

# Effectiveness of therapeutic strategies for patients with neck pain

## Protocol for a systematic review and network meta-analysis

Qiang Gao, PhD<sup>a</sup>, Weipeng Gao, BS<sup>a</sup>, Qing Xia, MSc<sup>b</sup>, Chunyu Xie, MSc<sup>c</sup>, Jian Ma, PhD<sup>c,\*</sup>, Liangzhen Xie, MSc<sup>c,\*</sup>

### Abstract

**Background:** Neck pain is a common discomfort or more intense forms of pain in the cervical region. Neck pain has a large impact on individuals and their families, communities, healthcare systems, and businesses throughout the world. Therapeutic strategies are widely used for patients with neck pain in clinical practice, but the effectiveness of each therapeutic strategy is still unclear. The aim of this study is to assess the efficacy and safety of therapeutic strategies for neck pain.

**Method:** Seven electronic databases will be searched regardless of publication date or language. Randomized controlled trials will be included if they recruited participants with neck pain for assessing the effect of each therapy. Primary outcomes will include pain score. The risk of bias will be assessed by 2 authors using the Cochrane tool of risk of bias. Network meta-analysis in random effects model will be conducted to estimate the indirect and mixed effects of therapeutic strategies for neck pain by R-3.5.1 software. The confidence in cumulative evidence will be assessed by grading of recommendations assessment, development, and evaluation.

**Results:** This study will be to assess the effect and safety of therapeutic strategies for neck pain.

**Conclusions:** This study will assess the effect of different therapeutic strategies for neck pain and provide reliable evidence for the choice of treatments.

**Systematic review registration:** PROSPERO (CRD42019102385).

**Abbreviations:** CIs = confidence intervals, NMA = network meta-analysis, NP = neck pain.

**Keywords:** neck pain, network meta-analysis, protocol, therapeutic strategy

## 1. Introduction

Neck pain (NP) defined as discomfort or more intense forms of pain in the cervical region, is common, disabled and costly throughout the world. NP and its disability associated with NP have a large impact on individuals and their families, communities, healthcare systems, and businesses. NP has become the fourth leading cause of disability and more than 80% of individuals are affected.<sup>[1,2]</sup> From a 2010 survey in American, about 10.2 million individuals visited the physician offices and

hospitals for NP every year.<sup>[3]</sup> A higher prevalence was found in officers, computer workers, women, and middle-aged people.<sup>[4]</sup> In terms of global burden,<sup>[5]</sup> NP was ranked as the 21st, whose DALYs added up to 33.6 M in 2010. Thus, NP is still a common and serious public health problem, and effective therapeutic strategies are required for the prevention.

The safety and effective method to relieve pain is important for individuals who suffer from long-term NP. Several therapeutic strategies are used to alleviate NP and its associated disorders, including conservative therapy, alternative, and complementary medicine treatments (acupuncture, massage, traction, Yoga and exercise, etc), injection, and surgery.<sup>[1,6]</sup> Additionally, the evidence showed that the differential effectiveness of many therapeutic strategies for NP were based on subpopulations (such as age, sex, race, and stage) and therapeutic dosage was in terms of duration, intensity, and frequency.

To our knowledge, various therapeutic strategies were widely used for patients with NP in clinical practice, but the effectiveness of each therapeutic strategy was still unclear.<sup>[1,6]</sup> Although some meta-analyses had been published,<sup>[7–12]</sup> there was a lack of multiple comparisons in clinical studies so that it was more difficult to make the ideal choice. Network meta-analysis (NMA) was a way to assess the effects of more than 2 treatments for the same condition by direct and indirect comparisons.<sup>[13]</sup> Therefore, we conducted the first NMA that comprehensively integrated the eligible randomized controlled trials (RCTs). Meanwhile, we intended to assess the effect of different therapeutic strategies for NP and provide reliable evidence for the choice of treatments.

*This study is supported by the Science and Technology development project of Taian (2016NS1179).*

*This study is a protocol for network meta-analysis of therapeutic strategies for neck pain. This review will be published in a journal and disseminated in print by peer-review.*

*The authors have no conflicts of interest to disclose.*

<sup>a</sup> Taian City Central Hospital, Taian, <sup>b</sup> Heilongjiang University of Chinese Medicine,

<sup>c</sup> First Affiliated Hospital, Heilongjiang University of Chinese Medicine, Harbin, China.

\* Correspondence: Liangzhen Xie, No.26 Heping Road, Harbin 150040, China (e-mail: littleblack1984050@163.com), Jian Ma, No.26 Heping Road, Harbin 150040, China (e-mail: majian1961@163.com).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Medicine (2019) 98:11(e14890)

Received: 19 February 2019 / Accepted: 21 February 2019

<http://dx.doi.org/10.1097/MD.00000000000014890>

## 2. Methods

### 2.1. Objectives and registration

This review will be to assess the efficacy and safety of therapeutic strategies for patients with NP. This review protocol has been registered in the PROSPERO that is the International Prospective Register of Systematic Reviews (<https://www.crd.york.ac.uk/PROSPERO>), and its registered number was CRD42019102385.

### 2.2. Inclusion criteria

**2.2.1. Types of studies.** The inclusion criteria of studies will be RCTs in this systematic review regardless of publication status and language.

**2.2.2. Types of participants.** In our study, participants will be diagnosed as NP regardless of their age, sex, or race.

**2.2.3. Types of interventions.** In our study, we will evaluate the efficacy of every therapy for patients with NP in clinical practice.

**2.2.4. Types of outcome measures.** In our study, primary outcomes will include pain score. Secondary outcomes will include neck function and disability, health-related quality of life, and adverse events.

### 2.3. Search methods for the identification of studies

We will search the 7 electronic databases regardless of publication date or language, including Cochrane Library, MEDLINE, EMBASE, Chinese BioMedical Database, China National Knowledge Infrastructure, Chinese VIP Information (VIP), and Wangfang Database. We will conduct different strategies for databases based on trial terms (random, trial, group), symptom terms (neck, cervical, pain, ache), treatment terms (manual therapy, massage, traction, mobilization, acu-

puncture, collar, Yoga and exercise, training, injection, surgery, corticosteroid, nonsteroidal anti-inflammatory drugs).

### 2.4. Data collection

Two reviewers (QG and WPG) will independently assess the titles and abstracts of all articles identified from electronic databases. Full-text articles will be scanned for all potentially relevant articles. If there is any disagreement on the selection of articles, they will be discussed with the third author (LZX). Two reviewers (QG and WPG) will independently extract the relevant information based on a standard data extraction table. Information will include baseline characteristics (publication of year, author, country, and sample size), participants (age and sex), intervention and control, outcomes. A PRISMA flow chart will be used to show the whole process (Fig. 1).

### 2.5. Assessment of the risk of bias

Two reviewers (QG and WPG) will independently assess the risk of bias by the Cochrane tool of risk of bias (V.5.1.0). The following items will be assessed: random sequence generation (selection bias), allocation concealment (selection bias), blinding (performance bias and detection bias), incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other bias. The judgments of evaluated domains will include high, low and unclear. Disagreements will be resolved by discussion by arbiter (LZX).

### 2.6. Data synthesis and statistical analysis

**2.6.1. Intervention comparisons: direct.** For continuous variables, mean difference or standardized mean difference with their 95% confidence intervals (CIs) will be reported. For categorical variables, risk ratios or odds ratio with their 95% CIs

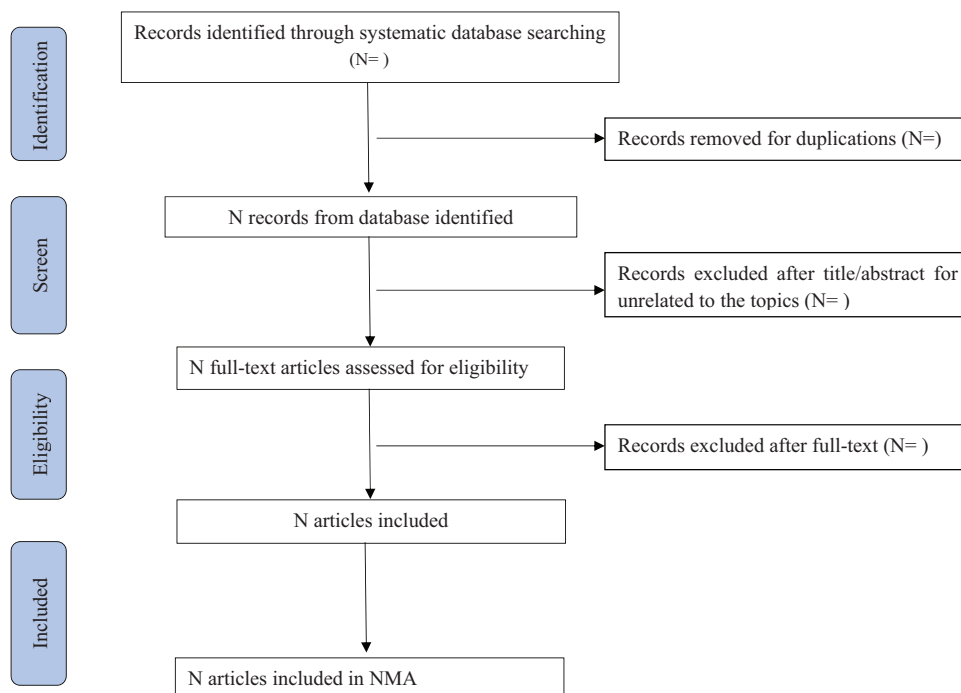


Figure 1. Flow chart of study selection.

will be summarized. Standard pairwise meta-analysis in random effects model will be conducted by R-3.5.1 software where heterogeneity of interventions permit. For insufficient or missing data, we will contact the authors by e-mail or phone as much as possible.

**2.6.2. Intervention comparisons: indirect and mixed.** NMA in random effects model will be conducted to estimate the indirect and mixed effects of therapeutic strategies for NP by package netmeta version 1.13 of R-3.5.1 software. The inconsistency between direct and indirect comparisons was assessed by node-splitting method. The rank of each treatment for different outcomes will be summarized and evaluated by surface under the cumulative ranking curve.

**2.6.3. Subgroup and sensitivity analysis.** Heterogeneity will be tested by standard Chi-squared statistic and Higgins  $I^2$  statistic. Considered of possible significant heterogeneity or inconsistency, subgroup analysis will be performed in order to explore the differences in age, sex, methodological quality, subtypes, and race/ethnicity. Additionally, if there are sufficient studies, sensitivity analysis will be performed in order to test the robustness of findings.

**2.6.4. Reporting biases.** Funnel plots will be drawn to identify whether there will be the potential for small study bias if there are sufficient studies. If there are asymmetry of funnel plots that suggest possible small study effects, the results of analysis will be explained cautiously.<sup>[14,15]</sup>

**2.6.5. Confidence in cumulative evidence.** Based on the grading of recommendations assessment, development, and evaluation, the level of evidence on outcomes will be assessed. The quality of the body of evidence will be assessed based on 5 factors, including study limitations, effect consistency, imprecision, indirectness, and publication bias. The assessments will be categorized as high, moderate, low, and very low quality.

### 3. Ethics and dissemination

Ethical approval is not appropriate, on account of this protocol for NMA. In our study, there will be no patients recruited, and no data gathered from patients. This review will be disseminated by the approach of peer-reviewed publications.

### Author contributions

LZX and JM developed the study protocol. QG and WPG developed the search strategy with the supervision of LZG. QG and WPG will scan the included studies, extract the data and assess the risk of bias. QG and QX will perform data analysis with the supervision of LZG and JM. All authors (QG, WPG, QX, CYX, JM, and LZG) will contribute to data interpretation.

QG, WPG, QX, CYX, JM, and LZG drafted and revised the manuscript. All authors have read and approved the final version of the manuscript.

**Conceptualization:** Jian Ma, Liangzhen Xie.

**Data curation:** Qiang Gao, Weipeng Gao, Qing Xia.

**Formal analysis:** Qiang Gao.

**Funding acquisition:** Qiang Gao.

**Methodology:** Weipeng Gao, Qing Xia, Liangzhen Xie.

**Software:** Qiang Gao, Weipeng Gao, Qing Xia.

**Supervision:** Jian Ma, Liangzhen Xie.

**Writing – original draft:** Qiang Gao, Weipeng Gao, Qing Xia, Chunyu Xie, Jian Ma, Liangzhen Xie.

**Writing – review and editing:** Qiang Gao, Weipeng Gao, Qing Xia, Chunyu Xie, Jian Ma, Liangzhen Xie.

### References

- [1] Cohen SP. Epidemiology, diagnosis, and treatment of neck pain. *Mayo Clin Proc* 2015;90:284–99.
- [2] Hogg-Johnson S, van der Velde G, Carroll LJ, et al. The burden and determinants of neck pain in the general population: results of the bone and joint decade 2000–2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S46–60.
- [3] Riddle DL, Schappert SM. Volume and characteristics of inpatient and ambulatory medical care for neck pain in the United States: data from three national surveys. *Spine (Phila Pa 1976)* 2007;32:132–40.
- [4] Cote P, van der Velde G, Cassidy JD, et al. The burden and determinants of neck pain in workers: results of the bone and joint decade 2000–2010 task force on neck pain and its associated disorders. *J Manipulative Physiol Ther* 2009;32(2 Suppl):S70–86.
- [5] Hoy D, March L, Woolf A, et al. The global burden of neck pain: estimates from the global burden of disease 2010 study. *Ann Rheum Dis* 2014;73:1309–15.
- [6] Blanpied PR, Gross AR, Elliott JM, et al. Neck pain: revision 2017. *J Orthop Sports Phys Ther* 2017;47:A1–83.
- [7] Bai Z, Guan Z, Fan Y, et al. The effects of qigong for adults with chronic pain: systematic review and meta-analysis. *Am J Chin Med* 2015; 43:1525–39.
- [8] Fredin K, Loras H. Manual therapy, exercise therapy or combined treatment in the management of adult neck pain – a systematic review and meta-analysis. *Musculoskelet Sci Pract* 2017;31:62–71.
- [9] Gross AR, Paquin JP, Dupont G, et al. Exercises for mechanical neck disorders: a cochrane review update. *Man Ther* 2016;24:25–45.
- [10] Monticone M, Cedraschi C, Ambrosini E, et al. Cognitive-behavioural treatment for subacute and chronic neck pain. *Cochrane Database Syst Rev* 2015;519:CD010664.
- [11] Seo SY, Lee KB, Shin JS, et al. Effectiveness of acupuncture and electroacupuncture for chronic neck pain: a systematic review and meta-analysis. *Am J Chin Med* 2017;45:1573–95.
- [12] Yang JD, Tam KW, Huang TW, et al. Intermittent cervical traction for treating neck pain: a meta-analysis of randomized controlled trials. *Spine (Phila Pa 1976)* 2017;42:959–65.
- [13] Faltinsen EG, Storebo OJ, Jakobsen JC, et al. Network meta-analysis: the highest level of medical evidence? *BMJ Evid Based Med* 2018;23:56–9.
- [14] Lau J, Ioannidis JPA, Terrin N, et al. The case of the misleading funnel plot. *BMJ (online)* 2006;333:597–600.
- [15] Sterne JA, Egger M, Smith GD. Systematic reviews in health care: Investigating and dealing with publication and other biases in meta-analysis. *BMJ* 2001;323:101–5.