Effectiveness of manual joint mobilization techniques in the treatment of Non-Specific Neck Pain. Systematic review with meta-analysis and meta-regression of randomized controlled trials.

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EDITOR's Comments:

06-Dec-2024

Re: Manuscript JOS-06-24-12836-LR.R1: Effectiveness of manual joint mobilization techniques in the treatment of Non-Specific Neck Pain. Systematic review with meta-analysis and meta-regression of randomized controlled trials.

Dear Dr Rossettini:

Thank you for submitting your work to JOSPT. We think it will interest our readers. The review team has read your manuscript and provided constructive feedback. You will find their comments (if any) at the end of this email. The review team has suggested ways to make the manuscript even more helpful to our readers. We invite you to incorporate these suggestions (and any other minor edits) to your manuscript. As you revise your manuscript, please mark, highlight, underline, or bold, changes to the text, to facilitate the review of the revised manuscript. We prefer authors to resubmit a file that uses the tracking feature of Microsoft Word, which helps the review team see exactly what you have changed. Deleted text can simply be removed – do not leave strike-through text in the revised manuscript.

Please ensure you unblind any details that were blinded in your original manuscript, including author and affiliation details. Any details redacted for the purposes of blinding should be replaced with the relevant information. Making those corrections at this time will help the production stage of the manuscript.

Please ensure you include a statement about author contributions, data sharing, and patient involvement in the research. You will find a detailed guide on how to formulate the statements in the instructions for authors (page 1 and 2). We ask all authors to provide these statements, irrespective of manuscript type.

Your cover letter can simply state the specific changes made in response to specific comments of the review team, and any other changes you have made to the manuscript. Submission of your revised manuscript should be done through our online submission and

review system that you can access at the following web address: http://mc.manuscriptcentral.com/jospt.

When re-submitting your revised manuscript, please follow the instructions on the Author Centre dashboard page of the site. We ask you to submit (i) a clean version of your manuscript (i.e. no changes tracked) and (ii) a marked version with the changes/edits highlighted using the Word track changes function.

As the revisions are minor, we would appreciate your resubmission of the revised manuscript within 4 weeks, if possible. Please do not hesitate to contact me if you have any questions.

Thank you for your continued effort on this manuscript. I am looking forward to seeing your revised manuscript soon.

Sincerely,

Clare L. Ardern, PT, PhD

Editor-in-Chief

Dear Editor,

We would like to thank the JOSPT editor and reviewers for their interest in our manuscript number JOS-06-24-12836-LR.

We have carefully considered their useful comments, which have greatly improved the quality of the manuscript, taking into consideration the criticism and feedback of experts in the field. We hope to address all these concerns.

Please find below our point-by-point responses to the peer reviewers' comments; each change has been highlighted in green in the body of the manuscript. Accordingly, we have revised and modified only the manuscript.

Thank you again for allowing us to revise the manuscript thoroughly for full consideration.

Kindly regards.

ASSOCIATE EDITOR Comments:

Associate Editor: Martinez-Calderon, Javier

Comments to the Author:

(There are no comments.)

Dear Associate Editor,

Thanks for your interest in our manuscript number JOS-06-24-12836-LR. We are happy that you liked the final version of the manuscript. We hope to see it published soon.

Reviewer(s)' Comments to Author:

REVIEWER: 1

Comments to the Author

The revisions are appropriate. Congratulations on the excellent work. Best regards.

Dear Reviewer 1,

Thanks for your interest in our manuscript number JOS-06-24-12836-LR. We are happy that you liked the final version of the manuscript. We hope to see it published soon.

REVIEWER: 2

Comments to the Author

Thank you for undertaking this review. You have made a lot of changes based on reviewer feedback and it has improved the quality of the review. Some small mistakes - change blindness to blinding. The findings are "in favour of". Find some suggestions in text (see attached PDF)

Dear Reviewer 2,

Thanks for your interest in our manuscript number JOS-06-24-12836-LR. We are happy that you liked the final version of the manuscript. We have followed all your suggestions. Accordingly, we have revised and modified only the manuscript. We hope to see the paper published soon.

Title:

Effectiveness of manual joint mobilization techniques in the treatment of Non-Specific Neck Pain. Systematic review with meta-analysis of randomized controlled trials.

Authors

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Public protocol registration

The protocol was prospectively registered on the International Prospective Register of Systematic Reviews database (PROSPERO) with n° CRD42023391701.

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LFM and GR teach manual therapy at postgraduate university masters. GR leads education programs on placebo, nocebo effects and contextual factors in healthcare to under- and post-graduate students along with private CPD courses. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. All co-authors have seen and agreed with the content of the manuscript and there is no financial interest to report. We certify that the submission is original work and is not under review at any other publication.

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None.

Authors' contribution:

AB: was responsible for systematic research, article selection, critical appraisal and ROB analysis, and article writing. SB was involved in methodological management, article writing and checking, and statistical analysis. GB was engaged in critical appraisal, ROB analysis, and article checking. GR was involved in the article writing and checking. LFM was responsible for the original idea, articles selection, statistical analysis, article writing and checking. All authors contributed to the interpretation of the data for the work and revising it critically for important intellectual content. All the authors finally approved the manuscript. All authors have read and agreed to the published version of the manuscript.

Patient involvement statement:

Not applicable.

Data sharing statement:

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

Title

Effectiveness of manual joint mobilization techniques in the treatment of Non-Specific Neck Pain. Systematic review with meta-analysis of randomized controlled trials.

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None.

Financial disclosures and conflict of interest

I affirm that I have no financial affiliation (including research funding) or involvement with any commercial organization that has a direct financial interest in any matter included in this manuscript, except as disclosed and cited in the manuscript. Any other conflict of interest (i.e., personal associations or involvement as a director, officer, or expert witness) is also disclosed and cited in the manuscript.

ABSTRACT

Objective: To investigate the effects of cervical joint mobilization techniques (JMTs) on pain and disability in adults with non-specific neck pain (NSNP).

Design: Intervention systematic review with meta-analysis and meta-regression of randomized controlled trials (RCTs).

Literature Search: We searched MEDLINE, Cochrane CENTRAL, EMBASE, CINAHL, PEDro and Web of Science databases, including references from other reviews or clinical practice guidelines up to October 16, 2024.

Study Selection Criteria: Eligible RCTs evaluated JMTs compared to routine physiotherapy, minimally active interventions or no treatment. The primary outcome was pain; secondary outcomes were disability, Global Perceived Effect (GPE), quality of life, psychosocial status and adverse events.

Data Synthesis: Meta-analyses and meta-regression were conducted for pain, disability and GPE. The risk of bias was assessed with Cochrane RoB 2.0 Tool; the certainty of the evidence was assessed with the Grading of Recommendations, Assessment, Development, and Evaluations (GRADE) approach. We used The Template for the Intervention Description and Replication (TIDieR) checklist to evaluate the quality of reporting of interventions delivered.

Results: Results from 16 RCTs were pooled (n = 1157 participants), reporting non-clinically positive results on pain reduction (Mean Difference (MD): -0.86 (95% CI: [-1.35; -0.36]), disability (MD: -2.45 [-4.32; -0.59]) and GPE (Standardized Mean Difference: 0.11 ([-0.15; 0.37]) and high heterogeneity. The meta-regressions did not identify any covariates associated with the treatment effects. Minor side effects (increased neck pain and headache) were reported.

Conclusion: There was very low certainty evidence supporting the efficacy of JTMs for reducing pain and improving disability in people with NSNP.

Key words: Non-specific neck pain, Cervical joint mobilizations, Pain intensity, Disability.

INTRODUCTION

Non-Specific Neck Pain (NSNP) is a widespread disorder with a global prevalence of 203 million cases. Assuming the estimated increase of up to 33% by 2050, 269 million people around the world will experience NSNP[15,28,77]. The neck pain can interfere with activities of daily living, resulting in decreased quality of life (QoL) and increased disability[19,41,48]. In 2019, the Global Burden of Disease study (GBD) found neck pain ranked 11th out of the 369 conditions in terms of people living Years Lived with Disability (YLDs), which increased by 76.2%, from 11.5 million in 1990 to 20.2 million in 2020[28]. It accounts for approximately 1 in every 4 outpatient physiotherapy visits,[41] and has a relapse rate of up to 85%[39]. NSNP is a serious public health problem that must be addressed as it drastically affects public healthcare spending directly (e.g. visits and treatments) and indirectly (e.g. sick leave and related loss of productivity)[19,48].

According to clinical practice guidelines (CGP)[5,14,33], treatment for NSNP should focus on a multimodal intervention including education on self-management strategies, exercise and manual therapy[19,34,35,41,60,83]. Manual therapy techniques include High-Velocity Low-Amplitude Techniques (HVLATs) and Joint Mobilization Techniques (JMTs)[16]. Systematic reviews of randomized controlled trials (RCTs) have analyzed the role of manual therapy in managing people with NSNP[40,85]. Despite promising evidence, the lack of a pragmatic approach and incomplete reporting of treatments limit their external validity and replicability by clinicians and researchers[18,55,67]. A recent systematic review studied the effectiveness of HVLATs and mobilizations together in treating people with NSNP[60]. However, HVLATs are more challenging to perform and might be contraindicated under some circumstances[23]. Conversely, mobilizations are simpler to perform, involving gentle passive movements within the joint physiological range of motion[3]. Considering the difference in execution and type of techniques, we aimed to investigate the effectiveness of cervical JMTs compared with other

interventions in reducing pain in individuals with acute, subacute or chronic NSNP. Secondly, we aimed to analyze the effects of JMTs on disability, QoL, cervical range of motion (ROM), Global Perceived Effect (GPE), psychosocial status and adverse events.

METHODS

This systematic review with meta-analysis and meta-regression was developed, implemented and conducted according to the "Cochrane Handbook for Systematic Reviews"[44] and reported following the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) Statement[65]. The protocol was prospectively registered on the International Prospective Register of Systematic Reviews database (PROSPERO, n° CRD42023391701). Different from what we reported in the protocol, we considered RCTs published in all languages, and we conducted a meta-regression of the results to understand the effect of different covariates on the results.

Eligibility Criteria

Eligibility criteria were defined according to the Population, Intervention, Comparators, Outcome Measures and Study Design (PICOS) model[56].

- *Population:* we included adults (≥ 18 years old) with acute (< 6 weeks), subacute (6-12 weeks) or chronic (> 12 weeks) NSNP. People with comorbidities, major specific pathologies (e.g. fracture or dislocation, neoplasm or whiplash-associated disorder) or neurological conditions (e.g. cervical radiculopathy or myelopathy) were excluded.
- *Interventions:* we considered different JMTs for the cervical spine: Posterior-Anterior glide (PA), Mulligan techniques (Natural Apophyseal Glide or NAG, Sustained Natural Apophyseal Glide or SNAG), Maitland and Kaltenborn techniques. Studies that used a multimodal approach were considered only if they included at least one JMT. Pharmacological or medical intervention (e.g. injection) were excluded.
- *Comparators:* we considered other physiotherapy interventions such as exercise,

HVLATs, minimally active interventions (wait list, sham therapy or placebo treatment) or no treatment were considered.

- *Outcome measures:* the primary outcome was pain intensity measured with 0-100 or 0-10 Visual Analogue Scale (VAS), 0-10 Numeric Pain Rating Scale (NPRS) or similar unidimensional scales. After data extraction, pain scales were normalized to 0-10. As secondary outcomes we considered: disability and QoL measured by at least one of the scales chosen from Neck Disability Index (NDI), Neck Pain and Disability scale (NPDS), Neck Bournemouth Questionnaire (NBQ), 36-items Short Form Health Survey (SF-36) or 12-items Short Form Health Survey (SF-12), Nottingham Health Profile (NHP), Health Status Questionnaire, Sickness Impact Profile and McGill Pain Score; active or passive cervical ROM; GPE and patient satisfaction; psychosocial status (e.g. depression, kinesiophobia) and adverse events.
- *Study design:* we included only randomized controlled trials (RCTs) with no limitation on publication date or language. Protocols of unpublished studies were excluded.

Search Strategy and Sources of Information

In adherence to the recommendations outlined in the "Cochrane Handbook for Systematic Reviews for Interventions"[44], an advanced search strategy was performed across MEDLINE (accessed via PubMed), Cochrane Central Register of Controlled Trials (CENTRAL), and EMBASE (accessed through Scopus). Additionally, supplementary databases based on the specific research question were consulted: Cumulative Index to Nursing and Allied Health Literature (CINAHL; accessible via EBSCOhost), Physiotherapy Evidence Database (PEDro), and Web of Science. Finally, we searched the reference lists of other systematic reviews[8,13,19,29,31,32,34,35,41,52,54,59,73,74,81-83,86] and CPGs[5,9,10,14,17,33,50,62] (**SUPPLEMENTARY APPENDIX A**). Last search was conducted on October 16, 2024.

Study Selection and Data Collection Process

After excluding duplicates and inappropriate records based on title and abstract, two independent authors (AB, LFM) assessed the suitability of full-text articles based on eligibility criteria. The selection process was performed using the Rayyan platform (http://rayyan.qcri.org) to guarantee reviewers' blinding during the entire screening process[64]. Two blinded reviewers (AB, LFM) extracted data from the included RCTs. Data were organized in a custom table, including first author, year of publication, study design, duration and follow-up period, sample size and characteristics, diagnosis, intervention, control and outcome measures. The outcomes' results were separately collected in a table containing mean values, standard deviations and follow-up period. Any disagreement was resolved by discussion and consensus.

Assessment of Risk of Bias in Individual Studies and Certainty of the Evidence

Two independent authors (AB, GB) judged the Risk of Bias (RoB) using the revised Cochrane RoB tool 2.0[78]. The tool assesses each of the following domains: selection bias (randomization process and concealment of assignments), performance bias (blinding of participants and personnel), attrition bias (missing or incomplete data), detection bias (blinding of evaluators), outcome reporting bias (selection of reported outcomes)[42–44]. Any disagreement was resolved by consensus. The certainty of the evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach[37]. Two reviewers (LFM, AB) independently assessed the certainty of the evidence through the GRADEpro (GDT) software[75]. Two reviewers (AB, GB) assessed the trials with the TIDieR (Template for Intervention Description and Replication) checklist to evaluate the quality of reporting of the interventions in included RCTs[45].

Data Analysis and Synthesis

Treatment measure was evaluated by comparing the mean and the Standard Deviation (SD) between the groups at the end of the treatment period, as suggested by Higgins et al.[44]. The

Mean Difference (MD) was used in case of homogeneous scales; the Standardized Mean Difference (SMD) was used in case of non-homogeneous scales[44]. In trials with multiple comparisons, participants of the intervention or control groups were equally split[27,46,49,61,70,79,80] to avoid a double-counting error, as suggested by Higgins et al.[44]. When possible, the meta-analysis was conducted for each outcome of interest.

The primary analyses compared the effect of mobilizations with different comparators. The effect was expressed through 95% confidence intervals (95% CI). Statistical heterogeneity of trials was evaluated using the I^2-test and the chi^2-test[5]. An I^2 value less than 25%, 50% and 75%, respectively, indicated a low, moderate and high heterogeneity[85]. In meta-analyses including at least three trials, a sensitivity analysis (SA) was conducted to examine the influence of trials with high-RoB or particular comparators (e.g. HVLATs) on results[43].

Meta-analyses were performed using RevMan 5.4 software[69]. A descriptive synthesis was provided if meta-analysis was not possible (e.g. missing or incomplete data). Sub-group analyses were conducted based on pain duration (less or more than three months) and specific mobilizations, classified as active-assisted (SNAG) or passive techniques (NAG, PA glide, Maitland or Kaltenborn). Trials that did not specify symptom duration or included both acute and chronic NSNP were excluded from the sub-groups analysis[21,63,70]. The results of the individual trials were combined with a random-effects model[56].

Random-effect meta-regression analyses were performed to investigate whether covariates (year of publication, sample size, mean age, active/passive treatment, acute/chronic NSNP and risk of bias) accounted for the treatment effect. We calculated regression coefficients (β) as the estimated increase or decrease in the effect size units of the covariates on particular outcomes and its 95% CI. The meta-regression analyses were only possible for the outcomes 'pain' and 'disability' as they were the only outcomes with greater than ten trials[44]. Meta regressions were performed with Stata 18 (StataCorp LLC, College, Texas) with the function

'meta regress'.

RESULTS

The search identified 1342 records. After removing duplicates, 1034 records were screened for title and abstract; 995 were excluded. Of the remaining 39 studies screened for full-text, 23 were excluded, while 16 fulfilled the inclusion criteria. Of these, 14 trials were included in the quantitative synthesis[21,26,27,30,46,49,53,61,63,70,76,79,80,84] and 2 in the qualitative synthesis: Buyukturan et al.[11] did not report SD values, and Desai et al.[20] did not report individual measurements related to pain and disability. Duymaz et al.[21] and Ghulam et al.[30] did not report whether participants had acute or chronic NSNP; Rezkallah et al.[70] and Ozlu et al.[63] did not differentiate the population's data into people with acute and chronic NSNP. Two authors (AB, GR) requested the missing data from the corresponding authors of the trials, obtaining one reply[30]. The study selection process is reported in **FIGURE 1**. A list of excluded studies with the reasons for their exclusion is available in **SUPPLEMENTARY APPENDIX B**.

Characteristics of Included Trials

The characteristics of the included trials were summarized in **TABLE 1.**

Population: The pooled population consisted of 1157 people with a mean age of 38.44 ± 7.34 years. Individuals had chronic[11,20,26,46,49,61,63,70,76,79,80,84] or acute/subacute[27,30,53,63,70] NSNP. One trial did not specify the duration of symptoms[21]. It was not possible to quantify the percentages of individuals divided by sex or duration of NSNP because, in some trials, those pieces of information were not specified[11,20,30,49,63,76,79].

Diagnosis: In one case, an orthopedic surgeon made the diagnosis[61], while in the remaining trials, the participants were evaluated by physicians specialized in physical medicine and rehabilitation, general medicine, or experienced physiotherapists.

Treatment Techniques and Sessions: The treatments proposed in the trials included different JMTs: PA glide[26,30,46,80,84], Mulligan[11,20,21,27,46,61,63,70,76,79,80], Kaltenborn[49,] and Maitland

techniques[27]. Leaver et al.[53] used one or more passive JMTs of the therapist's choice. Eleven trials[11,21,26,27,30,61,63,70,76,79,80] combined the JMTs with other physiotherapy treatments (e.g. TE, MMTs, patient education, physical therapies).

The number of treatments ranged from 4 sessions in 2 weeks[46,53] to a maximum of 24 sessions in 8 weeks[61,84]. The follow-up period ranged from a minimum of 1 week (after the beginning of treatment)[30] to a maximum of 12 weeks (after the end of treatment)[27,46].

Outcome measures: all trials measured pain intensity by 0-10 VAS[11,21,27,30,46,49,63,70,76,79], 0-100 VAS[21,84] or 0-10 NPRS[20,53,61,80]. Fifteen trials measured the disability level by 0-35 or 0-50 NDI[11,20,21,26,27,30,46,53,61,70,76,79,80,84] or by NPDS[63]. Five trials measured QoL (SF-36, SF-12 or NHP)[11,21,53,63,79], two trials measured depression (BDI)[11,21], two trials measured GPE[46,53], one trial measured kinesiophobia[11], eleven trials measured A-CROM[11,20,26,27,30,46,61,63,70,76,79] and one trial measured P-CROM[49]. Two trials[21,80] did not specify the type of CROM measured.

Risk of Bias Assessment

Two trials[11,46] had an overall low RoB. Five trials had an uncertain RoB due to the absence of a study protocol (outcome reporting bias)[26,70,84], the use of an inadequate randomization method (selection bias)[76] or the lack of participants and personnel's blindness (performance bias)[79,84]. Nine trials were at high RoB due to: inadequate randomization method and/or concealment of the assignment sequence[20,21,49,53,61], lack of participants' and personnel's blindness or absence of the intention-to-treat analysis (ITT)[20,21,27,49,61], lack of dropouts' data[49,63,80] or outcome examiners' blindness[20,30,46,63,80], inappropriate outcome measurement methods[21,61] or absence of a study protocol[20,21,27,49,61]. The RoB analysis for each trial is described in **FIGURE 2** and **SUPPLEMENTARY APPENDIX C.** Funnel plot analysis excluded the presence of publication bias within the included trials for the primary outcome (**SUPPLEMENTARY APPENDIX D**). TIDieR analysis revealed that seven

RCTs[20,21,26,61,63,70,79] did not report sufficient information about the intervention delivered (**SUPPLEMENTARY APPENDIX E**).

Effects of Interventions

Synthesis of Findings and GRADE tables were reported in **TABLE 2.** Raw data extracted from each trial were reported in **SUPPLEMENTARY APPENDIX F.** As per the meta-regression analyses, none of the explored covariates had any effect on pain and disability outcomes (**SUPPLEMENTARY APPENDIX G**).

Effects on Pain Intensity

The primary meta-analysis included 14 RCTs (961 participants)[21,26,27,30,46,49,53,61,63,70,76,79,80,84] and 21 comparisons (**FIGURE 3**). Eight trials had a high RoB[21,27,30,49,53,61,63,80], five trials had an uncertain RoB[26,70,76,79,84] and one trial was at a low RoB[46]. The analysis showed an MD = -0.86 (95% CI: [-1.35; -0.36]; I^2 = 92%) in favour of mobilizations. The sensitivity analysis removing the trials at high RoB reported an MD = -0.69 (95% CI: [-1.44; -0.05]; I^2 = 91%) in favour of mobilizations. The sensitivity analysis removing the trials at high RoB and the HVLATs as comparator reported an MD = -0.89 (95% CI: [-1.75; -0.02]; I^2 = 93%) in favour of mobilizations. The certainty of the evidence for all analyses was very low.

Sub-group analyses included 11 RCTs (811 participants)[26,27,30,46,49,53,61,76,79,80,84] and 17 comparisons, stratified by pain duration and mobilization techniques (**FIGURE 3**, continued). For pain < 3 months, the MD was -0.10 (95% CI: [-0.97, 0.77]) for active-assisted mobilizations and -0.30 (95% CI: [-1.45, 0.86]; I^2 = 87%) for passive mobilizations. For pain > 3 months, the MD was -0.41 (95% CI: [-1.24, 0.42]; I^2 = 95%); for active-assisted mobilizations, the MD was -0.86 (95% CI: [-2.12, 0.40]; I^2 = 89%); for passive mobilizations the MD was -0.24 (95% CI: [-1.13, 0.65]; I^2 = 84%) for mixed techniques. The overall effect showed a MD = -0.49 (95% CI: [-0.96, -0.01]; I^2 = 91%) in favour of mobilizations. The certainty of the evidence for all analyses was very low.

Effects on Disability (0-50 NDI)

The primary meta-analysis included 12 RCTs (897 participants)[21,26,27,30,46,53,61,70,76,79,80,84] and 18 comparisons (**FIGURE 4**). Six trials had a high RoB[21,27,30,53,61,80], five trials had uncertain RoB[26,70,76,79,84] and one trial had a low RoB[46]. The analysis showed an MD of -2.45 (95% CI: [-4.32; -0.59]; I^2 = 97%) in favour of mobilizations (very low certainty). The sensitivity analysis removing the trials at high RoB reported a MD: -3.22 (95% CI: [-6.25; -0.18]; I^2 =93%) in favour of mobilizations. The sensitivity analysis removing the trials at high RoB and the HVLATs as comparator reported an MD = -4.57 (95% CI: [-7.80; -1.34]; I^2 = 94%) in favour of mobilizations. The certainty of the evidence for sensitivity analysis was low.

The sub-group analyses included 10 RCTs (787 participants)[26,27,30,46,53,61,76,79,80,84] and 15 comparisons, stratified by pain duration and mobilization techniques (**FIGURE 4**, continued). For pain that lasted < 3 months, the MD of disability was 4.70 (95% CI: [-0.74, 10.14]) for active-assisted mobilizations, and 0.54 (95% CI: [-2.41,3.49]; I^2 = 82%) for passive mobilizations. For pain > 3 months, the MD of disability was -2.23 (95% CI: [-5.70, 1.24]; I^2 = 98%) for active-assisted mobilizations, -5.81 (95% CI: [-13.56, 1.94]; I^2 = 86%) for passive mobilizations and -0.63 (95% CI: [-2.59, 1.33]; I^2 = 79%) for mixed techniques. Overall effect showed an MD = -1.55 (95% CI: [-3.63, 0.54]; I^2 = 97%) in favour of mobilizations. The certainty of the evidence for all analyses was very low.

Effects on Global Perceived Effect

Primary meta-analysis included 2 RCTs (238 participants)[46,53] and 3 comparisons (**FIGURE 5**). Pérez et al.[46] used the GROC scale (-7 to +7), and Leaver et al.[53] used a self-generated scale from -5 to +5. For pain < 3 months, the SMD was 0.18 (95% CI: [-0.12, 0.47]) (very low certainty). For pain >3 months, the MD was -0.10 (95% CI: [-0.65, 0.44]; I^2 = 0%; low certainty). The overall effect was MD = 0.11 (95% CI: [-0.15, 0.37]; I^2 = 0%; low certainty).

Manual Mobilizations vs HVLATs

Two RCTs (238 participants)[46,53] directly compared different manual mobilizations and HVLATs in patients with chronic[46] and acute[53] neck pain (**FIGURE 6**). None of the comparisons revealed any difference between the groups for any of the assessed outcomes (pain, disability and GPE). All comparisons indicated no heterogeneity ($I^2 = 0\%$); the certainty of evidence was moderate.

Descriptive summary

Pain: Two RCTs [11,20] did not show any differences between groups.

Quality of life: Four trials[11,21,63,79] showed greater improvement in favour of NAG/SNAG in addition to exercise (MD: 23.57; SD: 9.49)[21] or multimodal treatments (MD: 16.1; 95% CI: [8.9; 20.21])[11] (MD: 6.0; SD: 16.10)[63], when compared to the control (MD: -1.59; SD: 7.48)[21] (MD: 10.5; 95% CI: [4.3; 12.4])[11] (MD: -2.25; SD: 13.22)[63]. In Buyukturan et al.[11] this result applied exclusively to the physical component of the SF-36 scale; there was no difference between groups in the mental component of the scale.

Depression: Two trials[11,21] found greater improvement favoring the use of SNAG in addition to exercise[21] (MD: 8.05; SD: 4.90) or multimodal treatments[11] (MD: -7; 95% CI: [-10; -4]) instead of the control group (MD: 0.60; SD: 1.04)[21] (MD: -8; 95% CI: [-11; -4])[11].

Kinesiophobia: Buyukturan et al.[11] reported TSK higher scores and rates of improvement in the treatment group (MD: 5; 95% CI: [4; 8]) rather than the control group (MD: 3; 95% CI: [4; 6]).

Range of movement: Four RCTs reported an improvement in the PA[26] or SNAG[46,63,76] group for all possible directions of active cervical range of motion (A-CROM). In Buyukturan et al.[11], only flexion-extension and right lateral flexion were superior in the NAG/SNAG group. In Tabassum et al.[80], adding post-isometric relaxation techniques to the multimodal approach reached better ROM in flexion, rotation and side-bending compared to SNAG+PA. In Sun et al.[79], the comparisons between groups showed that the cervico-thoracic self-mobilizations

group had medium to large effect sizes compared to exercise or self-SNAG. Mohamed et al.[61] and Shamsi et al.[76] presented an increase of A-CROM in the experimental group when compared to positional release technique or ultrasound therapy in addition to a multimodal treatment program. No differences were observed by Ghulam et al.[30]. Duymaz et al.[21] and Rezkallah et al.[70] identified a difference favoring the SNAG group compared to exercise for all possible movement directions, in contrast with Ganesh et al.[27]. Pérez et al.[46] found no difference between JMTs and HVLATs.

Kim et al.[49] showed an increase in each direction of P-CROM in groups undergoing JMTs or ART compared to Kaltenborn mobilizations.

Adverse events

Some participants who received SNAG reported local muscle and joint soreness[27]. Increased neck pain and headache have been reported without difference in the incidence between 28 participants treated with HVLATs (31.8%) and 24 with JMTs (27%)[53].

DISCUSSION

We reviewed the effectiveness of JMTs in reducing pain and disability in adults with acute/subacute[27,30,53,63,70] or chronic[11,20,26,46,49,61,63,70,76,79,80,84] NSNP. Due to high heterogeneity, our main findings revealed very low certainty evidence supporting the use of JTMs in NSNP. Therefore, we cannot conclude whether JMTs were effective in managing NSNP. Our meta-regression found no effect on outcomes from any covariates examined, including mean age, type of mobilization technique, acute or chronic NSNP, and RoB.

Pooled data showed only statistical, but not clinically relevant, change favoring mobilizations with a narrow CI reflecting a reduction of 1.35 points at the lower margin[7,68]. Global effect size decreased when considering sensitivity analyses excluding trials with high RoB, while it increased when excluding trials that used HVLATs as a comparison. In our analysis, Mobilizations and HVLATs did not show significant post-treatment differences between

groups for any of the considered outcomes (pain, disability or GPE) or any timing of symptoms (acute or chronic).

Our findings agreed with those of other systematic reviews[19,35,60], resulting in some interesting clinical implications as HVLATs are often indicated in the treatment of people with NSNP[32]. However, their administration is only sometimes possible due to general contraindications[23], physiotherapist inexperience or patient preferences and expectations (e.g. negative prior experience)[25]. If further research confirms the effectiveness of HVLATs and JMTs in alleviating pain or improving GPE in NSNP, considering that there are no discernible differences between them, prioritizing JMTs due to their potentially higher safety profile compared to HVLATs could be justified[23,60]. The results of the sub-group analyses indicated that the best variations were observed in people with chronic NSNP, regardless of whether active or passive techniques were used. However, the pooled results were highly heterogeneous and clinically irrelevant.

The results related to the outcome disability, assessed using the NDI scale, suggested favoring mobilizations, with multiple trials reporting average values that met the MCID of the NDI scale (3.5 points)[47,57]. However, the pooled mean results were not clinically significant, achieving a reduction of 4.32 points at the lower end of the CI. In this instance, the sensitivity analyses that excluded both high-RoB trials and those comparing mobilizations to HVLATs showed a significant enhancement in overall outcomes, which, in the latter case, achieved the MCID with a mean reduction of 4.57 points and a reduction of 7.80 at the lower margin of the CI. However, the strength of this evidence remained low due to significant heterogeneity. Sub-group analyses indicated, similarly to the pain assessments, a more favorable trend reported by people with chronic NSNP that was neither clinically nor statistically relevant. As in other musculoskeletal disorders, the impact of NSNP on disability is important, especially in long-lasting forms[38,48]. Because the NDI aims to assess several aspects, including pain

intensity, our disability-related results can be considered a logical consequence of pain reduction. It is reasonable to expect that participants who experienced lower levels of pain would also report lower functional limitations. However, because of the low level of evidence, these results should be taken with caution[37,60].

The positive results on psychosocial status are encouraging. Several studies[1,6,22] showed that the presence of high levels of depression resulted in a negative impact on recurrent or persistent NSNP. According to Alghamdi et al.[1], increased levels of depression often correlate with worsening NSPS. This finding suggested the importance of considering the possible presence of psychosocial distress in people with NSNP[6]. Similarly, the presence of kinesiophobia was significantly correlated with pain intensity, functional performance and QoL in people with chronic NSNP[2,36]. More studies are needed to understand the effect of manual therapy techniques on psychological outcomes and the relationship between them. The positive results obtained on kinesiophobia might be justified by the relationship between kinesiophobia and proprioception[2]. An improvement in cervical ROM results in an improvement in cervical proprioception with a relative reduction of kinesiophobia[11].

According to other studies[4,24,52], the positive results on A-CROM could be justified by the analgesic and neuro-modulating effect of JMTs on pain, related to neurophysiological and biomechanical mechanisms (sympathoexcitation, decreased neural mechanosensitivity etc.)[52]. The reduction of pain intensity would consequently lead to improved muscle recruitment and function and increased A-CROM. The absence of differences between JMTs and HVLATs is in line most of the findings by Minnucci et al.[60] that only showed a greater effect of HVLATs in improving rotational CROM. However, according to Kim et al.[49], JMTs are not as effective as active release techniques in improving P-CROM.

Only two trials[27,53] reported minor adverse effects in groups undergoing JMTs, while no serious adverse events[51] were reported in any trial. The risk of major adverse events when

undergoing JMTs is lower than the one from taking drugs [13]. However, some authors[12,13,66] reported that about half of people treated with manual therapy may experience minor adverse events, especially after the first treatment session, which usually resolves within 72 hours[13].

Clinical implications

As our results are hampered by the very low certainty of the evidence, we cannot state that the use of mobilizations is truly effective in people with NSNP. The overlapping results with manipulations make JMTs preferable to HVLATs when the latter is contraindicated, regardless of the reasons (e.g. health risks and individuals' preferences). The insufficient information regarding the intervention, limited the external validity of the findings and their reproducibility in clinical settings, highlighting a common issue observed in RCTs across various musculoskeletal pain conditions (e.g. NSPN and low back pain)[18,55,58,67,72]. According to other systematic reviews[19,40,41,59,60,74,85], the absence of adverse events showed that JMTs are safe to use in a multimodal approach that includes first-line interventions such as exercise and education on self-management strategies[60] and considers patients' expectations, preferences and previous experiences.

Limitations

Although we conducted sensitivity analyses and meta-regression, the high heterogeneity could not be explained. Even if we ensured a sound methodology, the need to pool or exclude some groups from the analysis of trials with multiple comparisons or interventions[7,9,26,43,56,57,61] may have reduced the power of the results. The high variability of the delivered treatments prevented us from identifying the most effective technique among those proposed. This represents an interesting insight for future research by adopting more suitable analysis tools (e.g. network meta-analysis)[71].

CONCLUSION

There was very low certainty evidence supporting the use of JTMs in acute and chronic NSNP,

preventing us from concluding whether these techniques are truly effective for this condition.

KEY POINTS

Findings: The certainty of evidence ranged from low to very low for most outcomes, preventing definitive conclusions regarding the effectiveness of JMTs on individuals with NSNP despite these treatments being recommended by clinical practice guidelines. No discernible differences were observed between mobilizations and manipulations.

Implications: JMTs should be a part of a multimodal approach, including exercise, education, and self-management strategies as first-line strategies. Given the high heterogeneity and risk of bias, physiotherapists should not rely solely on JMTs but instead tailor treatments to individual patient needs, preferences, and expectations, prioritizing patient safety and considering contraindications.

Cautions: Our results are limited by insufficient information on the intervention, reducing the external validity and reproducibility of the findings in clinical settings. Clinicians should exercise caution when applying these findings in practice. High-quality RCTs with consistent protocols, appropriate controls, and extended follow-up are needed to establish reliable conclusions for clinical practice.

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FIGURE CAPTIONS

FIGURE 1. Study selection flow diagram, according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[24]

FIGURE 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included trials

FIGURE 3. Forest plots for Primary Analysis, Sensitivity Analyses and Sub-groups Analyses on Pain Intensity

FIGURE 4. Forest plots for Primary Analysis, Sensitivity Analyses and Sub-groups Analyses on Disability Level

FIGURE 5. Forest plots for Sub-groups Analyses on Global Perceived Effect (GPE)

FIGURE 6. Forest plots for Manual mobilizations vs High Velocity Low Amplitude Techniques (HVLAT) for outcome Pain, Disability and Global Perceived Effect (GPE).

TABLES

TABLE 1. General Characteristics of the Included Trials

Author, Year (Setting)	Study Design, Treatment Duration, Follow up	Sample, Demographic characteristics, Diagnosis	Intervention Group Characteristics	Control Group Characteristics	Outcome Measures
Buyukturan et al. 2018 **(Physical Therapy and Rehabilitation Center, Ahi Evran University, Turkey)**	RCT Duration: 10 sessions in 2 weeks Follow/Up: End of the 2 weeks of treatment	N = 44 NSNP >3 months (Chronic)	N = 22 Mean age: 69 (range: 65–70.5) MMT + NAG/SNAG	N = 22 Mean age: 67 (range: 65.5–72) MMT (exogenous thermotherapy, antalgic electrotherapy, therapeutic exercise)	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-35) Kinesiophobia (TSK) Depression (BDI) Quality of life (SF-36)
Desai et al. 2012 **(Pravara Rural Hospital, India)**	RCT Duration: 6 weeks Follow/Up: End of the first session (NPRS, A-CROM) and of 3 and 6 weeks of treatment	N = 112 NSNP >3 months (Chronic)	N = 39 Mean age: 37.23 (SD: 9.1) SNAG	CG 1: N = 35 Mean age: 37.23 (SD: 9.29) MMT (exogenous thermotherapy, therapeutic exercise) CG 2: N = 38 Mean age: 33.6 (SD: 7.36) Self-SNAG	Pain (NPRS 0-10) A-CROM (UG) Disability (NDI 0-50)
Duymaz et al. 2018 **(Dept. of Physiotherapy and Rehabilitation, Istanbul Bilim University School of Health, İstanbul)**	RCT Duration: 10 sessions in 2 weeks Follow/Up: End of the 2 weeks of treatment and 1 and 3 months after treatment	N = 40 (35 F) NSNP (Unspecified duration)	N =20 Mean age: 33.35 (SD: 6.09) Therapeutic exercise + SNAG	N = 20 Mean age: 34.25 (SD: 8.66) Home Exercises	Pain (VAS 0-100) Disability (NDI 0-50) Quality of life (NHP) Depression (BDI) CROM (UG) PPT (algometer) Muscle endurance (chronometer) Muscle strength (dynamometer)
Farooq et al. 2018 **(National Institute of Rehabilitation Medicine, Islamabad, Pakistan)**	RCT Duration: 10 sessions in 4 weeks Follow/Up: End of the 4 weeks of treatment	N = 68 (44 F) NSNP >3 months (Chronic)	N = 34 Mean age: 41.82 (SD: 10.94) MMT + Central and Lateral PA glide	N =34 Mean age: 44.00 (SD: 12.80) MMT (exogenous thermotherapy, antalgic electrotherapy, therapeutic exercise)	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-50) Muscle endurance (chronometer)
Ganesh et al. 2014 **(Swami Vivekanand National Institute of Rehabilitation Training and Research, India)**	RCT Duration: 10 sessions in 2 weeks + 4 weeks of exercise at home Follow/Up: End of the 2 weeks of treatment and 12 weeks after treatment	N = 80 (41 F) Mean age: 41.7 (SD: 9.8) NSNP < 3 months (acute/subacute)	N = 26 IG 1: Therapeutic exercise + Maitland joint mobilization (grade 1-4) N = 27 IG 2: Therapeutic exercise + Mulligan joint mobilization (SNAG)	N = 27 Therapeutic exercise	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-50)
Ghulam et al. 2023 **(Physiotherapy department of Najran University, Saudi Arabia)**	RCT Duration: 9 sessions in 3 weeks Follow/Up: End of the 1st, 2nd and 3rd week of treatment	N = 30 Mean age: 30.87 (SD: 4.45) NSNP < 3 months (acute/subacute)	N = 15 MMT + Central PA glide	N = 15 MMT (MHP, therapeutic exercise, PIR)	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-50) PPT (algometer)

Kim et al. 2015 **(Gangnamgu Hospital, Republic of Korea)**	RCT Duration: 6 sessions in 3 weeks Follow/Up: End of the 3 weeks of treatment	N = 24 NSNP >3 months (Chronic)	N = 8 Mean age: 39.3 (SD: 14.9) Kaltenborn joint mobilization (grade 1-3)	CG 1: N = 8 Mean age: 40.0 (SD: 10.4) ART N = 8 CG 2: Mean age: 47.0 (SD: 10.0) No treatment	Pain (VAS 0-10) P-CROM (UG) PPT (algometer)
Leaver et al. 2010 **(Private physiotherapy, chiropractic, and osteopathy clinics, Sydney, Australia)**	RCT Duration: 4 sessions in 2 weeks Follow/Up: End of the 2 weeks of treatment (NPRS, GPE), 4 (NDI, PSFS, SF-12) and 12 weeks after randomization	N = 182 (118 F) Mean age: 38.9 (SD: 10.7) NSNP < 3 months (acute/subacute)	N = 91 Passive Joint mobilization techniques of therapist's choice.	N = 91 Cervical HVLATs	Recovery time Pain (NPRS 0-10) Disability (NDI 0-50) Function (PSFS) Global perceived effect (scale +5 / -5) Health-related Quality of life (SF-12)
Mohamed et al. 2020 **(Hospital of October 6 University, Egypt)**	RCT Duration: 24 sessions in 8 weeks Follow/Up: End of the 8 weeks of treatment	N = 120 (70 F) NSNP >3 months (Chronic)	N = 40 Mean age: 35.22 (SD: 3.68) MMT + SNAG	CG 1: N = 40 Mean age: 34.02 (SD: 4.73) MMT (exogenous thermotherapy, therapeutic exercise) CG 2: N = 40 Mean age: 34.42 (SD: 3.75) MMT + PRT	Pain (NPRS 0-10) A-CROM (UG) Disability (NDI 0-50)
Ozlu et al. 2024 **(Lifemed Medical Center, Instanbul, Turkey)**	RCT Duration: 10 sessions in 2 weeks Follow/Up: End of the 2 weeks of treatment	N = 46 NSNP lasting for at least 2 weeks (Acute/subacute and Chronic)	N = 24 Mean age: 41.35 (SD: 12.39) MMT + SNAG	N = 22 Mean age: 50.15 (SD: 12.46) MMT (ultrasound, antalgic electrotherapy, exogenous thermotherapy, therapeutic exercise)	Pain (VAS 0-10) Disability (NPDS 0-100) Quality of life (SF-36) A-CROM (UG)
Pérez et al. 2014 **(Valleaguado Primary Health Care Centre, Coslada, Spain)**	RCT Duration: 4 sessions in 2 weeks Follow/Up: End of the 2 weeks of treatment and 1, 2 and 3 months after treatment	N = 61 (51 F) Mean age: 36.5 (SD: 9.4) NSNP >3 months (Chronic)	N = 21 IG 1: Lateral PA glide N = 21 IG 2: SNAG	N = 19 Cervical HVLATs	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-50) Global perceived effect (GROC)
Rezkallah et al. 2018 **(School of physical therapy, Cairo University, Egypt)**	RCT Duration: 12 sessions in 4 weeks Follow/Up: End of the 4 weeks of treatment	N = 70 (40 F) NSNP lasting from 3 weeks to 6 months (Acute/subacute and Chronic)	N = 25 Mean age: 30.06 (SD: 2.86) Therapeutic exercise (5 times a week at home) + SNAG	CG 1: N = 23 Mean age: 30.06 (SD: 4.37) Home Exercises + MFR CG 2: N = 22 Mean age: 29.4 (SD: 3.77) Home Exercises	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-50)

Shamsi et al. 2021 **(Raj Nursing Home, Saudi Arabia)**	RCT Duration: 6 sessions in 2 weeks Follow/Up: End of the 2 weeks of treatment	N = 100 Mean age: 30.82 (SD: 6.75) NSNP >3 months (Chronic)	N = 50 MMT + SNAG	N = 50 MMT (MHP, therapeutic exercises) + Ultrasound-therapy	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-50)
Sun et al. 2024 **(Sports Rehabilitation Laboratory of the Capital University of Physical Education, Beijing, China)**	RCT Duration: 18 sessions in 6 weeks Follow/Up: End of the 6 weeks of treatment	N = 30 NSNP >3 months (Chronic)	N = 10 Therapeutic exercise + self-SNAG	CG 1: N = 10 Therapeutic exercise CG 2: N = 10 Therapeutic exercise + cervico-thoracic self-mobilizations	Pain (VAS 0-10) A-CROM (UG) Disability (NDI 0-50) Quality of life (SF-36) Muscle endurance (chronometer) Muscle strength (dynamometer)
Tabassum et al. 2024 **(Physical Therapy and Rehabilitation Department, Heavy Industries Taxila Hospital, Pakistan)**	RCT Duration: 6 sessions in 2 weeks + 4 weeks of exercise at home Follow/Up: End of the 2 weeks of treatment and 4 weeks after treatment	N = 105 (67 F) NSNP >3 months (Chronic)	N = 35 Mean age: 40.14 (SD: 4.57) MMT + PA glide + SNAG	CG 1: N = 35 Mean age: 40.09 (SD: 4.29) MMT (MHP, antalgic electro-therapy) + PIR CG2: N = 35 Mean age: 39.26 (SD: 5.19) MMT (MHP, antalgic electrotherapy, therapeutic exercises)	Pain (NPRS 0-10) CROM (UG) Disability (NDI 0-50) Cervical lordosis (X-rays)
Voulgarakis et al. 2021 **(International Hellenic University, Greece)**	RCT Duration: 24 sessions in 8 weeks Follow/Up: End of the 8 weeks of treatment	N = 45 (30 F) NSNP >3 months (Chronic)	N = 15 Mean age: 41 (SD: 7.69) Cervical and Thoracic PA glide (grade 3)	CG 1: N = 15 Mean age: 40 (SD: 3.93) Acupuncture CG 2: N = 15 Mean age: 44 (SD: 4.3) No treatment	Pain (VAS 0-100) Disability (NDI 0-50)

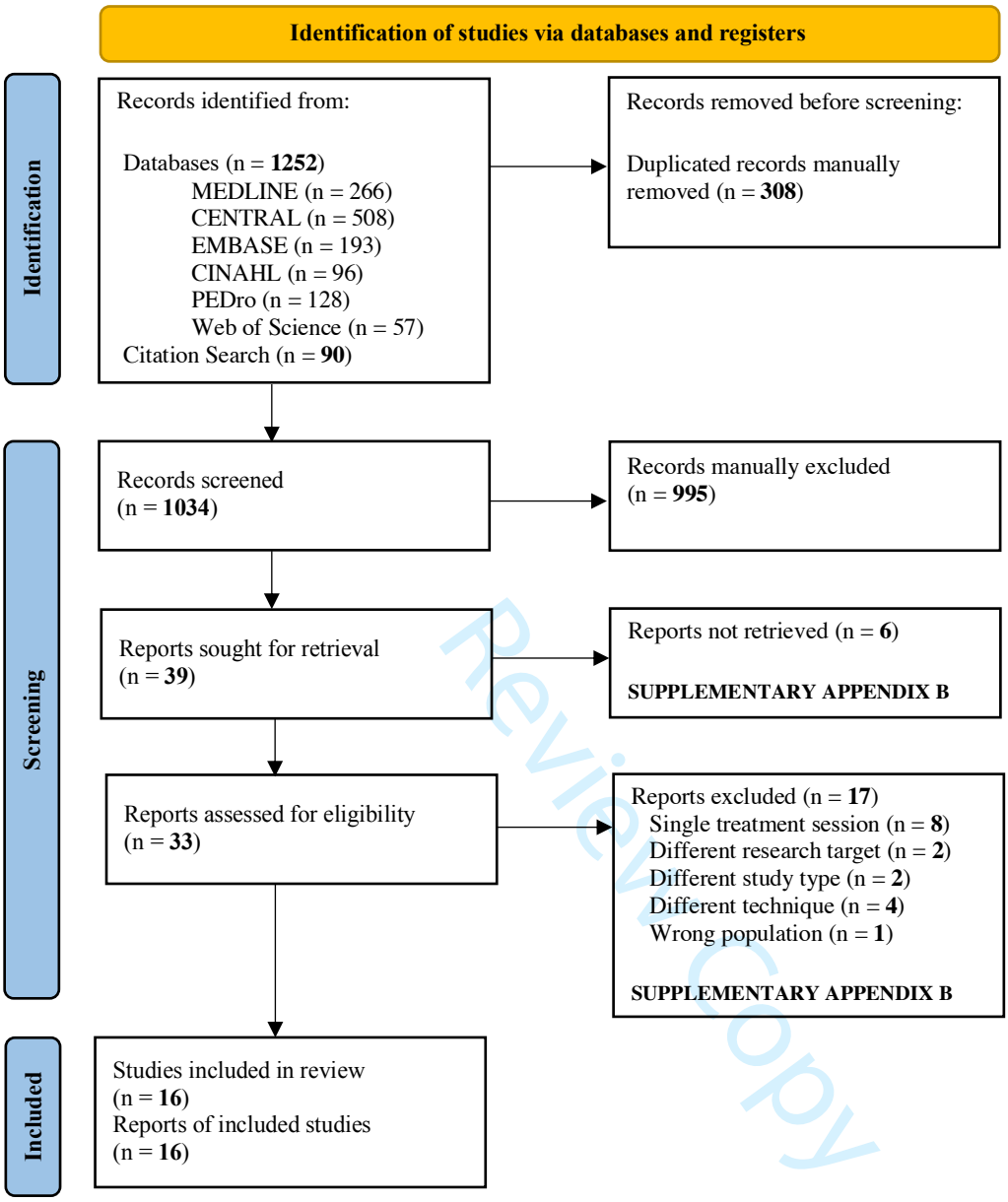
Abbreviations: NSNP: Non Specific Neck Pain; RCT: Randomized Controlled Trial; CG: Control Group; IG: Intervention Group; NAG: Natural Apophyseal Glide; SNAG: Sustained Natural Apophyseal Glide; SD: Standard Deviation; MMT: Multi Modal Treatment; PA Glide: Posterior-Anterior Glide; ART: Active Release Technique; MHP: Moist Hot Pack; PIR: Post Isometric Relaxation; MFR: Myo-Fascial Release; PRT: Positional Release Technique; HVLATs: High Velocity and Low Amplitude Techniques; VAS: Visual Analogue Scale; NPRS: Numeric Pain Rating Scale; NPDS: Neck Pain and Disability Scale; SF-36: 36-items Short Form Health Survey; SF-12: 12-items Short Form Health Survey; PPT: Pressure Pain Threshold; TSK: Tampa Scale of Kinesiophobia; BDI: Beck Depression Inventory; NDI: Neck Disability Index; PSFS: Patient Specific Functional Scale; NHP: Nottingham Health Profile; GROC: Global Rating of Change Scale; P-CROM: Passive Cervical Range of Motion; A-CROM: Active Cervical Range of Motion; UG: Universal Goniometer.

TABLE 2. Summary of Treatment Effects and GRADE Summary of Finding Among Trials Included in the Systematic Review

Certainty assessment						№ of patients		Effect	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	JMTs	Other treatment	Absolute (95% CI)	

A. Outcome PAIN (0-10 NPRS)									
Primary Analysis: Mobilization vs Other Treatments									
14	RCT	serious[a]	very serious[b]	not serious	not serious	448	513	MD **0.86 lower** (1.35 lower to 0.36 lower)	⊕◯◯◯ Very low[b,d,e]
Sensitivity Analysis w/o High RoB studies									
6	RCT	not serious	very serious[b]	not serious	serious[e]	176	183	MD **0.69 lower** (1.44 lower to 0.05 higher)	⊕◯◯◯ Very low[b,d,e]
Sensitivity Analysis w/o High RoB and HVLAs studies									
5	RCT	not serious	very serious[b]	not serious	serious[e]	134	164	MD **0.89 lower** (1.75 lower to 0.02 lower)	⊕◯◯◯ Very low[b,d,e]
Sub-groups Analysis: Overall effect considering Symptoms Duration and Different Techniques									
11	RCT	serious[a]	very serious[b]	not serious	not serious[c]	383	428	MD **0.49 lower** (0.96 lower to 0.01 lower)	⊕◯◯◯ Very low[b,d,e]
Symptoms <3 months - Active Mobilization									
1	RCT	very serious[d]	not serious	not serious	extremely serious[e]	22	10	MD **0.1 lower** (0.97 lower to 0.77 higher)	⊕◯◯◯ Very low[b,d,e]
Symptoms <3 months - Passive Mobilization									
3	RCT	very serious[d]	very serious[b]	not serious	very serious[e]	127	114	MD **0.3 lower** (1.45 lower to 0.86 higher)	⊕◯◯◯ Very low[b,d,e]
Symptoms >3 months - Active Mobilizations									
4	RCT	serious[d]	very serious[b]	not serious	very serious[e]	121	159	MD 0.41 **lower** (1.24 lower to 0.42 higher)	⊕◯◯◯ Very low[b,d,e]
Symptoms >3 months - Passive Mobilizations									
4	RCT	not serious	very serious[b]	not serious	very serious[e]	78	75	MD **0.86 lower** (2.12 lower to 0.40 higher)	⊕◯◯◯ Very low[b,d,e]
Symptoms >3 months - Active + Passive Mobilization combined									
1	RCT	very serious[d]	very serious[b]	not serious	extremely serious[e]	35	70	MD **0.24 lower** (1.13 lower to 0.65 higher)	⊕◯◯◯ Very low[b,d,e]
B. Outcome DISABILITY (0-50 NDI)									
Primary Analysis: Mobilization vs Other Treatments									
12	RCT	serious[a]	very serious[b]	not serious	not serious	420	477	MD **2.45 lower** (4.32 lower to 0.59 lower)	⊕◯◯◯ Very low[a,b]
Sensitivity Analysis w/o High RoB									
6	RCT	not serious	very serious[b]	not serious	serious[e]	166	163	MD **3.22 lower** (6.25 lower to 0.18 lower)	⊕⊕◯◯ Low[b,e]
Sensitivity Analysis w/o High RoB and HVLAs									
5	RCT	not serious	very serious[b]	not serious	serious[e]	124	144	MD **4.57 lower** (7.8 lower to 1.34 lower)	⊕⊕◯◯ Low[b,e]
Sub-groups Analysis: Overall effect considering Symptoms Duration and Different Techniques									
10	RCT	serious[a]	very serious[b]	not serious	serious[c]	375	412	MD **1.55 lower** (3.63 lower to 0.54 higher)	⊕◯◯◯ Very low[a,b,c]
Symptoms <3 months - Active Mobilization									
1	RCT	very serious[d]	not serious	not serious	extremely serious[e]	22	10	MD **4.7 higher** (0.74 lower to 10.14 higher)	⊕◯◯◯ Very low[d,e]
Symptoms <3 months - Passive Mobilization									
3	RCT	very serious[d]	very serious[b]	not serious	very serious[e]	127	114	MD **0.54 higher** (2.41 lower to 3.49 higher)	⊕◯◯◯ Very low[d,e]
Symptoms >3 months - Active Mobilizations									
4	RCT	serious[d]	very serious[b]	not serious	very serious[e]	121	159	MD 2.23 **lower** (5.7 lower to 1.24 higher)	⊕◯◯◯ Very low[d,e]
Symptoms >3 months - Passive Mobilizations									
3	RCT	not serious	very serious[b]	not serious	very serious[e]	63	59	MD **5.73 lower** (13.42 lower to 1.95 higher)	⊕◯◯◯ Very low[d,e]
Symptoms >3 months - Active + Passive Mobilization combined									
1	RCT	very serious[d]	very serious[b]	not serious	extremely serious[e]	35	70	MD **0.63 lower** (2.59 lower to 1.33 higher)	⊕◯◯◯ Very low[d,e]
C. Outcome GLOBAL PERCEIVED EFFECT									
Sub-groups Analysis: Overall effect considering Symptoms Duration									
2	RCT	not serious	not serious	not serious	very serious[e]	130	108	SMD **0.11 higher** (0.15 lower to 0.37 higher)	⊕⊕◯◯ Low[e]
Symptoms <3 months									
1	RCT	very serious[d]	not serious	not serious	extremely serious[a]	88	89	SMD **0.18 higher** (0.12 lower to 0.47 higher)	⊕◯◯◯ Very low[a,d]
Symptoms >3 months									
1	RCT	not serious	not serious	not serious	very serious[e]	42	19	SMD **0.1 lower** (0.65 lower to 0.44 higher)	⊕⊕◯◯ Low[e]
D. Mobilizations vs HVLAs									
Analysis on PAIN									
2	RCT	not serious	not serious	not serious	serious[e]	130	108	SMD **0.05 higher** (0.21 lower to 0.31 higher)	⊕⊕⊕◯ Moderate[e]
Analysis on DISABILITY									
2	RCT	not serious	not serious	not serious	serious[e]	130	108	SMD **0.11 higher** (0.15 lower to 0.37 higher)	⊕⊕⊕◯ Moderate[e]
Analysis on GLOBAL PERCEIVED EFFECT									
2	RCT	not serious	not serious	not serious	serious[e]	130	108	SMD **0.11 higher** (0.15 lower to 0.37 higher)	⊕⊕⊕◯ Moderate[e]

Abbreviations: CI: confidence interval; MD: mean difference; SMD: Standardised Mean Difference; RCT: Randomized controlled trial; JMTs: Joint Mobilization Techniques; NPRS: Numeric Pain Rating Scale; NDI: Neck Disability Index; [a)]7 trials had high Risk of Bias; [b)]Hight heterogeneity; [c)]One group less than 400 subjects; [d)]High Risk of Bias; [e)]Less than 400 subjects for each group.


Identification of studies via databases and registers
Identification
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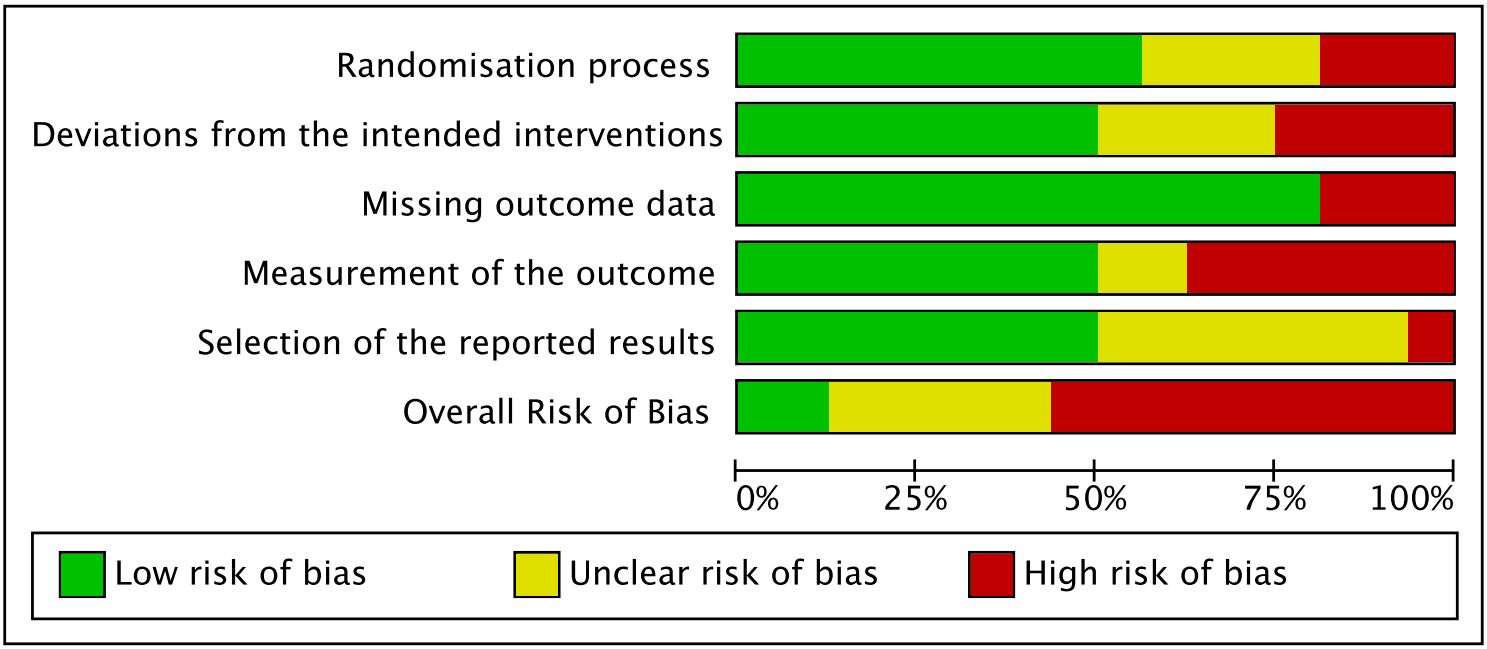
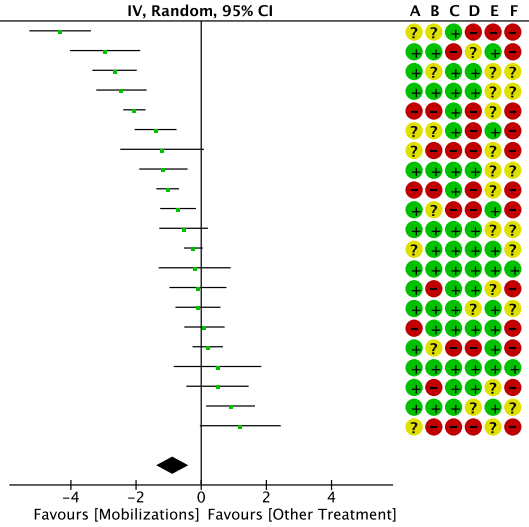
Databases (n = 1252)
MEDLINE (n = 266)
CENTRAL (n = 508)
EMBASE (n = 193)
CINAHL (n = 96)
PEDro (n = 128)
Web of Science (n = 57)
Citation Search (n = 90)
Records removed before screening:
Duplicated records manually removed (n = 308)
Screening
Records screened (n = 1034)
Records manually excluded (n = 995)
Reports sought for retrieval (n = 39)
Reports not retrieved (n = 6)
SUPPLEMENTARY APPENDIX B
Reports assessed for eligibility (n = 33)
Reports excluded (n = 17)
Single treatment session (n = 8)
Different research target (n = 2)
Different study type (n = 2)
Different technique (n = 4)
Wrong population (n = 1)
SUPPLEMENTARY APPENDIX B
Included
Studies included in review (n = 16)
Reports of included studies (n = 16)


Randomisation process
Deviations from the intended interventions
Missing outcome data
Measurement of the outcome
Selection of the reported results
Overall Risk of Bias
0%
25%
50%
75%
100%
Low risk of bias
Unclear risk of bias
High risk of bias

Pain: Overall Primary Analysis

Study or Subgroup	Mobilizations Mean	SD	Total	Other Treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Duymaz 2018 (1)	1.47	1.27	20	5.8	1.74	20	4.6%	−4.33 [−5.27, −3.39]
Ozlu 2024 (2)	0.6	1.14	20	3.55	2.18	20	4.3%	−2.95 [−4.03, −1.87]
Voulgarakis 2021 (3)	3.13	0.88	15	5.79	1.02	15	5.0%	−2.66 [−3.34, −1.98]
Rezkallah 2018 (4)	2.69	0.97	13	5.14	1.35	22	4.8%	−2.45 [−3.22, −1.68]
Mohamed 2020 (5)	2.12	0.64	20	4.17	0.63	40	5.3%	−2.05 [−2.39, −1.71]
Ghulam 2023 (6)	2.86	0.83	15	4.26	0.96	15	5.0%	−1.40 [−2.04, −0.76]
Kim 2015 (7)	4.3	1	4	5.5	1.2	8	4.0%	−1.20 [−2.49, 0.09]
Farooq 2018 (8)	2	1.3	34	3.16	1.78	34	4.9%	−1.16 [−1.90, −0.42]
Mohamed 2020 (9)	2.12	0.64	20	3.15	0.66	40	5.3%	−1.03 [−1.38, −0.68]
Tabassum 2024 (10)	4.26	0.85	17	4.97	1.12	35	5.1%	−0.71 [−1.26, −0.16]
Rezkallah 2018 (11)	2.69	0.97	12	3.23	1.24	23	4.9%	−0.54 [−1.29, 0.21]
Shamsi 2021 (12)	0.44	0.6	50	0.68	0.85	50	5.4%	−0.24 [−0.53, 0.05]
Pérez 2014 (13)	0.8	1.6	21	1	1.4	10	4.3%	−0.20 [−1.31, 0.91]
Ganesh 2014 (14)	1.8	1.1	22	1.9	1.2	10	4.7%	−0.10 [−0.97, 0.77]
Sun 2024 (15)	3.2	0.63	5	3.3	0.67	10	4.9%	−0.10 [−0.79, 0.59]
Leaver 2010 (16)	2.5	2.2	88	2.4	2	89	5.0%	0.10 [−0.52, 0.72]
Tabassum 2024 (17)	4.26	0.85	18	4.06	0.76	35	5.2%	0.20 [−0.27, 0.67]
Pérez 2014 (18)	1.5	2.3	21	1	1.4	9	3.9%	0.50 [−0.84, 1.84]
Ganesh 2014 (19)	2.4	1.5	24	1.9	1.2	10	4.5%	0.50 [−0.46, 1.46]
Sun 2024 (20)	3.2	0.63	5	2.3	0.82	10	4.9%	0.90 [0.15, 1.65]
Kim 2015 (21)	4.3	1	4	3.1	1.1	8	4.1%	1.20 [−0.04, 2.44]
Total (95% CI)			**448**			**513**	**100.0%**	**−0.86 [−1.35, −0.36]**

Heterogeneity: Tau² = 1.16; Chi² = 260.66, df = 20 (P < 0.00001); I² = 92%
Test for overall effect: Z = 3.41 (P = 0.0007)



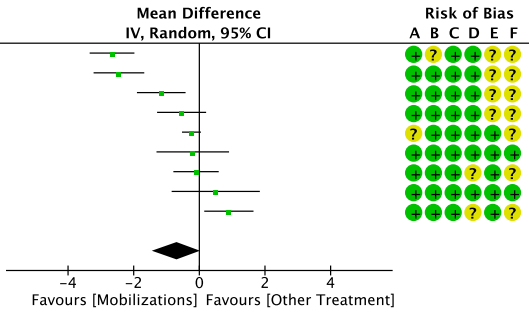
Footnotes
(1) SNAG + ET vs ET
(2) SNAG + MMT vs MMT
(3) PA vs No Treatment
(4) SNAG + ET vs ET
(5) SNAG + MMT vs MMT
(6) PA + MMT vs MMT
(7) Kalterborn VS no treatment
(8) PA + MMT vs MMT
(9) SNAG + MMT vs PRT + MMT
(10) SNAG + PA + MMT vs MMT
(11) SNAG + ET vs MFR + ET
(12) SNAG + MMT vs US + MMT
(13) PA vs HVLATs
(14) SNAG + ET vs ET
(15) SNAG + ET vs ET
(16) Passive Joint mobilization vs HVLATs
(17) SNAG + PA + MMT vs PIR + MMT
(18) SNAG vs HVLATs
(19) Maitland + ET vs ET
(20) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET
(21) Kalterborn vs ART

Risk of bias legend
(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

Pain: Sensitivity Analysis excluding Studies with High RoB

Study or Subgroup	Mobilizations Mean	SD	Total	Other Treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Voulgarakis 2021 (1)	3.13	0.88	15	5.79	1.02	15	11.6%	−2.66 [−3.34, −1.98]
Rezkallah 2018 (2)	2.69	0.97	13	5.14	1.35	22	11.3%	−2.45 [−3.22, −1.68]
Farooq 2018 (3)	2	1.3	34	3.16	1.78	34	11.4%	−1.16 [−1.90, −0.42]
Rezkallah 2018 (4)	2.69	0.97	12	3.23	1.24	23	11.3%	−0.54 [−1.29, 0.21]
Shamsi 2021 (5)	0.44	0.6	50	0.68	0.85	50	12.6%	−0.24 [−0.53, 0.05]
Pérez 2014 (6)	0.8	1.6	21	1	1.4	10	10.0%	−0.20 [−1.31, 0.91]
Sun 2024 (7)	3.2	0.63	5	3.3	0.67	10	11.5%	−0.10 [−0.79, 0.59]
Pérez 2014 (8)	1.5	2.3	21	1	1.4	9	9.0%	0.50 [−0.84, 1.84]
Sun 2024 (9)	3.2	0.63	5	2.3	0.82	10	11.3%	0.90 [0.15, 1.65]
Total (95% CI)			**176**			**183**	**100.0%**	**−0.69 [−1.44, 0.05]**

Heterogeneity: Tau² = 1.13; Chi² = 85.72, df = 8 (P < 0.00001); I² = 91%
Test for overall effect: Z = 1.82 (P = 0.07)



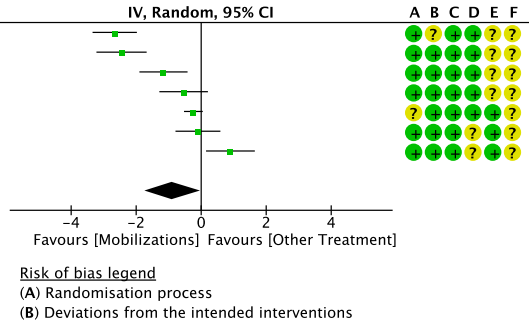
Footnotes
(1) PA vs No Treatment
(2) SNAG + ET vs ET
(3) PA + MMT vs MMT
(4) SNAG + ET vs MFR + ET
(5) SNAG + MMT vs US + MMT
(6) PA vs HVLATs
(7) SNAG + ET vs ET
(8) SNAG vs HVLATs
(9) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET

Risk of bias legend
(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

Pain: Sensitivity Analysis excluding Studies with High RoB and HVLAs as comparator

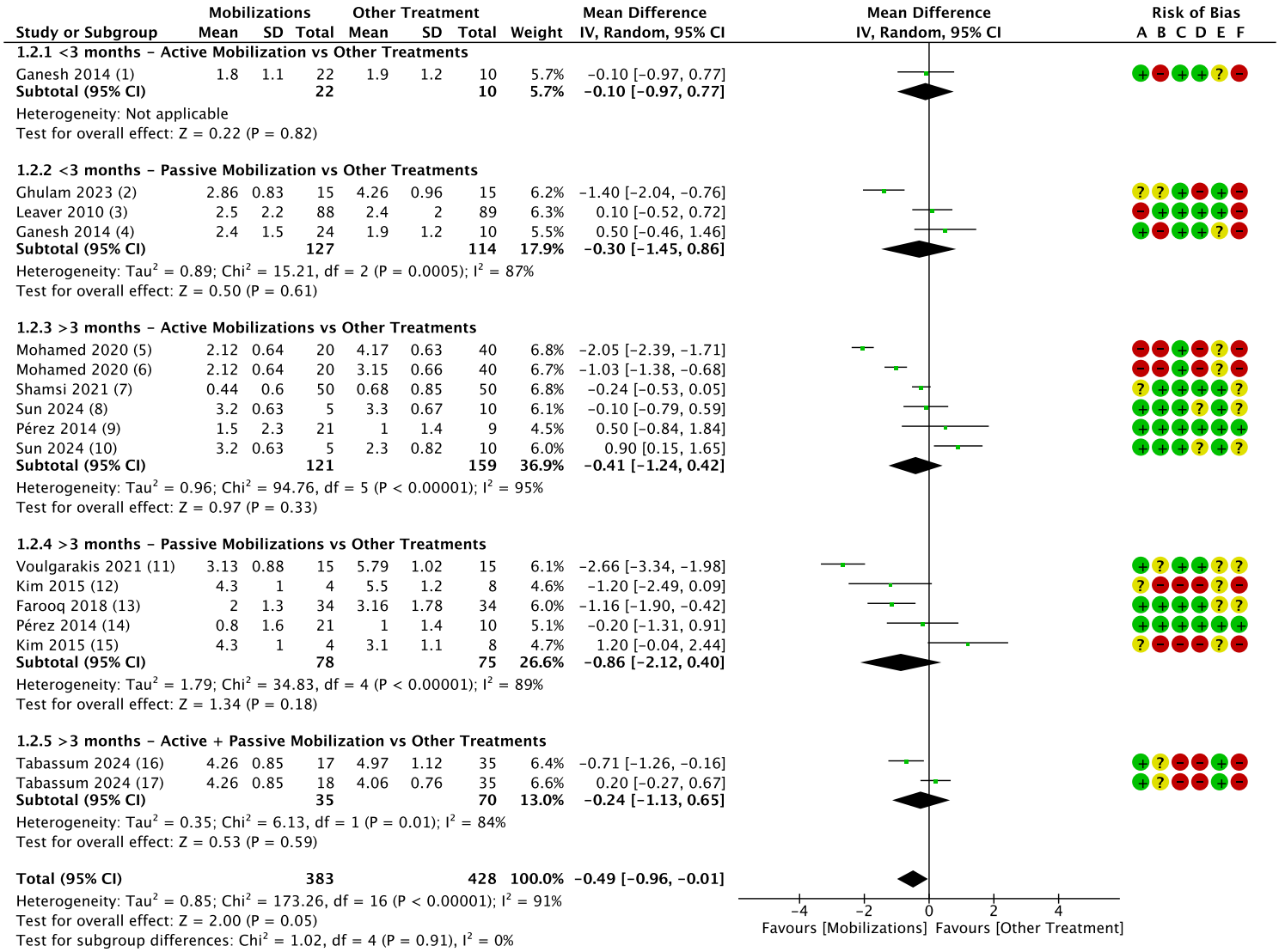
Study or Subgroup	Mobilizations Mean	SD	Total	Other Treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Voulgarakis 2021 (1)	3.13	0.88	15	5.79	1.02	15	14.3%	−2.66 [−3.34, −1.98]
Rezkallah 2018 (2)	2.69	0.97	13	5.14	1.35	22	13.9%	−2.45 [−3.22, −1.68]
Farooq 2018 (3)	2	1.3	34	3.16	1.78	34	14.1%	−1.16 [−1.90, −0.42]
Rezkallah 2018 (4)	2.69	0.97	12	3.23	1.24	23	14.0%	−0.54 [−1.29, 0.21]
Shamsi 2021 (5)	0.44	0.6	50	0.68	0.85	50	15.4%	−0.24 [−0.53, 0.05]
Sun 2024 (6)	3.2	0.63	5	3.3	0.67	10	14.3%	−0.10 [−0.79, 0.59]
Sun 2024 (7)	3.2	0.63	5	2.3	0.82	10	14.0%	0.90 [0.15, 1.65]
Total (95% CI)			**134**			**164**	**100.0%**	**−0.89 [−1.75, −0.02]**

Heterogeneity: Tau² = 1.23; Chi² = 82.66, df = 6 (P < 0.00001); I² = 93%
Test for overall effect: Z = 2.01 (P = 0.04)



Footnotes
(1) PA vs No Treatment
(2) SNAG + ET vs ET
(3) PA + MMT vs MMT
(4) SNAG + ET vs MFR + ET
(5) SNAG + MMT vs US + MMT
(6) SNAG + ET vs ET
(7) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET

Risk of bias legend
(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias



Footnotes

(1) SNAG + ET vs ET
(2) PA + MMT vs MMT
(3) Passive Joint mobilization vs HVLATs
(4) Maitland + ET vs ET
(5) SNAG + MMT vs MMT
(6) SNAG + MMT vs PRT + MMT
(7) SNAG + MMT vs US + MMT
(8) SNAG + ET vs ET
(9) SNAG vs HVLATs
(10) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET
(11) PA vs No Treatment
(12) Kalterborn VS no treatment
(13) PA + MMT vs MMT
(14) PA vs HVLATs
(15) Kalterborn vs ART
(16) SNAG + PA + MMT vs MMT
(17) SNAG + PA + MMT vs PIR + MMT

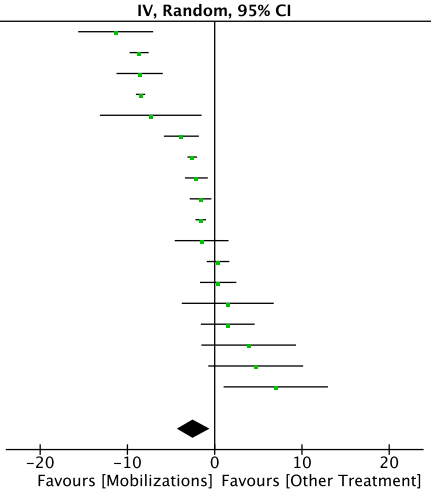
Risk of bias legend

(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

Disability: Overall Primary Analysis

Study or Subgroup	Mobilizations Mean	SD	Total	Other Treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Voulgarakis 2021 (1)	15.65	5.61	15	27	6.37	15	4.9%	−11.35 [−15.65, −7.05]
Rezkallah 2018 (2)	5.86	1.25	13	14.52	2.04	22	6.4%	−8.66 [−9.75, −7.57]
Duymaz 2018 (3)	2.9	3.12	20	11.5	5.18	20	5.8%	−8.60 [−11.25, −5.95]
Mohamed 2020 (4)	10.6	1.03	20	19.1	0.9	40	6.5%	−8.50 [−9.03, −7.97]
Farooq 2018 (5)	12.06	8.54	34	19.39	15.09	34	4.0%	−7.33 [−13.16, −1.50]
Shamsi 2021 (6)	14.48	3.68	50	18.3	6.23	50	6.1%	−3.82 [−5.83, −1.81]
Mohamed 2020 (7)	10.6	1.03	20	13.17	1.03	40	6.5%	−2.57 [−3.12, −2.02]
Rezkallah 2018 (8)	5.86	1.25	12	7.96	2.7	23	6.4%	−2.10 [−3.41, −0.79]
Tabassum 2024 (9)	18.89	2.18	17	20.51	2.04	35	6.4%	−1.62 [−2.86, −0.38]
Ghulam 2023 (10)	14.6	0.83	15	16.2	0.86	15	6.5%	−1.60 [−2.20, −1.00]
Sun 2024 (11)	19.5	2.5	5	21	3.5	10	5.6%	−1.50 [−4.58, 1.58]
Tabassum 2024 (12)	18.89	2.18	18	18.51	2.47	35	6.4%	0.38 [−0.92, 1.68]
Leaver 2010 (13)	6.9	7.3	88	6.5	6.8	89	6.1%	0.40 [−1.68, 2.48]
Pérez 2014 (14)	10.7	9.4	21	9.2	5.5	10	4.3%	1.50 [−3.77, 6.77]
Sun 2024 (15)	19.5	2.5	5	18	3.5	10	5.6%	1.50 [−1.58, 4.58]
Pérez 2014 (16)	13.1	9.5	21	9.2	5.5	9	4.2%	3.90 [−1.52, 9.32]
Ganesh 2014 (17)	14.9	9.5	22	10.2	6	10	4.2%	4.70 [−0.74, 10.14]
Ganesh 2014 (18)	17.2	11.7	24	10.2	6	10	3.9%	7.00 [1.02, 12.98]
Total (95% CI)			**420**			**477**	**100.0%**	**−2.45 [−4.32, −0.59]**

Heterogeneity: $Tau^2 = 13.78$; $Chi^2 = 589.22$, df = 17 ($P < 0.00001$); $I^2 = 97\%$
Test for overall effect: Z = 2.58 (P = 0.010)



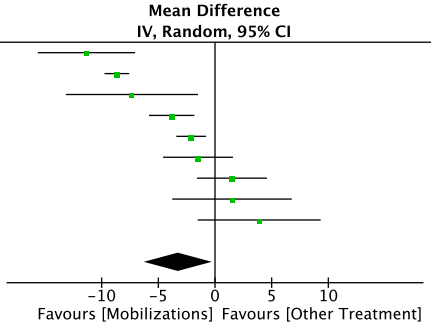
Footnotes
(1) PA vs No Treatment
(2) SNAG + ET vs ET
(3) SNAG + ET vs ET
(4) SNAG + MMT vs MMT
(5) PA + MMT vs MMT
(6) SNAG + MMT vs US + MMT
(7) SNAG + MMT vs PRT + MMT
(8) SNAG + ET vs MFR + ET
(9) SNAG + PA + MMT vs MMT
(10) PA + MMT vs MMT
(11) SNAG + ET vs ET
(12) SNAG + PA + MMT vs PIR + MMT
(13) Passive Joint mobilization vs HVLATs
(14) PA vs HVLATs
(15) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET
(16) SNAG vs HVLATs
(17) SNAG + ET vs ET
(18) Maitland + ET vs ET

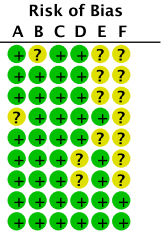
Risk of bias legend
(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

Disability: Sensitivity Analysis excluding Studies with High RoB

Study or Subgroup	Mobilizations Mean	SD	Total	Other Treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Voulgarakis 2021 (1)	15.65	5.61	15	27	6.37	15	10.5%	−11.35 [−15.65, −7.05]
Rezkallah 2018 (2)	5.86	1.25	13	14.52	2.04	22	13.0%	−8.66 [−9.75, −7.57]
Farooq 2018 (3)	12.06	8.54	34	19.39	15.09	34	8.9%	−7.33 [−13.16, −1.50]
Shamsi 2021 (4)	14.48	3.68	50	18.3	6.23	50	12.5%	−3.82 [−5.83, −1.81]
Rezkallah 2018 (5)	5.86	1.25	12	7.96	2.7	23	12.9%	−2.10 [−3.41, −0.79]
Sun 2024 (6)	19.5	2.5	5	21	3.5	10	11.7%	−1.50 [−4.58, 1.58]
Sun 2024 (7)	19.5	2.5	5	18	3.5	10	11.7%	1.50 [−1.58, 4.58]
Pérez 2014 (8)	10.7	9.4	21	9.2	5.5	10	9.5%	1.50 [−3.77, 6.77]
Pérez 2014 (9)	13.1	9.5	21	9.2	5.5	9	9.3%	3.90 [−1.52, 9.32]
Total (95% CI)			**176**			**183**	**100.0%**	**−3.22 [−6.25, −0.18]**

Heterogeneity: $Tau^2 = 18.08$; $Chi^2 = 110.64$, df = 8 ($P < 0.00001$); $I^2 = 93\%$
Test for overall effect: Z = 2.08 (P = 0.04)





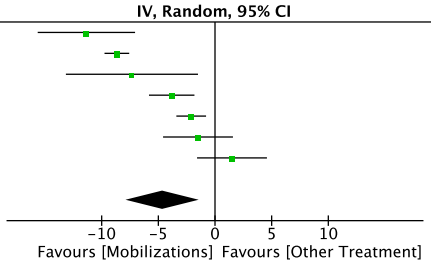
Footnotes
(1) PA vs No Treatment
(2) SNAG + ET vs ET
(3) PA + MMT vs MMT
(4) SNAG + MMT vs US + MMT
(5) SNAG + ET vs MFR + ET
(6) SNAG + ET vs ET
(7) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET
(8) PA vs HVLATs
(9) SNAG vs HVLATs

Risk of bias legend
(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

Disability: Sensitivity Analysis excluding Studies with High RoB and HVLAs as comparator

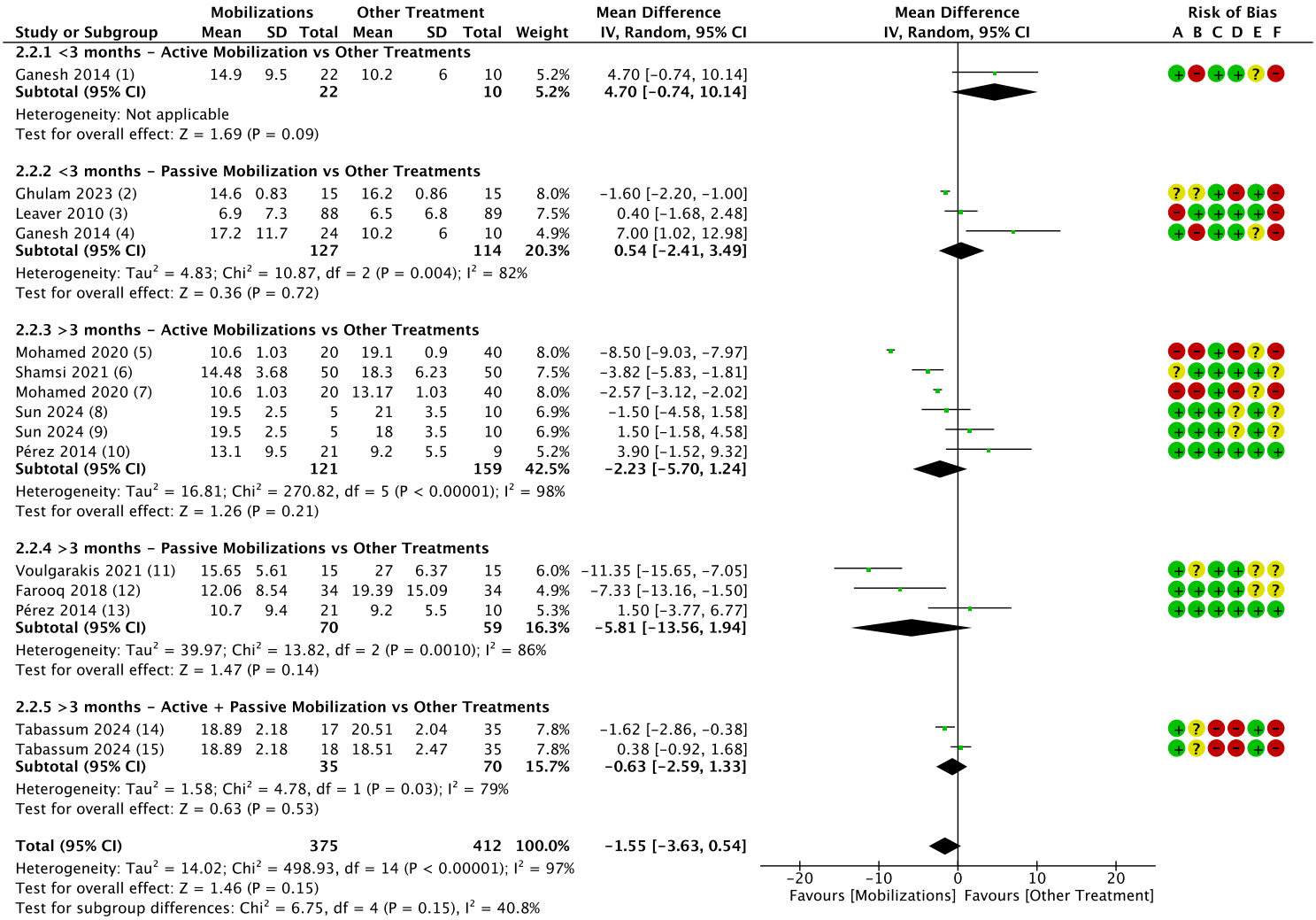
Study or Subgroup	Mobilizations Mean	SD	Total	Other Treatment Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Voulgarakis 2021 (1)	15.65	5.61	15	27	6.37	15	12.8%	−11.35 [−15.65, −7.05]
Rezkallah 2018 (2)	5.86	1.25	13	14.52	2.04	22	16.2%	−8.66 [−9.75, −7.57]
Farooq 2018 (3)	12.06	8.54	34	19.39	15.09	34	10.7%	−7.33 [−13.16, −1.50]
Shamsi 2021 (4)	14.48	3.68	50	18.3	6.23	50	15.5%	−3.82 [−5.83, −1.81]
Rezkallah 2018 (5)	5.86	1.25	12	7.96	2.7	23	16.1%	−2.10 [−3.41, −0.79]
Sun 2024 (6)	19.5	2.5	5	21	3.5	10	14.3%	−1.50 [−4.58, 1.58]
Sun 2024 (7)	19.5	2.5	5	18	3.5	10	14.3%	1.50 [−1.58, 4.58]
Total (95% CI)			**134**			**164**	**100.0%**	**−4.57 [−7.80, −1.34]**

Heterogeneity: $Tau^2 = 16.50$; $Chi^2 = 94.06$, df = 6 ($P < 0.00001$); $I^2 = 94\%$
Test for overall effect: Z = 2.77 (P = 0.006)



Footnotes
(1) PA vs No Treatment
(2) SNAG + ET vs ET
(3) PA + MMT vs MMT
(4) SNAG + MMT vs US + MMT
(5) SNAG + ET vs MFR + ET
(6) SNAG + ET vs ET
(7) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET

Risk of bias legend
(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

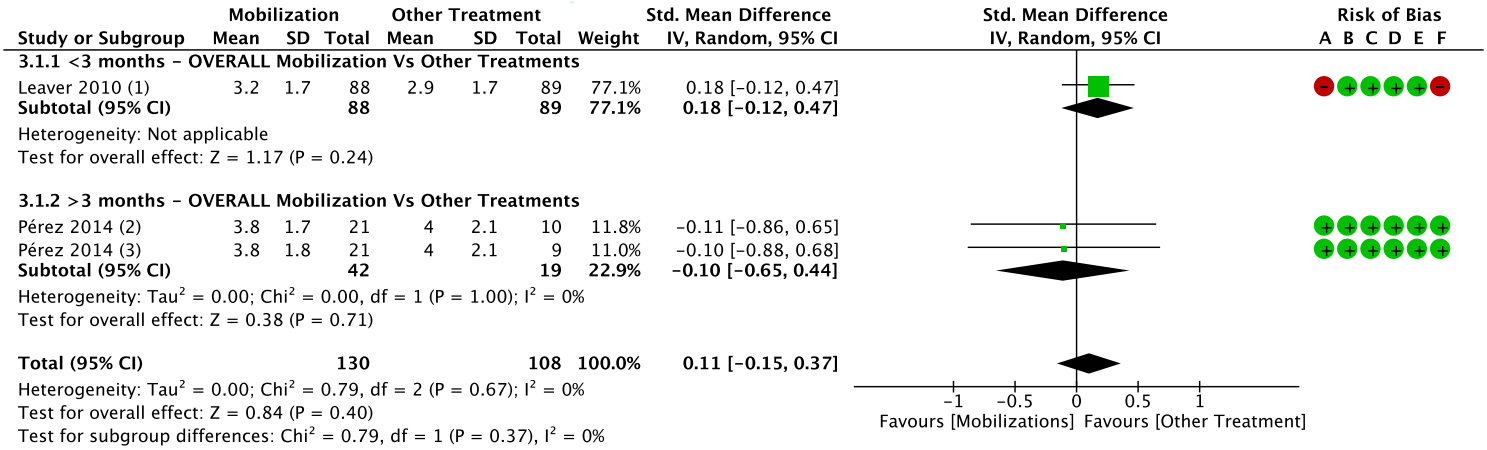


Footnotes

(1) SNAG + ET vs ET
(2) PA + MMT vs MMT
(3) Passive Joint mobilization vs HVLATs
(4) Maitland + ET vs ET
(5) SNAG + MMT vs MMT
(6) SNAG + MMT vs US + MMT
(7) SNAG + MMT vs PRT + MMT
(8) SNAG + ET vs ET
(9) Self Cervical SNAG + ET vs Self Cervicothoracic Mobilizations + ET
(10) SNAG vs HVLATs
(11) PA vs No Treatment
(12) PA + MMT vs MMT
(13) PA vs HVLATs
(14) SNAG + PA + MMT vs MMT
(15) SNAG + PA + MMT vs PIR + MMT

Risk of bias legend

(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

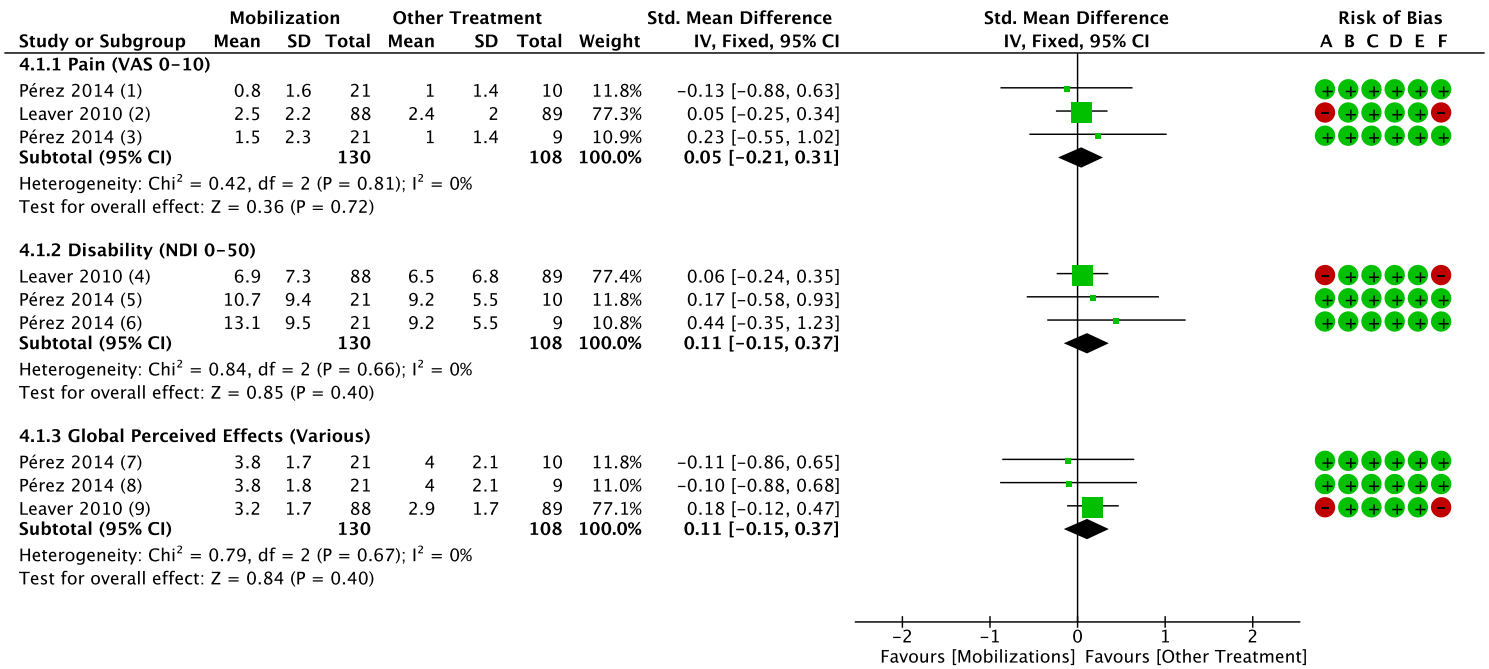


Footnotes

(1) Passive Joint mobilization vs HVLATs
(2) PA vs HVLATs
(3) SNAG vs HVLATs

Risk of bias legend

(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias



Footnotes
(1) PA vs HVLATs
(2) Passive Joint mobilization vs HVLATs
(3) SNAG vs HVLATs
(4) Passive Joint mobilization vs HVLATs
(5) PA vs HVLATs
(6) SNAG vs HVLATs
(7) PA vs HVLATs
(8) SNAG vs HVLATs
(9) Passive Joint mobilization vs HVLATs

Risk of bias legend
(**A**) Randomisation process
(**B**) Deviations from the intended interventions
(**C**) Missing outcome data
(**D**) Measurement of the outcome
(**E**) Selection of the reported results
(**F**) Overall Risk of Bias

APPENDIX A. Search strategies for each scientific database

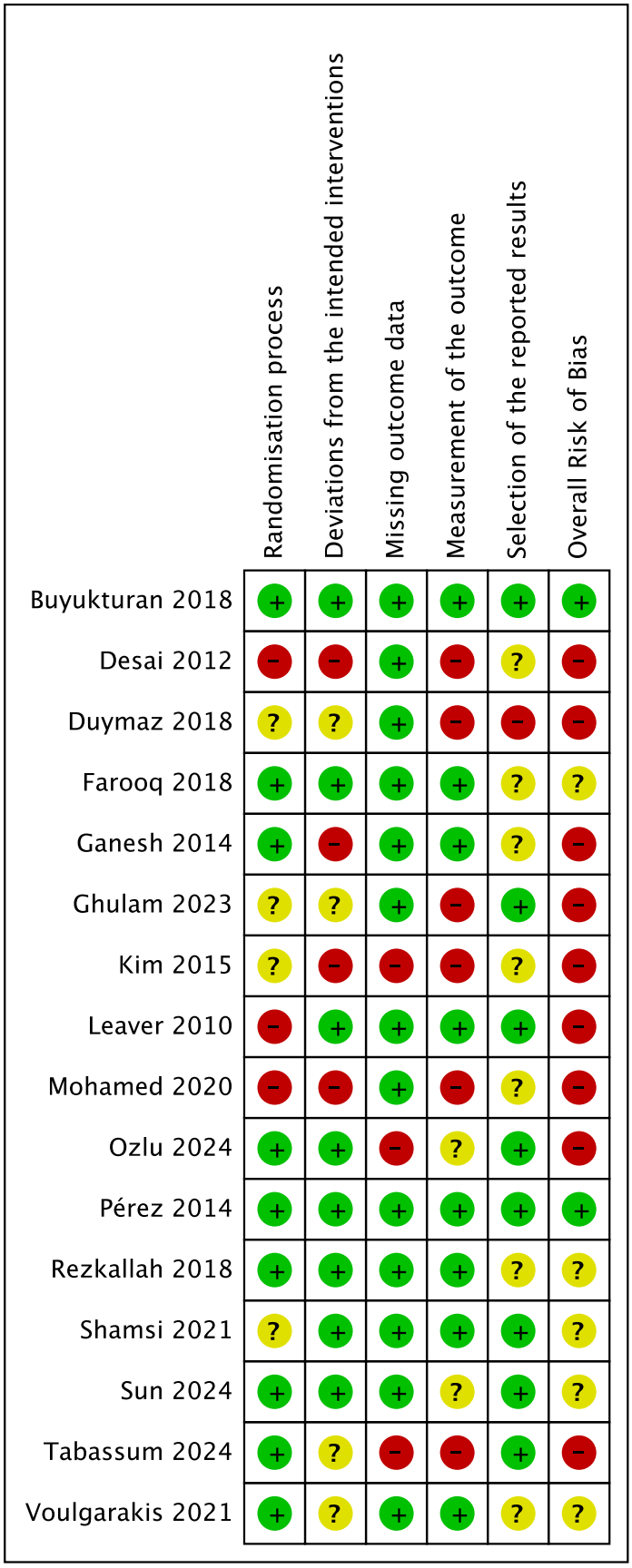
MEDLINE (Pubmed):	(("Neck Pain"[Mesh] OR "Pain, Neck" OR "Neck Pain*") OR ("Cervicalgia" OR "Cervical Pain" OR "Cervical Spine Pain" OR "Cervical*" OR "Cervico*") OR "Non-Specific Neck Pain" OR "Chronic Neck Pain" OR "Mechanical Neck Pain" OR "Acute Neck Pain" OR "Neck Injur*" OR ("Atlanto-Axial Joint" OR "Axis" OR "Atlas")) AND (("Mulligan Mobilization" OR "Mulligan") OR ("Joint Mobilization" OR "Joint Mobilizations" OR "Joint Mobilisation" OR "Joint Mobilisation*") OR ("Mobilization Therapy" OR "Mobilization Therapies") OR ("Mobilization Technique" OR "Mobilization Techniques" OR "Mobilisation Technique") OR ("Mobilization with Movement" OR "Mobilizations with Movement") OR ("Sustained Natural Apophyseal Glide" OR "SNAG" OR "Natural Apophyseal Glides") OR ("Maitland" OR "Maitland Mobilization" OR "Maitland Mobilisation" OR "Maitland*") OR ("Cervical Spine Mobilization" OR "Cervical Mobilization")) AND (("Pain"[Mesh] OR "Pain Relief" OR "Pain Reduction" OR "Pain Intensity") OR "Quality of Life"[Mesh] OR ("Function" OR "Functional Ability" OR "Functional Disability" OR "Disability" OR "Function*") OR ("Patient Satisfaction" OR "Global Perceived Effect") OR ("Adverse Event" OR "Adverse Effect*" OR "Adverse Event*" OR "Side Effect*" OR "Complication*" OR "Consequence*"))
CENTRAL*:	("Neck Pain" OR "Cervical Pain" OR "Cervical*" OR "Cerviço*" OR "Axis" OR "Atlas") AND (("Mulligan Mobilization" OR "Mulligan") OR ("Joint Mobilization" OR "Mobilization Therapy" OR "Mobilization Technique") OR "Mobilization with Movement" OR ("Sustained Natural Apophyseal Glide" OR "SNAG" OR "Natural apophyseal glides") OR "Maitland*" OR ("Cervical Spine Mobilization" OR "Cervical Mobilization")) AND ("Pain" OR "Quality of Life" OR "Disability" OR "Function*" OR "Patient Satisfaction" OR "Side Effect*" OR "Complication*")
EMBASE (Scopus)*:	("Neck Pain") AND ("Mulligan Mobilization" OR "Joint Mobilization" OR "Mobilization Therapy" OR "Mobilization Technique" OR "Mobilization with Movement" OR "Sustained Natural Apophyseal Glide" OR "Maitland Mobilization" OR "Cervical Mobilization") AND ("Pain Intensity" OR "Quality of Life" OR "Disability" OR "Function") AND ("Randomized Control Trial" OR "RCT")
CINAHL (EBSCOhost)*:	("Neck Pain" OR "Cervical*" OR "Neck Injur*") AND ("Joint Mobilization" OR "Joint Mobilisation*" OR "Mobilization Technique*" OR "Mobilization with Movement" OR "SNAG" OR "Natural Apophyseal Glides" OR "Cervical Spine Mobilization" OR "Cervical Mobilization") AND ("Pain" OR "Function" OR "Consequence*")
PEDro:	"Neck Pain" AND Mobilization
Web of Science:	("Neck Pain" OR "Cervical Pain" OR "Cervical*" OR "Cervico*" OR "Axis" OR "Atlas") AND (("Mulligan Mobilization" OR "Mulligan") OR ("Joint Mobilization*" OR "Joint Mobilisation*") OR "Mobilization Therap*" OR ("Mobilization Technique*" OR "Mobilisation Technique") OR "Mobilization with Movement" OR ("SNAG" OR "Natural Apophyseal Glides") OR ("Maitland" OR "Maitland Mobilization") OR ("Cervical Spine Mobilization" OR "Cervical Mobilization")) AND ("Pain" OR "Function*" OR "Adverse Effect*" OR "Adverse Event*" OR "Complication*" OR "Consequence*") AND ("Randomized Control Trial" OR "RCT" OR "Randomized Clinical Trial*")

*Some filters were used on CENTRAL (filter for "trials"), CINAHL and EMBASE (filter for "academic journals" and "randomized controlled trials") databases.

APPENDIX B. Full-text articles excluded with the reasons for their exclusion

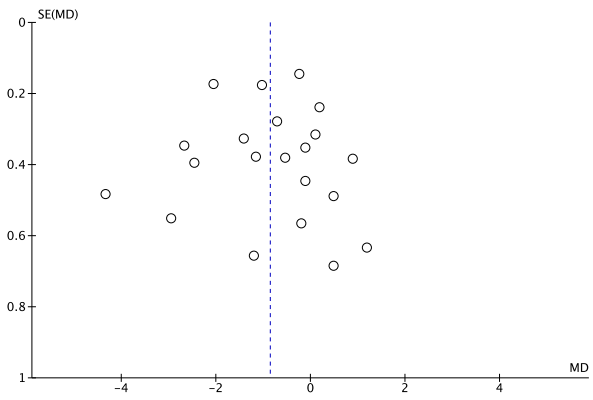
Reason of Exclusion	**Article / Year**
Reports not retrieved	Brodin 1984
	Cassidy 1992
	Kanlayanaphotporn 2010
	Hurwitz 2003
	Tamer 2016
	Abbas 2024
Single Treatment Session	Dunning 2012
	Kanlayanaphotporn 2009
	Lascurain-Aguirrebena 2018
	Lluch 2014
	Lopez-Lopez 2015
	Martinez-Segura 2006
	Snodgrass 2014
	Valera-Calero 2019
Different Research Target	Alansari 2021
	Waqas 2017
Different Study Design	Sterling 2001
	Vijayan 2022
Different Technique	Hoving 2002
	Korthals-de Bos 2003
	Groeneweg 2017
	Ali 2014
Wrong population	Bahar 2012

APPENDIX C. Risk of bias summary: review authors' judgements about each Risk of Bias item for each included study.

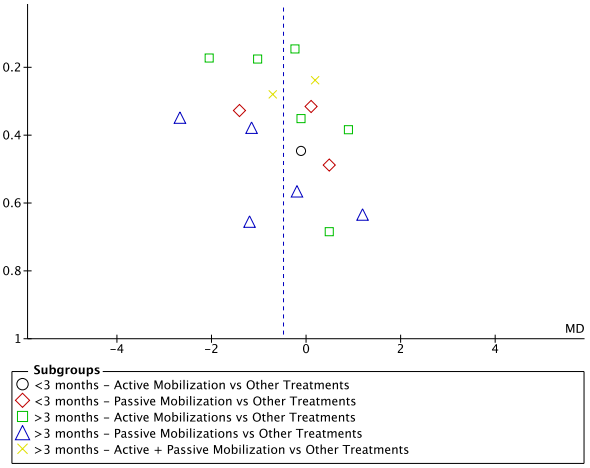


APPENDIX D. Funnel Plots of Comparisons for Pain and Disability Outcomes

Pain

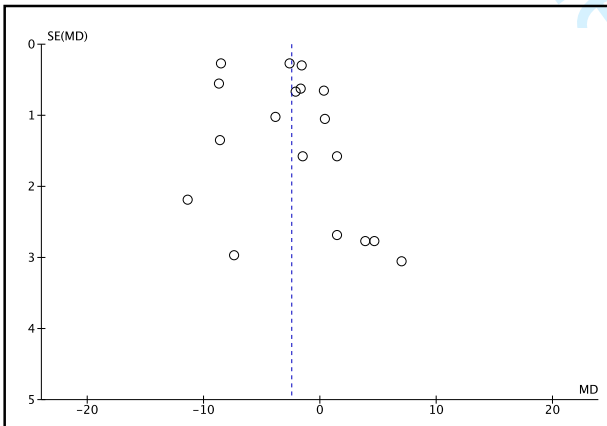


Funnel plot of comparison: 1 PAIN-Joint mobilization VS other treatment, outcome: 1.1 Pain - OVERALL.

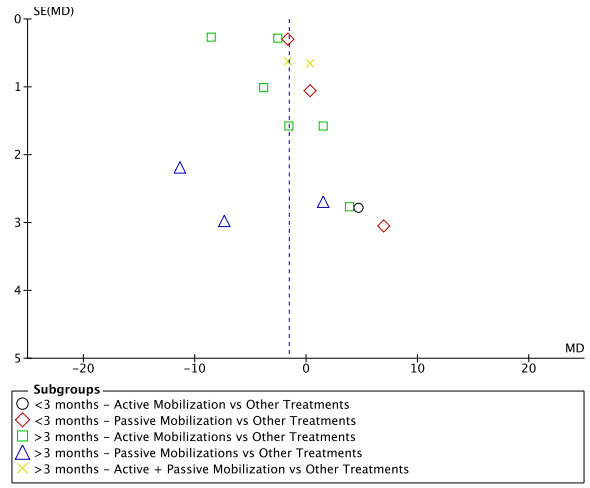


Funnel plot of comparison: 1 PAIN-Joint mobilization VS other treatment, outcome: 1.2 Pain - Subgroup Analysis.

Disability



Funnel plot of comparison: 2 DISABILITY-Joint mobilization VS other treatment, outcome: 2.1 Function - OVERALL.



Funnel plot of comparison: 2 DISABILITY-Joint mobilization VS other treatment, outcome: 2.2 Function - Subgroup Analysis.

APPENDIX E. Template for Intervention Description and Replication (TIDieR) Checklist Overview. Results were ordered by the percentage of reported outcomes.

Study / Year	TIDieR Checklist												% of reported
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**items**
Buyukturan et al. 2018	1	1	2	2	2	2	2	2	2	2	3	3	100%
Ganesh et al. 2014	100	99	100	100	100	100	99	100	100	100	100	100	100%
Ghulam et al. 2023	2	2	3	2-3	3	3	3	3	3	3	3	3	100%
Kim et al. 2015	2464	2464	2464	2464	2464	2464	2464	2464	2464	2464	2464	2464	100%
Leaver et al. 2010	1313	1313	1314	1313-1314	1313-1315	1314	1313	1314	1314	1315	1314	1315	100%
Pérez et al. 2014	216	215-216	216	216	216	216	216	216-217	216	217-218	216-217	217	100%
Shamsi et al. 2021	200	200	200-202	200-202	201	201-202	200	200-201	201	201	200	200	100%
Tabassum et al. 2024	12	11	11-12	11-12	11	12	11	12	12	12	12	12	100%
Voulgarakis et al. 2021	232	232	232-233	232-233	233	233	232-233	232-233	233	234	234	234	100%
Desai et al. 2012	9	10	12	12	9	12	9	12	N/A	14	12	13-14	91,7%
Ozlu et al. 2024	227	227	227	227	226-227	227	226	227	N/A	226	226	226-227	91,7%
Rezkallah et al. 2018	137-138	136	136-139	136-139	N/A	137-138	136	136-138	138	136	136-137	136-137	91,7%
Sun et al. 2024	2	4	4	4	3-4	4	2	3-4	3-4	N/A	2-4	2-4	91,7%
Mohamed et al. 2020	385-386	385	385-386	385-386	385	386	386	385-386	386	N/A	N/A	N/A	75%
Duymaz et al. 2018	N/A	304-305	305-306	305	305	N/A	306	N/A	N/A	N/A	N/A	N/A	41,7%
Farooq et al. 2017	N/A	25-26	26	26	26-27	N/A	27	N/A	N/A	N/A	N/A	N/A	41,7%

APPENDIX F. Raw data extracted from each study included in the systematic review

TABLE 1. Treatment Effects

Outcome	Study	Type of NSNP	Intervention	Control	Outcome measure	Gruoup	Randomized	Available	Drop out	Baseline	Post treatment	Follow up 1	Follow up 2	Follow up 3
Pain Intensity														
	Buyukturan et al. 2018	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (NAG and SNAG)	Multimodal treatment	VAS 0-10	Intervention	22	21	1	4 (2-5.5)	0			
						Control	22	19	3	5 (4-7)	2 (0-3)			
	Duymaz et al. 2018	NSNP	Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	VAS 0-100	Intervention	20	20	0	72.75 ± 15.95	14.65 ± 12.69			
						Control	20	20	0	67.95 ± 16.50	57.95 ± 17.44			
	Farooq et al. 2018	NSNP chronic	Multimodal treatment + Centrale and lateral PA glide	Multimodal treatment	VAS 0-10	Intervention	34	34	1	5.97 ± 1.78	2 ± 1.30			
						Control	34	34	2	5.56 ± 1.94	3.16 ± 1.78			
	Ganesh et al. 2014	NSNP acute, subacute	1) Therapeutic exercise + Maitland joint mobilization 2) Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	VAS 0-10	Intervention 1	26	20	6	6.7 ± 2.0	2.4 ± 1.5 (N = 24)	2.2 ± 1.3 (N = 20)		
						Intervention 2	27	20	7	5.7 ± 0.9	1.8 ± 1.1 (N = 22)	1.5 ± 1.0 (N = 20)		
						Control	27	20	7	5.9 ± 1.3	1.9 ± 1.2 (N = 20)	1.2 ± 0.8 (N = 20)		
	Ghulam et al. 2023	NSNP acute, subacute	Multimodal treatment + Central PA glide	Multimodal treatment	VAS 0-10	Intervention	15	15	0	6.53 ± 0.516	2.86 ± 0.83			
						Control	15	15	0	6.60 ± 0.507	4.26 ± 0.96			
	Kim et al. 2015	NSNP chronic	Kaltenborn joint mobilization	1) ART 2) No treatment	VAS 0-10	Intervention	8	8	0	6.2 ± 0.7	4.3 ± 1.0			
						Control 1	8	8	0	6.0 ± 0.9	3.1 ± 1.1			
						Control 2	8	8	0	6.0 ± 1.3	5.5 ± 1.2			
	Leaver et al. 2010	NSNP acute, subacute	Joint mobilization techniques of therapist's choice PASSIVE	HVLATs	NPRS 0-10	Intervention	91	88	3	5.9 ± 2.0	2.5 ± 2.2	/	1.4 ± 1.7	
						Control	91	89	2	6.1 ± 2.1	2.4 ± 2.0	/	1.6 ± 2.0	
	Mohamed et al. 2020	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	1) Multimodal treatment 2) Multimodal treatment + PRT	NPRS 0-10	Intervention	40	40	0	6.32 ± 0.8	2.12 ± 0.64			
						Control 1	40	40	0	6.27 ± 0.68	4.17 ± 0.63			
						Control 2	40	40	0	6.05 ± 0.67	3.15 ± 0.66			
	Ozlu et al. 2024	NSNP acute subacute chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	Multimodal treatment	VAS 0-10	Intervention	24	20	4	6.5 ± 1.60	0.6 ± 1.14			
						Control	22	20	2	6.65 ± 2.39	3.55 ± 2.18			
	Pérez et al. 2014	NSNP chronic	1) Lateral PA glide 2) Mulligan joint mobilization (SNAG)	HVLATs	VAS 0-10	Intervention 1	21	18	3	2.7 ± 1.9	0.8 ± 1.6 (N = 21)	0.6 ± 1.1 (N = 21)	0.6 ± 1.0 (N = 19)	0.6 ± 1.1 (N = 18)
						Intervention 2	21	16	5	2.9 ± 2.2	1.5 ± 2.3 (N = 21)	1.1 ± 1.9 (N = 21)	1.2 ± 2.0 (N = 18)	1.2 ± 1.9 (N = 16)
						Control	19	17	2	3.0 ± 1.9	1.0 ± 1.4 (N = 19)	0.9 ± 1.3 (N = 19)	0.8 ± 1.4 (N = 18)	1.0 ± 1.7 (N = 17)
	Rezkallah et al. 2018	NSNP acute subacute chronic	Therapeutic exercise + Mulligan joint mobilization (SNAG)	1) Therapeutic exercise + MFR 2) Therapeutic exercise	VAS 0-10	Intervention	25	25	0	7.73 ± 1.05	2.69 ± 0.97			
						Control 1	23	23	0	8.15 ± 1.007	3.23 ± 1.24			
						Control 2	22	22	0	7.71 ± 1.1	5.14 ± 1.35			
	Shamsi et al. 2021	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	Multimodal treatment + Ultrasound therapy	VAS 0-10	Intervention	50	50	0	6.48 ± 1.09	0.44 ± 0.60			
						Control	50	50	0	6.34 ± 1.27	0.68 ± 0.85			
	Sun et al. 2024	NSNP chronic	Therapeutic exercise + Mulligan joint self-mobilization (self-SNAG)	1) Therapeutic exercise 2) Therapeutic exercise + cervico-thoracic self-mobilizations	VAS 0-10	Intervention	10	10	0	5.70 ± 1.70	3.20 ± 0.63			
						Control 1	10	10	0	5.70 ± 2.06	3.30 ± 0.67			
						Control 2	10	10	0	5.80 ± 1.40	2.30 ± 0.82			
	Tabassum et al. 2024	NSNP chronic	Multimodal treatment + PA glide + Mulligan joint mobilization (SNAG)	1) Multimodal treatment + PIR 2) Multimodal treatment	VAS 0-10	Intervention	35	35	1	6.51 ± 1.040	4.26 ± 0.852	2.74 ± 1.039		
						Control 1	35	35	3	6.69 ± 1.207	4.06 ± 0.765	2.89 ± 1.388		
						Control 2	35	35	2	6.46 ± 1.221	4.97 ± 1.124	4.17 ± 1.150		
	Voulgarakis et al. 2021	NSNP chronic	Cervical and thoracic PA glide	1) Acupuncture* 2) No treatment	VAS 0-100	Intervention	15	15	0	59.22 ± 8.64	31.34 ± 8.78			
						Control 1	15	15	0	60.21 ± 9.28	22.25 ± 9.35			
						Control 2	15	15	0	58.72 ± 10.21	57.92 ± 10.21			
Disability														
	Buyukturan et al. 2018	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (NAG and SNAG)	Multimodal treatment	NDI 0-35	Intervention	22	21	1	18 (16-20)	5 (4-6)			
						Control	22	19	3	17 (15-18)	7 (4-8)			
	Duymaz et al. 2018	NSNP	Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	NDI 0-50	Intervention	20	20	0	15.00 ± 5.54	2.90 ± 3.12			
						Control	20	20	0	13.50 ± 5.06	11.50 ± 5.18			
	Farooq et al. 2018	NSNP chronic	Multimodal treatment + Centrale and lateral PA glide	Multimodal treatment	NDI 0-50	Intervention	34	34	1	35.57 ± 17.40	12.06 ± 8.54			
						Control	34	34	2	31.16 ± 17.59	19.39 ± 15.09			
	Ganesh et al. 2014	NSNP acute, subacute	1) Therapeutic exercise + Maitland joint mobilization 2) Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	NDI 0-50	Intervention 1	26	20	6	33.9 ± 17.7	17.2 ± 11.7 (N = 24)	13.2 ± 9.9 (N = 20)		
						Intervention 2	27	20	7	36 ± 14.7	14.9 ± 9.5 (N = 22)	9.4 ± 5.3 (N = 20)		
						Control	27	20	7	34.8 ± 11.5	10.2 ± 6.0 (N = 20)	6.7 ± 3.5 (N = 20)		
	Ghulam et al. 2023	NSNP acute, subacute	Multimodal treatment + Central PA glide	Multimodal treatment	NDI 0-50	Intervention	15	15	0	18.93 ± 0.961	14.60 ± 0.83			
						Control	15	15	0	19.40 ± 1.183	16.20 ± 0.86			
	Leaver et al. 2010	NSNP acute, subacute	Joint mobilization techniques of therapist's choice	HVLATs	NDI 0-50	Intervention	91	88	3	14.8 ± 6.6	/	6.9 ± 7.3	5.5 ± 6.6	
						Control	91	89	2	16.1 ± 8.2	/	6.5 ± 6.8	5.3 ± 6.2	
	Mohamed et al. 2020	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	1) Multimodal treatment 2) Multimodal treatment + PRT	NDI 0-50	Intervention	40	40	0	22.65 ± 1.07	10.6 ± 1.03			
						Control 1	40	40	0	22.97 ± 1.32	19.1 ± 0.9			
						Control 2	40	40	0	22.5 ± 1.22	13.17 ± 1.03			
	Ozlu et al. 2024	NSNP acute subacute chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	Multimodal treatment	NPDS	Intervention	24	20	4	54 ± 1.48	18.8 ± 1.09			
						Control	22	20	2	52.05 ± 2.03	39.35 ± 1.89			
	Pérez et al. 2014	NSNP chronic	1) Lateral PA glide 2) Mulligan joint mobilization (SNAG)	HVLATs	NDI 0-50	Intervention 1	21	18	3	16.5 ± 7.8	10.7 ± 9.4 (N = 21)	10.7 ± 9.0 (N = 21)	11.3 ± 9.6 (N = 19)	11.1 ± 8.7 (N = 18)
						Intervention 2	21	16	5	17.9 ± 7.3	13.1 ± 9.5 (N = 21)	11.1 ± 9.2 (N = 21)	10.8 ± 9.9 (N = 18)	11.1 ± 8.8 (N = 16)
						Control	19	17	2	15.0 ± 5.5	9.2 ± 5.5 (N = 19)	10.4 ± 5.9 (N = 19)	9.4 ± 8.1 (N = 18)	12.1 ± 8.1 (N = 17)

Rezkallah et al. 2018	NSNP acute subacute chronic	Therapeutic exercise + Mulligan joint mobilization (SNAG)	1) Therapeutic exercise + MFR 2) Therapeutic exercise	NDI 0-50	Intervention	25	25	0	18.95 ± 2.3	5.86 ± 1.25			
					Control 1	23	23	0	20.11 ± 1.7	7.96 ± 2.7			
					Control 2	22	22	0	19.47 ± 1.16	14.52 ± 2.04			
Shamsi et al. 2021	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	Multimodal treatment + Ultrasound therapy	NDI 0-50	Intervention	50	50	0	33.24 ± 5.96	14.48 ± 3.68			
					Control	50	50	0	31.24 ± 7.52	18.3 ± 6.23			
Sun et al. 2024	NSNP chronic	Therapeutic exercise + Mulligan joint self-mobilization (self-SNAG)	1) Therapeutic exercise 2) Therapeutic exercise + cervico-thoracic self-mobilizations	NDI 0-50	Intervention	10	10	0	0.44 ± 0.08	0.39 ± 0.05			
					Control 1	10	10	0	0.53 ± 0.14	0.42 ± 0.07			
					Control 2	10	10	0	0.45 ± 0.10	0.36 ± 0.07			
Tabassum et al. 2024	NSNP chronic	Multimodal treatment + PA glide + Mulligan joint mobilization (SNAG)	1) Multimodal treatment + PIR 2) Multimodal treatment	NDI 0-50	Intervention	35	35	1	34.06 ± 3.88	18.89 ± 2.18	10.97 ± 2.77		
					Control 1	35	35	3	33.83 ± 3.97	18.51 ± 2.47	10.37 ± 4.06		
					Control 2	35	35	2	34.06 ± 3.55	20.51 ± 2.04	16.94 ± 2.48		
Voulgarakis et al. 2021	NSNP chronic	Cervical and thoracic PA glide	1) Acupuncture* 2) No treatment	NDI 0-50	Intervention	15	15	0	27.11 ± 5.23	15.65 ± 5.61			
					Control 1	15	15	0	26.90 ± 4.25	12.11 ± 6.34			
					Control 2	15	15	0	27.01 ± 4.21	27.00 ± 6.37			
Global Perceived Effect													
Leaver et al. 2010	NSNP acute, subacute	Joint mobilization techniques of therapist's choice	HVLATs	Scale -5 to +5	Intervention	91	88	3	/	3.2 ± 1.7	/	3.4 ± 1.9	
					Control	91	89	2	/	2.9 ± 1.7	/	3.3 ± 1.7	
Pérez et al. 2014	NSNP chronic	1) Lateral PA glide 2) Mulligan joint mobilization (SNAG)	HVLATs	GROC	Intervention 1	21	18	3	/	3.8 ± 1.8	3.3 ± 2.3	3.2 ± 2.4 (N = 19)	3.3 ± 2.1 (N = 18)
					Intervention 2	21	16	5	/	3.8 ± 1.7	4.0 ± 2.7	4.2 ± 2.8 (N = 18)	4.2 ± 2.8 (N = 16)
					Control	19	17	2	/	4.0 ± 2.1	2.8 ± 2.6	3.3 ± 3.0 (N = 18)	3.3 ± 2.9 (N = 17)
Quality of Life													
Buyukturan et al. 2018	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (NAG and SNAG)	Multimodal treatment	SF-36	Intervention	22	21	1	72.4 (70.2-75.9)	88.2 (85.4-89.1)			
					Control	22	19	3	70.5 (69.2-76.7)	80.3 (78-85.5)			
Duymaz et al. 2018	NSNP	Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	NHP	Intervention	20	20	0	175.21 ± 97.95	69.89 ± 50.96			
					Control	20	20	0	152.23 ± 111.92	152.63 ± 110.31			
Leaver et al. 2010	NSNP acute, subacute	Joint mobilization techniques of therapist's choice	HVLATs	SF-12	Intervention	91	88	3	43.6 ± 7.9 (Physical) 48.9 ± 9.4 (Mental)	/	47.3 ± 7.7 (Physical) 51.5 ± 9.3 (Mental)	50.6 ± 7.8 (Physical) 52.7 ± 8.7 (Mental)	
					Control	91	89	2	42.9 ± 8.2 (Physical) 46.0 ± 11.62 (Mental)	/	47.9 ± 7.1 (Physical) 49.1 ± 8.8 (Mental)	50.2 ± 6.2 (Physical) 52.2 ± 8.9 (Mental)	
Ozlu et al. 2024	NSNP acute subacute chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	Multimodal treatment	SF-36	Intervention	24	20	4	72.5 ± 12.72 (Physical) 60.0 ± 16.97 (Mental)	78.50 ± 13.48 (Physical) 63.20 ± 16.13 (Mental)			
					Control	22	20	2	60.25 ± 25.10 (Physical) 60.40 ± 19.18 (Mental)	58 ± 23.64 (Physical) 59.7 ± 15.27 (Mental)			
Sun et al. 2024	NSNP chronic	Therapeutic exercise + Mulligan joint self-mobilization (self-SNAG)	1) Therapeutic exercise 2) Therapeutic exercise + cervico-thoracic self-mobilizations	SF-36	Intervention	10	10	0	0.12 ± 0.08 (Physical) -0.31 ± 0.04 (Mental)	0.23 ± 0.07 (Physical) -0.20 ± 0.16 (Mental)			
					Control 1	10	10	0	0.11 ± 0.10 (Physical) -0.34 ± 0.03 (Mental)	0.17 ± 0.10 (Physical) -0.31 ± 0.04 (Mental)			
					Control 2	10	10	0	0.11 ± 0.08 (Physical) -0.31 ± 0.06 (Mental)	0.26 ± 0.06 (Physical) -0.19 ± 0.16 (Mental)			
Depression													
Buyukturan et al. 2018	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (NAG and SNAG)	Multimodal treatment	BDI	Intervention	22	21	1	13 (10-14)	6 (4-8)			
					Control	22	19	3	15 (7-19)	7 (3-9)			
Duymaz et al. 2018	NSNP	Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	BDI	Intervention	20	20	0	8.85 ± 5.32	1.20 ± 1.54			
					Control	20	20	0	7.95 ± 4.85	6.90 ± 4.96			
Kinesiophobia													
Buyukturan et al. 2018	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (NAG and SNAG)	Multimodal treatment	TSK	Intervention	22	21	1	40 (39-42)	36 (35-40)			
					Control	22	19	3	41 (40-41)	38 (37-41)			

*Abbreviations: NSNP: Non Specific Neck Pain; NAG: Natural Apophyseal Glide; SNAG: Sustained Natural Apophyseal Glide; PA Glide: Posterior-Anterior Glide; ART: Active Release Technique; MFR: Myo-Fascial Release; PRT: Positional Release Technique; HVLATs: High Velocity and Low Amplitude Techniques; PIR: Post Isometric Relaxation; VAS: Visual Analogue Scale; NPRS: Numeric Pain Rating Scale; NPDS: Neck Pain and Disability Scale; SF-36: 36-items Short Form Health Survey; SF-12: 12-item Short Form Health Survey; NDI: Neck Disability Index; GROC: Global Rating of Change Scale; NHP: Nottingham Health Profile; BDI: Beck Depression Inventory; TSK: Tampa Scale of Kinesiophobia. *Control group excluded from the meta-analysis and described qualitatively*

TABLE 2. Cervical ROM Results

Study	Type of NSNP	Intervention	Control	Outcome measure	Group	Randomized	Available	Drop out	Movement direction	Baseline	Post treatment	Follow up 1	Follow up 2	Follow up 3
Buyukturan et al. 2018	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (NAG and SNAG)	Multimodal treatment	Universal goniometer (A-CROM)	Intervention	22	21	1	Flexion	35 (33.3-36.5)	46 (40.8-47.5)			
									Extension	33 (32.5-36.4)	41 (37.4-45.2)			
									Right lateral flexion	33 (30.4-38.5)	42 (40.2-48.5)			
									Left lateral flexion	34 (31.6-36.3)	40 (38.4-45.7)			
									Right rotation	45 (39.6-46.5)	52 (45.7-53.5)			
									Left rotation	35 (32.7-36.5)	48 (45.5-52.4)			
					Control	22	19	3	Flexion	34 (32.2-36.3)	41 (39.2-43.3)			
									Extension	35 (34.6-36.2)	40 (35.4-42.3)			
									Right lateral flexion	32 (30.2-33.4)	38 (35.7-39.7)			
									Left lateral flexion	32 (29.6-34.3)	37 (34.5-39.6)			
									Right rotation	42 (39.2-43.1)	45 (40.01-44.8)			
									Left rotation	39 (34.4-42.5)	42 (39.2-44.03)			
Duymaz et al. 2018	NSNP	Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	Universal goniometer	Intervention	20	20	0	Flexion	39.65 ± 9.04	59.65 ± 5.86			
									Extension	37.30 ± 3.79	49.60 ± 1.98			
									Lateral flexion	29.15 ± 5.26	38.80 ± 2.69			
									Rotation	41.40 ± 5.21	53.87 ± 1.64			
					Control	20	20	0	Flexion	44.45 ± 7.29	47.25 ± 8.68			
									Extension	40.75 ± 7.62	43.20 ± 7.40			
									Lateral flexion	31.97 ± 4.79	34.87 ± 4.37			
									Rotation	44.52 ± 5.88	46.77 ± 5.68			
Farooq et al. 2018	NSNP chronic	Multimodal treatment + Central and lateral PA glide	Multimodal treatment	Universal goniometer (A-CROM)	Intervention	34	34	1	Flexion - Extension	85.69 ± 20.04	101.08 ± 18.09			
									Lateral flexion	63.5 ± 16.85	78.65 ± 14.93			
									Rotation	120.49 ± 22.83	136.20 ± 19.06			
					Control	34	34	2	Flexion - Extension	89.33 ± 19.93	96.48 ± 22.63			
									Lateral flexion	66.82 ± 17.85	75.91 ± 20.26			
									Rotation	114.88 ± 20.53	122.74 ± 18.94			
Ganesh et al. 2014	NSNP acute, subacute	1) Therapeutic exercise + Maitland joint mobilization 2) Therapeutic exercise + Mulligan joint mobilization (SNAG)	Therapeutic exercise	Universal goniometer (A-CROM)	Intervention 1	26	20	6	Extension	34 ± 7	46 ± 6 (N = 24)	44 ± 5 (N = 20)		
									Right lateral flexion	27 ± 10	36 ± 8 (N = 24)	36 ± 7 (N = 20)		
									Left lateral flexion	28 ± 7	37 ± 7 (N = 24)	35 ± 8 (N = 20)		
									Right rotation	44 ± 11	58 ± 9 (N = 24)	58 ± 8 (N = 20)		
									Left rotation	43 ± 12	55 ± 8 (N = 24)	53 ± 7 (N = 20)		
					Intervention 2	27	20	7	Extension	31 ± 9	43 ± 6 (N = 22)	43 ± 5 (N = 20)		
									Right lateral flexion	24 ± 10	36 ± 7 (N = 22)	36 ± 8 (N = 20)		
									Left lateral flexion	24 ± 9	34 ± 8 (N = 22)	37 ± 8 (N = 20)		
									Right rotation	44 ± 8	57 ± 8 (N = 22)	55 ± 8 (N = 20)		
									Left rotation	41 ± 11	53 ± 7 (N = 22)	54 ± 7 (N = 20)		
					Control	27	20	7	Extension	35 ± 10	43 ± 5 (N = 20)	43 ± 6 (N = 20)		
									Right lateral flexion	27 ± 11	37 ± 7 (N = 20)	36 ± 9 (N = 20)		
									Left lateral flexion	29 ± 9	36 ± 7 (N = 20)	37 ± 8 (N = 20)		
									Right rotation	47 ± 9	57 ± 8 (N = 20)	57 ± 7 (N = 20)		
									Left rotation	44 ± 9	54 ± 7 (N = 20)	54 ± 7 (N = 20)		
Ghulam et al. 2023	NSNP	Multimodal treatment + Central PA glide	Multimodal treatment	Universal goniometer (A-CROM)	Intervention	15	15	0	Lateral flexion (unaffected side)	36.00 ± 1.512	38.80 ± 1.47			
					Control	15	15	0	Lateral flexion (unaffected side)	35.40 ± 1.595	38.13 ± 1.64			
Kim et al. 2015	NSNP chronic	Kaltenborn joint mobilization	1) ART 2) No treatment	Universal goniometer (P-CROM)	Intervention	8	8	0	Flexion	36.4 ± 2.5	41.5 ± 2.7			
									Extension	50.9 ± 5.7	57.9 ± 5.5			
									Right lateral flexion	38.4 ± 4.6	46.3 ± 4.8			
									Left lateral flexion	38.9 ± 5.0	45.1 ± 4.0			
									Right rotation	57.8 ± 7.6	63.6 ± 6.3			
									Left rotation	61.3 ± 5.8	67.2 ± 2.9			
					Control 1	8	8	0	Flexion	37.4 ± 12.7	48.1 ± 12.4			
									Extension	47.0 ± 7.9	54.1 ± 7.7			
									Right lateral flexion	30.5 ± 5.7	43.8 ± 5.4			
									Left lateral flexion	34.7 ± 5.4	41.9 ± 4.3			
									Right rotation	48.6 ± 6.8	57.4 ± 6.9			
									Left rotation	57.4 ± 3.4	65.6 ± 3.5			
					Control 2	8	8	0	Flexion	36.3 ± 6.2	36.3 ± 6.0			
									Extension	44.9 ± 5.5	45.4 ± 6.1			
									Right lateral flexion	39.0 ± 4.4	38.7 ± 5.5			
									Left lateral flexion	32.7 ± 5.5	32.5 ± 6.8			
									Right rotation	47.8 ± 7.0	47.6 ± 8.4			
									Left rotation	50.3 ± 9.6	48.9 ± 7.4			
Mohamed et al. 2020	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	1) Multimodal treatment 2) Multimodal treatment + PRT	Universal goniometer (A-CROM)	Intervention	40	40	0	Flexion	23.85 ± 1.14	39.32 ± 0.72			
									Extension	27.2 ± 0.99	47.27 ± 1.01			
									Right lateral flexion	26.02 ± 1.25	43.62 ± 1.27			
									Left lateral flexion	25.95 ± 1.28	44.27 ± 1.28			
									Right rotation	32.7 ± 1.2	57.97 ± 1.12			
									Left rotation	33.82 ± 0.98	58.32 ± 1.07			
					Control 1	40	40	0	Flexion	24.05 ± 1.41	32.65 ± 0.97			
									Extension	27.32 ± 1.04	36.92 ± 1.14			
									Right lateral flexion	25.45 ± 1.19	35.8 ± 1.4			
									Left lateral flexion	25.42 ± 1.23	35.07 ± 1.16			
									Right rotation	33.02 ± 1.05	46.57 ± 0.95			
									Left rotation	34.12 ± 1.15	47.85 ± 1.25			
					Control 2	40	40	0	Flexion	24.45 ± 1.2	36.2 ± 0.75			
									Extension	26.9 ± 0.92	40.77 ± 1.27			
									Right lateral flexion	25.82 ± 1.3	39.15 ± 1.07			
									Left lateral flexion	25.37 ± 1.23	38.47 ± 1.01			
									Right rotation	32.87 ± 1.04	50.52 ± 1.01			
									Left rotation	33.72 ± 1.08	51.12 ± 1.36			
Ozlu et al. 2024	NSNP acute subacute chronic	Multimodal treatment + Mulligan joint	Multimodal treatment	Universal goniometer (A-CROM)	Intervention	24	20	4	Flexion	30.95 ± 1.34	50.90 ± 1.11			
									Extension	49.75 ± 7.34	60.85 ± 15.66			
									Right lateral flexion	20 ± 7.77	31.10 ± 6.19			
									Left lateral flexion	21.25 ± 7.58	32.85 ± 7.13			
									Right rotation	63 ± 6.56	77.35 ± 6.06			

		mobilization (SNAG)							Left rotation	60.25 ± 8.65	79.10 ± 5.99		
					Control	22	20	2	Flexion	32.5 ± 1.17	34.10 ± 1.06		
									Extension	47.75 ± 12.40	49.35 ± 13.59		
									Right lateral flexion	21.50 ± 8.90	23.25 ± 10.42		
									Left lateral flexion	23.40 ± 7.61	22.65 ± 8.70		
									Right rotation	56.75 ± 10.29	57.10 ± 1.37		
									Left rotation	53.8 ± 1.41	54.6 ± 1.36		
Pérez et al. 2014	NSNP chronic	1) Lateral PA glide 2) Mulligan joint mobilization (SNAG)	HVLATs	Universal goniometer (A-CROM)	Intervention 1	21	18	3	Flexion	45.1 ± 15.4	55.7 ± 12.8 (N = 21)	54.9 ± 13.9 (N = 21)	54.6 ± 13.1 (N = 19)	55.1 ± 14.1 (N = 18)
									Extension	49.6 ± 13.8	59.4 ± 13.4 (N = 21)	53.8 ± 15.1 (N = 21)	50.7 ± 16.6 (N = 19)	51.6 ± 14.6 (N = 18)
									Lateral flexion	68.7 ± 17.2	83.1 ± 20.2 (N = 21)	77.1 ± 16.4 (N = 21)	74.9 ± 22.7 (N = 19)	75.3 ± 20.5 (N = 18)
									Rotation	119.1 ± 32.9	131.3 ± 26.3 (N = 21)	128.1 ± 27.4 (N = 21)	126.7 ± 25.4 (N = 19)	127.6 ± 23.7 (N = 18)
					Intervention 2	21	16	5	Flexion	40.0 ± 13.3	48.3 ± 13.2 (N = 21)	52.4 ± 13.9 (N = 21)	51.2 ± 16.1 (N = 18)	52.6 ± 14.1 (N = 16)
									Extension	44.4 ± 10.1	57.7 ± 11.2 (N = 21)	55.0 ± 9.7 (N = 21)	53.9 ± 10.8 (N = 18)	51.2 ± 11.2 (N = 16)
									Lateral flexion	64.4 ± 14.9	76.8 ± 16.8 (N = 21)	76.9 ± 12.7 (N = 21)	76.5 ± 11.6 (N = 18)	72.0 ± 12.3 (N = 16)
									Rotation	111.9 ± 26.0	124.5 ± 23.4 (N = 21)	126.1 ± 25.7 (N = 21)	121.7 ± 16.7 (N = 18)	121.4 ± 21.9 (N = 16)
					Control	19	17	2	Flexion	37.7 ± 11.6	50.4 ± 10.0 (N = 19)	49.2 ± 11.1 (N = 19)	52.3 ± 15.5 (N = 18)	50.9 ± 13.7 (N = 17)
									Extension	43.6 ± 21.9	63.3 ± 14.9 (N = 19)	56.6 ± 16.9 (N = 19)	54.3 ± 17.5 (N = 18)	53.9 ± 18.4 (N = 17)
									Lateral flexion	66.4 ± 19.4	78.0 ± 20.5 (N = 19)	77.1 ± 21.5 (N = 19)	70.4 ± 22.9 (N = 18)	71.4 ± 25.1 (N = 17)
									Rotation	112.8 ± 26.4	130.6 ± 30.3 (N = 19)	124.4 ± 33.9 (N = 19)	123.0 ± 36.1 (N = 18)	120.5 ± 33.9 (N = 17)
Rezkallah et al. 2018	NSNP acute subacute chronic	Therapeutic exercise + Mulligan joint mobilization (SNAG)	1) Therapeutic exercise + MFR 2) Therapeutic exercise	Universal goniometer (A-CROM)	Intervention	25	25	0	Flexion	43.56 ± 2.84	50.56 ± 2.8			
									Extension	50.6 ± 2.74	69.17 ± 2.28			
									Right lateral flexion	32.56 ± 2.04	40.56 ± 1.03			
									Left lateral flexion	32.82 ± 2.2	41.26 ± 1.21			
									Right rotation	58.21 ± 1.59	65.26 ± 1.68			
									Left rotation	56.39 ± 5.53	63.6 ± 1.61			
					Control 1	23	23	0	Flexion	42.84 ± 2.29	48.76 ± 3.7			
									Extension	51.03 ± 2.63	67.69 ± 3.88			
									Right lateral flexion	33.15 ± 1.56	39.57 ± 2.15			
									Left lateral flexion	32.65 ± 1.86	39.69 ± 2.3			
									Right rotation	57.26 ± 3.48	63.88 ± 4.5			
									Left rotation	58.92 ± 2.05	64 ± 1.76			
					Control 2	22	22	0	Flexion	43 ± 2.77	44.71 ± 2.05			
									Extension	52.19 ± 3.48	55.42 ± 3.57			
									Right lateral flexion	33.33 ± 1.27	37.04 ± 1.53			
									Left lateral flexion	33.09 ± 2.5	35.57 ± 1.63			
									Right rotation	58.42 ± 1.24	60.28 ± 1.18			
									Left rotation	57.04 ± 3.15	59.66 ± 2.97			
Shamsi et al. 2021	NSNP chronic	Multimodal treatment + Mulligan joint mobilization (SNAG)	Multimodal treatment + Ultrasound therapy	Universal goniometer (A-CROM)	Intervention	50	50	0	Flexion	22.38 ± 3.46	43.64 ± 3.95			
									Extension	23.32 ± 3.55	42.9 ± 4.42			
									Right lateral flexion	22.04 ± 3.01	36.46 ± 2.53			
									Left lateral flexion	21.82 ± 2.70	36.48 ± 2.79			
									Right rotation	43.18 ± 6.22	64.92 ± 5.21			
									Rotazione sx	43.04 ± 4.95	66.1 ± 4.91			
					Control	50	50	0	Flexion	21.48 ± 3.73	34.02 ± 3.88			
									Extension	21.04 ± 2.68	33.32 ± 3.02			
									Right lateral flexion	21.08 ± 3.32	33.66 ± 3.97			
									Left lateral flexion	20.02 ± 2.72	32.54 ± 3.68			
									Right rotation	43.01 ± 7.34	55.03 ± 7.07			
									Left rotation	40.48 ± 6.29	53.94 ± 6.14			
Sun et al. 2024	NSNP chronic	Therapeutic exercise + Mulligan joint self-mobilization (self-SNAG)	1) Therapeutic exercise 2) Therapeutic exercise + cervicothoracic self-mobilization	Universal goniometer (A-CROM)	Intervention	10	10	0	Flexion	26.76 ± 6.72	37.40 ± 5.68			
									Extension	42.40 ± 5.80	52.07 ± 3.64			
									Right lateral flexion	34.68 ± 7.75	41.31 ± 3.39			
									Left lateral flexion	34.37 ± 6.42	43.51 ± 3.53			
									Right rotation	49.03 ± 6.42	53.80 ± 3.80			
									Left rotation	42.63 ± 7.67	49.41 ± 4.34			
					Control 1	10	10	0	Flexion	26.52 ± 6.90	37.20 ± 6.22			
									Extension	39.56 ± 7.50	44.02 ± 6.89			
									Right lateral flexion	34.84 ± 8.29	38.57 ± 4.46			
									Left lateral flexion	36.27 ± 8.14	41.33 ± 4.67			
									Right rotation	50.58 ± 4.40	50.08 ± 2.51			
									Left rotation	46.32 ± 8.82	47.25 ± 6.31			
					Control 2	10	10	0	Flexion	28.70 ± 7.04	40.34 ± 3.30			
									Extension	42.40 ± 5.79	51.59 ± 4.87			
									Right lateral flexion	38.07 ± 6.11	46.11 ± 4.89			
									Left lateral flexion	37.92 ± 5.45	45.76 ± 2.47			
									Right rotation	49.23 ± 6.75	58.02 ± 6.27			
									Left rotation	42.75 ± 5.57	54.72 ± 5.61			
Tabassum et al. 2024	NSNP chronic	Multimodal treatment + PA glide + Mulligan joint mobilization (SNAG)	1) Multimodal treatment + PIR 2) Multimodal treatment	Universal goniometer (CROM)	Intervention	35	35	1	Flexion	39.89 ± 3.29	54.49 ± 3.07	56.01 ± 6.95		
									Extension	39.80 ± 3.54	56.23 ± 2.07	59.03 ± 4.26		
									Right lateral flexion	30.63 ± 2.32	41.91 ± 2.68	41.74 ± 3.28		
									Left lateral flexion	31.74 ± 2.29	42.80 ± 3.80	42.40 ± 3.72		
									Right rotation	56.46 ± 2.63	70.97 ± 5.11	71.97 ± 5.11		
									Left rotation	57.17 ± 2.54	69.09 ± 4.853	72.57 ± 4.85		
					Control 1	35	35	3	Flexion	38.53 ± 3.79	49.17 ± 4.87	58.51 ± 5.72		
									Extension	40.06 ± 3.43	47.03 ± 4.18	50.43 ± 3.58		
									Right lateral flexion	29.54 ± 2.46	40.08 ± 2.74	44.71 ± 2.91		
									Left lateral flexion	30.53 ± 2.06	40.90 ± 2.50	44.02 ± 2.47		
									Right rotation	55.26 ± 3.03	69.14 ± 5.169	75.11 ± 5.17		
									Left rotation	56.09 ± 2.41	72.26 ± 5.187	74.29 ± 5.10		
					Control 2	35	35	2	Flexion	39.57 ± 3.30	43.06 ± 2.35	47.46 ± 3.58		
									Extension	40.09 ± 3.76	44.74 ± 2.07	45.09 ± 3.06		
									Right lateral flexion	29.75 ± 2.65	37.77 ± 2.42	39.66 ± 2.89		
									Left lateral flexion	30.69 ± 2.67	36.97 ± 2.74	39.29 ± 2.57		
									Right rotation	56.43 ± 2.68	61.89 ± 3.40	63.89 ± 3.40		
									Left rotation	57.49 ± 2.33	62.20 ± 3.41	64.20 ± 3.41		

Abbreviations: NSNP: Non Specific Neck Pain; NAG: Natural Apophyseal Glide; SNAG: Sustained Natural Apophyseal Glide; PA Glide: Posterior-Anterior Glide; PIR: Post Isometric Relaxation; ART: Active Release Technique; MFR: Myo-Fascial Release; PRT: Positional Release Technique; HVLATs: High Velocity and Low Amplitude Techniques; P-CROM: Passive Cervical Range Of Motion; A-CROM: Active Cervical Range Of Motion.

APPENDIX G. Sub-group Meta-Regression Analyses, considering year of publication, sample size, mean age, active/passive treatment, acute/chronic NSNP and Risk of Bias as covariates.

Outcomes	Covariates	Coefficient [95% CI]
Pain	Year of Publication	- 0.1 [-0.4; 0.1]
	Sample size (Control)	- 0.1 [-0.2; 0.1]
	Sample size (Intervention)	0.08 [-0.1; 0.2]
	Age	- 0.1 [-0.3; 0.1]
	Acute Treatment (Yes VS No)	- 1.7 [-4.8; 1.5]
	Active Treatment (Yes VS No)	0.5 [-0.8; 1.8]
	RoB (High VS Medium VS Low)	- 1.4 [-3.5; 0.7]
Disability	Year of Publication	- 1.1 [-3.4; 1.3]
	Sample size (Control)	- 0.3 [-1.2; 0.7]
	Sample size (Intervention)	0.2 [-0.8; 1.1]
	Age	- 0.6 [-2.5; 1.2]
	Acute Treatment (Yes VS No)	- 5.5 [-47.6; 36.6]
	Active Treatment (Yes VS No)	1.6 [-11.3; 14.5]
	RoB (High VS Medium VS Low)	- 7.6 [-36.3; 20.9]

Abbreviations: CI: confidence interval; RoB: Risk Of Bias.