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Review

The effectiveness of manual therapy in people with chronic non-specific low back pain: an umbrella review with meta-analysis

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ABSTRACT

Background: Chronic nonspecific low back pain (CNLBP) is a widely recognized condition worldwide. Its clinical management must be based on the best current evidence to achieve optimal outcomes, yet there is still a lack of consensus on its clinical approach.
Objective: To evaluate the effectiveness of manual therapy (MT) on pain intensity, frequency, disability, and quality of life in adults with chronic nonspecific low back pain (CNLBP).
Methods: A comprehensive search was conducted in 8 databases, covering January 2014 to October 2024. Inclusion criteria included adults with CNLBP, MT interventions provided by healthcare professionals, and systematic reviews (SRs) of randomized controlled trials (RCT). Data on pain intensity, pain frequency, disability, and quality of life measured using validated scales were extracted. The results were shown according to the type of intervention and the period evaluated (short, medium, or long term).
Results: About 21 SRs with 35,711 participants were included. MT included spinal manipulation, soft-tissue techniques, myofascial techniques, massage, and neuromeningeal techniques. MT outperforms other interventions regarding pain (MD −10.52; 95% CI −13.71 to −7.33) and disability (SMD −0.60; 95% CI−0.80 to −0.40) in the short term, and this effect diminishes over time.
Conclusions: MT offers significant short-term benefits in reducing pain and disability in individuals with CNLBP. Like most interventions for CNLBP, the effects of MT tend to diminish over time. Nevertheless, MT may serve as a valuable treatment option for short-term pain relief and functional improvement. Limitations in the methodological quality and long-term follow-up of included studies constrain the conclusions that can be drawn about long-term efficacy.
Registration: PROSPERO, CRD42023382825.

List of abbreviations: AMSTAR-2, Assessment Tool for Systematic Reviews-2; CAA, Corrected Covered Area; CI(s), Confidence Interval(s); CINAHL, Cumulative Index of Nursing and Allied Literature Complete; CNLBP, Chronic Nonspecific Low Back Pain; CNS, Central Nervous System; COVID-19, Coronavirus Disease 2019; GBD, Global Burden of Disease; GRADE, Grading of Recommendations, Assessment, Development, and Evaluations; GROOVE, Graphical Representation of Overlap for Overview; HeLP, Healthy Lifestyle Program; HPA, Hypothalamic-Pituitary-Adrenal; IL-6, Interleukin 6; LGI, Low-Grade Inflammation; MA, Meta-analysis; MD(s), Mean Difference(s); MET, Muscle Energy Techniques; MFR, Myofascial Release; MT, Manual Therapy; NPRS, Numeric Pain Rating Scale; NSAIDs, Non-Steroidal Anti-Inflammatory Drugs; NSLBP, Nonspecific Low Back Pain; ODI, Oswestry Disability Index; PEDro, Physiotherapy Evidence Database; PICO, Population, Intervention, Comparison, and Outcome; PNI, Psychoneuroimmunology; PRIOR, Preferred Reporting Items for Overviews of Reviews; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; PROSPERO, International Prospective Register of Systematic Reviews; QBPDS, Quebec Back Pain Disability Scale; RCT(s), Randomized Controlled Trial(s); RMDQ, Roland-Morris Disability Questionnaire; RoB, Risk of Bias; ROBIS, Risk Of Bias in Systematic Reviews; SD(s), Standard Deviation (s); SMD(s), Standardized Mean Difference(s); SMT, Spinal Manipulative Therapy; SNS, Sympathetic Nervous System; SR(s), Systematic Review(s); TNF-α, Tumor Necrosis Factor-α; VAS, Visual Analogue Scale

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Introduction

Low back pain is a globally increasing health concern [1] defined as pain located below the costal margin and above the lower gluteal folds, with or without irradiation to the legs [2]. According to the latest update of the Global Burden of Disease (GBD) study, in 2020, the number of people with low back pain reached 619 million worldwide, 10% of the world's population [3]. These Fig.s may be underestimated, as the GBD 2021 data do not account for the impact of Coronavirus Disease 2019 (COVID-19). A recent meta-analysis reported an increase in both the intensity and prevalence of low back pain during the pandemic [4]. Low back pain continues to be the global leading cause of years lived with disability [3], and not only negatively affects people's quality of life [5] but also implies a great economic threat to health systems [6]. In Spain, the annual cost of low back pain amounts to 10 million euros per year [7].

Chronic low back pain is defined as persisting for 12 weeks or longer [8]. In 85% of cases, it is classified as chronic nonspecific low back pain (CNLBP), indicating an absence of a specific pathology detectable through objective examination [6,9]. For this reason, CNLBP is not understood as a disease but as a behavioral and neurobiological response orchestrated by the central nervous system in response to a perception of threat [6], and its chronification has been attributed mainly to central mechanisms [10,11]. However, the vision of chronic pain where no damage is found as an exclusively cerebral mechanism has been questioned by recent literature [12], since there is some evidence of the involvement of peripheral mechanisms in the chronification of pain, such as pathological changes in small diameter fibers [13,14], microvascular dysfunction [15], or low-grade inflammation [16,17].

About 65% of people with CNLBP still have pain one year after onset [18]. Some clinical guidelines recommend non-pharmacological approaches as first-line treatments for CNLBP, while others may include pharmacological therapies depending on the clinical context [19,20]. Due to the persistence of symptoms, many people seek complementary therapies for pain management, among which are different manual therapy (MT) approaches. Although some clinical guidelines do not consider MT within the arsenal of interventions for CNLBP [20,21], other reviews recommend it as an adjunctive treatment [22–24].

Due to the wide variety of manual interventions (physiotherapy, osteopathy, massage, chiropractic, acupressure, etc.) and the heterogeneity of studies, their results should be interpreted with caution. Therefore, this study aims to perform an umbrella review with meta-analysis to critically evaluate the quality of systematic reviews (SR) on MT and CNLBP and synthesize their efficacy in terms of pain intensity, pain frequency, disability, and quality of life in people suffering from CNLBP.

Materials and methods

Design

This study is an umbrella review (UR) with meta-analysis.

Regulatory and ethical aspects

This UR follows the Preferred Reporting Items for SRs and Meta-Analyses (PRISMA) and incorporates the Preferred Reporting Items for Overviews of Reviews (PRIOR) checklist [25]. The protocol was registered in PROSPERO (CRD42023382825) before commencement.

Inclusion criteria

Following the population, intervention, comparison, and outcome (PICO) framework [26], inclusion criteria were:

- Population: Adult participants (≥18 years) diagnosed with CNLBP.
- Intervention: MT administered by healthcare providers alone or combined with other therapies. We decided to include any therapeutic act performed with the hand as MT. Although MT involves a large number of different interventions, the current comprehensive models that attempt to explain neurophysiological interactions are common to the different approaches [27,28].
- Comparison: Control groups could entail diverse interventions when it was possible to isolate and assess the effectiveness of MT.
- Outcomes: Pain intensity, pain frequency, disability, and/or quality of life.
- Trials were excluded if they focused on people aged <18 years, or if they included other types of low back pain such as acute or subacute pain, or pain due to specific underlying conditions (eg, radiculopathy, spinal stenosis, malignancy).

Study design

Systematic reviews (SRs) with or without meta-analyses of randomized controlled trials (RCTs) were eligible for inclusion. Following international criteria, no language restrictions were applied [29].

Search strategy

A comprehensive search was conducted in several databases, including PubMed, Cochrane, Web of Science, Scopus, Physiotherapy Evidence Database (PEDro), ProQuest, Cumulative Index of Nursing and Allied Literature Complete (CINAHL), and Dialnet. The literature search covered studies published from January 2014 to October 2024, ensuring the inclusion of recent advancements in the field. Details of the search strategy can be found in supplementary material S1. Two independent reviewers (OCV and JGC) conducted the search using a standardized protocol, with any disagreements resolved by consensus. In addition, reference lists of relevant studies were screened manually, and authors were contacted for additional information when necessary.

Selection criteria and data extraction

The 2 independent reviewers initially screened titles, abstracts, and keywords to identify relevant SRs. In case of reviewers' disagreement or insufficient abstract data, full-text reviews were conducted. Studies that met the inclusion criteria were then subjected to full-text analysis by the 2 reviewers. Disagreements were resolved by discussion, with the involvement of a third reviewer when necessary [30]. To ensure that we covered the entire literature, in cases where MT was combined with other interventions, or where the SRs investigated multiple treatment modalities, we included the review only if it was possible to isolate and extract data specific to MT in participants with CNLBP.

Methodological quality and risk of bias assessment

The methodological quality of the included SRs was assessed using the Assessment Tool for Systematic Reviews (AMSTAR-2) [31], which consists of 16 items rated as "yes," "partly yes," or "no." Overall ratings classified SRs as critically low, low, moderate, or high quality. Risk of bias (RoB) was assessed using the Risk of Bias in Systematic Reviews (ROBIS) tool, which assesses 3 phases: relevance assessment (optional), identification and selection of studies, and data collection and assessment. The ROBIS tool includes signaling questions that are scored as "yes," "probably yes," "probably no," "no," or "no information," resulting in a RoB score of "low," "high," or "unclear" [32]. The 2 independent reviewers performed both assessments.

Overlapping analysis

To quantify the extent of overlap between primary studies included in the systematic reviews (SRs) analyzed, we employed the Graphical Representation of Overlap for Overviews (GROOVE) tool [33]. This instrument provides a systematic approach to the evaluation and

quantification of the number of primary studies included in each review through an evidence matrix, identifying studies that are included in more than one SR, thus providing a clear visual representation of the degree of overlap. The GROOVE tool generates graphical representations of the overlap percentages between each pair of SRs, calculating the overall Corrected Covered Area (CCA), which serves as a standardized metric for interpreting the extent of overlap. Following the authors' guidelines, the CCA is classified as follows: slight overlap if CCA is less than 5%, moderate overlap if it ranges from 6% to 9%, high overlap if it is between 10% and 14%, and very high overlap if CCA is 15% or greater.

Certainty of evidence

The certainty of the evidence was assessed by 2 authors following the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) [34] guidelines. This approach considers potential study limitations, including RoB, inconsistency, indirectness, imprecision, and publication bias. Inconsistency refers to the variation in results across studies. Indirectness refers to the applicability of studies evaluating similar interventions of interest. Imprecision refers to the variability of effect estimates and the width of 95% confidence intervals. Publication bias includes issues such as small-study effects and the non-reporting of studies with nonsignificant (negative) results. The certainty ratings were determined using GRADEpro software [35].

Data synthesis and analysis

Data from primary studies included in SRs were extracted and analyzed according to the following criteria: i) for outcomes assessed at multiple time points within the same follow-up period (eg, at 1 month and 3 months within the short term), only the final measurement point was included in the meta-analysis (MA); ii) for trials with multiple intervention arms applying MT, pooled means and standard deviations (SDs) from intervention groups were used. The same was done for multiple control/comparison groups.

Interventions were defined as any form of MT, including spinal manipulation, soft-tissue techniques, myofascial techniques, massage, and neuromeningeal mobilization. Control groups included non-manual therapies (eg, electrotherapy, cold/heat application), exercise, placebo, or waiting lists.

The MA was conducted using the inverse variance method within a random-effects model to compare mean differences (MDs) in pain scores (0−100 scale) across studies. For disability outcomes, standardized mean differences (SMDs) were calculated due to variability in measurement scales. Effect sizes (MDs and SMDs) were reported with 95% confidence intervals (CIs) to indicate precision.

Heterogeneity was assessed using the I^2 statistic and Cochran's Q-test, with interpretation thresholds as follows: I^2 values of 0%−40% were considered potentially unimportant, 30%−60% moderate, 50%−90% substantial, and 75%−100% considerable. Statistical heterogeneity reflects the proportion of total variation across studies attributable to inconsistency rather than chance. Analyses were performed in Review Manager 5.4 using the DerSimonian and Laird approach. Forest plots were used to visualize the results.

Potential small-study effects were assessed visually using funnel plots and statistically using Egger's test through R software [36]. SMDs were classified as small (0.2), moderate (0.5), or large (0.8) regarding Cohen's thresholds.

Results

Study selection and data extraction

The study screening strategy is shown in the flow chart (Fig. 1). The initial search retrieved 921 articles; ultimately, 21 SRs met the inclusion criteria [37−57], fourteen of which included meta-analysis [37−39,41−44,47,51−53,55−57]. The list of excluded studies, with reasons, is available in Supplementary Material (Table S2).

Characteristics of the included SRs

The main study characteristics, including design, population, interventions, controls, and outcomes, are detailed in Supplementary Material (Tables S3 and S4). 7 SRs focused on spinal manipulative treatment (SMT) and/or mobilization exclusively [38,41,43,47,48,51,53], 3 on myofascial therapy [37,49,55], 2 on muscle energy techniques (MET) [44,52], 5 on multiple MT interventions [39,40,42,46,56], 1 on neural mobilization [54], 1 on acupressure [45], 1 on Mulligan mobilization [50], and 1 on Tuina therapy [57]. Pain intensity was primarily assessed using the Visual Analogue Scale (VAS) and Numeric Pain Rating Scale (NPRS), while disability was evaluated using the Quebec Back Pain Disability Scale (QBPDS), Roland-Morris Disability Questionnaire (RMDQ), and Oswestry Disability Index (ODI). No results were found for pain frequency, and only 6 SRs include quality of life parameters, which seems insufficient to draw rigorous conclusions.

Results of the methodological quality (AMSTAR-2) and risk of bias assessment (ROBIS)

According to the AMSTAR-2 scale, 6 studies were classified as low quality and 15 studies as critically low. The result of each domain of the scale can be seen in Table 1. Regarding RoB, 4 studies had low risk and 17 had high risk according to the ROBIS scale (Fig. 2 in text and Tables S5.A and S5.B in Supplementary Material).

Overlap analysis

The overlap analysis showed a CCA of 2%, meaning a slight overlap among SRs. Considering structural zeros among primary studies included in the different SRs, the adjusted CCA is 3%. A graphical representation of overlapping and the matrix of evidence can be seen in Supplementary Material S6 and S7.

GRADE assessment

The certainty of the evidence was low or very low for the pain and disability items. The ratings for each domain, with their respective explanations, can be found in Table 2.

Qualitative analysis

Spinal manipulative treatment (SMT, thrust) and mobilization (non-thrust) have been shown to be effective in reducing pain and improving function in persons with CNLBP [38,43,46], with manipulation showing slightly greater effects, although not always statistically significant [38,47]. Spinal manipulation has been found to be comparable to other recommended treatments, such as non-steroidal anti-inflammatory drugs (NSAIDs) and exercise [41,43,47], and better than non-recommended therapies [51], supporting its role as a viable option within a multimodal treatment approach. Targeted manipulation at the vertebral level does not appear to provide additional benefits over non-targeted approaches [53]. There is considerable heterogeneity across studies in treatment protocols, populations, and assessment methods, which limits direct comparisons and generalizability of findings. Manipulation offers small short-term benefits (up to 12 weeks) for pain and function [43], but long-term effects may diminish, suggesting a potential need for ongoing treatment.

Myofascial Release (MFR) has shown potential benefits for CNLBP, particularly in reducing disability, though its effects on pain are less consistent across studies. Evidence suggests that MFR significantly improves disability outcomes [37,49,55], with benefits observed after multiple

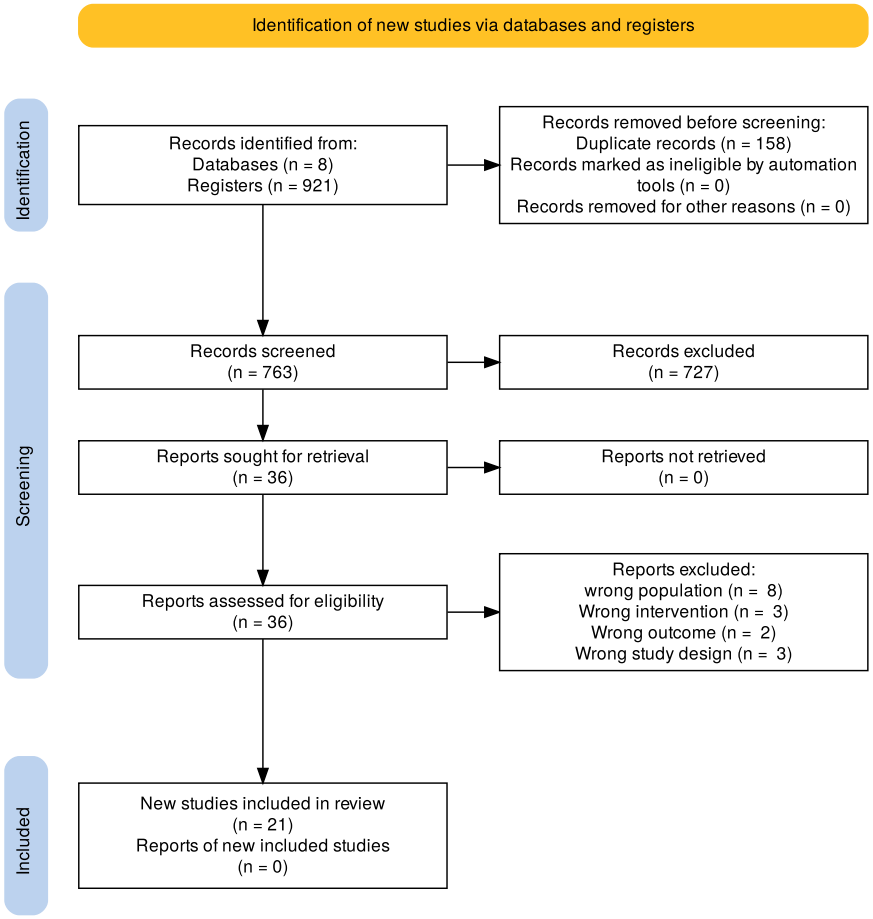

Fig. 1. PRISMA flowchart.

sessions and even following a single application [49]. However, while some studies report a reduction in pain intensity [49,55], others do not find a significant effect when considering all the data together [37]. The effectiveness of MFR may depend on treatment duration and technique variety [49]. Moreover, combining MFR with other interventions, such as physical therapy or exercise, may enhance its therapeutic impact [37]. Despite these promising findings, study heterogeneity in treatment protocols and populations limits the generalizability of results.

The findings for MET on CNLBP suggest a small but significant effect on pain reduction, while its impact on disability remains inconclusive. The study of Santos et al [52] found a minor yet statistically significant reduction in pain with MET, whereas Franke et al [44] reported no additional benefit when MET was combined with other therapies. Neither review found consistent improvements in disability. Both studies highlight methodological limitations.

Other SRs investigated the effects of various types of massage, including acupressure, Tuina, Swedish massage, and traditional Thai massage, and they found some benefits in reducing pain and disability in persons with CNLBP, though effect sizes and evidence quality vary. Acupressure appears to be a cost-effective and safe approach, showing significant pain reduction, functional improvements, and enhanced sleep quality [45,56]. Tuina demonstrates moderate effects on pain and disability, with combination therapy yielding superior functional outcomes [57]. Swedish and Thai massage are effective, particularly in older adults, with Swedish massage offering longer-lasting benefits [40,42]. One SR focused on neural mobilization [54], showing evidence of pain reduction in most of the studies analyzed. Finally, the study of Pourahmadi et al. [50] found that Mulligan techniques can reduce pain and disability in people with lower back pain, though the strength of this conclusion is moderate.

Results of the meta-analysis

About 150 primary studies were extracted from the included SRs after removing duplicates. Then, k = 48 articles were chosen according to the inclusion criteria for MA purposes. Table S8 in Supplementary Material shows the SRs, their primary studies after removing duplicates, the type of MT performed, and the exclusion reasons for each article (and/or advice notes). The risk of bias in each article is presented according to the domains of the RoB tool [58], as older SRs present this scale instead of the newer RoB-2. We respected the RoB qualifications of the SRs' authors where presented; otherwise, we qualified the RCT, as many articles were rated following other risk of bias or methodological quality scales as PEDro [37,40,48,49,52], the Cochrane Back and Neck Review Group scale [46,50], and the Scottish Intercollegiate Guidelines Network [38]. The RoB for each study included in the meta-analysis can be found in the Supplementary Material S9.A and S9.B.

The results are presented for the 2 primary outcomes: pain and disability. For pain, the MD on a 0-100 point scale was calculated. For disability, we calculated SMD. Subgroup analyses were conducted based on the follow-up period, examining short-term (0 to 3 months), medium-term (4-6 months), and long-term (7-12 months) outcomes.

Pain

A total of 48 primary studies reported on pain outcomes, encompassing 7,021 participants [59–80]. When the data presented in the article were not on a 0-100 scale, they were transformed mathematically to enable calculations on this scale (Fig.s 3 and 4 in text, Supplementary Material S10 and S11).

Table 1
Results of the methodological quality assessment (AMSTAR-2)

STUDY	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	SCORE
Chen et al. [37]	Y	N	Y	N	Y	Y	N	Y	Y	N	Y	Y	Y	Y	N	Y	**CL**
Coulter et al. [38]	Y	PY	Y	N	Y	Y	N	PY	Y	N	Y	N	Y	Y	N	Y	**CL**
dal Farra et al. [39]	Y	Y	Y	N	Y	Y	Y	Y	Y	N	Y	N	Y	Y	N	Y	**CL**
de Luca et al. [40]	Y	N	Y	N	N	N	N	PY	Y	N	N/A	N/A	N	N	N/A	Y	**CL**
de Zoete et al. [41]	Y	Y	Y	Y	Y	Y	N	PY	Y	N	Y	Y	Y	Y	N	Y	**CL**
do Nascimento et al. [42]	Y	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	**L**
Fernández Alimán [43]	Y	N	Y	N	N	N	N	PY	Y	N	Y	N	N	N	N	Y	**CL**
Franke et al. [44]	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	**L**
Godley & Smith [45]	Y	N	Y	N	Y	N	N	PY	N	N	N/A	N/A	N	N	N/A	Y	**CL**
Hidalgo et al. [46]	Y	PY	Y	N	Y	Y	Y	Y	Y	N	N/A	N/A	N	N	N/A	N	**CL**
Jenks et al. [47]	Y	Y	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	N	N	Y	**L**
Merepeza et al. [48]	Y	N	Y	N	N	N	N	PY	Y	N	N/A	N/A	Y	N	N/A	N	**CL**
Ozóg et al. [49]	Y	Y	Y	N	Y	Y	N	Y	Y	N	N/A	N/A	Y	N	N/A	Y	**CL**
Pourahmadi et al. [50]	Y	Y	Y	N	Y	Y	Y	Y	Y	N	N/A	N/A	Y	N	N/A	Y	**L**
Rubinstein et al. [51]	Y	Y	N	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	**L**
Santos et al. [52]	Y	Y	Y	Y	Y	Y	Y	PY	Y	N	Y	N	N	N	N	Y	**CL**
Sorensen et al. [53]	Y	Y	N	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Y	**L**
Souza de Faria et al. [54]	N	N	N	N	N	N	N	N	Y	N	N/A	N/A	N	N	N/A	Y	**CL**
Wu et al. [55]	Y	Y	Y	N	Y	Y	N	Y	Y	N	Y	N	Y	N	N	Y	**CL**
Yang et al. [57]	Y	Y	Y	N	Y	N	N	PY	Y	N	Y	N	Y	N	N	Y	**CL**
Yeganeh et al. [56]	Y	N	Y	N	Y	Y	N	PY	Y	N	N	N	N	N	N	N	**CL**

CL, Critically Low; L, Low; 1: Did the research questions and inclusion criteria for the review include the components of PICO? 2: Did the report of the review contain an explicit statement that the review methods were established prior to the conduct of the review, and did the report justify any significant deviations from the protocol? 3: Did the review authors explain their selection of the study designs for inclusion in the review? 4: Did the review authors use a comprehensive literature search strategy? 5: Did the review authors perform study selection in duplicate? 6: Did the review authors perform data extraction in duplicate? 7: Did the review authors provide a list of excluded studies and justify the exclusions? 8: Did the review authors describe the included studies in adequate detail? 9: Did the review authors use a satisfactory technique for assessing the risk of bias in individual studies that were included in the review? 10: Did the review authors report on the sources of funding for the studies included in the review? 11: If meta-analysis was performed, did the review authors use appropriate methods for statistical combination of results? 12: If meta-analysis was performed, did the review authors assess the potential impact of risk of bias in individual studies on the results of the meta-analysis or other evidence synthesis? 13: Did the review authors account for risk of bias in individual studies when interpreting/ discussing the results of the review? 14: Did the review authors provide a satisfactory explanation for, and discussion of, any heterogeneity observed in the results of the review? 15: If they performed quantitative synthesis, did the review authors carry out an adequate investigation of publication bias (small study bias) and discuss its likely impact on the results of the review? 16: Did the review authors report any potential sources of conflict of interest, including any funding they received for conducting the review?

Short term

A total of 45 primary studies reported pain in the short term, with 3,953 participants [59–80]. The pooled MD was −10.52 (95% CI −13.71 to −7.33), indicating a significant reduction in pain levels with MT. The average outcome differed significantly from zero (Z = 6.47, $P < 10^{-5}$). According to the Q-test, a high level of heterogeneity was observed ($Q_{(44)} = 714.68$, $P < 10^{-5}$, $Tau^2 = 101.21$, $I^2 = 94\%$), potentially due to variability in the therapeutic applications, measurement methods, and the timing of sample collection.

Medium-term

Ten studies reported medium-term pain outcomes [62,66,69,74,79,80]; one of these included participants not analyzed in the short-term subgroup (204 participants). The total number of participants in this subgroup was 1,560. The MD was −4.93 (95% CI −8.77 to −1.08, Z = 2.51, $P = 0.01$). Significant heterogeneity was revealed according to Cochran's Q ($Q_{(9)} = 46.76$, $P < 10^{-5}$, $Tau^2 = 26.56$, $I^2 = 81\%$), likely attributable to differences in therapeutic approaches and the timing of outcome measurements. Although the effect diminished over time, it remained statistically significant.

Long-term

Ten studies reported long-term pain outcomes, including 1,508 participants. Two of the studies (97 participants) were not part of other subgroups. The pooled MD was −3.58 (95% CI −9.38 to 2.21, Z = 1.21, $P = 0.23$) indicating no statistically significant effect of MT on pain reduction in the long term compared to other interventions. Heterogeneity was considered high ($Q_{(9)} = 82.78$, $P < 10^{-5}$, $Tau^2 = 70.95$, $I^2 = 89\%$).

Disability

A total of 38 studies assessed disability outcomes, including 6,456 participants [59–62,64–66,68–71,74–80]. The main scales used were the RMDQ and ODI (Fig. 5 and 6 in text, Supplementary Material S12 and S13).

Short-term

A total of 36 primary studies reported short-term disability outcomes, including 3,445 participants [59–62,64–66,68–71,74–80]. The pooled SMD was −0.60 (95% CI −0.80 to −0.40, Z = 5.83, P

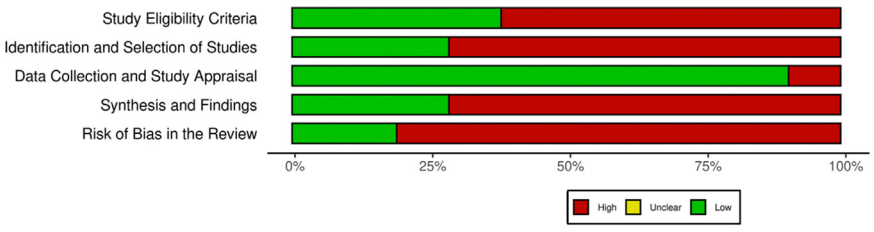

Fig. 2. ROBIS assessment summary plot.

Table 2
GRADE assessment

№ of studies	Study design	Risk of bias	Inconsistency	Certainty assessment Indirectness	Imprecision	Other considerations	№ of patients Manual therapy	other treatments or placebo	Effect Relative (95% CI)	Absolute (95% CI)	Certainty
Pain - Short-term (1-3 m)											
45	randomized trials	very serious[a]	not serious[b]	not serious	not serious	none	2100	1693	-	SMD **0.77 lower** (0.98 lower to 0.56 lower)	⊕⊕◯◯ Low[a,b]
Pain - Medium-term (4-6 m)											
10	randomized trials	very serious[a]	not serious[a,b,e]	not serious	not serious	none	735	667	-	SMD **0.42 lower** (0.78 lower to 0.05 lower)	⊕⊕◯◯ Low[a, a,b,e]
Pain - Long-term (7-12 m)											
10	randomized trials	very serious[a]	serious[c]	not serious	serious[d]	publication bias strongly suspected[e]	776	732	-	SMD **0.29 lower** (0.69 lower to 0.11 higher)	⊕◯◯◯ Very low[a,c,d, e]
Disability - Short-term (1-3 m)											
36	randomized trials	very serious[a]	not serious[b]	not serious	not serious	publication bias strongly suspected[e]	1745	1540	-	SMD **0.61 lower** (0.82 lower to 0.41 lower)	⊕◯◯◯ Very low[a,b,e]
Disability - Medium-term (4-6 m)											
10	randomized trials	very serious[a]	not serious[b]	not serious	not serious	none[e]	735	670	-	SMD **0.34 lower** (0.59 lower to 0.1 lower)	⊕⊕◯◯ Low[a,b,e]
Disability - Long-term (7-12 m)											
9	randomized trials	very serious[a]	serious[c]	not serious	serious[d]	none	746	704	-	SMD **0.97 higher** (0.04 higher to 1.91 higher)	⊕◯◯◯ Very low[a,c,d]

CI, confidence interval; SMD, standardized mean difference
Explanations:
[a] Downgraded if at least one item of the RoB tool is considered "High" risk of bias.
[b] Not downgraded despite high statistical heterogeneity, as all studies show effects in the same direction, with clinically meaningful improvements in pain, and differences in effect sizes are likely due to variability in the therapeutic applications, measurement methods, and the timing of sample collection.
[c] Downgraded once due to considerable heterogeneity with wide variability in effect sizes.
[d] Downgraded once due to wide confidence intervals, crossing the null effect, indicating uncertainty about the presence and magnitude of the intervention effect.
[e] Downgraded due to strong funnel plot asymmetry and statistically significant publication bias (Egger's test $P = 0.0145$)

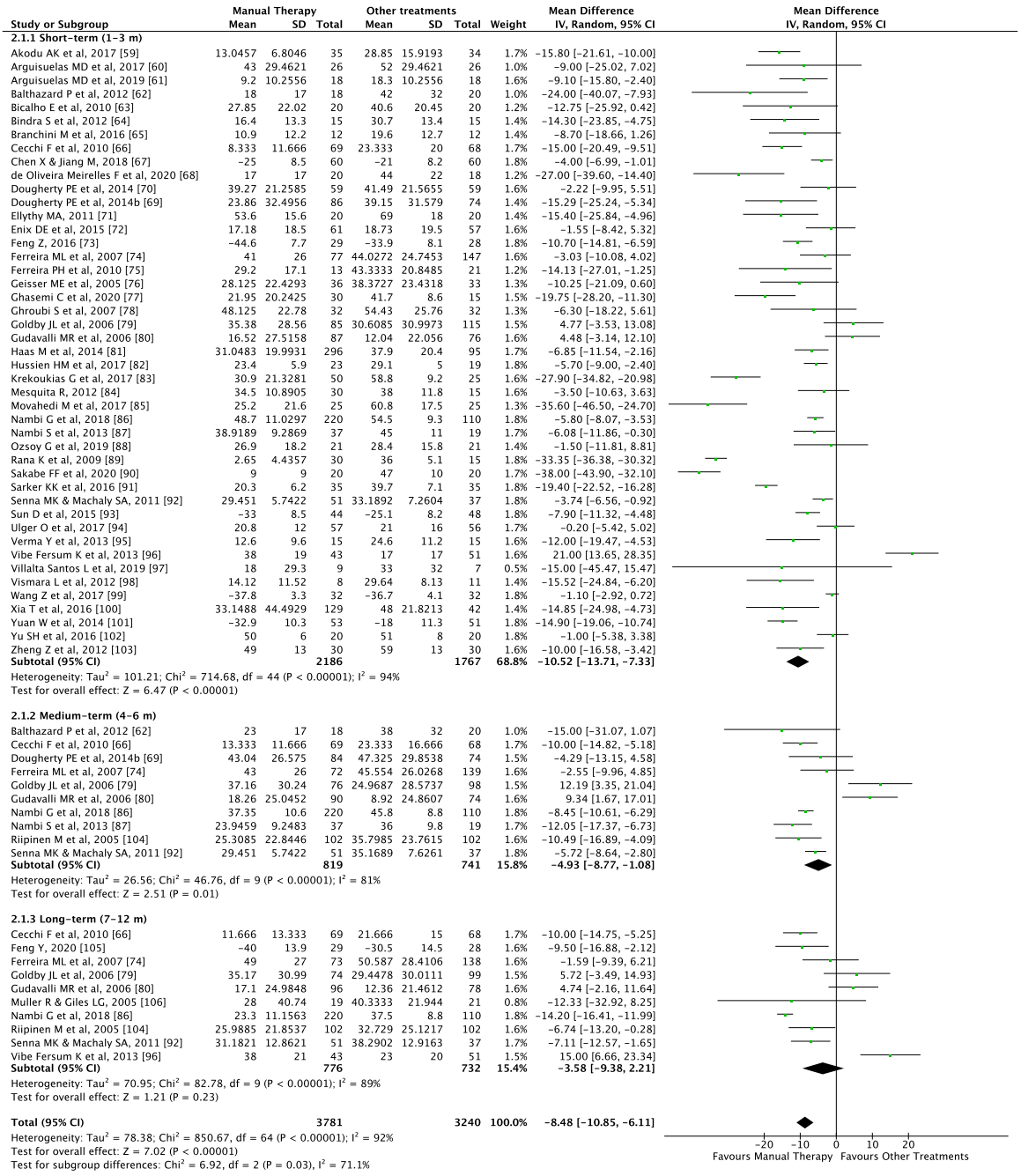

Fig. 3. Forest plot for pain.

$<10^{-5}$), suggesting a moderate improvement in disability. Heterogeneity was considerable ($Q_{(35)} = 254.32$, $P < 10^{-5}$, Tau² = 0.30, I² = 86%).

Medium-term

About 10 studies reported medium-term disability outcomes, encompassing 1,561 participants [62,66,70,74,79,80]. 1 out of the 10 includes 204 participants not analyzed in the short-term subgroup. The pooled SMD was −0.31 (95% CI −0.54 to −0.09, Z = 2.73, $P = 0.006$), indicating a small but statistically significant effect of MT on disability. The heterogeneity was considered high ($Q_{(9)} = 40.04$, $P < 10^{-5}$, Tau² = 0.10, I² = 78%).

Long-term

Nine studies reported long-term disability outcomes, including 1,450 participants, all of whom were also analyzed in other subgroups [66,74,79,80]. The pooled SMD was 0.97 (95% CI 0.04 to 1.91, Z = 2.04, $P = 0.04$), indicating no statistically significant effect of MT on disability in the long term. Heterogeneity was considerable ($Q_{(8)} = 492.34$, $P < 10^{-5}$, Tau² = 1.98, I² = 98%). Overall, the effect on disability was most pronounced in the short term, diminished over time, and disappeared in the long term.

Discussion

The findings of this UR and meta-analysis indicate that MT has a statistically significant effect on reducing pain intensity and disability in individuals with CNLBP in the short term. The pooled MD for pain in the short-term period was −10.52 (95% CI −13.71 to −7.33), indicating a significant reduction in pain levels. Similarly, disability outcomes demonstrated a pooled SMD of −0.60 (95% CI −0.80 to −0.40), suggesting

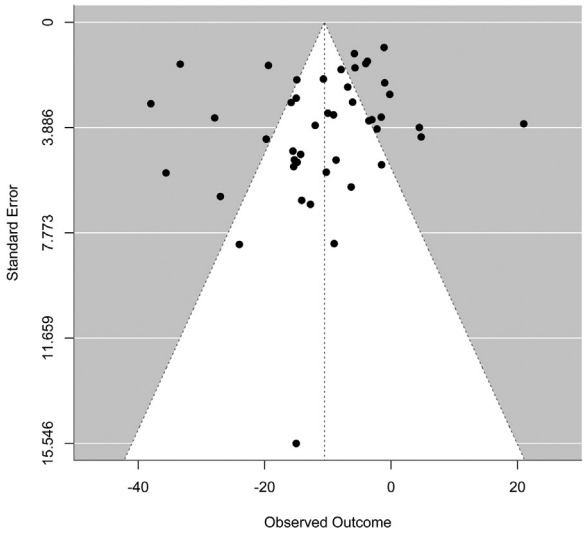

Fig. 4. Funnel plot for pain at short term.

moderate improvement. However, the effect sizes diminished over time, with medium-term results showing a reduced impact (MD −4.93, 95% CI −8.77 to −1.08 for pain and SMD −0.31, 95% CI −0.54 to −0.09 for disability), and long-term follow-ups revealing no statistically significant effect (MD −3.58, 95% CI −9.38 to 2.21 for pain and SMD 0.97, 95% CI 0.04 to 1.91 for disability). These findings highlight that, as with most treatments for CNLBP, the benefits of MT are more pronounced within the first 3 months, gradually diminishing over time. This pattern was observed through subgroup analyses based on follow-up duration (short-, medium-, and long-term), showing progressively smaller effect sizes over time.

Several factors may explain the transient benefits of MT in CNLBP. A potential mechanism involves the neurophysiological modulation of central pain processing, inducing short-term hypoalgesia [27]. Previous studies suggest that MT activates segmental inhibition, mechanoreceptor stimulation, and descending pain modulation pathways, contributing to an immediate but short-lived reduction in pain perception. However, the lack of long-term benefits may stem from the absence of sustained biomechanical or neuroplastic adaptations following MT. Additionally, the heterogeneity in techniques (eg, spinal manipulation, myofascial release, and mobilization) and

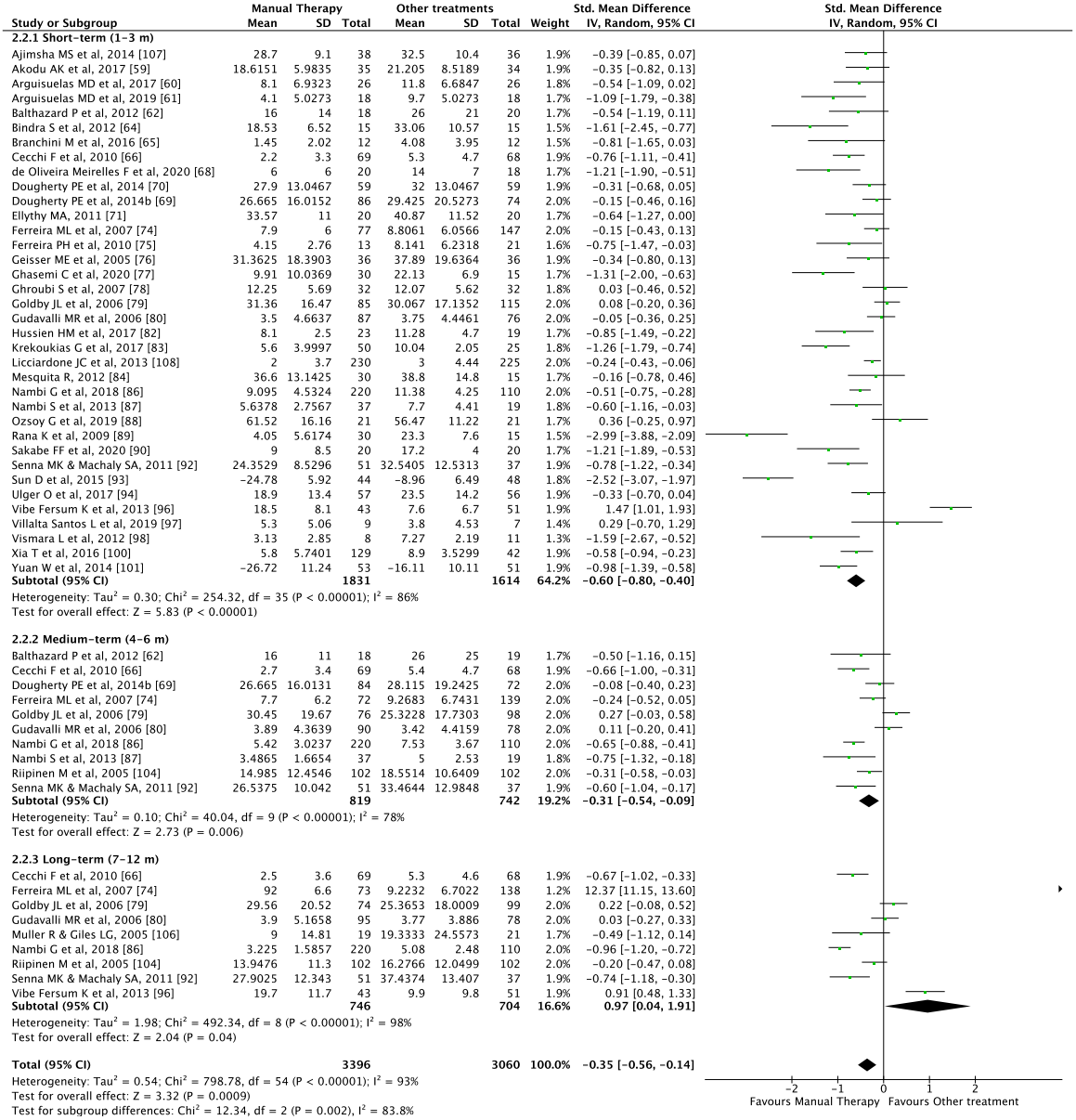

Fig. 5. Forest plot for disability.

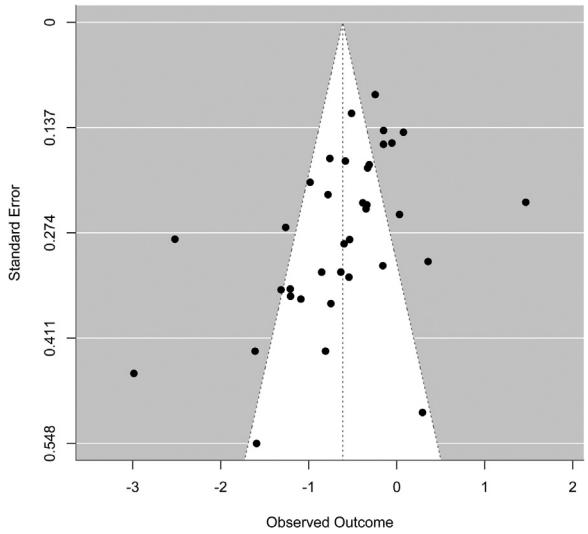

Fig. 6. Funnel plot for disability at short term.

their application across studies likely contribute to variations in outcomes [19,24]. Recent evidence further suggests that the specific procedural application of spinal manipulative therapy may not significantly influence treatment outcomes for spinal pain. A network meta-analysis by Nim et al found that variations in SMT application (ie, targeted versus general approaches) did not lead to meaningful differences in clinical effectiveness. These findings challenge the assumption that precise localization of MT techniques is critical for achieving optimal outcomes, reinforcing the idea that broader neuromodulatory effects, rather than localized biomechanical changes, drive pain relief in CNLBP. Additionally, the review highlights that many spinal manipulative therapy interventions have comparable effects to guideline-recommended treatments, including exercise and personal education, further supporting a multimodal approach to CNLBP management.

The influence of psychosocial factors, such as person expectations and therapist-participant interactions, may also play a role in short-term efficacy, further complicating the interpretation of long-term results . Moreover, touch itself has been identified as a critical component of therapeutic interventions. A SR and multivariate MA by Packheiser et al found that touch-based interventions significantly reduce pain and anxiety, suggesting that the tactile stimulation provided by MT may contribute to immediate symptom relief. This finding aligns with the growing recognition that the context in which MT is delivered, including human contact and perceived care, can influence clinical outcomes beyond the mechanical effects of the intervention itself.

The term CNLBP has been widely used in clinical and research settings; however, its definition and application remain contentious. A discursive analysis by Hebron et al. highlights that CNLBP is often framed through different conceptual models, each carrying distinct assumptions about causality and treatment. The biomedical discourse views CNLBP as a condition with an undetectable but inherently biological origin, fueling a persistent search for an underlying pathoanatomical cause. In contrast, neurocentric models attribute CNLBP to changes in central nervous system (CNS) processing, emphasizing nociplastic mechanisms. Other perspectives, such as the multifactorial and biopsychosocial approaches, acknowledge the interaction between biological, psychological, and social factors but often struggle to integrate these domains into a cohesive clinical framework. Hebron et al. argue that such varied discourses both enable and constrain research and treatment approaches, as they shape clinical decision-making and participant experiences. Importantly, the NSLBP Otherwise Discourse (nonspecific low back pain) by these authors challenges traditional classifications by shifting the focus from individual pathology to societal and systemic influences on pain. This evolving debate underscores the need for critical reflection on how CNLBP is defined and managed, as rigid classifications may inadvertently overlook the complexity of chronic pain and its broader implications for healthcare and person outcomes.

In this regard, Psychoneuroimmunology (PNI) provides a crucial framework for understanding the multifactorial nature of CNLBP. PNI research highlights the bidirectional interactions between the brain, immune system, and endocrine pathways, emphasizing the role of psychosocial stressors, lifestyle behaviors, and systemic inflammation in chronic pain conditions. Modern contextual risk factors such as chronic stress, sedentary lifestyle, poor nutrition, social isolation, and environmental toxins trigger low-grade inflammation (LGI), primarily mediated by pro-inflammatory cytokines as interleukin 6 (IL-6) and tumor necrosis factor-α (TNF-α), and neuroendocrine imbalances. As outlined by Pruimboom et al. , the immune-brain connectome is constantly shaped by environmental inputs, with psychological stressors activating the Hypothalamic-Pituitary-Adrenal (HPA) axis and sympathetic nervous system (SNS), leading to neuroinflammatory responses and altered pain processing. In the case of CNLBP, chronic stress and emotional distress may sensitize nociceptive pathways, contributing to central sensitization and the persistence of pain despite the absence of structural pathology.

Furthermore, lifestyle factors such as poor dietary habits (high-glucose diet, micronutrient deficiencies), lack of exercise, and disrupted sleep contribute to gut dysbiosis and systemic endotoxemia, which in turn exacerbate neuroimmune dysregulation. Evidence suggests that holistic interventions targeting physical activity, nutrition, stress management, and social support can modulate inflammatory pathways, promote neuroplasticity, and restore homeostasis, offering a PNI-based therapeutic perspective for CNLBP. This integrative approach moves beyond traditional mechanistic models, embracing the contextual and adaptive nature of pain, thereby opening new avenues for more personalized and effective treatment strategies.

Recent clinical evidence supports the use of lifestyle-based interventions in managing CNLBP. The Healthy Lifestyle Program (HeLP) trial by Mudd et al demonstrated that integrating lifestyle modifications, including physical activity, dietary improvements, and smoking cessation, alongside guideline-based physiotherapy care, led to small but significant improvements in disability, weight reduction, and quality of life in individuals with CNLBP. These findings reinforce the PNI hypothesis that chronic pain is not merely a biomechanical issue, but a condition modulated by systemic inflammation, stress physiology, and lifestyle determinants. Neuroimmune interactions underlying pain chronification suggest that LGI, metabolic dysfunction, and altered HPA axis activity contribute to the persistence of CNLBP. The HeLP study's results align with PNI principles, demonstrating that targeting modifiable risk factors, such as sedentarism, poor nutrition, and psychosocial stressors, can positively influence immune and neuroendocrine responses, thereby attenuating pain perception and improving functional outcomes. These findings advocate for a multidisciplinary, integrative treatment model, where lifestyle medicine, neuroimmunology, and MT converge to optimize long-term recovery in CNLBP participants.

Clinical implications

The findings of this UR highlight the potential utility of MT as part of a short-term management strategy for CNLBP. Clinicians may consider applying MT to achieve immediate symptom relief, particularly in participants with high baseline pain or functional limitation that hinders engagement with active therapies such as exercise or education. The short-term reduction in pain and disability observed across multiple MT modalities supports its use as a facilitating tool in the early stages of treatment. Moreover, short-term improvements are highly valued by people and can enhance treatment satisfaction, functioning, and adherence.

Given the limited long-term efficacy of most treatments for CNLBP, including MT, clinicians are encouraged to apply a person-centered, multimodal approach in line with current guidelines. MT can provide

meaningful short-term benefits in pain relief and function and should be considered as one of several complementary strategies—alongside patient education, physical activity, and psychosocial support—tailored to individual needs and expectations.

Furthermore, touch-based interventions such as MT may play a valuable role in enhancing participants' satisfaction, therapeutic adherence, and perceived support, elements that are particularly relevant in persistent pain conditions. In this sense, MT may serve not only as a biomechanical or neurophysiological stimulus but also as a relational and contextual therapeutic resource. These aspects should be considered when integrating MT into clinical practice to optimize person-centered care and long-term functional outcomes.

Strengths and weaknesses

One of the major strengths of this UR is its rigorous methodological approach, which included a comprehensive evaluation of SRs using AMSTAR-2 and ROBIS tools to assess quality and RoB. The overlap analysis revealed a low degree of redundancy among included reviews (CCA = 2%), minimizing the risk of duplicated evidence. Additionally, using GRADE criteria provided a transparent assessment of the certainty of the evidence. However, several limitations must be acknowledged. First, the high heterogeneity (I^2 >80% for most outcomes) limits the generalizability of the results. Second, the inclusion of diverse MT modalities with varying treatment protocols introduces potential confounders, making it difficult to identify the most effective approach. It is important to acknowledge that MT encompasses a wide range of techniques, including spinal manipulation, mobilization, and soft-tissue approaches, each of which may differ in terms of biomechanical application, duration, and intensity. While some research indicates that variations in the application of SMT—such as targeted versus general approaches—do not result in meaningful differences in clinical effectiveness, recent studies suggest that specific differences in technique parameters may influence participant outcomes. This apparent inconsistency in the literature reflects the complex and multifactorial nature of MT and underscores the need to interpret pooled effect sizes with caution, particularly considering the inherent heterogeneity across interventions and study designs included in meta-analyses.

Lastly, publication bias remains a concern, as the potential overrepresentation of positive findings may have influenced the pooled effect sizes. Specifically, the Egger test detected statistically significant publication bias in short-term disability outcomes ($P = 0.013$) and long-term pain outcomes ($P = 0.014$), suggesting that these results should be interpreted with caution. Although medium-term pain ($P = 0.284$) and disability ($P = 0.657$) outcomes did not show strong evidence of bias, the presence of asymmetry in funnel plots indicates potential reporting distortions. The observed bias may be partially attributed to the selective publication of studies with positive outcomes, as well as variations in methodological quality across included MAs.

Prospective

Future research should address these limitations by conducting high-quality, well-powered randomized controlled trials with standardized MT protocols and long-term follow-up periods. Comparative studies evaluating the efficacy of MT against other conservative interventions, such as exercise therapy or cognitive-behavioral approaches, are also necessary. Additionally, investigating person-specific factors, such as baseline pain chronicity, psychosocial determinants, and biomechanical profiles, may help identify subgroups that are more likely to benefit from MT. Lastly, emerging evidence on neuroplastic changes following MT should be further explored to determine whether sustained adaptations can be achieved through adjunctive or integrative therapeutic strategies.

Conclusion

This UR and meta-analysis support the use of MT as a clinically valuable option for reducing pain and disability in individuals with CNLBP, particularly in the short term. As with most treatments for CNLBP, the benefits of MT tend to decrease over time, highlighting the need for further investigation into strategies that prolong its clinical efficacy. Current evidence supports the inclusion of MT within a person-centered, multimodal management approach tailored to individual needs and preferences. However, methodological limitations and a lack of long-term follow-up in many of the included studies constrain the strength of the conclusions. Future research should emphasize methodological rigor and explore the durability of treatment effects to further clarify the role of MT in CNLBP management.

Author contribution

JGC and OCV conceptualized, designed, and performed the literature searches, data extraction and assessment of quality, RoB, and certainty of evidence. JGC, OCV, and SNL did the initial write-up and revision. OCV performed the meta-analysis. SNL and LBP reviewed the manuscript and Supplementary Material and provided a critical review. All authors read the manuscript and approved its definitive version.

Data Sharing

All data relevant to the study are included in the article or are available as supplemental files.

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Declaration of Generative AI and AI-assisted technologies in the writing process

None.

Fig. S7: Graphical representation of overlapping.
Fig. S9.A: RoB assessment of the primary studies.
Fig. S9.B: RoB assessment of the primary studies summary plot.
Fig. S10: Funnel plot for pain at medium-term.
Fig. S11: Funnel plot for pain at long term.
Fig. S12: Funnel plot for disability at medium-term.
Fig. S13: Funnel plot for disability at long term.

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S1. Search Strategy.
S2. Excluded systematic reviews and reasons.
S3. Characteristics of the systematic reviews included in the review.
S4. Detailed interventions of the studies included in the review.
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S5.A: Summary of ROBIS assessment.
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S6. Overlapping of systematics reviews (GROOVE tool).
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S8. Primary studies detailed classification.
S9. Risk of Bias (RoB) assessment of the primary studies.
S9.A: RoB assessment of the primary studies.
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S15. Supplemental references.

Declaration of competing interest

None.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.rehab.2025.102049.

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