

Does adding manual therapy improve long-term outcomes in patients with chronic neck pain? A systematic review and meta-analysis

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ABSTRACT

Introduction Chronic neck pain (CNP) is a prevalent, recurrent disorder imposing substantial physical, psychological, and economic burdens. However, the long-term effects of manual therapy (MT) remain unclear. This study was designed to evaluate the durable efficacy and safety of MT for the management of CNP. **Methods** Randomized controlled trials (RCTs) evaluating manual therapy for CNP were retrieved from Chinese and English databases from inception through October 29, 2024 (updated to June 30, 2026). The Cochrane Risk of Bias Assessment tool 2.0 was used to assess the risk of bias. Data were analyzed using Review Manager 5.4 software. The certainty of the evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation approach. **Results** Eighteen RCTs were included. Manual therapy may provide pain relief (mean difference [MD] = -1.01 points, 95% confidence interval [CI]: -1.54, -0.49; $P < 0.001$) and functional improvement (MD = -3.78%, 95% CI: -5.26, -2.31; $P < 0.001$) for at least three months post-treatment. Moreover, when combined with active control (e.g., NSAIDs, exercise, or physical therapy), these benefits may persist for up to six months (MD = -1.20 points, 95% CI: -1.74, -0.66; $P < 0.001$; MD = -5.55%, 95% CI: -8.73, -2.37; $P = 0.0006$). Although overall quality-of-life results were inconsistent, physical health may improve for up to six months (MD = 9.63 points, 95% CI: 5.84, 13.43; $P < 0.001$). Five studies reported adverse event rates ranging from 3.3% to 41.3%; however, but they were mild and transient. **Conclusion** Moderate- to very-low- quality evidence indicates that manual therapy may provide pain relief and functional improvement lasting at least 3 months post-treatment in patients with CNP compared with placebo therapy, no-treatment, or active control. When combined with active control, these effects may persist for up to six months and demonstrate an acceptable safety profile.

Registration: The study protocol was registered with the International Prospective Register of Systematic Reviews (<https://www.crd.york.ac.uk/PROSPERO/>, CRD42025632884).

KEYWORDS

durable effect, manual therapy, chronic neck pain, systematic review, meta-analysis

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1. Introduction

Chronic neck pain (CNP) refers to pain in the region extending from the head to the upper edge of the scapula, the lateral area above the clavicle, and the suprasternal fossa that persists for more than three months.¹ In recent years, changes in lifestyle and work patterns, such as mobile phone use, driving, computer-based work, and physical labor, have led to prolonged poor posture (e.g., forward head posture and neck flexion), resulting in an increased prevalence of neck pain.² According to a survey, the global age-standardized prevalence and incidence rates of neck pain are 3551.1 per 100 000 and 806.6 per 100 000, respectively.³ Approximately 50% to 85% of these cases may develop into CNP.⁴ CNP is characterized by a high recurrence rate and a prolonged disease duration. Approximately 25% to 60% of patients continue to experience pain one year or more after symptom onset,⁵ and this proportion increases to 60% to 80% among manual workers.⁶ Over time, CNP affects patients' physical and mental health, work, and quality of life, and increases medical expenses and the economic burden.

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Clinical guidelines recommend oral medications and various interventions for managing CNP. Nonsteroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used medications for relieving pain and improving neck function recovery in CNP management.⁷ However, their potential side effects and adverse reactions raise significant safety concerns. In studies reporting adverse drug reactions (ADRs), the incidence of NSAID-related ADRs ranges from 20% to 25%,⁸ and severe adverse reactions, such as gastrointestinal bleeding, anaphylactic shock, liver damage, and even death, have been reported.⁹ Physical therapy and exercise are also commonly used to relieve pain. Although they offer short-term benefits, their long-term efficacy depends on patient adherence. Due to the demands and stress of daily life and work, treatment may be interrupted or performed intermittently, potentially leading to symptom recurrence and poor outcomes. Given the safety concerns regarding pharmacological treatments and the limitations of current interventions in achieving sustained effects, there is an urgent need to explore effective, safe, and longer-lasting treatment strategies for CNP.

Many patients are dissatisfied with conventional treatments and seek complementary or alternative medicine (CAM). Manual therapy has demonstrated lasting effects in the treatment of various diseases and may also alleviate CNP.^{10,11} Current reviews either overlook the long-term effects of manual therapy or focus solely on its sustained benefits for pain relief,^{12,13} failing to comprehensively evaluate its post-treatment effects on functional improvement and quality of life. This meta-analysis aimed to systematically assess the

durable effects of manual therapy on CNP, with a focus on pain, function, quality of life, and safety.

2. Methods

This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.¹⁴

2.1. Eligibility criteria

Participants: Adults with neck pain lasting more than 3 months due to mechanical neck disorders, myofascial pain syndrome, cervical spondylosis, cervical spine disease with radiating pain, or myalgia were included.

Intervention: The intervention group underwent various manual therapies, including tuina, massage, manipulation, mobilization, inhibitory suboccipital technique, high velocity low amplitude, among others. Studies comparing manual therapy combined with other interventions with the same interventions administered alone were included.

Comparison: The control group received active treatment (NSAIDs, exercise, or physical therapy), placebo/sham treatment, or no treatment.

Outcomes: This study evaluated the sustained effects of manual therapy on CNP over a follow-up period of at least 3 months post-treatment. The primary outcomes were neck pain intensity (assessed using the visual analog scale [VAS] or numerical rating scale [NRS]) and neck dysfunction (evaluated using the neck disability index [NDI] or Northwick Park Neck Pain Questionnaire [NPQ]). The secondary outcome was quality of life (assessed using the 36-item short form health survey [SF-36]).

Study design: Only randomized controlled trials (RCTs) with a follow-up period of at least 3 months post-treatment were included.

2.2. Exclusion criteria

Studies involving patients with myelopathy, other serious diseases (e.g., cardiovascular or cerebrovascular diseases), or whiplash injuries were excluded. Patients with cervical headache or vertigo without neck pain were also excluded. Additionally, studies evaluating acupuncture, those comparing manual therapy with Chinese herbal medicine, or studies published repeatedly or lacking complete data were excluded.

2.3. Search strategy

We conducted a literature search of PubMed, Embase, the Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journals Database (VIP), and SinoMed for Chinese and English studies related to manual therapy for CNP from inception to October 29, 2024. The search was updated through June 30, 2026, and one additional eligible article was identified. The search terms included CNP (e.g., cervical pain, cervicodynia, and cervicgia), manual therapy (e.g., tuina, massage, musculoskeletal manipulations, and manipulative therapy), and RCT. Detailed search strategies and results (e.g., PubMed) are provided in Appendix 1.

2.4. Study selection and data extraction

Records retrieved from Chinese and English databases were imported into NoteExpress 4.0 (Beijing Aegean Software Co., Ltd., Beijing, China). Two reviewers (WJW and YNS) independently screened the titles and abstracts after deduplication, and subsequently reviewed the full texts according to the predefined inclusion and exclusion criteria. Any disagreements were resolved by consensus. Data extraction was performed by two authors (WJW and YNS) using a predesigned form and supervised by a senior researcher (CHY). Extracted data included the first author, interventions, controls, sample size, disease duration, follow-up period, outcome measures, and adverse events.

2.5. Study risk of bias assessment

Using the Cochrane Risk of Bias 2.0 tool,¹⁵ a revised framework developed by the Cochrane Collaboration for assessing RCTs, two independent investi-

gators (WJW and YNS) evaluated the risk of bias in the included studies. Discrepancies were resolved through discussion with a third investigator (XYW), who was consulted when consensus could not be reached.

2.6. Data analysis

Statistical analyses were conducted using Review Manager 5.4 (Cochrane Collaboration, Oxford, UK). The mean difference (MD) and 95% confidence interval (CI) were calculated for continuous outcomes. Based on the method described by Wan et al.,¹⁶ the medians and quartile ranges of continuous data were converted into means and standard deviations. The Cochrane Q *P*-value and *I*² statistics were used to assess heterogeneity across all meta-analyses. When the *P*-value was < 0.05 or *I*² > 50%, indicating significant heterogeneity, a random-effects model was used. Otherwise, a fixed-effect model was used. Statistical significance was set at *P*-value < 0.05.

Subgroup and sensitivity analyses were also performed. Subgroup analyses were conducted based on the type of manual therapy or active control (exercise-based vs. non-exercise-based) to explore potential sources of heterogeneity and assess the robustness of the results. A subgroup analysis based on the type of manual therapy was not performed because the interventions were insufficiently described in some studies, precluding appropriate categorization. Differences in effect estimates between subgroups were considered indicative of potential effect modification. Sensitivity analyses examined heterogeneity sources and result stability by bias risk (low, high, or potential) and sample size (*n* ≥ 60 as a cutoff). Excluding studies one by one was used to assess the robustness of the results by determining whether the direction of the effect remained unchanged.

Pain scores were assessed using an 11-point NRS ranging from 0 to 10, with 0 representing no pain and 10 representing the highest level of imaginable pain. For studies reporting pain scores on a 100-mm VAS, scores were converted to the 0–10 NRS scale by dividing the VAS score by 10.¹⁷ The minimum clinically important difference (MCID) for the NRS score (0–10) was set at 2.5 points, based on a previous study in patients with neck pain.¹⁸ The MCID for the NDI was 3 points.¹⁹ Additionally, we used a funnel plot and Egger's test (only for results containing 10 or more studies) to evaluate publication bias. The Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology was used to assess the quality of evidence.²⁰

When fewer than 10 studies were available, Egger's test was not performed because of the limited statistical power to detect publication bias. Therefore, potential publication bias could not be completely ruled out.

3. Results

3.1. Study selection

A total of 4907 studies were identified through preliminary retrieval. After excluding 1940 duplicates, 2967 studies remained. After title and abstract screening, 126 studies were considered potentially relevant and retrieved for full-text assessment. Following detailed full-text screening, 18 studies were included in the review.^{21–38} The detailed search and selection process is shown in Figure 1.

3.2. Study characteristics

A total of 18 studies^{21–38} were included. Five studies^{21,22,31,32,36} were conducted in China, and 13^{23–30,33–35,37,38} were conducted in other countries (e.g. United States of America, Australia, Spain, Germany, and the Netherlands). In terms of publication year, five studies^{25,27,31,37,38} were published within the past 5 years, and 10^{23–27,31,32,35,37,38} studies were published within the past 10 years. According to the type of manual technique, 4 studies^{29,32,35,36} used traditional Chinese massage, 3^{22,28,31} used energy techniques, and 11^{21,23–27,30,33,34,37,38} used soft tissue techniques. The sample size, interventions, follow-up duration, and results are presented in Table 1. The interventions included spinal manipulation, massage, and joint loosening. Eight studies^{21–28} combined manual therapy with

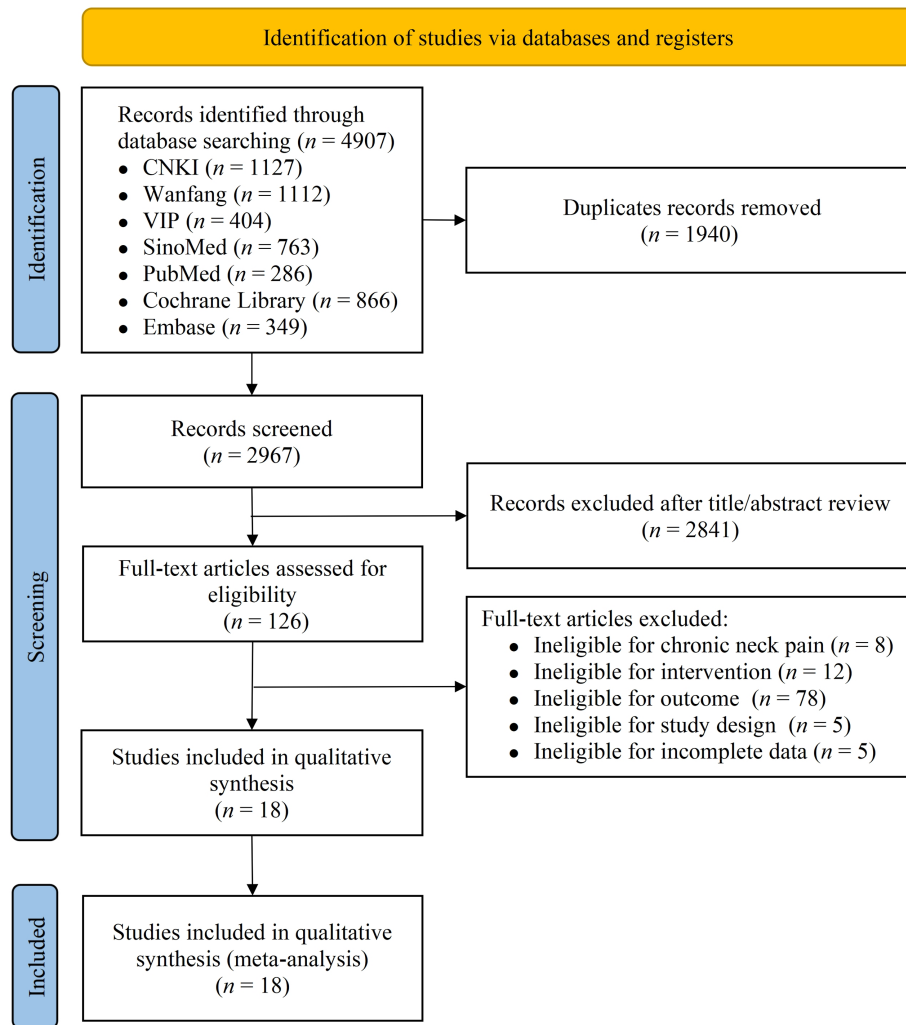


Figure 1 PRISMA Study flow diagram

Notes: CNKI: China National Knowledge Infrastructure; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; VIP: Chinese Scientific Journals Database.

traction, exercise, or other treatments. The control group (CG) was categorized into three groups: placebo therapy, no therapy, and other active therapies (e.g., exercise therapy, traction therapy, self-care). Four studies^{23,27,29,30} were three-arm trials, one of which evaluated the efficacy of three different manipulations.

3.3. Risk of bias in studies

Among the 18 studies included in the meta-analysis, 17²²⁻³⁸ used rigorous randomization methods, while one²¹ randomized participants based on the order of admission, indicating a high risk of bias in this domain. One study²¹ lacked detailed descriptions of the intervention and adequate blinding, thereby posing a potential risk of bias. Regarding missing outcome data, 17 studies²²⁻³⁸ provided details on participant withdrawals and their inclusion in the final analysis, while one study²¹ failed to provide a study flowchart, obscuring the exact number of patients lost to follow-up and resulting in a high risk of bias. Nine studies^{21,25,26,28,29,32,36-38} exhibited unclear selective reporting bias because they lacked protocol registration, whereas the remaining nine studies^{22-24,27,30,31,33-36} had a low risk of bias in this area (Figure 2).

3.4. Outcomes

3.4.1. Manual therapy versus placebo therapy

At 3 months post-treatment, moderate-quality evidence from two

studies^{33,34} indicated that manual therapy was more effective than placebo therapy in reducing neck pain intensity (MD = -1.68 points, 95% CI: -2.70 , -0.65 ; $P < 0.001$, $I^2 = 0\%$; Figure 3). However, the magnitude of this improvement did not reach the MCID threshold of 2.5 points.

At 3 months post-treatment, Haller et al.³³ observed that manual therapy provided a better improvement in neck function (NDI: MD = -5.40% , 95% CI: -10.14 , -0.66 ; $P = 0.03$), meeting the MCID of 3 points. However, Schwler et al.³⁴ did not report a statistically significant improvement in neck function as assessed by the NPQ (MD = -14.00% , 95% CI: -34.24 , 6.24 ; $P = 0.18$).

3.4.2. Manual therapy versus no-treatment control

The study by Pach et al.³⁵ found that manual therapy reduced pain intensity at 3 months post-treatment (VAS: MD = -1.80 points, 95% CI: -2.68 , -0.92 ; $P < 0.001$). However, this improvement did not reach the MCID.

Low-quality evidence from three studies^{35,37,38} indicated that manual therapy can improve neck function at 3 months post-treatment (NDI: MD = -6.12% , 95% CI: -9.81 to -2.44 , $P < 0.05$; $I^2 = 69\%$) (Figure 4). This improvement reached the MCID.

Two studies by Munk et al.^{37,38} investigated the effect of manual therapy on quality of life using the SF-36. Manual therapy did not significantly improve either the mental component summary (MCS) scores (MD = 3.42 points, 95% CI: -0.00 , 6.84 ; $P = 0.05$) or the physical component summary (PCS) scores (MD = 0.56 points, 95% CI: -1.30 , 2.41 ; $P = 0.56$) at 3 months post-treatment (Figure 5).

Table 1 Characteristics of included studies

Study ID	Diagnosis	Sample size	Duration of disease (mean [SD]/ median [IQR]; months)	Intervention	Comparison	Follow-up period (months)	Outcomes	AE (IG/CG)
Qin 2012 ²¹	Chronic non-specific neck pain	IG: 15; CG: 15	44.73 (45.00)	MTIP + SET	SET	3	VAS, NDI	NR
Lau 2011 ²²	Chronic mechanical neck pain	IG: 60; CG: 60	≥ 3	TM + IRR	IRR	IG: 3 CG: 6	NRS, NPQ, SF-36	0%/0%
González-Rueda 2020 ²³	Chronic mechanical neck pain	IG: 26, 26; CG: 26	19.81 (19.25)	IST + CPT UCTM + CPT	CPT	3	NRS, NDI	0%/0%
Rodríguez-Sanz 2020 ²⁴	CNP	IG: 29; CG: 29	IG: 96.97 (96.73) CG: 124.38 (148.17)	MT + ET	ET	IG: 3 CG: 6	VAS, NDI	0%/10.3%
Groisman 2023 ²⁵	CNP	IG: 45; CG: 45	≥ 3	OMT+ ET	ET	IG: 3 CG: 6	NRS, NDI	0%/0%
Lytras 2020 ²⁶	Chronic mechanical neck pain	IG: 20; CG: 20	≥ 3	INIT + ET	ET	IG: 3 CG: 6	VAS, NDI, SF-36	NR
Lytras 2023 ²⁷	CNP	IG: 20, 20; CG: 20	≥ 3	INIT + ET SM + ET	ET	6	VAS, NDI, SF-36	NR
Maiers 2014 ²⁸	CNP	IG: 80; CG: 79	IG: 78.0 (24.0, 228.0); CG: 60.0 (24.0, 180.0)	SM + ET	ET	3	NRS, NDI, SF-36	0%/0%
Zaproudina 2007 ²⁹	CNP	IG: 35, 33; CG: 34	IG: 140 (74) (TBS), 134 (88) (M); CG: 127 (78)	TBS M	PT	IG: 6 CG: 12	NDI	0%/0%
Izquierdo Pérez 2014 ³⁰	CNP	IG: 22; CG: 22, 22	20.74 (24.49)	SNAG	HVLA Mob	3	VAS, NDI	0%/0%
Luo 2022 ³¹	Chronic non-specific neck pain	IG: 15; CG: 15	IG: 10.9 (2.1) CG: 9.7 (2.5)	SM	Conventional physiotherapy treatment	3	VAS, NDI	NR
Yang 2020 ³²	Cervical vertigo	IG: 30; CG: 30	≥ 3	TORT	Traction treatment	3	VAS	Overall: 3.3%
Haller 2016 ³³	CNP	IG: 27; CG: 27	9.6 (8.9)	CST	simulate CST	3	VAS, NDI	22.2%/29.6%
Schwerla 2008 ³⁴	Chronic non-specific neck pain	IG: 23; CG: 18	≥ 3	Osteopathy treatment	Sham treatment	3	NRS, NPQ	0%/0%
Pach 2018 ³⁵	CNP	IG: 46; CG: 46	IG: 109.2-138.0; CG: 134.4-136.8	Tuina	No-intervention waiting list	3	VAS, NDI	41.3%/0%
Lin 2013 ³⁶	Chronic mechanical neck pain	IG: 33; CG: 30	IG: 37.06 (35.20); CG: 39.23 (28.73)	LM	Tuina	3	NRS, NPQ	No-specifical description
Munk 2024 ³⁷	CNP	IG: 102; CG: 101	≥ 6	CA-M	WL-C ₀	3	NDI SF-36	NR
Munk 2026 ⁸	CNP	IG: 145; CG: 145	≥ 6	TT-M	WL-C	3	NDI, SF-36	NR

Notes: AE: adverse event; CA-M: care ally-assisted massage (trained non-professional care ally-delivered massage); CG: control group; CNP: chronic neck pain; CPT: conventional physiotherapy treatment; CST: craniosacral therapy; ET: exercise therapy; HVLA: high velocity low amplitude; IG: intervention group; INIT: integrated neuromuscular inhibition technique; IQR: interquartile range; IRR: infrared radiation therapy; IST: inhibitory suboccipital technique; LM: Long's manipulation; M: massage; Mob: mobilization; MT: manual therapy; NDI: neck disability index; NPQ: neck pain questionnaire; NR: not reported; NRS: numerical rating scale; OMT: osteopathic manipulative treatment; PT: physiotherapy; SD: standard deviation; SET: sling exercise therapy; SF-36: 36-item short form health survey; SM: spinal manipulation; SNAG: sustained natural apophyseal glide; TBS: traditional bone setting; TM: thoracic manipulation; TORT: technique of relieving tendons; TT-M: therapist-treated massage; UCTM: upper cervical translatoric mobilization; VAS: visual analog scale; WL-C: waitlist control.

3.4.3. Manual therapy versus active control

Moderate-quality evidence from two studies^{31,32} indicated that manual therapy reduced pain intensity at 3 months post-treatment compared with active control (MD = -1.35 points, 95% CI: -1.66, -1.04; $P < 0.001$, $I^2 = 0\%$; Figure 6), but this improvement did not reach the MCID.

At 3 months post-treatment, the study by Luo³¹ found that manual therapy exhibited superior performance in neck disability compared to active control (MD = -5.60%, 95% CI: -9.65 to -1.55, $P = 0.007$), exceeding the MCID. However, the study by Zaproudina et al.²⁹ showed no superior performance at 6 months (MD = -2.98%, 95% CI: -8.67, 2.70; $P = 0.30$, $I^2 = 50\%$; Figure 7A) and 12-month post-treatment (MD = -2.85%, 95% CI = -9.81, 4.11; $P = 0.42$,

$I^2 = 51\%$; Figure 7B).

3.4.4. Manual therapy with active control versus active control alone

Low-quality evidence demonstrated that manual therapy combined with active control provided a greater performance in neck pain intensity than active control alone (MD = -1.01 points, 95% CI: -1.53, -0.49; $P = 0.0001$, $I^2 = 62\%$; Figure 8A).^{21-26,28} Low-quality evidence showed that the effect size slightly increased at 6 months post-treatment (MD = -1.20 points, 95% CI: -1.72, -0.68; $P < 0.001$, $I^2 = 65\%$; Figure 8B). However, neither improvement reached the MCID.^{22,24-27}

At 3 months post-treatment, moderate-quality evidence determined that manual therapy combined with active control resulted in amelioration of

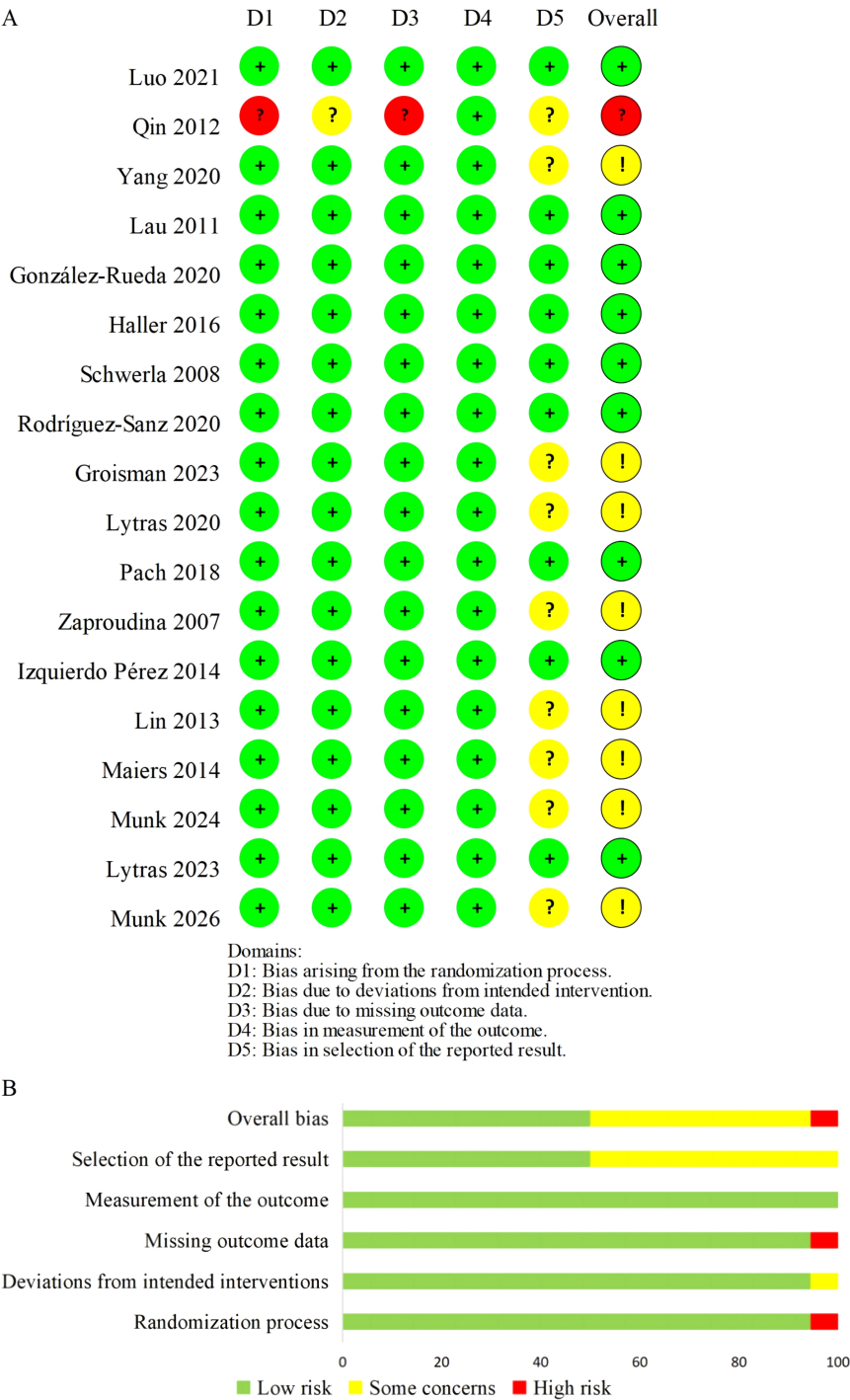


Figure 2 Risk of bias 2 (A) risk of bias summary; (B) risk of bias graph

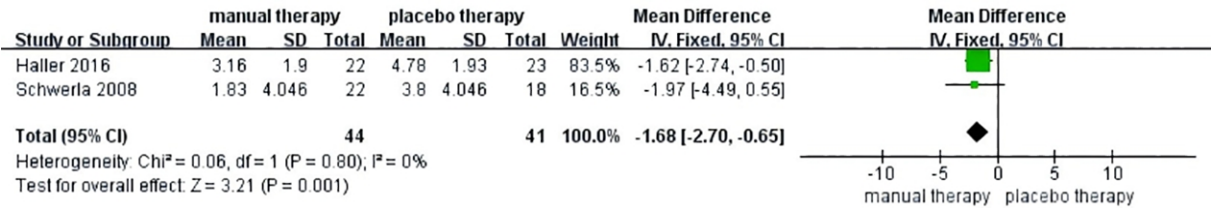


Figure 3 Forest plot comparing the mean difference in pain scores between manual therapy and placebo control at the 3-month follow-up after intervention for CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; P: probability; SD: standard deviation.

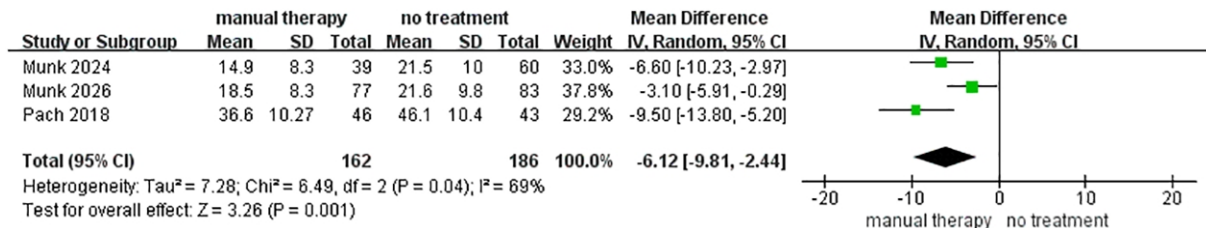


Figure 4 Forest plot of the mean difference in NDI scores between the manual therapy and no-treatment control groups at 3-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; NDI: neck disability index; P: probability; SD: standard deviation.

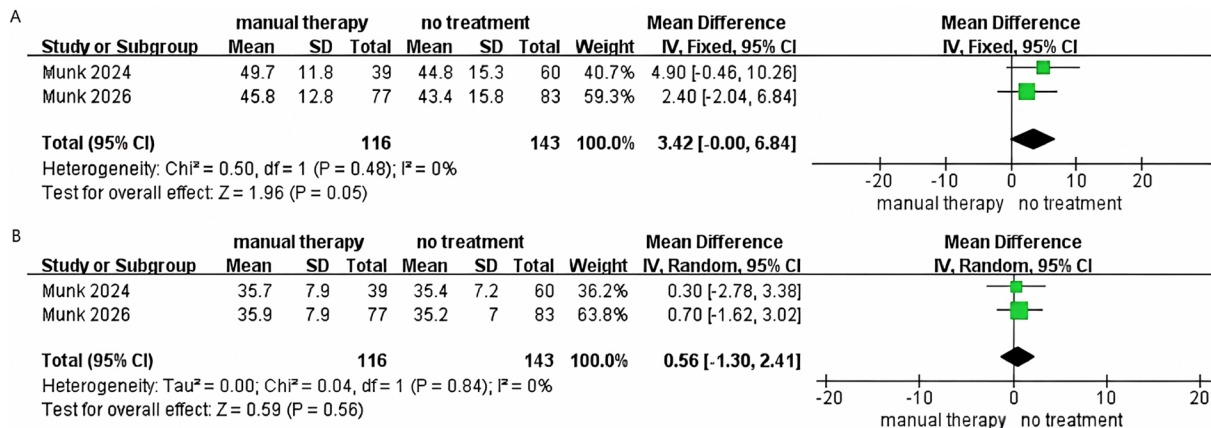


Figure 5 Forest plots of the mean difference in (A) SF-36 MCS and (B) SF-36 PCS scores between the manual therapy and no-treatment control groups at 3-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; MCS: mental component summary; P: probability; PCS: physical component summary; SD: standard deviation; SF-36: 36-item short form health survey.

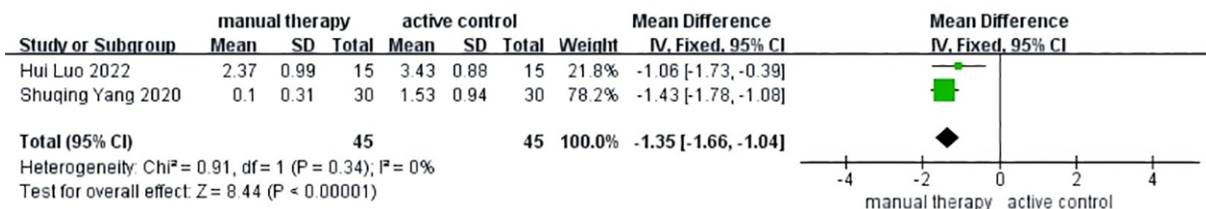


Figure 6 Forest plot comparing the mean difference in pain scores between manual therapy and active control at the 3-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; P: probability; SD: standard deviation.

neck disability (MD = -3.65%, 95% CI: -5.09, -2.21; $P < 0.001$, $F = 42\%$; [Figure 9A](#)). This effect persisted at 6 months post-treatment (MD = -5.63%, 95% CI: -8.66, -2.61; $P = 0.0003$, $F = 61\%$; [Figure 9B](#)). Both improvements exceeded the MCID.

The study by Lau et al.²² also reported an improvement in NPQ scores with manual therapy with active control (MD = -7.56%, 95% CI: -13.64, -1.48; $P = 0.01$). However, it was not observed at 6 months post-treatment (MD = -6.03%, 95% CI: -12.09, 0.03; $P = 0.05$).

At 3 months post-treatment, pooling data from three studies^{22,26,28} produced low-quality evidence demonstrating that manual therapy combined with active control provided larger benefits in terms of physical component summary (PCS) (MD = 6.73 points, 95% CI: 0.94, 12.52; $P = 0.02$, $F = 87\%$; [Figure 10A](#)). However, it was not found in terms of MCS (MD = 1.07 points, 95% CI: -1.04, 3.18; $P = 0.32$, $F = 21\%$; [Figure 10B](#)).

At 6 months post-treatment, a similar improvement was observed in terms of PCS (MD = 9.83 points, 95% CI: 6.10, 13.56; $P < 0.001$, $F = 56\%$; [Figure](#)

[11A](#)) and MCS (MD = 4.09 points, 95% CI: -0.13, 8.31; $P = 0.06$, $F = 63\%$; [Figure 11B](#)).^{22,26,27}

3.4.5. Comparison of different manual therapies

The study by Izquierdo Perez et al.³⁰ compared three manual therapies and analyzed their effects separately because of substantial heterogeneity with other studies. At 3 months post-treatment, no significant differences were observed in pain relief (MD = -0.42 points, 95% CI: -1.29, 0.46; $P = 0.35$) or functional improvement (MD = -0.68%, 95% CI: -4.00, 2.63; $P = 0.69$).

At 3 months post-treatment, low-quality evidence from three studies^{23,26,27} did not reveal different alleviation of pain intensity (MD = -1.55 points, 95% CI: -3.40, 0.30; $P = 0.10$, $F = 77\%$; [Figure 12](#)). A similar result (MD = -0.27 points, 95% CI: -0.65, 0.10; $P = 0.15$) was observed at 6 months post-treatment in the study by Lytras et al.²⁷

Gonzalez-Rueda et al.²³ and Lin et al.³⁶ found different improvements in neck function at 3 months post-treatment (NDI: MD = -2.77%, 95% CI:

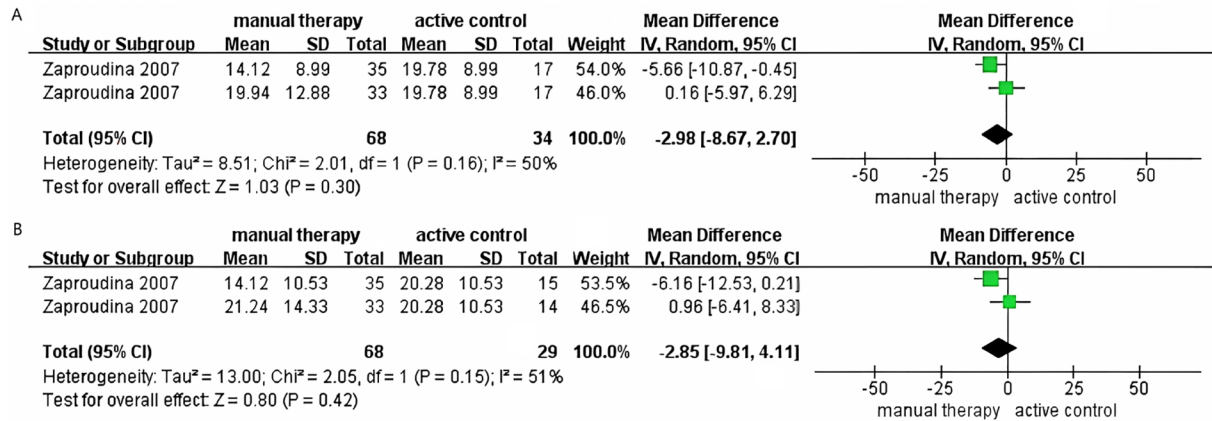


Figure 7 Forest plots of the mean difference in NDI scores between the manual therapy and active control groups at the (A) 6-month and (B) 12-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; NDI: neck disability index; P: probability; SD: standard deviation.

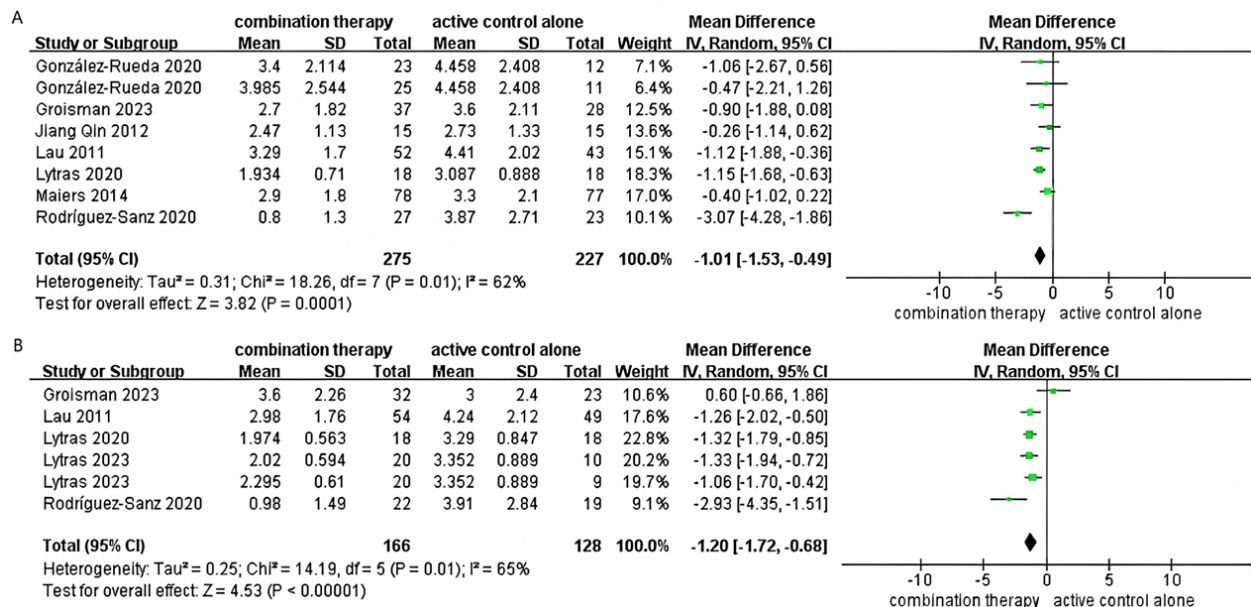


Figure 8 Forest plots of the mean difference in pain scores between manual therapy plus active control and active control alone at the (A) 3-month and (B) 6-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; SD: standard deviation.

-5.07, -0.47, $P = 0.02$; NPQ: MD = -10.81%, 95% CI: -17.09, -4.53, $P = 0.0007$). However, very low-quality evidence from two studies^{27,29} suggested that the difference was not reported at 6 months post-treatment (MD = -2.93%, 95% CI: -7.86, 1.99; $P = 0.24$; $I^2 = 57\%$; Figure 13),^{27,29} while Zaproudina et al.²⁹ found it at 12 months post-treatment (MD = -7.30%, 95% CI: -13.49, -1.11, $P = 0.02$), exceeding the MCID threshold of 3%.

The study by Lytras et al.²⁷ used the SF-36 to compare the quality of life at 6 months post-treatment and found no statistical significance in either the PCS or MCS scores (MD = -0.70 points, 95% CI: -5.72, 4.32, $P = 0.78$; MD = 0.50 points, 95% CI: -4.29, 5.29, $P = 0.84$).

3.5. Evidence of effect of interventions

The results of the GRADE assessment are presented in Appendix 2. Of the 29 comparisons, 14 were investigated in only a single study, and most had small sample sizes.

3.6. Subgroup and sensitivity analyses

Subgroup analysis based on whether the active control was exercise-based showed differences in the effect sizes of neck pain reduction (total: MD = -1.01 points, 95% CI: -1.53, -0.49; $P = 0.0001$, $I^2 = 62\%$; exercise-based: MD = -1.27 points, 95% CI: -2.13, -0.40; $P = 0.004$, $I^2 = 80\%$; non-exercise: MD = -0.76 points, 95% CI: -1.28, -0.24; $P = 0.004$, $I^2 = 0\%$) and functional improvement (total: MD = -3.65%, 95% CI: -5.55, -1.74, $P = 0.0002$, $I^2 = 42\%$; exercise-based: MD = -4.73%, 95% CI: -7.39, -2.08; $P = 0.0005$, $I^2 = 51\%$; non-exercise: MD = -2.05%, 95% CI: -4.36, 0.25, $P = 0.08$, $I^2 = 0\%$) at 3 months post-treatment (Appendix 3).

Sensitivity analysis based on risk of bias revealed altered results (high/potential: $P > 0.05$; low: $P < 0.05$) for neck pain intensity and dysfunction at 6 months post-treatment, as well as PCS at 3 months post-treatment. However, the results from low-risk studies provided greater support for the robustness of these results. No reversal in the direction of effect was observed in any comparison. Sensitivity analyses based on sample size and sequential

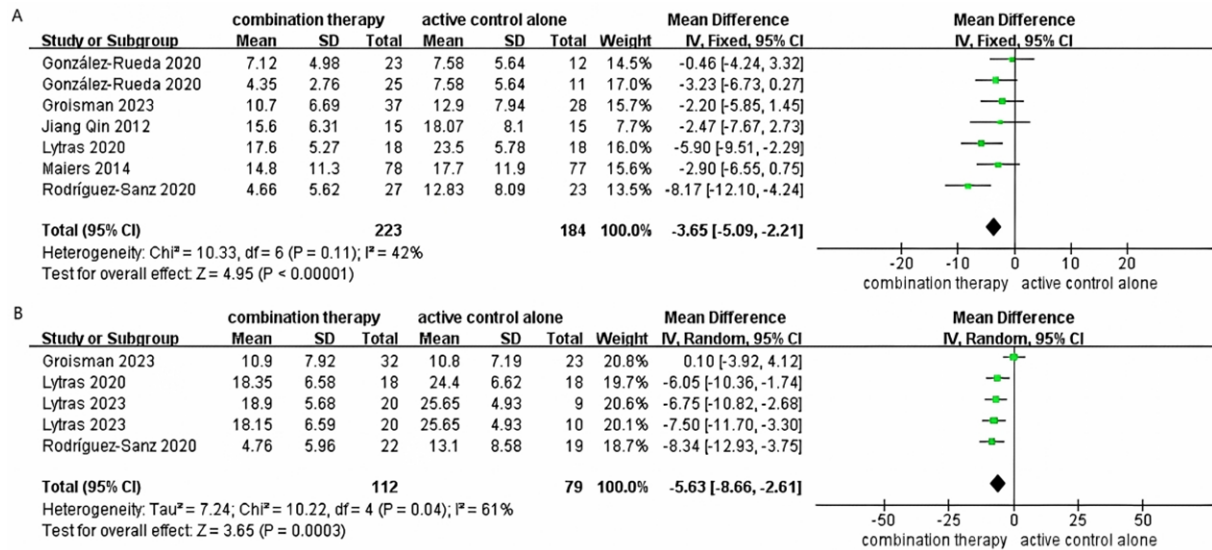


Figure 9 Forest plots of the mean difference in NDI scores between manual therapy plus active control and active control alone at the (A) 3-month and (B) 6-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; NDI: neck disability index; SD: standard deviation.

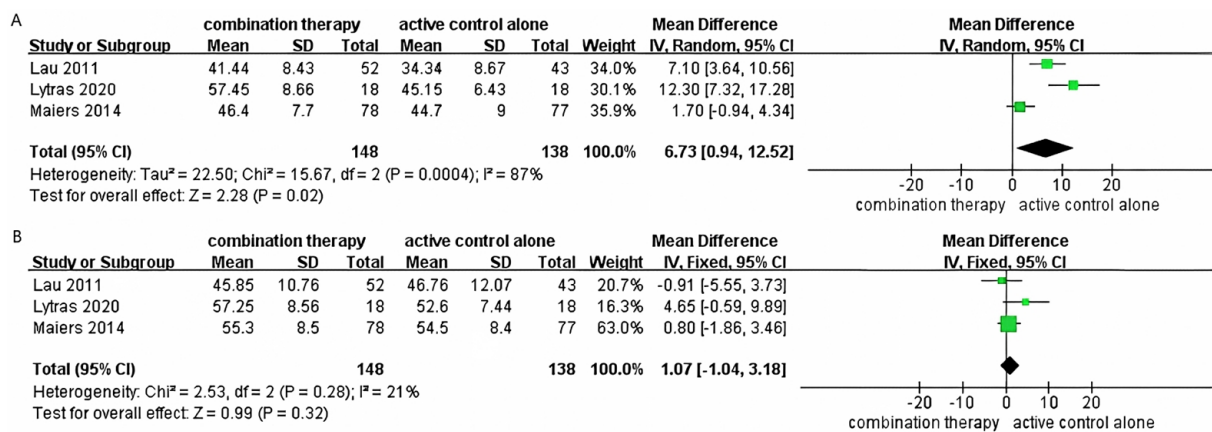


Figure 10 Forest plots of the mean difference in (A) SF-36 PCS and (B) SF-36 MCS scores between the manual therapy plus active control and active control alone at the 3-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; MCS: mental component summary; P: probability; PCS: physical component summary; SD: standard deviation; SF-36: 36-item short form health survey.

study removal also showed robust results for neck pain and dysfunction. However, the results for the secondary outcome of quality of life were less robust, primarily linked to Groisman et al.²⁵, Maiers et al.²⁸, Rodríguez-Sanz et al.²⁴, or Lau et al.²² This may have been due to differences in sample size, effect size, or dropout rates that affected the robustness of the findings. The details are shown in Appendix 4.

3.7. Safety assessment

Seven studies^{22,23,25,28-30,34} did not report adverse events, whereas six^{21,26,27,31,37,38} did not mention adverse events at all. Five studies^{24,32,33,35,36} reported mild or suspected adverse events, with no serious adverse events observed. However, one³⁶ of these studies did not provide detailed information on the adverse events. The incidence of adverse events ranged from 3.3% to 41.3% in the manual therapy group, was 29.6% in the placebo group, and ranged from 3.3% to 10.3% in the active control group. The highest incidence (41.3%) was reported in one study,³⁵ in which all adverse events were mild and transient and did not lead to treatment discontinuation. No adverse events were

observed in the group receiving manual therapy combined with the active control. The majority of adverse events were considered minor, as they either resolved spontaneously or were effectively treated.

4. Discussion

4.1. Summary of evidence

For the treatment of CNP in adults, moderate-quality evidence indicates that manual therapy provides long-term pain relief and functional improvement (exceeding the MCID) lasting for at least three months. Low-quality evidence shows that when manual therapy is combined with active control therapy, these effects may persist for at least 6 months. Low- to very low-quality evidence suggests that the improvement in quality of life (PSC) with combined manual therapy and active control therapy lasts for at least 6 months. These findings may inform recommendations for future clinical guidelines.

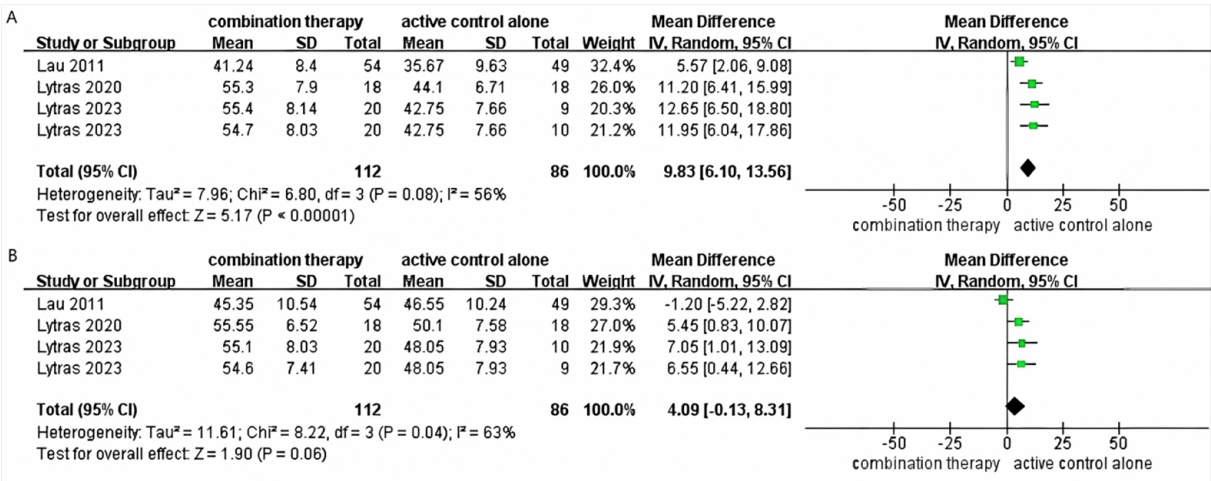


Figure 11 Forest plots of the mean difference in (A) SF-36 PCS and (B) SF-36 (MCS) scores between manual therapy plus active control and active control alone at the 6-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; MCS: mental component summary; P: probability; PCS: physical component summary; SD: standard deviation; SF-36: 36-item short form health survey.

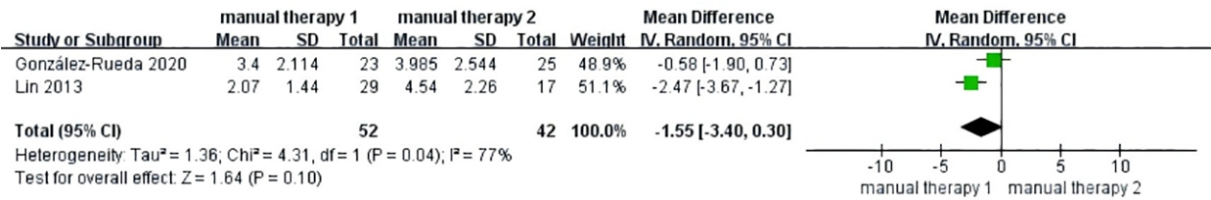


Figure 12 Forest plot of the mean difference in pain scores between the two manual therapies at the 3-month follow-up in patients with CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; SD: standard deviation.

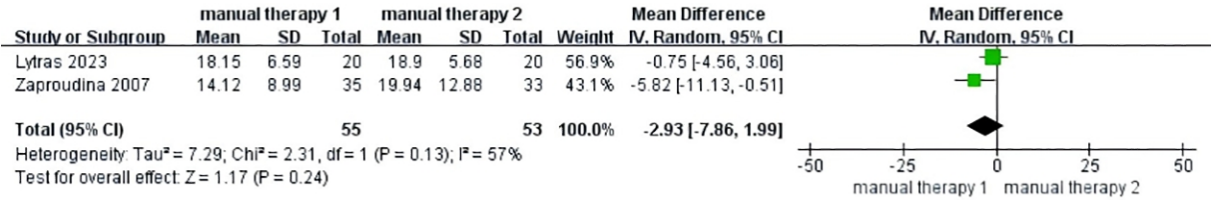


Figure 13 Forest plot of the mean difference in NDI scores between the two manual therapies at the 6-month follow-up after intervention for CNP

Notes: CI: confidence interval; CNP: chronic neck pain; df: degrees of freedom; IV: inverse variance; NDI: neck disability index; SD: standard deviation.

4.2. Manual therapy for CNP

This study demonstrated that manual therapy provided benefits in alleviating neck pain for at least 3 months. However, the results regarding functional improvement were not entirely consistent. This discrepancy may be attributed to several factors. First, the placebo effect, including the influence of patient expectations and beliefs, may influence treatment outcomes. Second, differences in the type or intensity of manual therapy or control interventions between the two studies may have contributed to the inconsistent findings. Additionally, the NDI score assesses the impact of cervical dysfunction on activities of daily living, whereas the NPQ score focuses on the severity of neck pain and its influence on patients' quality of life.

Compared with active controls, manual therapy may provide sustained effects in pain relief and functional improvement for at least 3 months. However, these benefits were not maintained at the 6- and 12-month follow-ups. These findings suggest two possible explanations. First, the effects of manual therapy on reducing CNP severity may not persist beyond 3 months. Second, active control interventions may exhibit delayed therapeutic effects. In con-

trast, combining manual therapy with active treatment may maintain benefits in pain relief and functional improvement for up to 6 months. This indicates that manual therapy, when used as an adjunctive treatment, may significantly enhance the efficacy of conventional interventions and provide more durable therapeutic effects. A recent systematic review indicated that manual therapy combined with exercise was superior to either treatment in isolation for CNP.³⁹ Guidelines recommend personalized multimodal therapy for CNP.⁴⁰ Combining manual therapy with active treatment, which involves both relaxation of local myofascial tissues plus strengthening of muscle function, yields better overall improvement.

Regarding the quality of life, the study found that combining manual therapy and active treatment resulted in a sustained improvement in PCS for at least 6 months. This may be attributed to the fact that manual therapy primarily exerts local effects through muscle relaxation, fascial adjustment, and meridian unblocking, whereas active treatment promotes the recovery of motor function, thereby contributing to overall physical health. Additionally, mental health is influenced by multiple factors.

In the comparison of different manual therapies, the effects on functional improvement were not entirely consistent, possibly because of significant differences among the techniques. However, no statistically significant differences were found in pain relief or quality of life, suggesting that different manual therapies may have similar therapeutic effects. Similar findings have been reported in other studies.^{41,42}

Our findings are consistent with those of a review by Castellini et al.⁴³ which included 119 studies with 12 496 participants. The authors synthesized outcomes across multiple follow-up time points and found that manual therapy provided pain relief for at least 1 month, with most mild adverse events reported after acupuncture or dry needling interventions. Additionally, manual therapy combined with exercise improved dysfunction at 3–6 months follow-up. Our study extends these findings by specifying the exact follow-up time points (3, 6, and 12-months post-treatment) and evaluating the sustained effects of manual therapy, including its contribution to improvements in quality of life. We also found that manual therapy had an acceptable safety profile, consistent with the good safety profile reported in previous studies.^{44–46}

The mechanisms underlying manual therapy are complex and have not yet been fully elucidated. Some scholars have proposed that the regulatory and therapeutic effects are achieved through two mechanisms: nerve conduction and mechanical conduction.⁴⁷ Other scholars have proposed a close relationship between the nervous system and the myofascial system,⁴⁸ suggesting that manipulation may directly adjust pathological changes in the fascia through the “neuro-myofascial network.” Collectively, these perspectives may help explain the therapeutic effects of manual therapy.

4.3. Quality of included trials and evidence

The risk of bias in the included studies was primarily related to blinding and missing outcome data. Most patients signed informed consent before enrollment and were aware of their group allocation at the start of treatment. Most therapists (66.7%) and assessors (33.3%) were aware of the patient group allocation during the procedure. Owing to the long follow-up period, there were many dropouts. The overall dropout rate was 22.43% at 3 months post-treatment (manual therapy, 21.06%; non-manual therapy, 24.33%) and 20.85% at 6 months post-treatment (manual therapy, 14.89%; non-manual therapy, 29.81%). A study flow diagram was missing in 5.6% of the cases.

The GRADE evidence quality evaluation revealed that the evidence for manual therapy for CNP was downgraded mainly because of imprecision, as many studies had small sample sizes, leading to wide confidence intervals and reduced result reliability. Additionally, when high risk of bias or $P \geq 50\%$ (inconsistency) was present in the comparisons, the evidence quality was also downgraded by one level.

4.4. Strengths and limitations

Through meta-analysis and GRADE assessment, we found moderate- to very-low-quality evidence suggesting that manual therapy may provide sustained benefits in pain and function, with an acceptable safety profile. These findings highlight its potential role as an adjunct to conventional treatments rather than as a replacement for them. We focused on the post-treatment effects of manual therapy for CNP, particularly at longer-term follow-up time points. The study found that manual therapy not only yields statistically significant functional improvement in patients with CNP, but also demonstrated clinical meaningful effects. Notably, when combined with exercise-based active interventions, the benefits for pain relief and functional improvement may persist for at least 6 months.

Our study has certain limitations. First, most of the included studies were published in Chinese and English, which may have introduced language bias, although the inclusion of studies in these languages is unlikely to substantially compromise the robustness of the results.^{49,50} Second, the types of manual therapy included in this review were diverse (e.g., tuina, osteopathy, muscle energy techniques), with substantial heterogeneity in their mechanisms and applications. Although we attempted subgroup analyses by manual therapy category in the supplementary material, the small number of studies in each subgroup limited the reliability and interpretability of these findings; there-

fore, the subgroups are not emphasized in the main text. Therefore, pooling these heterogeneous manual therapies under the single label of “manual therapy” has limitations that must be fully considered when interpreting the results. In addition, heterogeneity may have existed across comparisons because of differences in sample size, types of manual therapy, or positive control types. Sensitivity and subgroup analyses were performed to identify the sources of heterogeneity and confirm the robustness of the results. Furthermore, whether patients received other treatments during follow-up was not fully reported, and any additional treatments could have influenced post-treatment outcomes. Therefore, our results should be interpreted with caution.

4.5. Clinical and research implications

Manual therapy, as a complementary and alternative therapy for CNP, is effective in reducing pain intensity and improving functional limitations. When combined with exercise-based positive controls, it demonstrated better sustained effects, lasting at least 6 months. Beyond addressing local physiological issues in the neck, manual therapy may also contribute to improvements in overall physical health.

Previous studies have reported long-term benefits of cervical manipulation for pain relief and functional improvement, particularly when combined with supervised progressive neck muscle contraction training. However, evidence regarding the long-term effects remains limited. Future research should involve larger sample sizes, rigorous designs, standardized long-term follow-up periods, and comprehensive outcome assessments to facilitate future meta-analyses. Additionally, well-designed placebo-controlled groups (e.g., sham treatments or simulated techniques) are essential to accurately assess the true and placebo effects of manual therapy through consistent outcome measures.

5. Conclusion

Moderate- to very-low-quality evidence indicates that manual therapy may alleviate neck pain and improve function in patients with CNP for at least 3 months post-treatment compared to placebo therapy, no-treatment, or active control. When combined with active controls, these effects may persist for up to six months. Although the results on quality of life were inconsistent across studies, combined treatment may provide sustained improvement in physical health for at least 6 months. Despite the need for further research with larger sample sizes, standardized procedures, and meticulous designs, current evidence suggests that manual therapy has enduring therapeutic effects and an acceptable safety profile. Manual therapy may therefore be a useful complementary approach for managing CNP.

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Data Availability

All data supporting the findings of this study are available within the article and its Supplementary Material.

Author Contribution Statement

Wei-jiao Wang: Data curation, investigation, formal analysis, and writing – original draft. **Ya-nan Sun:** Conceptualization, methodology, visualization, and writing – original draft. **Xi-you Wang:** Conceptualization, supervision, project administration, and writing – review & editing. **Chang-he Yu:** Conceptualization, supervision, project administration, and writing – review & editing.

Use of AI Statement

None.

Declaration of Competing Interest

The authors have no competing interests to declare that are relevant to the content of this article.

Electronic Supplementary Material

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