Olson Hunt (2014)	39, neck pain, 18–60 years	Matched group: supine thoracic manipulation at limited segment (n = 19) Unmatched group: seated thoracic global manipulation $(n = 20)$	1 session	Immediately post- intervention	Pain (NRS)	Difference in pain intensity between groups in favor of matched group: $-1.2$ , p < .05
Martínez-Segura et al. (2006)	70, mechanical neck pain for more than 1 month, positive lateral gliding test (limitation C3-C5)	Matched group: cervical manipulation at limited segment (n = 34) Unmatched group: cervical mobilization held for 30" similar to the manipulation without thrust $(n = 37)$	1 session	Immediately post- intervention	Pain (VAS)	Difference in pain intensity between groups in favor of matched group: $-3.1$ , p < .01
Puentedura et al. (2011)	24, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>+</sup>	Matched group: cervical manipulation at limited segment plus exercise $(n = 14)$ Unmatched group: thoracic global manipulation plus exercise (n = 10)	5 sessions over 2 weeks	4 weeks, 6 months	Pain (NRS)	Difference in pain intensity between groups in favor of matched group: $-1.83$ , p < .001 at short term, -2.2 p < .001 at intermediate-term
Puntumetakul et al. (2015)	48, chronic neck pain, NDI > 10%	Matched group: multiple level thoracic manipulation at limited segments ( $n = 16$ ) Unmatched group: T6–7 spinal manipulation ( $n = 16$ ) Sham manipulation group ( $n = 16$ )	1 session	1 week after intervention	Pain (VAS) Disability (NDI)	Incomplete data
MATCHING CRITERIA	A: MANUALLY ASSESSED DIR	ECTION OF MOVEMENT LIMITATION	N			
Karas et al. (2018)	69, mechanical neck pain, 18–60 years	Matched group: supine thoracic manipulation at limited segment in the direction of the movement limitation ( $n = 34$ ) Unmatched group: supine thoracic manipulation at limited segment in the opposite direction of the movement limitation ( $n = 35$ )	1 session	Immediately post- intervention	Pain (NRS) Disability (NDI)	No statistically significant difference in pain intensity between groups. No statistically significant difference
						in disability between groups.

(Continued)

Participants	Interventions	# of sessions	Follow-ups	Outcome	Std Mean difference (95%Cl)
					( )
A: CLINICAL PREDICTION ROL 140, neck pain, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>+</sup>	Matched group: 3 manipulations to mid-thoracic spine plus specific exercise, CPR+ $(n = 33)$ Unmatched group: 3 manipulations to mid-thoracic spine plus specific exercise, CPR- $(n = 27)$	5 sessions over 4 weeks	4 weeks, 6 months	Pain (NRS) Disability (NDI)	No statistically significant difference in pain intensity between groups at short and intermediate-term No statistically significant difference in disability between groups at short and intermediate-term
60, unilateral neck pain, VAS at rest > 2	Matched group: cervical unilateral postero-anterior cervical mobilization ( $n = 30$ ) Unmatched group: cervical random mobilization ( $n = 30$ )	1 session	Immediately post- intervention	Pain (VAS)	No statistically significant difference in disability between groups
60, central or bilateral neck pain, VAS at rest > 2	Matched group: cervical central postero-anterior cervical mobilization ( $n = 30$ ) Unmatched group: cervical random mobilization ( $n = 30$ )	1 session	Immediately post- intervention	Pain (VAS)	No statistically significant difference in disability between groups
A: UNDEFINED CLINICAL ASS 20, acute neck pain, 18–60 years, 2 <vas <7<="" td=""><td>ESSMENT Matched group: pragmatic cervical mobilization (<i>n</i> = 10) Unmatched group: C1–2 and T1–2 unilateral mobilization (<i>n</i> = 10)</td><td>1 session</td><td>48 hours after intervention</td><td>Pain (VAS) Disability (NDI)</td><td>No statistically significant difference in pain intensity between groups. No statistically significant difference in disability between groups.</td></vas>	ESSMENT Matched group: pragmatic cervical mobilization ( <i>n</i> = 10) Unmatched group: C1–2 and T1–2 unilateral mobilization ( <i>n</i> = 10)	1 session	48 hours after intervention	Pain (VAS) Disability (NDI)	No statistically significant difference in pain intensity between groups. No statistically significant difference in disability between groups.
48, chronic neck pain, women, repetitive work task, tightness and tenderness of upper trapezius	Matched group: Specific neck/ shoulder strength training neck/ shoulder ( $n = 18$ ) Unmatched group: general aerobic training ( $n = 16$ ) Other group:no treatment ( $n = 14$ )	3 sessions per week over 10 weeks	10 weeks, 5 months	Pain (VAS)	Difference in pain intensity between groups in favor of matched group: $-2.5$ , p < .001 on short term, -1.3 p < .001 on intermediate-term
A: CLINICAL PREDICTION RUL 140, neck pain, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>+</sup>	<b>E FOR THORACIC MANIPULATION</b> Matched group: Stretching and strengthening CPR+ ( <i>n</i> = 29) Unmatched group: Stretching and strengthening, CPR- ( <i>n</i> = 25)	5 sessions over 4 weeks	4 weeks, 6 months	Pain (NRS) Disability (NDI)	No statistically significant difference in pain intensity between groups at short and intermediate-term No statistically significant difference in disability between groups at short and intermediate-term
	Participants   A: CLINICAL PREDICTION RUL   140, neck pain, 18–60 years,   NDI > 20%, CPR for thoracic manipulation <sup>+</sup> A: PAIN LOCATION   60, unilateral neck pain, VAS at rest > 2   60, central or bilateral neck pain, VAS at rest > 2   60, central or bilateral neck pain, VAS at rest > 2   A: UNDEFINED CLINICAL ASSE 20, acute neck pain, 18–60 years, 2   20, acute neck pain, 18–60 years, 18, tightness and tenderness of upper trapezius   A: CLINICAL PREDICTION RUL   140, neck pain, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>+</sup>	Participants Interventions   A: CLINICAL PREDICTION RULE FOR THORACIC MANPULATION 140, neck pain, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>+</sup> Matched group: 3 manipulations to mid-thoracic spine plus specific exercise, CPR+ (n = 33) Unmatched group: cervical unilateral postero-anterior cervical mobilization (n = 30) Unmatched group: cervical random mobilization (n = 30)   60, unilateral neck pain, VAS at rest > 2 Matched group: cervical random mobilization (n = 30)   60, central or bilateral neck pain, VAS at rest > 2 Matched group: cervical random mobilization (n = 30)   60, central or bilateral neck pain, VAS at rest > 2 Matched group: cervical random mobilization (n = 30)   CUNDEFINED CLINICAL ASSESSMENT 20, acute neck pain, VAS  Matched group: cervical random mobilization (n = 10)   CUNDEFINED CLINICAL ASSESSMENT 20, acute neck pain, VAS  Matched group: pragmatic cervical mobilization (n = 10)   STUDIES *   STUDIES *   STUDIES *   * CLINICAL PREDICTION RULE FOR THORACIC MANIPULATION 140, neck pain, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>+</sup> Matched group: Specific neck/ shoulder (n = 18)   140, neck pain, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>+</sup> Matched group: Stretching and strengthening CPR+ (n = 29)	Participants Interventions sectors   A: CLINICAL PREDICTION RULE FOR THORACIC MANIPULATION 140, neck pain, 18–60 years, NDI > 20%, CPR for thoracic manipulation <sup>**</sup> Matched group: 3 manipulations to mid-thoracic spine plus specific exercise, CPR + (n = 33) Unmatched group: 3 manipulations to mid-thoracic spine plus specific exercise, CPR - (n = 27) 5 sessions   A: PAIN LOCATION 60, unilateral neck pain, VAS at rest > 2 Matched group: cervical unilateral postero-anterior cervical mobilization (n = 30) Unmatched group: cervical random mobilization (n = 30) 1 session   60, central or bilateral neck pain, VAS at rest > 2 Matched group: cervical random mobilization (n = 30) 1 session   20, acute neck pain, 18–60 years, 2 <vas 7<="" <="" td=""> Matched group: pragmatic cervical mobilization (n = 10) 1 session   20, acute neck pain, 18–60 years, 2<vas 7<="" <="" td=""> Matched group: Specific neck/ shoulder strength training neck/ shoulder (n = 18) 1 session   3 Matched group: Specific neck/ shoulder (n = 18) 3 sessions   48, chronic neck pain, women, repetitive work task, tightness and tenderness of upper trapezius Matched group: Specific neck/ shoulder (n = 18) 3 sessions   40, neck pain, 18–60 years, NDI &gt; 20%, CPR for thoracic manipulation<sup>**</sup> Matched group: Specific neck/ shoulder (n = 18) 3 sessions   410, neck pain, 18–60 years, NDI &gt; 20%, CPR for thoracic manipulation<sup>**</sup> Matched group: Specific neck/ strengthening CPR + (n = 29)<!--</td--><td>Participants Interventions sessions Follow-ups   EX CLINICAL PREDICTION RULE FOR THORACIC MANIPULATION 140, neck pain, 18–60 years, manipulation* Matched group: 3 manipulations to mid-thoracic spine plus specific exercise, CPR+ (n = 33) 4 weeks, 6   MDI &gt; 20%, CPR for thoracic manipulation* Unmatched group: cervical unilateral at rest &gt; 2 1 session mobilization (n = 30) 1 session unmatched group: cervical random mobilization (n = 30) Immediately post- intervention   60, central or bilateral pain, VAS at rest &gt; 2 Matched group: cervical central poster-onterior cervical mobilization (n = 30) Immediately post- mobilization (n = 30) Immediately post- mobilization (n = 30)   60, central or bilateral pain, VAS at rest &gt; 2 Matched group: cervical central mobilization (n = 30) I session mobilization (n = 10) Immediately post- intervention   61 UNDEFINED CLINICAL ASSESSMENT 20, acute neck pain, 18–60 Matched group: pragmatic cervical mobilization (n = 10) I session week 48 hours after intervention   51 TRAPEZIUS MYALGIA 48, chroin cerk pain, women, repetitive work tenderness of upper trapezius Matched group: Specific neck/ shoulder (n = 18) 3 sessions veeks 10 weeks, 6 months   61 Other group: nore treatment (n = 14) Numatched group: Stretching and strengthening, CPR- (n = 25) 5 sessions weeks 4 weeks, 6</td><td>Participants   Interventions   assions   Follow-ups   Outcome     4: CLINICAL PREDICTION BULE FOR THORACIC MANIPULATION 140, neck pain, 18–60 years, manipulation<sup>1</sup>   A weeks, (PR + (n = 33)) umatched group: a manipulations to mid-thoracic spine plus specific exercise, CPR- (n = 27)   S sessions over 4 weeks   4 weeks, 6 months   Pain (NRS)     60, unilateral neck pain, VAS at rest &gt; 2 pain, VAS at rest &gt;</td></vas></vas>	Participants Interventions sessions Follow-ups   EX CLINICAL PREDICTION RULE FOR THORACIC MANIPULATION 140, neck pain, 18–60 years, manipulation* Matched group: 3 manipulations to mid-thoracic spine plus specific exercise, CPR+ (n = 33) 4 weeks, 6   MDI > 20%, CPR for thoracic manipulation* Unmatched group: cervical unilateral at rest > 2 1 session mobilization (n = 30) 1 session unmatched group: cervical random mobilization (n = 30) Immediately post- intervention   60, central or bilateral pain, VAS at rest > 2 Matched group: cervical central poster-onterior cervical mobilization (n = 30) Immediately post- mobilization (n = 30) Immediately post- mobilization (n = 30)   60, central or bilateral pain, VAS at rest > 2 Matched group: cervical central mobilization (n = 30) I session mobilization (n = 10) Immediately post- intervention   61 UNDEFINED CLINICAL ASSESSMENT 20, acute neck pain, 18–60 Matched group: pragmatic cervical mobilization (n = 10) I session week 48 hours after intervention   51 TRAPEZIUS MYALGIA 48, chroin cerk pain, women, repetitive work tenderness of upper trapezius Matched group: Specific neck/ shoulder (n = 18) 3 sessions veeks 10 weeks, 6 months   61 Other group: nore treatment (n = 14) Numatched group: Stretching and strengthening, CPR- (n = 25) 5 sessions weeks 4 weeks, 6	Participants   Interventions   assions   Follow-ups   Outcome     4: CLINICAL PREDICTION BULE FOR THORACIC MANIPULATION 140, neck pain, 18–60 years, manipulation <sup>1</sup> A weeks, (PR + (n = 33)) umatched group: a manipulations to mid-thoracic spine plus specific exercise, CPR- (n = 27)   S sessions over 4 weeks   4 weeks, 6 months   Pain (NRS)     60, unilateral neck pain, VAS at rest > 2 pain, VAS at rest >

	Participants	Interventions	# of sessions	Follow-ups	Outcome	Std Mean difference (95%Cl)
MATCHING CRITERIA	: CRANIO-VERTEBRAL ANGL	E				
lm, Kim, Chung, and Hwang (2016)	15, chronic neck pain, shoulder flexion > 130°, CVA < 44°	Matched group: scapular stabilization exercises $(n = 8)$ Unmatched group: relaxation exercises $(n = 7)$	12 sessions over 4 weeks	4 weeks	Pain (NRS)	Difference in pain intensity between groups in favor of matched group: $-1.3$ , p < .001
					Disability (NDI)	Difference in disability between groups in favor of matched group: -5.6 p < .001
Kang, Im, and Kim (2021)	32, neck pain, 20–60 years, VAS > 4, CVA < 53°	Matched group: scapular stabilization and thoracic extension exercise ( $n = 16$ ) Unmatched group: cervical stabilization and stretching exercises ( $n = 16$ )	18 sessions over 6 weeks	6 weeks	Pain (NRS)	Difference in pain intensity between groups in favor of matched group: $-1.1$ , p < .013
					(NDI)	No statistically significant difference in disability between groups at short and intermediate-term
Abd El-Azeim, Mahmoud, Mohamed, and El- Khateeb (2022)	60, chronic neck pain, 20– 60 years, CVA < 50°	Matched group: Scapular stabilization exercises and postural correction exercises (n = 30) Unmatched group: postural correction exercises (n = 30)	30 sessions over 10 weeks	10 weeks	Disability (NDI)	Difference in disability between groups in favor of matched group: -4.9, <i>p</i> < .001
Arif, Rehman, and Ikram (2022)	40, chronic neck pain, NDI 5–15, CVA < 50°	Matched group: cervical stabilization, heating pad, TENS, cervical isometric exercises (n = 20) Unmatched group: heating pad,	12 sessions over 4 weeks	4 weeks	Pain (NPRS)	Difference in pain between groups in favor of matched group: -1.05, p <.001
		TENS, cervical isometric exercises $(n = 20)$			Disability (NDI)	Difference in disability between groups in favor of matched group: -3.3, p <.001
MATCHING CRITERIA	: MANUALLY ASSESSED MO	VEMENT LIMITATION				
Lee and Kim (2016)	46, chronic neck pain, 18– 60 years, NDI > 20, limited upper cervical and thoracic spine in flexion/extension	Matched group: deep neck flexors strengthening and stretching exercises ( $n = 15$ ) Unmatched group: active mobility exercises ( $n = 15$ ) Other group: manual therapy, deep	30 sessions over 10 weeks	10 weeks	Pain (NRS)	Difference in pain intensity between groups in favor of matched group: $-1.3$ , p < .001
		neck flexors strengthening and stretching exercises ( <i>n</i> = 16)			Disability (NDI)	Difference in disability between groups in favor of matched group: $-9.7 p < .001$
Petersen et al. (2015)	72, neck pain	Matched group: pragmatic manual therapy plus movement direction specific exercise (n = 36) Unmatched group: pragmatic	1 session	4 days after intervention	Pain (NRS)	No statistically significant difference in pain intensity between groups
		manuai therapy plus general exercises (n = 36)			(NDI)	No statistically significant difference in disability between groups

(Continued)

	/•					
	Participants	Interventions	# of sessions	Follow-ups	Outcome	Std Mean difference (95%Cl)
MATCHING CRITERIA Jull et al. (2007)	ABNORMAL JOINT POSITIC 58, chronic neck pain, abnormal joint position sense	DN SENSE Matched group: proprioceptive training exercise $(n = 28)$ Unmatched group: deep neck flexors strengthening exercises (n = 30)	6 sessions over 6 weeks	7 weeks	Pain (NRS) Disability (NDI)	No statistically significant difference in pain intensity between groups No statistically
<b>MATCHING CRITERIA</b> Kjellman and Öberg (2002)	<b>MECHANICAL DIAGNOSIS</b> 77, neck pain provoked by active/sustained movement, foraminal test, upper limb tension test	AND THERAPY CRITERIA Matched group: mechanical diagnosis and therapy criteria ( <i>n</i> = 28) Unmatched group: general exercises ( <i>n</i> = 23)	16 sessions over 8 weeks	8 weeks, 6 months, 12 months	Pain (NRS)	No statistically significant difference in disability between groups No statistically significant difference in pain intensity between groups at
		Other group: ultrasound ( <i>n</i> = 26)			Disability (NDI)	short and intermediate-term No statistically significant difference in disability between groups at short and intermediate-term
Takasaki and Yamasaki (2023)	19, neck pain, direction preference for cervical retraction or extension	Matched group: seated repeated retraction exercise ( <i>n</i> = 9) Unmatched group: Supine repeated cranio-cervical flexion exercise ( <i>n</i> = 10)	1 session	Immediately post- intervention	Pain (NRS)	No statistically significant difference in pain intensity between groups
MATCHING CRITERIA: Kotteeswaran and Nayak (2021)	<b>MUSCLE WEAKNESS</b> 30, neck pain, 20–60 years	Matched group: weak scapular muscle strengthening exercises plus interferential therapy (n = 15) Unmatched group: resisted neck isometric exercises plus interferential therapy $(n = 15)$	12 sessions over 4 weeks	4 weeks	Disability (NDI)	Incomplete data
Giménez-Costa et al. (2022)	46, women, chronic neck pain, VAS 3–5/10, <250s neck extensor resistance test	Matched group: specific neck extensor exercise and home exercise program ( $n = 23$ ) Unmatched group: general neck extensor exercise and home exercise program ( $n = 23$ )	6 sessions over 6 weeks	6 weeks,	Pain (NPRS)	No statistically significant difference in pain intensity between groups at short term
		nome exercise program (r 25)		6 weeks, 6 months	Disability (NDI)	No statistically significant difference in disability at short term and intermediate term
DIFFERENT TREATME	NT STUDIES					
MATCHING CRITERIA: Paoloni et al. (2012)	PHYSIOTHERAPIST PREFEI 220, neck pain, VAS > 4	RENCE Matched group: combination of electrotherapy, exercise, manual therapy decided by physiotherapists ( <i>n</i> = 114) Unmatched group: medical doctor prescribed combination of	10 sessions over 3 weeks	4 weeks	Pain (VAS)	Difference in pain intensity between groups in favor of matched group: $-0.42$ , p < .05
		eiectrotnerapy, exercise, manual therapy ( <i>n</i> = 106)			Uisability (NPDS-I)	Difference in disability between groups in favor of matched group: -0.30, p < .05 (Continued)

			# of			Std Mean difference
	Participants	Interventions	sessions	Follow-ups	Outcome	(95%CI)
MATCHING CRITERIA Martín-Rodríguez, Sáez-Olmo, Pecos- Martín, and Calvo- Lobo (2019)	<b>ACTIVE TRIGGER POINTS</b> 34, neck pain, 20–58 years, sternocleidomastoid active trigger point	Matched group: dry needling on the trigger points ( $n = 17$ ) Unmatched group: dry needling 1.5 cm away from trigger points ( $n = 17$ )	1 session	1 month	Pain (VAS) Disability (NDI)	No statistically significant difference in pain intensity between groups No statistically significant difference
						in disability between groups
MATCHING CRITERIA	: CHINESE TRADITIONAL AC	UPUNCTURE POINTS				
Gu, Yan, Zhang, and Li (2019)	60, 18–70 years, spondilosys on X-rays	Matched group: 7 acupunture points needling plus mechanical traction ( $n = 30$ ) Unmatched group: random acupuncture needling plus mechanical traction ( $n = 30$ )	10 sessions over 11 days	11 days	Pain (VAS) Disability (NDI)	Difference in pain between groups in favor of matched group: $-0.54$ , $p < .05$ Difference in disability between groups in favor of matched
						group: –1.52, <i>p</i> < .05

+ CPR for thoracic manipulation: symptoms <30 days, no symptoms below the shoulder, cervical spine extension does not aggravate FABQPA < 12, cervical spine extension < 30°, decreased thoracic kyphosis.

Per-protocol	Unique ID	Study ID	Experimental	Comparator	Outcome	Weight	<u>D1</u>	DZ	D3	<u>D4</u>	<u>D5</u>	Overall		
	1	Andersen et al. 2008	Specific Strength Training	General Fitness Training	Pain	1		•	•	•			•	Low risk
	2	Aquino et al. 2009	Random MT	PT chosen MT	Pain	1	•	•	•	•	•	<u> </u>		Some concerns
	3	Cleland et al. 2010	MT+exs CPR+ and EX CPR+	MT +ex CPR- and EX CPR-	pain & disability	1	•	٠	•	•	•	•	•	High risk
	4	Gu et al. 2019	matched acupuncture	unmatched acupuncture	pain & disability	1	$\bullet$	•	•	$\bullet$				
	5	Im et al. 2016	Scapular stabilisation exercises	Relaxation exercises	pain & disability	1	!	•	+	•	1	•	D1	Randomisation process
	6	Joshi et al. 2020	Cx-Tx mobilisation	Tx manipulation	Pain	1	•	٠	+	•	1	•	D2	Deviations from the intended interventions
	7	Jull et al. 2007	Cx proprioceptive exs	CFT training	pain & disability	1	+	•	+	•	•	•	D3	Missing outcome data
	8	Kang et al. 2021	Scapular stab + Tx ex	Cx stab + stretching	pain & disability	1	+	•	+	•	•	•	D4	Measurement of the outcome
	9	Kanlayanaphotporn et al. 2009	Cx unilat PA matched with assessment	Cx random MT	pain	1	•	•	•	•	1	•	D5	Selection of the reported result
	10	Kanlayanatphotporn et al. 2014	Cx central PA matched with assessment	Cx random MT	pain	1	+	•	+	•	•	•		
	11	Karas et al. 2014	Targeted supine Tx manipulation	Seated Tx manipulation	pain	1	•	•	•	•	•	•		
	12	Karas et al. 2018	Tx manipulation in the direction of dysfunction	Tx manipulation in the opposite direction of dy	pain & disability	1	•	•	•	•	•	•		
	13	Kjellman et al. 2002	MDT treatment	General exercises	pain & disability	1	•	•	•	•				
	14	Kotteeswaran et al. 2021	Individualised scapular exercises	Resisted isometric Cx exercises	disability	1	1	•	+	•	1	()		
	15	Lagoutaris et al. 2020	Pragmatiic Cx MT	UpCx & CxTx MT	pain & disability	1	•	٠	٠	•	•	•		
	16	Lee et al. 2016	DCF training & stretching exercises	Active ROM exercises	pain & disability	1	1	•	•	•				
	17	Martin-Segura et al. 2006	Cx manipulation at dysfunctional level	Cx sustained premanipulative stretch	pain	1	•	•	( )	•		()		
	18	Martin-Rodriguez et al. 2019	TrP dry needling	Dry needling 1.5cm away from TrP	pain & disability	1	•	•	•	•	•	•		
	19	Petersen et al. 2015	MT + loc self mobilisation	MT + generalised exercise	pain & disability	1	•	•	( )	•	•	Ť		
	20	Paoloni et al. 2013	Patient oriented treatment	Prescription oriented treatment	pain & disability	1	•	•	•	•	•	()		
	21	Puentedura et al. 2011	Cx pragmatic manipulation	Tx unmatched manipulation	pain & disability	1	(		•					
	22	Puntumetakul et al. 2015	Patient oriented treatment	Prescription oriented treatment	pain & disability	1		ē.	( )	•		Ŏ		
	23	Schomacher 2009	Cx pragmatic manipulation+exs	Tx unmatched manipulation+exs	pain	1	ē.	õ	ē.	ē		ŏ		
	24	Abd El-Aziem et al. 2022	Scapular stab + Cx exercises	Cx exercises	disability	1	ē.	ē	<b>•</b>	ē		Ŏ		
	25	Arif et al. 2022	Cx stabilisation + hot packs and isom exercises	Hot packs+ isom exercises	Pain & disability	1	õ	ŏ	ě	ē		ŏ		
	26	Gimenéz-Costa et al. 2022	Specific extension Cx exercise	Global extension Cx exercise	pain & disability	1	ě	ă	ě.	ă	ě.	ĕ		
	27	Takasaky & Yamasaki 2023	matched retraction exercise	unmatched cranio-cervical flexion exercise	Pain	1	ă	ă	ě	ŏ	ě.	ŏ		

Figure 2. Risk of bias assessment.

more effective than unmatched manual therapy for improving short-term pain (SMD -0.48; 95% CI -1.12, 0.17) (Figure 3) or short-term disability (SMD -0.35; 95% CI -1.35, 0.66) (GRADE: Low) (Fig3 4). The Cohen's d was moderate for pain (Figure 3) and small for disability (Figure 4).

## Manual therapy matched vs unmatched - pain and disability intermediate-term

Two studies compared matched with unmatched manual therapy for pain and disability at intermediate-term. Matched manual therapy was not more effective than unmatched manual therapy for improving intermediate-

### **Manual Therapy Pain - Short-Term**

	Ma	atched		Unr	natche	d		Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Aquino et al. 2009	0	2.57	24	-0.54	2.48	24	9.3%	0.21 [-0.36, 0.78]	
Cleland et al. 2010	-2.7	1	33	-2.8	0.86	27	9.4%	0.11 [-0.40, 0.61]	- <b>-</b>
Joshi et al. 2020	-1.19	1.54	21	-1.29	1.25	21	9.2%	0.07 [-0.54, 0.68]	_ <del>_</del>
Kanlayanaphotporn et al. 2009	-1.08	1.14	30	-1.23	1.25	30	9.4%	0.12 [-0.38, 0.63]	- <b>-</b>
Kanlayanaphotporn et al. 2010	-1.83	1.96	30	-1.3	1.16	30	9.4%	-0.32 [-0.83, 0.18]	+
Karas et al. 2014	-2.3	0.9	19	-1.1	0.2	20	6.6%	-1.83 [-2.59, -1.07]	
Karas et al. 2016	-2.44	0.24	34	-2.74	0.24	35	9.4%	1.24 [0.72, 1.75]	
Lagoutaris et al. 2020	-2.1	1.6	10	-1.4	1.2	10	8.4%	-0.47 [-1.37, 0.42]	
Martinez-Segura et al. 2006	-3.5	1.2	34	-0.4	0.6	37	8.9%	-3.28 [-4.00, -2.55]	
Puentedura et al. 2011	-4.5	2.14	10	-1.3	0.96	10	7.6%	-1.85 [-2.93, -0.76]	
Puntumetakul et al. 2015	0	0	0	0	0	0		Not estimable	
Schomacher 2009	-1.3	1.2	59	-1.7	1.5	67	9.7%	0.29 [-0.06, 0.64]	+
Total (95% CI)			304			311	100.0%	-0.48 [-1.12, 0.17]	-
Heterogeneity: Tau <sup>2</sup> = 1.09; Chi <sup>2</sup> = 138.24, df = 10 (P < 0.00001); l <sup>2</sup> = 93% Test for overall effect: Z = 1.44 (P = 0.15)									-4 -2 0 2 4 Favours matched Favours unmatched

Figure 3. Forest plot of matched manual therapy compared to unmatched on pain at short-term follow-up.

Manual Therapy Disability (%NDI) Short Term



Figure 4. Forest plot of matched manual therapy compared to unmatched on disability at short-term follow up.

term pain (SMD –0.63; 95% CI –2.76,1.50) (Figure 5) or intermediate-term disability (SMD –0.55; 95% CI –2.16, 1.07) (GRADE: Very Low) (Figure 6) The Cohen's d was moderate for both outcomes (Figure 5 and 6).

## Exercise matched vs unmatched – pain and disability short-term

Twelve studies compared matched with unmatched exercise for pain and disability at short-term. Matched exercise therapy was significantly more effective compared to unmatched exercise for improving short-term pain (SMD -0.57; 95% CI -0.95, -0.18) (GRADE: Moderate) (Figure 8) or short-term disability (SMD -0.69; 95% CI -1.14, -0.23) (GRADE: Low) (Figure 9). The Cohen's d was large for pain and moderate for disability (Figure 8 and 9).

## Exercise matched vs unmatched - pain and disability intermediate-term

Three studies compared matched with unmatched exercise for pain and two studies for disability at intermediate-term. Matched exercise therapy was not more effective than unmatched exercise for pain (SMD -0.37; 95% CI -0.88, 0.15) (GRADE: Moderate) (Figures 7 and 8)(Figure 10), or disability (SMD 0.12; 95% CI -0.21, 0.45) (GRADE: High) (Figure 11). The Cohen's d was small for both outcomes (Figure 10 and 11 and 12).

### **Other interventions**

Gu, Yan, Zhang, and Li (2019) compared acupuncture applied using the Chinese medicine criteria with randomly applied acupuncture and found statistically significant results in favor of the matched group for pain (STD -0.54; 95% CI -1.06, -0.03), and disability (STD -1.52; 95% CI -2.09, -0.94) at short term with moderate and large Cohen's d respectively. Martín-Rodríguez, Sáez-Olmo, Pecos-Martín, and Calvo-Lobo (2019) compared dry needling applied on sternocleidomastoid trigger points with dry needling applied randomly away from trigger points. Randomly applied trigger points were statistically significantly better in terms of pain (STD 0.84; 95% CI 0.13, 1.54) with large Cohen's d, while disability did not differ significantly (STD 0.15.; 95% CI -0.53, 0.82) with small Cohen's d at short term.

### **Manual Therapy Pain - Intermediate-Term**





### Manual Therapy Disability (%NDI) Intermediate-Term





### **Exercise Pain - Short-Term**





### Exercise Disability (%NDI) - Short-Term



Figure 8. Forest plot of matched exercise compared to unmatched on pain at short-term follow up.

### **Exercise Pain - Intermediate-Term**





### Exercise Disability (%NDI) - Intermediate-Term





			Certainty ass	essment			Nº of	patients	Ef	fect			
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	matched manual therapy	unmatched manual therapy	Relative (95% CI)	Absolute (95% Cl)	Certainty	Importance	
Pain sho	Pain short-term (assessed with: VAS/NRS; Scale from: 0 to 10)												
12	randomised trials	not serious	very serious <sup>a</sup>	not serious	not serious	none	304	311	-	SMD 0.48 SD lower (1.12 lower to 0.17 higher)		CRITICAL	
Disabilit	Disability short-term (assessed with: %NDI; Scale from: 0 to 100)												
4	randomised trials	not serious	very serious <sup>a</sup>	not serious	not serious	none	91	82	-	SMD 0.35 SD lower (1.35 lower to 0.66 higher)	⊕⊕⊖O Low	CRITICAL	
Pain inte	ermediate-term	(follow-up	range 3 months	to 6 months; as	ssessed with: V	AS/NRS; Scale fro	om: 0 to 10)						
2	randomised trials	not serious	very serious <sup>a</sup>	not serious <sup>a,b</sup>	serious <sup>b</sup>	none	47	37	-	SMD 0.63 SD lower (2.76 lower to 1.5 higher)		IMPORTANT	
Disabilit	y intermediate-	term (follo	w-up: range 3 mo	nths to 6 month	ns; assessed w	ith: %NDI; Scale fr	om: 0 to 100	))	-	-			
2	randomised trials	not serious	very serious <sup>a</sup>	not serious	serious⁵	none	47	37	-	SMD 0.55 SD lower (2.16 lower to 1.07 higher)		IMPORTANT	

Figure 11. Forest plot of matched exercise compared to unmatched on disability at intermediate-term follow up.

			Certainty ass	essment			Nº of	patients	Ef	fect			
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	matched exercise	unmatched exercise	Relative (95% CI)	Absolute (95% CI)	Certainty	Importance	
Pain sho	Pain short-term (assessed with: VAS/NRS; Scale from: 0 to 10)												
11	randomised trials	not serious	seriousª	not serious	not serious	none	229	221	-	SMD 0.57 SD lower (0.95 lower to 0.18 lower)	⊕⊕⊕⊖ Moderate	CRITICAL	
Disabilit	Disability short-term (assessed with: %NDI; Scale from: 0 to 100)												
11	randomised trials	not serious	very seriousª	not serious	not serious	none	228	221	-	SMD 0.69 SD lower (1.14 lower to 0.23 higher)		CRITICAL	
Pain inte	ermediate-term	(follow-up:	range 3 months	to 6 months; as	sessed with: V	AS/NRS; Scale fro	m: 0 to 10)		•				
3	randomised trials	not serious	serious <sup>b</sup>	not serious	not serious	none	75	64	-	SMD 0.37 SD lower (0.88 lower to 0.15 lower)	⊕⊕⊕⊖ Moderate	IMPORTANT	
Disabilit	y intermediate-	term (follov	w-up: range 3 mo	nths to 6 month	is; assessed w	ith: %NDI; Scale fr	om: 0 to 10	))	•				
3	randomised trials	not serious	not serious	not serious	not serious	none	74	68	-	SMD 0.12 SD higher (0.21 lower to 0.45 higher)	⊕⊕⊕⊕ <sub>High</sub>	IMPORTANT	

Figure 12. Exercise, quality of the evidence (GRADE assessment).

Paoloni et al. (2012) found that matching a multimodal treatment to patient assessment was better, but not significantly better, than delivering it according to a standardized prescription by a medical doctor both in terms of pain (STD -0.42; 95% CI -0.68, 0.15), and disability (STD -0.30; 95% CI -0.57, 0.03) at short term with small and moderate Cohen's d respectively.

### Discussion

This systematic review investigated whether matched intervention led to better pain and disability outcomes compared to unmatched interventions for people with NSNP. Twenty-seven RCTs met the inclusion criteria, 12 were eligible for a meta-analysis on manual therapy, and 13 for exercise. Matched exercise therapy was significantly more effective than unmatched exercise for pain (GRADE: Moderate) and disability (GRADE: Low) at short term, but not in the intermediate-term. Matched manual therapy was not more effective than unmatched manual therapy for pain and disability either in the short or intermediate term.

### Matched vs unmatched exercise intervention

Our review found that matched exercise interventions were more effective than unmatched exercise interventions for improving pain and disability in the short term, but not in the intermediate-term. However, in a recent systematic review, Villanueva-Ruiz, Falla, and Lascurain-Aguirrebeña (2022) found no advantage to tailoring neck specific exercise to patients with motor control dysfunction compared to the same exercise prescribed to patients not tested for motor control dysfunction. However, considering that neck pain patients tend to have reduced capacity to sustain isometric cranio-cervical flexion (O'Leary, Jull, Kim, and Vicenzino, 2007) the studies that did not test patients for motor control dysfunction are likely to have included patients with neck flexors deficits which may have confounded the results. Furthermore, the only muscle function test used was the cranio-cervical flexion test, and a more comprehensive cluster of clinical tests may have better matched the intervention to the patients (Segarra et al., 2015). In their RCT, Svedmark et al. (2016) compared exercise interventions tailored to individual's functional limitations and symptoms such as cervical movement limitation, neck muscle strength impairments, impaired sensorimotor control, trapezius myalgia, and cervicogenic headache with semi-random unmatched interventions. However, even this attempt led to no difference in pain and disability at short, intermediate, and long term.

The conflicting results within our review could be explained in several ways. Firstly, inadequate matching processes may explain why no exercise modality seems clearly superior to another for musculoskeletal pain lasting more than three months (Gross et al., 2015). Secondly, optimal exercise dosage, in terms of load, volume and frequency of training is unknown, and the failure to increase or adapt some or all the parameters to the patient evolving situation may hinder the efficacy of the management over time (Svedmark et al., 2020; Wilhelm et al., 2020).

Thirdly, the studies reviewed matched exercise according only to patient presentation. It is possible that neglecting patient goals and perceived threats with exercise hindered the effects of matching in the intermediate-term. Fourthly, only three studies had intermediate-term follow-up for pain and for disability (Andersen et al., 2008; Cleland et al., 2010; Giménez-Costa et al., 2022; Kjellman and Öberg, 2002). The low number of studies with longer follow-up, and, the low number of participants, could, in part, explain the nonsignificant intermediate-term results.

Another possible explanation for these nonsignificant findings in the intermediate-term could relate to decline of exercise adherence. Maintaining adherence to exercise is a key factor for maintaining benefit over time (Jordan, Holden, Mason, and Foster, 2010). Of the three papers with intermediate-term follow-up only Andersen et al. (2008) reported high adherence in both groups measured through the compilation of logbooks. Thus, a progressive decrease of exercise adherence cannot be excluded.

The greatest difference between matched and unmatched treatments was demonstrated in the: trapezius myalgia (Andersen et al., 2008); CVA (Abd El-Azeim, Mahmoud, Mohamed, and El-Khateeb, 2022; Arif, Rehman, and Ikram, 2022; Im, Kim, Chung, and Hwang, 2016; Kang, Im, and Kim, 2021); and movement limitation sub-groups (Cleland et al., 2010; Lee and Kim, 2016), perhaps this result provides evidence for clinicians to use matched exercise intervention for these three subgroups and may therefore warrant further investigation.

### Matched vs unmatched manual therapy intervention

Our findings suggest that matched manual therapy is not more effective than unmatched manual therapy. Similarly, a recent systematic review found that there was no difference between spinal manual therapy applied to clinically relevant segments and manual therapy applied to randomly chosen segments (Nim et al., 2021). However, manual therapy has the capacity to activate peripheral, spinal and supraspinal pain inhibitory responses (Bialosky et al., 2018). For example, it can increase pressure pain threshold in the application site (Voogt et al., 2015), but also has remote pain modulation effects (Lascurain-Aguirrebena, Newham, and Critchley, 2016). Furthermore, a thorough assessment and manual therapy are part of the expectations of patients referred to physical therapy and may influence nociception through modulation of cortical networks and descending inhibitory pathways, in particular in chronic pain patients (Bialosky, Bishop, and Penza, 2017; Subialka et al., 2022). If the remote neurophysiological and psychological effects predominate, then potentially the site of application is less important, as well as any assessment process to decide where to apply it.

Only two studies reviewed (Cleland et al., 2010; Puentedura et al., 2011) used exercises with manual therapy, whereas the majority of international guidelines recommend the use of manual therapy in association with exercise and not as a stand-alone (Corp et al., 2021). A recent systematic review highlighted that combining different forms of manual therapy may augment the effect of manual therapy or exercise therapy performed in isolation because, possibly, manual therapy may increase the activity of deep neck flexors and reduce that of superficial muscles on the short term, or have some other unknown neurophysiological effect, thus increasing the exercises' efficacy (Hidalgo et al., 2017; Sterling, Jull, and Wright, 2001).

The matching criteria used to decide if and where to apply manual therapy were most painful and/or hypomobile segment or side or a set of criteria involving active movement limitation, pain duration, and location and low impact of fear avoidance beliefs. The studies that showed the best results in favor of matched treatment were those looking for movement limitation (Karas and Olson Hunt, 2014; Martínez-Segura et al., 2006; Puentedura et al., 2011) indicating that this could be a promising criterion to predict benefit from manual therapy.

### Strengths and limitations of this review

The main strengths of this review are that we conducted a search in seven databases, adopting all recommendations proposed by the Cochrane Handbook for Systematic Reviews (Higgins et al., 2019) and used the RoB 2 and the GRADE framework for evaluating the quality of evidence. Nevertheless, the review also has some limitations. First, two papers selected for the meta-analysis had incomplete data and, despite contacting the authors, it was not possible to include those results. Secondly, the high heterogeneity of the studies led to high variability in results and then to lower levels of certainty for some of the findings. Thirdly, there were few trials with intermediate-term and only one with long-term follow-up. Missing data meant that data extrapolation increased reliance on fewer trials. Again, this reduces the certainty of any advantages offered by a matching process to increase the effectiveness of treatments for patients with the neck pain.

### **Clinical implications**

Our review provides evidence to support the use of exercise that is matched to patient presentation in the short term for improving pain (moderate) and disability (low) for patients with NSNP. For example, neck/ shoulder strength training for women with trapezius myalgia, scapular stabilization, and thoracic spine extension exercise in case of CVA, or deep neck flexors strengthening in people with upper cervical spine flexion and thoracic spine extension movement limitation. In the intermediate-term the use of matched exercise is not supported, and it is possible that as treatment is progressed that greater focus can be given toward exercise-based strategies that are tailored to achieving the patients' functional goals.

### Implication for future research

The matching of treatment for patients with neck pain to the results of a clinical assessment can be supported only if a clear set of factors for predicting benefit from exercise therapy or manual therapy can be identified. The results of this review did not provide definite answers, and this might be due to the heterogeneity of the matching criteria investigated.

The revision of clinical practice guidelines for NP of the American Physical Therapy Association suggested to categorize patients according to acute or chronic stage and to the presence of movement limitation or movement coordination impairments (Blanpied et al., 2017). However, they suggested both exercise therapy and manual therapy interventions in presence of movement limitations and of movement coordination impairment, again, offering no clear guidance to clinicians. Further research into potentially useful matching criteria used in clinical practice by expert physiotherapists may support new directions for investigation and may also improve the management of neck pain in clinical practice. Qualitative research designs, investigating these criteria may be better suited to derive key clinical features than prospective cohort studies previously used in derivation stage of clinical prediction rules. Subsequently, RCTs with inclusion criteria based on those clinical features may support their usefulness into clinical practice.

### Conclusion

The results of this systematic review and meta-analysis suggest that matching exercise therapy to patient clinical features may lead to better results than unmatched treatments in neck pain patients, but only at short-term followup. Matched manual therapy was not superior to unmatched manual therapy at short or at intermediate term. The trials included in the meta-analysis used widely different matching criteria and this created a wide level of heterogeneity reducing the overall quality of evidence. Movement limitation, trapezius myalgia and forward head position could be useful criteria, perhaps able to predict a better outcome for patients receiving matched treatments but need further investigation.

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### **Appendix 1 - Search strategies**

#### EMBASE

"neck pain" OR (chronic AND neck AND pain) OR (mechanical AND neck AND pain) OR (cervical AND spine) AND

rehabil\* OR (manual AND therapy) OR manipul\* OR mobili\* OR exerc\* OR education OR train\* OR (endurance training) OR (motor control training) OR (neuromuscular training) OR (stabilization training) OR (deep cervical flexor training) OR (craniocervical flexor training)

neck AND pain NOT insulin NOT thyroid NOT arterial NOT nutrit\* NOT eating NOT tmd NOT temporomandibular NOT injur\* NOT dental NOT nerve NOT fusion NOT back NOT lumbar NOT trauma\* NOT crash NOT rheum\* NOT neur\* NOT palsy NOT diabetes NOT burn NOT fibromyalgia NOT hip NOT hand NOT knee NOT card\* NOT osteoporosis NOT arthritis NOT occlus\* NOT sedation NOT fracture NOT cord NOT surg\* NOT spondylitis NOT pulmonary NOT dizziness NOT radicul\* NOT headache NOT whiplash NOT stroke NOT discectomy NOT cancer NOT surgery NOT tumor

#### PUBMED

((chronic neck pain) OR (trapezius myalgia) OR (neck pain) OR (cervical spine) OR (mechanical neck pain))

AND

((rehabil\*) OR (manual therapy) OR (manipul\*) OR (mobil\*) OR (exerc\*) OR (train\*) OR (endurance training) OR (motor control training) OR (neuromuscular training) OR (stabilization training) OR (deep cervical flexor training) OR (craniocervical flexor training) OR (education)))

NOT

((insulin) OR (thyroid) OR (arterial) OR (nutrit\*) OR (eating) OR (TMD) OR (temporomandibular) OR (injur\*) OR (dental) OR (dogs) OR (nerve) OR (fusion) OR (back) OR (lumbar) OR (trauma\*) OR (rat) OR (crash) OR (rheum\*) OR (neur\*) OR (palsy) OR (diabetes) OR (burn) OR (fibromyalgia) OR (osteoporosis) OR (hip) OR (hand) OR (knee) OR (card\*) OR (osteoporosis) OR (arthritis) OR (occlus\*) OR (sedation) OR (fracture) OR (cord) OR (surg\*) OR (spondylitis) OR (pulmonary) OR (dizziness) OR (radicul\*) OR (headache) OR (whiplash) OR (stroke) OR (discectomy) OR (cancer) OR (needl\*) OR (taping) OR (tape) OR (surgery) OR (tumor)) Filters: English

### MEDLINE

((chronic neck pain) OR (trapezius myalgia) OR (neck pain) OR (cervical spine) OR (mechanical neck pain))

AND

((rehabil\*) OR (manual therapy) OR (manipul\*) OR (mobil\*) OR (exerc\*) OR (train\*) OR (endurance training) OR (motor control training) OR (neuromuscular training) OR (stabilization training) OR (deep cervical flexor training) OR (craniocervical flexor training) OR (education))

NOT

((insulin) OR (thyroid) OR (arterial) OR (nutrit<sup>\*</sup>) OR (eating) OR (TMD) OR (temporomandibular) OR (injur<sup>\*</sup>) OR (dental) OR (dogs) OR (nerve) OR (fusion) OR (back) OR (lumbar) OR (trauma<sup>\*</sup>) OR (rat) OR (crash) OR (rheum<sup>\*</sup>) OR (neur<sup>\*</sup>) OR (palsy) OR (diabetes) OR (burn) OR (fibromyalgia) OR (osteoporosis) OR (hip) OR (hand) OR (knee) OR (card\*) OR (osteoporosis) OR (arthritis) OR (occlus\*) OR (sedation) OR (fracture) OR (cord) OR (surg\*) OR (spondylitis) OR (pulmonary) OR (dizziness) OR (radicul\*) OR (headache) OR (whiplash) OR (stroke) OR (discectomy) OR (cancer) OR (needl\*) OR (taping) OR (tape) OR (surgery) OR (tumor))

Filters: human, English

#### COCHRANE

(chronic neck pain) OR (trapezius myalgia) OR (neck pain) OR (cervical spine) OR (mechanical neck pain)

AND

(rehabil\*) OR (manual therapy) OR (manipul\*) OR (mobil\*) OR (exerc\*) OR (train\*) OR (endurance training) OR (motor control training) OR (neuromuscular training) OR (stabilization training) OR (deep cervical flexor training) OR (craniocervical flexor training) OR (education)

AND a NOT

(insulin) NOT (thyroid) NOT (arterial) NOT (nutrit\*) NOT (eating) NOT (tmd) NOT (temporomandibular) NOT (injur\*) NOT (dental) NOT (nerve) NOT (fusion) NOT (back) NOT (lumbar) NOT (trauma\*) NOT (crash) NOT (rheum\*) NOT (neur\*) NOT (palsy) NOT (diabetes) NOT (burn) NOT (fibromyalgia) NOT (hip) NOT (hand) NOT (knee) NOT (card\*) NOT (osteoporosis) NOT (arthritis) NOT (occlus\*) NOT (sedation) NOT (fracture) NOT (cord) NOT (surg\*) NOT (spondylitis) NOT (pulmonary) NOT (dizziness) NOT (radicul\*) NOT (headache) NOT (whiplash) NOT (stroke) NOT (discectomy) NOT (cancer) NOT (surgery) NOT (tumor)

#### CINAHL

(chronic neck pain) OR (neck pain) OR (cervical spine) OR (mechanical neck pain)

AND

(rehabil\*) OR (manual therapy) OR (manipul\*) OR (mobil\*) OR (exerc\*) OR (train\*) OR (endurance training) OR (motor control training) OR (neuromuscular training) OR (stabilization training) OR (deep cervical flexor training) OR (craniocervical flexor training) OR (education)

NOT

(insulin) OR (thyroid) OR (arterial) OR (nutrit\*) OR (eating) OR (TMD) OR (temporomandibular) OR (injur\*) OR (dental) OR (dogs) OR (nerve) OR (fusion) OR (back) OR (lumbar) OR (trauma\*) OR (rat) OR (crash) OR (rheum\*) OR (neur\*) OR (palsy) OR (diabetes) OR (burn) OR (fibromyalgia) OR (osteoporosis) OR (hip) OR (hand) OR (knee) OR (card\*) OR (osteoporosis) OR (arthritis) OR (occlus\*) OR (sedation) OR (fracture) OR (cord) OR (surg\*) OR (spondylitis) OR (pulmonary) OR (dizziness) OR (radicul\*) OR (headache) OR (whiplash) OR (stroke) OR (discectomy) OR (cancer) OR (needl\*) OR (taping) OR (tape) OR (surgery) OR (tumor)

### psycINFO

(chronic neck pain) OR (neck pain) OR (cervical spine) OR (mechanical neck pain)

AND

(rehabil\*) OR (manual therapy) OR (manipul\*) OR (mobil\*) OR (exerc\*) OR (train\*) OR (endurance training) OR (motor control training) OR (neuromuscular training) OR (stabilization training) OR (deep cervical flexor training) OR (craniocervical flexor training) OR (education) NOT

(insulin) OR (thyroid) OR (arterial) OR (nutrit\*) OR (eating) OR (TMD) OR (temporomandibular) OR (injur\*) OR (dental) OR (dogs) OR (nerve) OR (fusion) OR (back) OR (lumbar) OR (trauma\*) OR (rat) OR (crash) OR (rheum\*) OR (neur\*) OR (palsy) OR (diabetes) OR (burn) OR (fibromyalgia) OR (osteoporosis) OR (hip) OR (hand) OR (knee) OR (card\*) OR (osteoporosis) OR (arthritis) OR (occlus\*) OR (sedation) OR (fracture) OR (cord) OR (surg\*) OR (spondylitis) OR (pulmonary) OR (dizziness) OR (radicul\*) OR (headache) OR (whiplash) OR (stroke) OR (discectomy) OR (cancer) OR (needl\*) OR (taping) OR (tape) OR (surgery) OR (tumor)

Filters: Human, English

### **SPORTDiscus**

(chronic neck pain) OR (neck pain) OR (cervical spine) OR (mechanical neck pain)

AND

(rehabil\*) OR (manual therapy) OR (manipul\*) OR (mobil\*) OR (exerc\*) OR (train\*) OR (endurance training) OR (motor control training) OR (neuromuscular training) OR (stabilization training) OR (deep cervical flexor training) OR (craniocervical flexor training) OR (education)

NOT

(insulin) OR (thyroid) OR (arterial) OR (nutrit\*) OR (eating) OR (TMD) OR (temporomandibular) OR (injur\*) OR (dental) OR (dogs) OR (nerve) OR (fusion) OR (back) OR (lumbar) OR (trauma\*) OR (rat) OR (crash) OR (rheum\*) OR (neur\*) OR (palsy) OR (diabetes) OR (burn) OR (fibromyalgia) OR (osteoporosis) OR (hip) OR (hand) OR (knee) OR (card\*) OR (osteoporosis) OR (arthritis) OR (occlus\*) OR (sedation) OR (fracture) OR (cord) OR (surg\*) OR (spondylitis) OR (pulmonary) OR (dizziness) OR (radicul\*) OR (headache) OR (whiplash) OR (stroke) OR (discectomy) OR (cancer) OR (needl\*) OR (taping) OR (tape) OR (surgery) OR (tumor)

Filters: English