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Bibliographic Data	
Authors	Gross A, Langevin P, Burnie SJ, and et al.
Title	Manipulation and mobilization for neck pain contrasted against an inactive control or another active treatment.- Cochrane Review
PMID	
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Other information if relevant	

Methods	
Aim of study	To assess the effects of manipulation or mobilization alone compared with those of an inactive control or another active treatment on pain, function, disability, patient satisfaction, quality of life and global perceived effect in adults experiencing neck pain with or without radicular symptoms and cervicogenic headache (CGH) at immediate- to long-term follow-up.
Design	Meta-analyses of randomized clinical trials and quasi RCTs.

PICOS	
Population from which participants are drawn	Adults age ≥18 or older recruited from primary, secondary, or tertiary care seeking care for neck pain or recruited from the community. Included neck pain with or without radicular findings, including whiplash, myofascial pain, degenerative changes, or no specific cause or cervicogenic headache. Some disorders were excluded: myelopathies or other long tract signs, headache not originating in or dominated by neck pain.
Intervention being evaluated	- Manipulation -high velocity low amplitude directed at specific spinal segments (not necessarily cervical segments alone), and - Mobilization -low velocity, small or large amplitude passive movements, or neuromuscular techniques within the patient's range of motion and under the patient's control
Comparison or control intervention	A control such as placebo, adjunct treatment (such as infrared radiation therapy plus manipulation compared to manipulation alone), wait list or no treatment, exercise, any intervention other than manipulation/mobilization, or one technique versus another technique.
Outcomes	Primary outcomes were pain and disability, and secondary outcomes were global perceived effect, patient satisfaction, and quality of life. There were no restrictions on the types of tools used to measure these outcomes.

Study types	Published and unpublished randomized controlled trials, including trials with quasi-random allocation procedures

Study selection	
Search date of literature review	November 2014
Databases in literature search	EMBASE, MEDLINE, CENTRAL, CINAHL, ClinicalTrials.gov, Manual Alternative and Natural Therapy Index System, and the Index to Chiropractic Literature. The search also included the reference lists of eligible papers.
How authors assessed study quality (risk of bias and other considerations	Cochrane risk of bias tool using the 12 criteria recommended by the Cochrane Collaboration and the Cochrane Cervical Overview Group. A low risk of bias was defined as studies fulfilling 6 or more of the 12 internal validity criteria, and high risk met fewer than 6 criteria. GRADE (Grades of Recommendation, Assessment, Development and Evaluation) of the Cochrane Collaboration profiles were used to evaluate the overall quality of the evidence and the strength of the recommendations. Studies were not excluded on the basis of results of the risk of bias assessments.
Additional information if relevant	Estimations were made of minimum clinically important differences for pain and function/disability. The minimum clinically important (MCID) difference was 10 on a 100-point pain intensity scale. A minimum clinically important difference of 5/50 units, or 10%, to be relevant for the Neck Disability Index (NDI). For other outcomes where guidelines on the MCID were not clear, Cohen's d was used: small (0.20), medium (0.50) or large (0.80).

Results	
Number of studies screened	360 records were screened
Number of studies selected for analysis of results	51 RCTS were selected of which 39 were on manipulation and 12 on mobilization with 2910 participants analyzed and 3294 participants randomly assigned. Included studies were published between 1977 and 2013.

Whether authors elected to perform meta-analysis to pool study results statistically and type of meta-analysis done (fixed effect or random effects, heterogeneity, etc)	Results were combined in a meta-analysis using a random-effects model based on the reasonableness of pooling on clinical grounds. It is unclear what constituted substantial heterogeneity for this review and whether heterogeneity affected the decision to pool studies. However, the evidence was downgraded for inconsistency in the quality of evidence assessment for substantial heterogeneity (I^2>?). In total, 17 pooled comparisons were made, where results for more than one study were pooled and a meta-analysis was performed. For continuous outcomes, effect sizes and standard mean differences (SMD) and 95% confidence intervals (CIs) were calculated for each analysis. For dichotomous variables, risk ratios (RR) with 95% confidence intervals (CIs) were used to calculate treatment effects.
Quality of studies as assessed by authors	A total of 41% (21 of 51) of the included trials had a low risk of bias. Twenty three trials met the criteria for adequate randomization and allocation concealment. A total of 6 trials attempted to blind the outcome assessor and blinded the participants. Thirty seven trials provided adequate information about missing data and kept this below 20% for short and intermediate-term outcomes. All but 2 included RCTs were at unclear risk of bias for selective reporting. The examination of publication bias with funnel plots suggests the presence of publication bias.

Effect sizes reported for primary outcomes (mean differences, standardized mean differences, response ratios, etc)	- Only one included study in this review was at low risk of bias, moderate to high quality, contained adequate sample size, and evaluated only chronic pain (Cheung Lau 2011). Results for this study are included below. - Cheung Lau (2011) assessed the effect multiple sessions of thoracic manipulation plus infrared radiation therapy (IRR) versus IRR in the inactive control (104 participants). This study showed that thoracic manipulation with IRR reduced chronic neck pain and improved disability compared with IRR alone with statistically significant and clinically important medium effect sizes for pain (standard mean difference SMD -0.60, 95% CI -0.99 to -0.20) and disability (SMD -0.50, 95% CI -0.89 to -0.10) at 3 months follow-up. - At 3 months follow-up, the between group difference for neck pain was 1.12 points lower on the Numeric Pain Rating Scale (NPRS) favoring the thoracic manipulation group (3.29) compared to the control group (4.41). This is a clinically meaningful reduction of 11%. The between group difference for disability was 7.56 points lower on the Northwick Park Neck Disability Questionnaire (NPQ) favoring the thoracic manipulation group (27.84) compared to the control group (35.40). This is a clinically meaningful improvement of 8%. - At intermediate term (6 months) follow-up the results were similar showing a statistically significant medium effect size for chronic neck pain (SMD -0.64, 95% CI -1.04 to -0.25) and a non-significant small effect size for disability (SMD -0.38, 95% CI -0.77 to 0.01) in favor of thoracic manipulation. The between group difference for neck pain was 1.26 points lower on the NPRS favoring the thoracic manipulation group (2.98) compared to the control group (4.24). This is a clinically meaningful reduction of pain of 13%. The between group difference for disability was 6.03 points lower on the NPQ favoring the thoracic manipulation group (28.77) compared to the control group (34.8). This result does not quite meet clinical significance.
Effect sizes reported for additional outcomes (mean differences, standardized mean differences, response ratios, etc)	Thoracic manipulation improved quality of life at both the short term (SMD -0.82, -1.23 to -0.42) and intermediate term follow-up (SMD -0.61 (-1.01 to -0.22) compared to a control intervention.
Additional information if relevant –summary of results	This review provides some evidence that multiple sessions of thoracic manipulation with infrared radiation therapy produced greater reductions in chronic neck pain, and improvements in function and quality of life when compared with multiple sessions of infrared radiation therapy alone at both short- and intermediate-term follow-up.

Authors' Conclusions	
Key conclusions of study authors	- This review found support for use of thoracic manipulation versus control for chronic neck pain, function and quality of life. - This review could not rule out publication bias. - The quality of reporting of clinical trials for manipulation and mobilization has not improved in recent years. - Until the number of high-quality studies within individual subgroups of neck pain increases, we will not be able to provide strong conclusions about which groups benefit most from manipulation or mobilization. In the future, there is an urgent need for large, high quality trials to evaluate manipulation and mobilization for both chronic neck and low back pain that include more than 40 participants in each trial. - Pilot studies of mobilization and manipulation exploring the minimally effective dose and the optimal dose should be conducted before a larger trial is undertaken. These pilot studies would serve a purpose similar to that of the small dose-finding studies conducted as part of pharmaceutical trials used to establish a minimally effective dose. - More trials are required to report on adverse events if meta-analysis is to be useful for obtaining a summary estimate of minor adverse events. Reporting of serious adverse events continues to be required.
Additional information if relevant	

Comments by DOWC staff

- This review found that thoracic manipulation had a clinically important effect for chronic neck pain reduction and improved disability and quality of life compared with a minimal intervention for chronic neck pain at short term and intermediate term follow-up.
- The randomization technique was appropriate and was adequately described and allocation concealment was sufficient in the Cheung Lau study. These criteria are important for minimizing selection bias, so that treatment is applicable to the general population. Without randomization and allocation concealment, it is unclear whether groups had baseline comparability, and whether study results are applicable to the general patient population.
- The main limitation noted in this review is that only five of the 51 trials included a sample size of more than 100 participants. Many trials were extremely small (20 to 30 participants). The quality of evidence is strongly limited by the large number of small trials.
- Other limitations of this review were the low number of high quality trials and small sample sizes per comparison, outcome and follow-up period, preventing sensitivity analyses from being conducted and the high likelihood of publication bias. As unpublished studies are more likely to report negative findings, it is possible that this review's conclusions are overly optimistic.

Comments by DOWC staff

- Unfortunately, this review did not split the topic into acute and chronic neck pain and perform separate analyses as is often done in Cochrane reviews. This created a needless muddle in the analysis of the results. This review consisted mostly of trials on acute neck pain, and only one high quality trial on chronic neck pain was found and reported on.
- Some significant errors were discovered in the Cochrane apparently the result of not carefully proofreading and editing the document. On page 168 and 169, Analyses 2.11 and 2.12 are labeled as funnel plots, when they are actually forest plots. Data in forest plots do not match the text as is the case on page 182 where the second subtotal in analysis 4.13 reports a pooled SMD of -0.01 with 95% CI from -0.21 to 0.18. However, the summary of findings on the top of page 28, and the text on the left hand column of page 20 under "Function and disability", reports the pooled SMD as 0.10 with 95% CI from -0.18 to 0.37. It would have been helpful if the text referred the reader to a specific analysis, as is often done in Cochrane reviews.
- On page 10, under "Assessment of heterogeneity," the text is very confusing. The authors were not clear in specifying their criteria for when it was appropriate to combine the data across studies as pooled effect measures into a meta-analysis. It is unclear what constituted substantial heterogeneity for this review and whether heterogeneity affected the decision to pool studies. It appears that data were pooled in the presence of substantial heterogeneity. Several meta-analyses were performed that reported a high degree of heterogeneity (I^2>80%) without any qualifying statement addressing it.
- Minor or no adverse events were reported in the included trials.
- Future studies should include larger studies in order to reduce wide confidence intervals resulting in nonsignificant results. If larger studies had been included in the pooled analyses, perhaps more conclusive results would have been found.

Assessment by DOWC	
Overall assessment as suitability of evidence for the guideline ☐ High quality ☒ Adequate ☐ Inadequate	Adequate quality Cochrane supporting some evidence that multiple sessions of thoracic manipulation was more effective in reducing short- and intermediate-term chronic neck pain, and improving function and quality of life when compared with multiple sessions of an inactive control for the treatment of patients with chronic neck pain.
If inadequate, main reasons for recommending that the article not be cited as evidence	

Additional references if relevant

Cheung Lau HM, Wing Chiu TT, Lam T. The effectiveness of thoracic manipulation on patients with chronic mechanical neck pain - a randomized controlled trial. *Manual Therapy* 2011; **16**:141–7.