
Design: Systematic Review of randomized clinical trials

PICOS
- **Patient population:** Adults with acute (<1 month) to chronic (>3 months) neck pain with or without radiculopathy or cervicogenic headache.
- **Intervention:** Manual therapy, including manipulation or mobilization techniques, combined with exercise.
- **Comparison:**
  - Placebo
  - A wait list/no treatment control
  - Adjunct treatment (e.g. mobilization and exercise plus ultrasound versus ultrasound)
  - Another treatment
- **Outcomes:** Pain, function/disability, quality of life (QOL), global perceived effect (GP), and patient satisfaction
  - Short-term follow-up - closest to 4 weeks
  - Long-term follow-up – closest to 12 months
  - Outcome from different scales e.g., VAS, Northwick Park Neck Pain Questionnaire (NPQ)
- **Studies:** Randomized clinical trials(RCTs) or quasi-RCTs published as full articles in peer reviewed journals

Study search and selection:
- Databases were searched through July 2009 and included CENTRAL, MEDLINE, EMBASE, Manual Alternative and Natural Therapy, CINAHL, and the Index to Chiropractic Literature
- Reference lists and personal communication with experts in the field were also searched for relevant articles
- References identified were retrieved and assessed independently by two authors
- Methodological quality and risk of bias of each study was independently assessed by at least 2 reviewers using the criteria recommended by the Cervical Overview Group. Three quality measures were used:
  - Jadad et al.,1996 criteria (maximum score = 5, high score > 2)
  - Cochrane Back Review Group criteria (maximum score 11, high score > 5)
  - Adapted Cochrane “Risk of Bias” method using a 12 point scale, (high score = 6-12 points or low risk of bias and a low score of 1-5 points is a high risk of bias).
- Unavoidable sources of bias common to all the studies included patient blinding and clinician blinding
  - Common avoidable sources of bias were unacceptable compliance with treatment, failure to ensure that co-interventions were avoided or
similar, and failure to describe or use appropriate concealment of allocation

- Studies of high risk of bias were not excluded from the analyses
- After assessment of risk of bias, other considerations for quality of evidence were assessed using the adopted GRADE (Grading of Recommendations Assessment, Development, and Evaluation) system, which considers the consistency, directness, precision and reporting of studies
  - Quality of evidence ratings represent the judgment of the authors regarding the robustness of the results to the likely effects of new information from further research
    - High quality means that further research is very unlikely to change the confidence in the measure of effect, meaning that there is enough consistent data with sufficient precision and few biases to warrant this judgment
    - Moderate quality means that further research is likely to have an important impact on confidence in the size of the effect and may change the estimate of effect
    - Low quality evidence means that further research is very likely to have an important impact on the estimate of effect and is likely to change that estimate
    - Very low quality evidence means that there is great uncertainty about the estimate of the effect

Results:

- 17 RCTs, analyzing 1317 patients, were selected assessing manual therapy, including manipulation and mobilization, combined with exercise for adults with neck pain as multi-modal interventions
- All trials were small; no study had more than 120 patients
- The combination of manipulation, mobilization, and exercise were compared to six different control groups reporting outcomes for pain, function and disability, quality of life, global perceived effect, and patient satisfaction. The 6 control groups are:
  - 1. Mock therapy or no treatment control
  - 2. Traditional care or general practitioner care (cervical collar and analgesics)
  - 3. Exercise advice
  - 4. Other treatment
  - 5. Manipulation or mobilization
  - 6. Exercise alone
- 5 trials had a low risk of bias and 12 a high risk of bias
- Pooled treatment effects were estimated for pain, function and disability, quality of life, and global perceived effect and reported as pooled standardized mean differences (pSMD)
  - Treatment effects were reported as
- pSMD = 0.2 to 0.5 is small
- pSMD = 0.5 to 0.8 is moderate
- pSMD > 0.8 is large
  - Some treatment effects that were not pooled were reported as relative risks (RR), where a “risk” of greater than 1 signifies that the treatment is effective.

- The quality of evidence was low or very low for most outcomes
- Results from moderate and high quality evidence are summarized below:
  - There was moderate quality evidence from 2 pooled trials with 148 patients (1 with low and one with high risk of bias) that the tri-modal therapy (manipulation, mobilization, and exercise) produced greater pain relief (pSMD = 0.97, large effect size) when compared to traditional care or general practitioner care for acute whiplash pain at short term follow-up.
  - There was moderate quality evidence from 2 pooled trials with 178 patients (1 with low and one with high risk of bias) that favored the tri-modal therapy over manipulation or mobilization alone at intermediate to long-term follow-up for chronic neck pain (pSMD = 0.48, borderline moderate effect size) and quality of life (pSMD = 0.48, borderline moderate effect size).
  - There was moderate quality evidence from 2 pooled trials with 221 patients (both with low risk of bias) that showed no statistically significant difference between the tri-modal therapy over exercise alone on quality of life for intermediate to long-term follow-up for chronic or mixed duration neck pain.
  - There was high quality evidence from 3 pooled trials with 320 patients (all 3 with low risk of bias) that the tri-modal therapy (manipulation, mobilization, and exercise) produced greater pain relief (pSMD = 0.50, moderate effect size) when compared to exercise alone for neck pain of mixed duration at short term follow-up only. No evidence was found for an effect on long term neck pain.
  - There was high quality evidence from 3 pooled trials with 320 patients (all 3 with low risk of bias) that showed no statistically significant difference between the tri-modal therapy over exercise alone on function and disability at both short-term and long-term follow-up for chronic or mixed duration neck pain.

- Side effects were reported in 18% (3/17) of trials. All side effects were benign and transient and included cervical and thoracic pain, headache, radicular symptoms, and dizziness. Occurrence of serious effects of stroke could not be established.
- Four of the trials measured the costs of care. There was moderate evidence favoring reduced costs for care consisting of manual therapy and exercise for acute, subacute, and chronic mechanical neck disorder compared to general
practitioner care (cervical collar and analgesics) or other treatments such as ultrasound, nerve stimulation, etc.

**Authors’ conclusions:**

- Manipulation or mobilization and exercise produce a greater long-term improvement in pain and global perceived effect when compared to no treatment for chronic neck pain.
- Manual therapy and exercise produce greater short-term pain relief than exercise alone, but produces no long-term difference across multiple outcomes for neck pain.
- The combination of manual therapy and exercise produces greater improvements in pain, function, quality of life, and patient satisfaction when compared to manipulation or mobilization alone for chronic neck pain.
- Manipulations, mobilizations and exercise are favored over traditional care (cervical collar, analgesics, advice, etc.) for reducing pain at short-term follow-up for acute whiplash, but may be no different at long-term follow-up for neck pain of chronic or mixed duration.
- There was insufficient evidence available to draw any conclusions for neck disorder with radicular findings.

**Comments:**

- The authors conclude that manipulation, mobilization and exercise produce a greater long-term improvement in pain and global perceived effect when compared to no treatment for chronic neck pain. The effect sizes were indeed large for both pain relief (pSMD = 0.87) and global perceived effect (SMD = 2.73). However, these conclusions are based on low and very low quality evidence and we would not endorse these conclusions as an evidence statement.
- The authors correctly conclude that manual therapy and exercise produce greater short-term pain relief than exercise alone, but produces no long-term difference across multiple outcomes for neck pain. This conclusion is based on high quality evidence. In the results section of the paper, the authors incorrectly concluded that the results were similar in the long-term which fails to match the data in Table 4 and the authors’ final conclusions.
- The authors’ conclusion that the combination of manual therapy and exercise produces greater improvements in pain, (pSMD = 0.48) function (pSMD = 0.31), quality of life (pSMD = 0.48), and patient satisfaction (SMD = 0.38) when compared to manipulation or mobilization alone for chronic neck pain are all based on statistically significant pSMD and SMD effect sizes. The pooled effects for pain and quality of life (borderline moderate effect sizes) originate from moderate quality evidence and would support an evidence statement. However, the small effect sizes for function and patient satisfaction arise from low quality evidence which would not support an evidence statement.
- Manipulations, mobilizations and exercise are favored over traditional care for reducing pain at short-term follow-up for acute whiplash (moderate quality evidence), but may be no different at long-term follow-up for neck pain of chronic or mixed duration (low quality evidence).
- 70% (12/17) of the included RCTs had a high risk of bias.
- The overall state of the evidence appears to be of low quality based on the size of the trials and the difficulty of controlling bias even though some of the effects were moderate to large.
- The literature search, assessment, and the integration of the studies into the GRADE system were of high quality.
- The table of results was comprehensive and compiled all the necessary data in an easily readable format.

**Assessment:** Moderate quality systematic review incorporating limited meta-analyses that added some support for the tri-modal therapy (manipulation, mobilization, and exercise):
- Some evidence that the tri-modal therapy provides greater pain relief when compared to any of the therapies alone or traditional care (cervical collar, analgesics, advice, etc.) for neck pain of mixed duration at short-term follow-up.
- There is also some evidence that the tri-modal therapy provides greater pain relief when compared to manipulation or mobilization alone for neck pain of mixed duration at long-term follow-up.
- There is some evidence that the tri-modal therapy provides no greater pain relief when compared to exercise alone for neck pain of mixed duration at long-term follow-up.
- There is insufficient evidence to comment on the effects of the tri-modal therapy on quality of life and function/disability.