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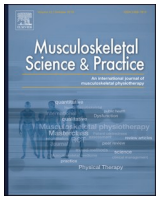

Systematic review

Cervical manipulation versus thoracic or cervicothoracic manipulations for the management of neck pain. A systematic review and meta-analysis☆,☆☆

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ABSTRACT

Background: Cervical and thoracic thrust or non-thrust manipulations have shown to be effective in patients with neck pain, but there is a lack of studies comparing both interventions in patients with neck pain.
Objective: To investigate the effects of cervical thrust or non-thrust manipulations compared to thoracic or cervicothoracic manipulations for improving pain, disability, and range of motion in patients with neck pain.
Design: Systematic review and meta-analysis.
Method: Searches were performed in PubMed, PEDro, Cochrane Library, CINHAL, and Web of Science databases from inception to May 22, 2023. Randomized clinical trials comparing cervical thrust or non-thrust manipulations to thoracic or cervicothoracic manipulations were included. Methodological quality was assessed with PEDro scale, and the certainty of evidence was evaluated using GRADE guidelines.
Results: Six studies were included. Meta-analyses revealed no differences between cervical thrust or non-thrust manipulations and thoracic or cervicothoracic manipulations in pain intensity, disability, or cervical range of motion in any plane. The certainty of evidence was downgraded to very low for pain intensity, to moderate or very low for disability and to low or very low for cervical range of motion.
Conclusion: There is moderate to very low certainty evidence that there is no difference in effectiveness between cervical thrust or non-thrust manipulations and thoracic or cervicothoracic manipulations for improving pain, disability, and range of motion in patients with neck pain.
Prospero registration: CRD42023429933.

1. Introduction

Neck pain (NP) is a common musculoskeletal condition that can affect more than 80% of people at least once in their lifetime (Dong et al., 2022). NP can be classified based on symptoms duration in acute, subacute, or chronic. Acute NP usually resolves within two months from the initial episode, being recurrent in 20–50% of people (Dong et al., 2022). Or it can be classified according to what aggravates it (Smith and Bolton, 2013). Mechanical NP is one of the most common, meaning that the symptoms are provoked by neck postures, neck movement or palpation of the cervical muscles (Childs et al., 2005).

The current clinical guidelines recommend physical therapy as the first management option for patients with NP (Blanpied et al., 2017; Fredin and Lorås, 2017; Silva et al., 2019). Manual therapy and exercise therapy are the most evidenced interventions being manual therapy the preferred approach by therapists (Childs et al., 2008; Joshi et al., 2019). Among the most used techniques are high-velocity low-amplitude (HVLA) thrust manipulations and non-thrust manipulations or

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mobilizations. These manual techniques have shown to be effective for improving pain and disability in patients with NP (Gross et al., 2010; Hidalgo et al., 2017). However, there is a risk of mild, moderate, or even serious adverse events associated with the used of these techniques. Even though clinicians consider the whole of the patient clinical presentation including several pre-manipulative screening tests to avoid these adverse events (Kerry and Taylor, 2009; Magarey et al., 2004; Rushton et al., 2023), some systematic reviews have described negative situations such as cervical edema, disc herniation, or vertebrobasilar artery dissection (Ernst, 2007; Kranenburg et al., 2017).

Recent systematic reviews and meta-analysis have concluded that thoracic HVLA thrust manipulations are also effective for improving pain and disability in patients with NP (Masaracchio et al., 2019; Tsegay et al., 2023). This approach may minimize the adverse events derived from the interventions targeting the cervical spine.

Despite the possible difference in the risk of adverse events between cervical or thoracic techniques, no systematic review and meta-analysis has been found comparing both interventions for decreasing pain intensity and improving disability and cervical range of motion (ROM) in patients with NP. Therefore, the aim of this study was to investigate the effects cervical thrust or non-thrust manipulations compared to thoracic or cervicothoracic manipulations for improving pain intensity, neck disability, and cervical ROM in patients with NP.

2. Methods

2.1. Study design

The protocol of this systematic review and meta-analysis was preregistered in the International Prospective Register of Systematic Reviews (PROSPERO: CRD42023429933) and followed the Preferred Reporting Items for Systematic Reviews and Meta-analysis (PRISMA) statement and Cochrane recommendations (Page et al., 2021).

2.2. Search strategy

The search strategy was conducted in PubMed (MEDLINE), Physiotherapy Evidence Database (PEDro), Cochrane Library, CINHAL, and Web of Science (WoS) from inception to May 22, 2023. The following Medical Subject Headings were used in the search strategy: spinal manipulation, orthopedic manipulation, and neck pain. These terms were combined with other keywords and linked with the Boolean operators AND/OR. The search strategy used in each database is shown in Appendix A. A hand search of the reference lists of all the included studies was performed.

2.3. Eligibility criteria

The inclusion criteria were developed according to the Population, Intervention, Comparison, Outcome, and Study design (PICOS) framework. All the studies met the following criteria: Population: patients diagnosed with NP; Intervention: cervical thrust or non-thrust manipulation; Comparison: thoracic or cervicothoracic thrust or non-thrust manipulations; Outcomes: pain intensity, neck disability, and cervical ROM; Study design: randomized controlled trials.

Studies were excluded if they: included patients with NP with associated comorbidities; the interventions applied passive soft tissue techniques; the outcome variables reported were not the outcomes of interest or were not measured using a valid and reliable instrument; the studies were not published in English, French or Spanish.

2.4. Data extraction

Once the searches were running in all databases, references were exported to Mendeley desktop, and duplicates were removed. Two reviewers (Sandra Jimenez (S.J.B) and Luis Ceballos (L.C.L)) ran the searches in each database independently and assessed the title and abstract to determine potential eligibility. A third reviewer (Andoni Carrasco (A.C.U)) was contacted in case of doubt.

The same two reviewers (Sandra Jimenez (S.J.B) and Luis Ceballos (L.C.L)) independently extracted the data from the included studies. A standardized form adapted from the Cochrane Collaboration was used to extract the data. The third reviewer (Andoni Carrasco (A.C.U)) solved any discrepancies.

2.5. Methodological quality

Methodological quality was assessed by the same independent reviewers (Sandra Jimenez (S.J.B) and Luis Ceballos (L.C.L)) using the PEDro scale. This scale is an 11-items scale based on a Delphi list to assess the methodological quality of clinical trials (Verhagen et al., 1998). A score of 7 or above was considered “high” quality, 5 to 6 was considered “fair” quality, and four or below was considered “poor quality”. The first item of the PEDro scale (eligibility criteria) is related to external validity and was not considered in the total score.

2.6. Data synthesis and analysis

Qualitative and quantitative synthesis was carried out with the following outcome variables: pain, disability, and cervical ROM.

Three subgroups of meta-analyses were performed for the outcome variables considering the intervention applied: cervical thrust or non-thrust manipulations versus thoracic manipulation, cervical manipulation plus exercise versus thoracic manipulation plus exercises, and cervical thrust or non-thrust manipulations versus cervicothoracic manipulations. The sample sizes from each group and the mean and standard deviation (SD) on the post-intervention were extracted. Mean Difference (MD) and 95% confidence interval (CI) were calculated based on the post-intervention means and SDs. A statistical significance value of $p < 0.05$ was determined. Data were presented using forest plots. The minimum clinically important difference (MCID) for pain intensity was stated as 2.1 (Cleland et al., 2008). For neck disability index (NDI) the MCID was stated in 7 points (Macdelilld et al., 2009). The standard error of measurements (SEM) reported for cervical ROM ranged from 1.6° to 4.1° in all the planes of movements (Audette et al., 2010).

Data were combined in forest plots when at least two trials were considered clinically homogeneous. The studies were considered homogeneous when intervention and outcome variables were similar. When a three-arm study was included, the data from the comparison group were divided (J Higgins et al., 2011). Random-effects meta--analysis was performed when the combination of intervention effects could incorporate an assumption that the studies are not all estimating the same intervention effect (Higgins et al., 2019). All meta-analyses were conducted using RevMan 5.4. Software.

To detect publication bias and to test each study’s influence, we visually examined the forest plot and performed an exclusion sensitivity analysis. Funnel plots, and Begg and Egger tests were not conducted in this study because the meta-analysis did not meet the rule of at least 10 trials included in each forest plot (Page et al., 2023).

2.7. Certainty of evidence

The certainty of evidence was assessed by GRADE Evidence Profiles by the same independent reviewers (Sandra Jimenez (S.J.B) and Luis Ceballos (L.C.L)). The categories of evidence were classified as “high”, “moderate”, “low”, or “very low”, to help researchers and clinicians on the importance of the results. The certainty was assessed according to the following domains: risk of bias, inconsistency, indirectness, imprecision, and other considerations.

The certainty of evidence was downgraded in accordance of the presence of the following: risk of bias (downgraded by one level if at least 25% of the participants were from studies with poor or fair

methodological quality; and two levels if at least 50% of the participants were from studies with poor or fair methodological quality: lack of allocation concealment, random allocation and/or sample size calculation, participant, and personnel blinding, blinding of outcome assessors), inconsistency of results (downgraded by one level if the I^2 value was ≥50%, and two levels if the I^2 was ≥75%) (Dantas et al., 2021; Guyatt et al., 2011b), indirectness of evidence (downgraded by one level if different populations, interventions, or comparators were included), and imprecision (downgraded by one level if fewer than 100 participants were included in each group or by two levels If < 30 participants were included in each group) (Dal Farra et al., 2021; Guyatt et al., 2011a). Single randomized trials were considered inconsistent and imprecise and provided "low certainty" evidence. This could be further downgraded to "very low" certainty if there was also a high risk of bias (Julian Higgins et al., 2011; Xie and Machado, 2021).

3. Results

Six studies were finally included in the qualitative and quantitative synthesis. Two studies were excluded, one was a pilot study (Ortega Santiago et al., 2012) and the other did not present the outcomes of interest (Bautista-Aguirre et al., 2017). The selection process is shown in the PRISMA flowchart diagram (Fig. 1).

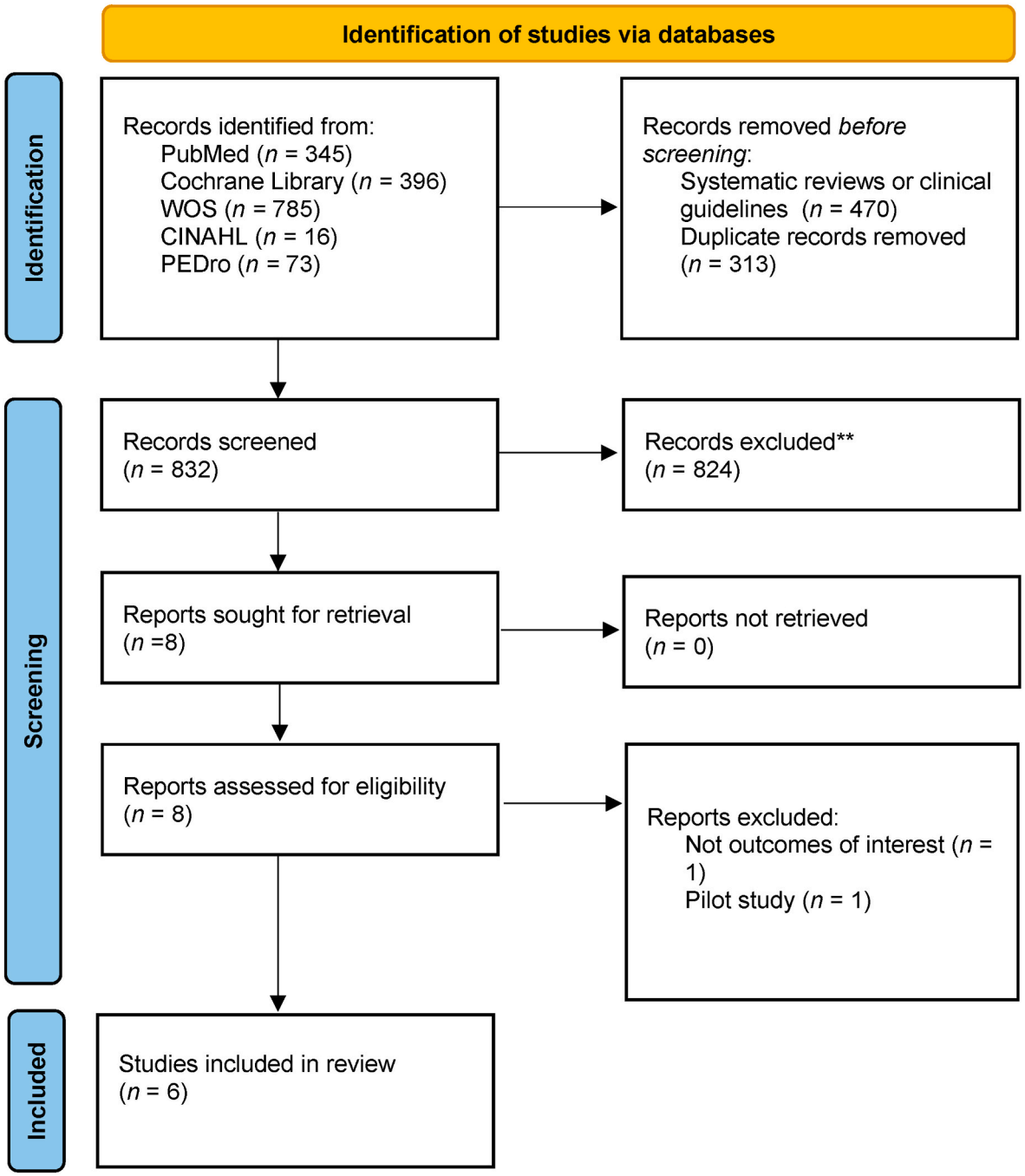


Fig. 1. Flowchart diagram
PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only.

3.1. Characteristics of the included studies

A total of six randomized controlled trials were included comprising 517 patients with NP. The sample size ranged from 20 to 186 patients.

Five of the studies included patients with mechanical NP and one did not specify the type of patients included (Puentedura et al., 2011). The inclusion criteria used in each study varied widely, but no one described a cervical ROM restriction as an inclusion criterion. The sociodemographic and clinical characteristics of the participants are shown in Table 1.

As can be seen in Table 1 the cervical manipulation groups consisted of HVLA manipulations in the cervical spine in four studies and two used anteroposterior non-thrust manipulations. The thoracic manipulation groups included HVLA manipulations of the thoracic spine in isolation or combined with thrust or non-thrust manipulations of the cervical spine. Concerning the sessions per week and the duration of the intervention, the most common treatment frequency was one session a week, and the intervention took one week in all the studies.

The outcome variables considered in the PICOS framework of this meta-analysis were pain intensity, disability, and cervical ROM. The instruments used in each study to measure the outcome variables are reported in Table 1. All the studies assessed pain intensity with the visual analogue scale (VAS) or the numeric pain rating score (NPRS), disability was measured in three studies with NDI, and cervical ROM was measured using CROM in three studies. All the studies assessed the outcome variables at baseline and the duration between the treatment and the follow-up measurements ranged from 10 m to 15 days.

3.2. Methodological quality

Two studies presented a high methodological quality scoring seven points in the PEDro scale, and four studies presented a fair methodological quality with scores between five and six points. None of the included studies met the blinding participants or therapist criteria. Outcome assessors were considered not blinded because self-reported outcome variables such as pain intensity were assessed in unblinded patients. Other studies did not describe if the allocation was concealed (Romero del Rey et al., 2022; Puentedura et al., 2011). The PEDro scale is shown in Table 2.

3.3. Synthesis of results

3.3.1. Pain intensity

Pain intensity was measured in all the studies. Very low certainty of evidence (downgraded for risk of bias and imprecision) suggested that cervical thrust or non-thrust manipulation provides no statistically significant improvement compared to thoracic manipulation (MD = −0.32; 95%CI -0.92, 0.28; 2 studies, 132 patients). Very low certainty of evidence (downgraded for risk of bias, inconsistency, and imprecision) suggested that cervical thrust or non-thrust manipulation provides no statistically significant improvement compared to cervicothoracic manipulation (MD = 0.41; 95%CI -0.49, 1.30; 3 studies, 332 patients). Very low certainty of evidence (downgraded for risk of bias and inconsistency) showed a statistically significant but clinically unimportant change in favor of cervical manipulation plus exercises

Table 1
Characteristics of the studies.

Author	Participants			Intervention		Frequency (days/ week)	Length (weeks)	Duration between treatment and follow-up	Outcome (tool)	Main results
	N (sex ratio)	Mean age (SD)	Diagnosis	CG	TG					
Martínez-Segura et al. (2012)	62 (31 M/ 31 F)	CG:35 (8) TG: 38 (7)	CMNP	Cervical manipulation (HVLA)	Thoracic manipulation (HVLA)	1	1	10 m	Pain (VAS) ROM	No between-groups differences
Martínez-Segura et al., (2012) B	61 (30 M/ 31 F)	CG:36 (9) TG: 38 (7)	CMNP	Cervical manipulation (HVLA)	Thoracic manipulation (HVLA)	1	1	10 m	Pain (VAS) ROM	No between-groups differences
Joshi et al. (2020)	42 (23 M/ 19 F)	CG:35.14 (10.13) TG: 38.47 (11.47)	MNP	Cervical non-thrust manipulation (AP)	Thoracic manipulation	1	1	30 m	Pain (NPRS) ROM	No between-groups differences
Puentedura et al. (2011)	20 (4 M/16 F)	CG:34.1 (7.0) TG: 33.1 (5.8)	NP	Cervical manipulation (HVLA) + exercise	Thoracic manipulation (HVLA) + exercise	3	1	7 days	Pain (NPRS) Disability (NDI)	↑NPRS, and NDI in CG vs TG
Saavedra-Hernández et al. (2013)	82 (41 M/ 41 F)	CG:45 (8) TG: 44 (9)	CMNP	Cervical manipulation (HVLA)	Cervical manipulation + thoracic manipulation (HVLA)	1	1	7 days	Pain (NPRS) ROM Disability (NDI)	↑NDI in TG vs CG
Masaracchio et al. (2013)	64 (14 M/ 50 F)	CG:34.5 (13.3) TG: 30.5 (9.5)	MNP	Cervical non-thrust manipulation (AP)	Cervical non-thrust manipulation (AP) + thoracic manipulation (HLVA)	2	1	2–3 days	Pain (NPRS) Disability (NDI)	No between-groups differences
Romero del Rey et al., 2022	186 (67 M/ 119 F)	CG:34 (11) TG: 32 (9.7)	MNP	Cervical manipulation (HVLA)	Cervical manipulation + thoracic manipulation (HVLA)	1	1	15 days	Pain (NPRS)	No between-groups differences

CG: cervical group; TG: thoracic group; M:male; F:female; NP: neck pain; MNP: mechanical neck pain; CMNP: chronic mechanical neck pain; HVLA: high velocity low amplitude; AP: anteroposterior; VAS: visual analogue scale; NPRS: numeric pain rating score; NDI: neck disability index.

Table 2
PEDro scores.

Author	1	2	3	4	5	6	7	8	9	10	11	Total score
Martínez-Segura et al. (2012)	Y	Y	Y	Y	N	N	N	Y	N	Y	Y	6/10
Joshi et al. (2020)	Y	Y	Y	Y	N	N	N	Y	N	Y	Y	6/10
Puentedura et al. (2011)	Y	Y	N	Y	N	N	N	N	Y	Y	Y	5/10
Saavedra-Hernández et al. (2013)	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7/10
Masaracchio et al. (2013)	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7/10
Romero del Rey et al., 2022	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6/10

Y: yes; N: no. 1. Eligibility criteria description; 2. Subjects were randomly allocated; 3. Allocation was concealed; 4. The groups were similar at baseline; 5. There was blinding of all subjects; 6. There was blinding of all therapists who administered the therapy; 7. There was blinding of all assessors who measured at least one key outcome; 8. Measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups; 9. All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analysed by intention to treat; 10. The results of between-group statistical comparisons are reported for at least one key outcome; 11. The study provides both point measures and measures of variability for at least one key outcome.

compared to thoracic manipulation plus exercise (MD = −2.00; 95%CI -3.00, −1.00; 1 study, 20 patients) (Fig. 2A).

3.3.2. *Disability*

Disability was measured in three studies. Very low certainty of evidence (downgraded for risk of bias, inconsistency, and imprecision) suggested that cervical manipulation plus exercise shows a statistically significant improvement compared to thoracic manipulation plus exercise, but the change was clinically unimportant (MD = −2.60; 95%CI -5.04, −0.16; 1 study, 20 patients). Moderate certainty of evidence (downgraded for imprecision) showed a statistically significant but clinically unimportant change in favor to cervicothoracic manipulation compared to cervical thrust or non-thrust manipulation (MD = 5.76; 95%CI 3.46, 8.06; 2 studies, 146 patients) (Fig. 2B).

3.3.3. *ROM*

Four studies measured cervical flexion, extension, lateral flexion, and rotation ROM. Very low (downgraded for risk of bias and imprecision) to low certainty of evidence (downgraded for inconsistency and imprecision) suggested that cervical thrust or non-thrust manipulation produces no statistically significant improvement compared to thoracic or cervicothoracic manipulation to improve cervical flexion, extension, lateral flexion, or rotation (Fig. 2C–H).

3.3.4. *Adverse events*

Four studies of the six included assessed adverse events derived from the interventions (Joshi et al., 2020; Martínez-Segura et al., 2012; Masaracchio et al., 2013; Puentedura et al., 2011). No adverse events were detected in any of them but Martinez-Segura et al. that described adverse events in 3% of the patients included (Martínez-Segura et al., 2012).

The overall certainty of evidence for pain intensity, disability, and cervical ROM was downgraded to moderate, low, or very low (Table 3).

4. Discussion

The aim of this systematic review and meta-analysis was to compare cervical thrust or non-thrust manipulations to thoracic or cervicothoracic manipulations in patients with NP. Moderate to very low certainty of evidence suggested that cervical interventions produce no statistically significant or clinical improvements compared to thoracic or cervicothoracic interventions for improving pain intensity, disability, and cervical ROM.

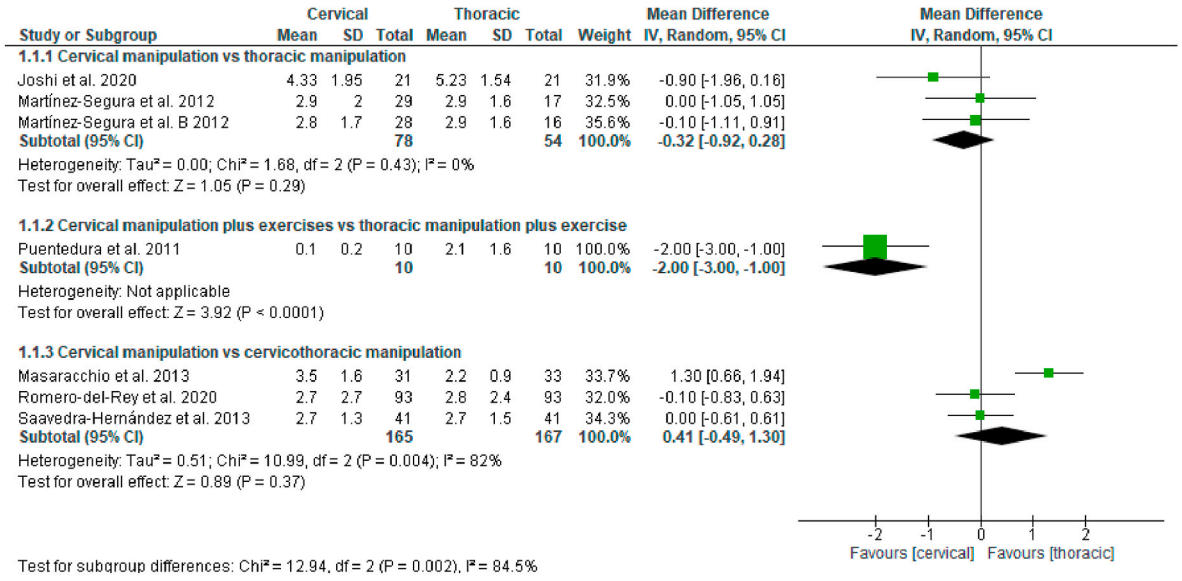
Concerning the methodological quality of the included clinical trials, the most common methodological flaws were the lack of blinding participants and therapists. Therapist blinding is not possible in most of physical therapy studies, which may introduce to bias, but is important to note that therapist blinding is not a part of clinical practice, as it plays no role in day-to-day treatment of patients (Kamper, 2018). Although most studies described the presence of blind examiners, outcome examiners could not be considered blinded because some self-reported outcome variables such as pain intensity were evaluated in unblinded patients.

Pain intensity showed no statistically significant improvement in any subgroup but in cervical manipulation plus exercise versus thoracic manipulation plus exercise, in which the cervical manipulation showed a statistically significant change but did not exceed the MCID described for patients with NP. Despite that all the studies measured pain intensity, the lack of standardization could influence the results. Patients with NP usually present pain on certain movements and positions, which difficult the measurement. In this sense, Masaracchio et al. (2013) and Puentedura et al. (2011) measured the current level of pain, and the worst and least amounts of pain in the previous 24 h, and Joshi et al. (2020) measured the most painful neck movement, while the other included studies measured pain at rest (Martínez-Segura et al., 2012; Saavedra-Hernández et al., 2013) or did not specify (Romero del Rey et al., 2022).

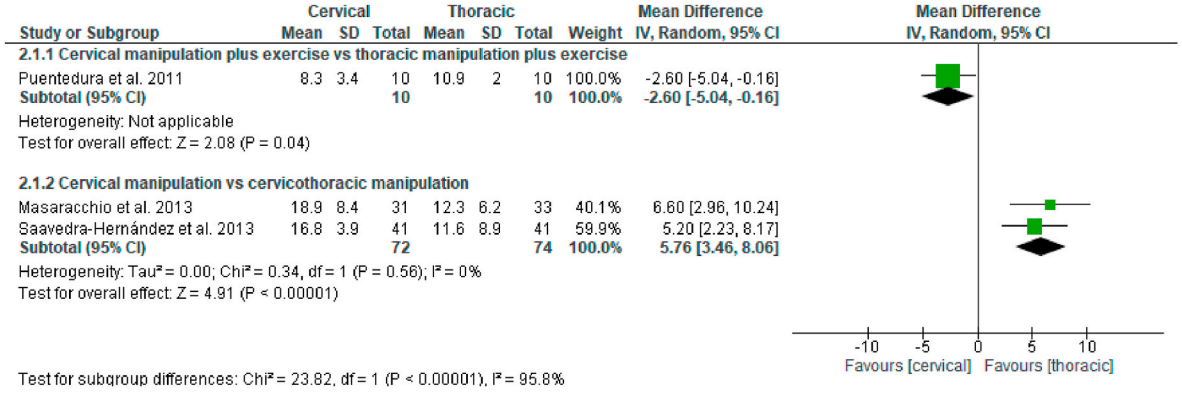
Disability measured with NDI showed a statistically significant improvement in both subgroups. Each subgroup showed statistically significant changes in opposite directions but none of them exceeded the MCID. The contradictory results found in this study could be related to the time between the intervention and the follow up. Masaracchio et al. (2013) applied two sessions and measured disability after two days, Puentedura et al. (2011) applied three sessions and registered disability after seven days, and Saavedra-Hernandez et al. (2013) applied a single session and assessed disability after seven days, so the elapsed time may not have been enough for patients to observe clear changes in all the daily life activities included in the NDI questionnaire for disability used in the three studies.

No statistically significant changes were observed for any subgroup in any plane of the cervical ROM. However, no study included cervical ROM restriction as an inclusion criterion, which means that the inclusion of patients with reduced cervical ROM could lead to different results. In this sense, considering the mean ROM values, the studies of Joshi et al. (2020) and Puentedura et al. (2011) presented cervical ROM mean values below the normative values (Thoomes-de Graaf et al., 2020), and the results of both studies seem to show a trend that cervical interventions are more effective than thoracic interventions for improving pain intensity and disability in patients with NP and limited ROM.

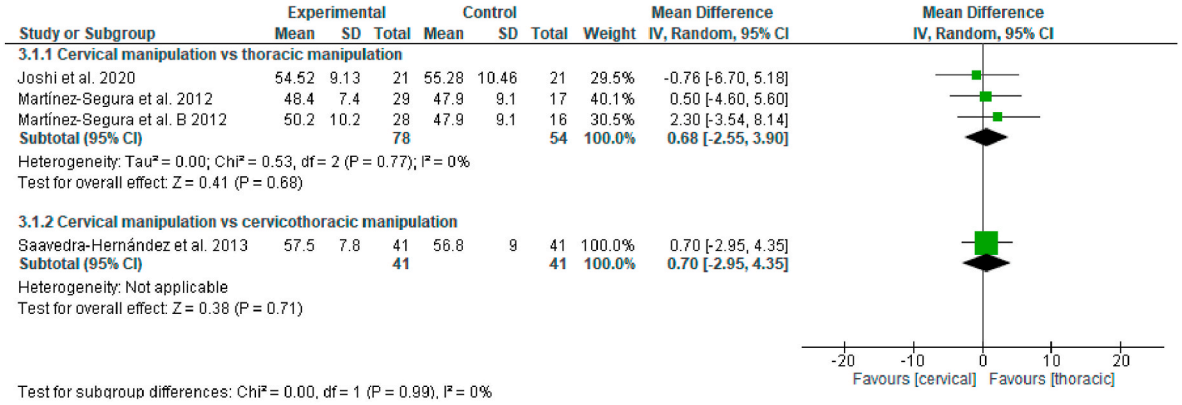
In this way, the results of this systematic review and meta-analysis suggest that cervical manipulation in isolation or combined with exercise is not more effective than thoracic manipulation in isolation or combined with exercise for improving the outcome variables assessed in this study. The combination of cervical and thoracic manipulations provides no more benefits compared to cervical manipulation in isolation in patients with NP. Therefore, thoracic manipulation seems to be as effective as cervical manipulation and its combination with cervical manipulation does not provide greater benefit. These results are in accordance with previous studies that showed that patients that received



A. Forest plot of pain intensity after the intervention.



B. Forest plot of disability after the intervention.



C. Forest plot of cervical flexion ROM after the intervention.

Fig. 2. Forest plot

Fig. 2A. Forest plot of pain intensity after the intervention. Fig. 2B. Forest plot of disability after the intervention. Fig. 2C. Forest plot of cervical flexion ROM after the intervention. Fig. 2D. Forest plot of cervical extension ROM after the intervention. Fig. 2E. Forest plot of cervical right lateral flexion ROM after the intervention. Fig. 2F. Forest plot of cervical left lateral flexion ROM after the intervention. Fig. 2G. Forest plot of cervical right rotation ROM after the intervention. Fig. 2H. Forest plot of cervical left rotation ROM after the intervention.

Table 3
Certainty of evidence according to GRADE recommendations.

Certainty assesment							Nº of patients		Effect	Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsisntency	Indirectness	Imprecission	Other considerations	[Cervical manipulation]	[thoracic or cervicothoracic manipulation]	Absolute (95% CI)		
Pain intensity. Cervical manipulation vs thoracic manipulation (VAS or NPRS)											
2	RCTs	Very serious	Not serious	Not serious	Serious	none	78	54	MD -0.32 (−0.92, 0.28)	⨁◯◯◯ [a] Very low	
Pain intensity. Cervical manipulation plus exercise vs thoracic manipulation plus exercise (NPRS)											
1	RCTs	Very serious	–	–	Very serious	none	10	10	MD **-2** (−3, −1)	⨁◯◯◯ [b] Very low	
Pain intensity. Cervical manipulation vs cervicothoracic manipulation (VAS or NPRS)											
3	RCTs	Serious	Very serious	Not serious	Not serious	none	165	167	MD **0.41** (0.49, 1.3)	⨁◯◯◯ [c] Very low	
Disability. Cervical manipulation plus exercise vs thoracic manipulation plus exercise (NDI)											
1	RCTs	Very serious	–	–	Very serious	none	10	10	MD **2.6** (−5.04, −0.16)	⨁◯◯◯ [b] Very low	
Disability. Cervical manipulation vs cervicothoracic manipulation (NDI)											
2	RCTs	Not serious	Not serious	Not serious	Serious	none	72	74	MD **5.76** (−3.46, 8.06)	⨁⨁⨁◯ [d] Moderate	
ROM. Cervical manipulation vs thoracic manipulation (CROM)											
2	RCTs	Very serious	not serious	not serious	Serious	none	78	54	Flexion MD 0.68 (−2.55,3.90) Extension MD 1.12 (−3.28,5.51) Right lateral flexion MD 1.26 (−1.41,3.93) Left lateral flexion MD 0.54 (−2.02,3.11) Right rotation MD -1.66 (−5.11,1.78) Left rotation MD 1.49 (−2.51,5.49)	⨁◯◯◯ [a] Very low	
ROM. Cervical manipulation vs cervicothoracic manipulation (CROM)											
1	RCTs	not serious	–	–	Serious	none	41	41	Flexion MD 0.70 (−2.95,4.35) Extension MD 2.6 (−1.78,6.98) Right lateral flexion MD 3.9 (0.09,7.71) Left lateral flexion MD 1.80 (−1.5, 5.1) Right rotation MD 2.1 (-2.75,6.95) Left rotation MD 2 (−1.05,5.04)	⨁⨁◯◯ [e] Low	

CI: Confidence interval; **MD:** Mean difference.
Explanations.
a. Downgraded two levels for risk of bias (more than 50% of the patients were from studies with fair methodological quality) and one level for imprecision (less than 100 patients were included in each group).
b. Downgraded two levels for risk of bias (more than 50% of the patients were from studies with fair methodological quality), one level for inconsistency (single study) and two levels for imprecision (less than 30 patients were included in each group).
c. Downgraded one level for risk of bias (more than 25% of the patients were from studies with fair methodological quality) and two levels for inconsistency (heterogeneity of results indicated by $I^2 = 82\%$).
d. Downgraded one level for imprecision (less than 100 patients per group).
e. Downgraded one level for inconsistency (single study) and for imprecision (less than 100 patients per group).
High: We are very confident that the true effect is close to the estimate of the effect.
Moderate: We are moderately confidence in the effect estimate. The true effect is close to the estimate of the effect, but the result can be different.
Low: Confidence in the effect estimate is limited, the true effect can be substantially different from the estimate of the effect.
Very Low: There is little confidence in the effect estimate, the true effect is likely to be substantially different from the estimate effect.

a higher number of manipulations exhibited similar decreases in neck pain to those receiving only one manipulation (Fernández-De-Las-Peñas et al., 2009).

Concerning adverse events, only two studies included pre-manipulative tests as part of their inclusion criteria to minimize potential risks for adverse events (Martínez-Segura et al., 2012; Saavedra-Hernández et al., 2013). Three studies specifically assessed vertebrobasilar insufficiency, while two studies examined the stability of the upper cervical spine using tests such as the Sharp-Purser test, alar ligament stress test, and transverse ligament test. Four studies asked patients to report any adverse events, and no severe events were reported (Joshi et al., 2020; Martínez-Segura et al., 2012; Masaracchio et al., 2013; Puentedura et al., 2011). However, it is important to note that numerous adverse events have been documented following HVLA thrust manipulation in the cervical spine. For this reason, the International Federation of Orthopedic Manipulative Physical Therapists recommended the use of other approaches for the treatment of patients with NP (Rushton et al., 2015, 2023). Considering that thoracic manipulations appear to have similar effects; these techniques may serve as substitutes for cervical manipulations.

The lack of superiority of the cervical manipulation over thoracic manipulations could be explained because spine manipulations seem to be not specific but have an effect on multiple vertebral joints; the effects may be related to biomechanical interactions and/or systemic effects such as changes in the functioning of descending anti-nociceptive system and central mechanisms of pain modulations; and the presence of other non-specific mechanisms such as patient expectation or therapeutic alliance (Nim et al., 2021).

From a clinical point of view, the current study found that cervical manipulations were not superior to thoracic manipulations, and its combination presented no more benefits than cervical manipulation in isolation for improving pain intensity, disability, and cervical ROM. Despite of that the results should be interpreted with caution because the certainty of the evidence was rated as moderate, low, or very low.

Four limitations should be pointed out in this study. First, our search strategy may have been limited by the omission of other databases, grey literature, or studies in other languages. Second, only six randomized controlled trials were included, which meant a small sample size. Third, three different subgroups were considered for statistical analysis and some subgroups comprised only one study, which complicates the interpretation of the results. Fourth, the quantitative analysis was performed using post-intervention scores instead of within-group changes scores due to the lack of variability data (Higgins and Deeks, 2023). Future studies should include ROM limitation as an inclusion criterion, assess longer periods of follow-up and the combination of different interventions to investigate the best effects, as well as their dose.

5. Conclusion

This systematic review and meta-analysis found moderate to very low certainty of evidence suggesting that cervical thrust or non-thrust manipulation in isolation or combined with exercise produce no significant or clinical changes compared to thoracic or cervicothoracic manipulation in isolation or combined with exercise for improving pain intensity, disability, and cervical ROM in patients with NP.

Ethical approval

Not required.

Patient consent for publication and participation

Note required.

Availability of data and material

All data relevant to the study are included in the manuscript or upload as supplementary information.

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Declaration of competing interest

None.

CRediT authorship contribution statement

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Appendix A. Supplementary data

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