BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021070
Article Type:	Research
Date Submitted by the Author:	08-Dec-2017
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Keywords:	Neck pain, Complementary Therapies, Meta-Analysis, Systematic Review

Is cupping therapy effective in neck pain patients?: a systematic review and meta-analysis

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ABSTRACT

Objectives: Neck pain is an important condition that is second only to depression as a cause of years lived with disability worldwide, which should prompt the search for effective treatment modalities. This systematic literature review aimed to investigate the effects of cupping on neck pain without limitations on language of publication.

Design: Systematic review and meta-analysis of randomised controlled trials

Setting: Nine databases, including Chinese, Korean and Japanese databases, through to July 2016 without language restriction

Participants: Neck pain patients

Interventions: Cupping therapy as the sole, or the add-on, intervention compared with no treatment or active control

Primary and secondary outcome measures: Pain severity, functional disability, and quality of life

Results: Seventeen RCTs were selected. Compared with the no intervention group, the cupping group exhibited a significant reduction in pain (standardized mean difference [SMD] -1.57 [95% CI -2.41 to -0.73]), improvement in function (SMD -0.59 [95% CI -1.01 to -0.17]), and improvement in quality of life (SMD 0.57 [95% CI 0.29 to 0.85]). Compared with active control, the cupping group reported a significant reduction in pain (P=0.0007) and significant improvement in quality of life (P=0.009). The group that received control treatment with cupping therapy (add-on group) exhibited a significant reduction in pain compared with the active control group (P=0.0004). Although the selected studies described mild side effects of cupping, none were serious.

Conclusions: Cupping was found to significantly lower pain in the no intervention, active control, and add-on comparisons. Depending on the type of control group, cupping also had significant effects on functional improvement and quality of life; however, it was difficult to draw definitive conclusions due to a low to very low quality of evidence. It is anticipated that well-designed studies in the future would be able to substantiate the effectiveness of cupping on neck pain.

Keywords: Neck pain, Complementary Therapies, Meta-Analysis, Systematic Review

ARTICLE SUMMARY

Strengths and limitations of this study

- This systematic review, investigating the efficacy of cupping in treating pain, placed no restrictions on publication language.
- Nine databases, from several countries, were searched for randomized controlled trials and included stringent inclusion and exclusion criteria.
- The analysis also addressed risk for bias, safety of cupping, and levels of evidence.
- This review may have been limited by heterogeneity across the selected studies, and low to very low levels of evidence.

INTRODUCTION

Studies analysing the 20 major causes of years lived with disability (YLD) from 2000 to 2012 worldwide reported that neck pain is the second leading cause of YLD following depression.[1] Furthermore, a Dutch study revealed that neck pain was associated with 1% of total medical expenditures and 0.1% of GDP, 77% of which were indirect medical expenses associated with absence from work or disability expenses.[2] As reported in the present review, neck pain is an important condition that directly escalates medical costs and negatively impacts productivity such as long-term absence(s) from work.

Neck pain is a common disease with a lifelong prevalence of 14.2% to 71% in adults, although these figures vary across studies.[3] The disease easily progresses to a chronic condition, with approximately 25% to 60% of patients progressing to chronic back or neck pain in the first year after onset.[4] Furthermore, neck pain is known to be most prevalent among the most active age group, particularly individuals 35 to 49 years of age, and subsides in subsequent years[5]; it is also more common in women.[3]

The standard first-line therapy for neck pain can be classified into drug and non-drug therapies. Drug therapy usually involves acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). However, acetaminophen and NSAIDs increase the risk for reduced liver function, liver failure, and haemorrhagic gastritis,[6] and these side effects may be more common when the drugs are used long-term for neck pain, which often becomes chronic. For these reasons, many studies have investigated and demonstrated the clinical efficacy of complementary and alternative medicine therapies, including acupuncture, on chronic pain such as spinal pain.[7]

Cupping is a physical treatment used by acupuncturists and other therapists that involves the use of a glass or bamboo cup to create suction on the skin over a painful area or acupuncture point. There are two types of cupping: dry and wet. Dry cupping is a technique in which cups are attached to the skin to create suction without drawing blood, whereas wet cupping is a technique in which blood is drawn before attaching the cups. Cupping therapy is used for post-stroke rehabilitation and hypertension, and has been reported to be effective for pain and musculoskeletal disorders.[8-10] In particular, cupping is a highly popular insurance-covered therapy in South Korea; insurance claims for cupping reached 215,079,729,000 won in 2013 alone.[11] Studies reporting the effects of cupping on neck pain include a systematic literature review published by Yuan et al. in 2015, which reported that cupping is effective in reducing pain and improving function(s) in chronic neck pain.[12] However, that systematic review searched articles published in or before 2013 and, because new clinical trials investigating cupping on neck pain have been published since, a new systematic review on the topic is needed. Moreover, Yuan et al[12] restricted the publication language of the articles. To review a more diverse pool of articles before drawing conclusions, however, the present review, in contrast, did not place any restrictions on language.

METHODS

The protocol of this systematic literature review was registered in the PROSPERO International prospective register of systematic reviews (CRD42016047218). This review was performed and reported in adherence with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA).[13]

Literature search

Studies that used cupping as the intervention for neck pain were searched in the Ovid-Medline (1946 to July 2016), Ovid-EMBASE (1980 to July 2016), Ovid-AMED (1985 to July 2016), and the Cochrane Central

Register of Controlled Trials (CENTRAL) to July 22, 2016. The Chinese database China National Knowledge Infrastructure (CNKI), Korean databases OASIS and NDSL, and Japanese databases J-stage and ISHUSHI, were also used. Search terms included a combination of MeSH terms such as neck pain (e.g., Neck pain, cervical spondylosis, cervical radiculopathy, cervical disc herniation, and myofascial pain syndrome) and cupping. Details of the search strategy are presented in Appendix 1. Importantly, there were no language restrictions.

Study inclusion and exclusion

Two or more investigators (YJL, SYK, and/or YMK) independently selected articles for analysis from the searched articles. After excluding duplicate publications, titles and abstracts were reviewed to primarily screen out articles according to the inclusion and exclusion criteria. The full texts of these articles were then reviewed to again secondarily screen out articles per the inclusion and exclusion criteria. Only randomized controlled clinical trials (RCTs) were considered. Any disagreement in the study selection process was resolved by discussion and, when an agreement was not reached, a third investigator intervened to reach consensus. Publication language of the study was not restricted. Subjects included adult patients with neck pain, including neck pain with neuropathy, without discriminating between acute and chronic. However, post-traumatic pain caused by whiplash or sports injuries was excluded because the natural history of neck pain may differ in such cases. Furthermore, patients with myelopathy or cervical headache/vertigo without neck pain were also excluded. All types of cupping therapies were included without restrictions dry or wet cupping; the type of cupping devices were also not restricted. Control groups included patients who underwent usual care for neck pain, such as physical therapy, NSAIDs, heat pad therapy, and acupuncture, as well as inactive controls, such as waitlist or no intervention groups. The outcome variables to assess the efficacy of cupping were pain intensity, neck disability index, and quality of life (QoL). Pain intensity was measured using a visual analogue scale (VAS), the McGill Pain Questionnaire, the Northwick Park Neck Pain Questionnaire (NPQ). The Neck Disability Index (NDI) was generally used to measure neck functional disability. QoL was assessed using the 36-item Short-form (SF-36) and EQ5D questionnaires. However, studies that did not use objective instruments and only reported outcomes in terms of improvement rates without a standard, or investigations that used an instrument without verified reliability and validity, were excluded.

Risk for bias evaluation and data extraction

Risk for bias in the RCTs was assessed according to seven categories per the Cochrane Risk of Bias. Studies that used appropriate methods for each item and specified the methods in the text were considered to have a low risk for bias; studies that did not perform or used inappropriate methods were considered to have a high risk for bias; and studies that did not mention or used ambiguous expressions were considered to have an unclear risk for bias. Two or more investigators independently assessed all research data, and disagreements were resolved by discussion. When an agreement could not be reached, a third investigator intervened to reach consensus. Two reviewers independently read the full text of all articles and extracted data according to a pre-determined format. Any disagreements were resolved by discussion between the two reviewers.

Data analysis

A meta-analysis was performed using the quantitative data from each study to assess the efficacy of cupping. The standardized mean difference (SMD) and 95% confidence interval (CI) were calculated using the Cochrane Collaboration software (Review Manager [RevMan] version 5.3, Copenhagen: The Nordic Cochrane Centre) for Windows (Microsoft Corporation, Redmond, WA USA). Heterogeneity across studies was assessed using the χ^2 (chi-squared) test with a significance of $P<0.10$ and the I^2 statistic. When heterogeneity was statistically significant, the cause of heterogeneity was analysed through subgroup analysis. A random effect model was applied, and publication bias was not assessed when the number of studies in the group was < 10.

Quality of evidence

The quality of evidence for each outcome was assessed in accordance with the Grading of Recommendations, Assessment, Development and Evaluation (GRADE). Quality of evidence was classified into high, moderate, low, or very low. To determine the quality of evidence, the following domains were assessed according to the standards suggested by the GRADE group: risk for bias; imprecision; inconsistency; indirectness; publication bias; large magnitude of effect; dose-response; and confounding.[14]

RESULTS

Search results

A total of 1861 articles were retrieved, including 53 from Ovid-Medline, 123 from Ovid-EMBASE, 17 from Ovid-AMED, 37 from the Cochrane Library, and 157 from a Chinese database. After the first and second round of screening, a total of 17 articles were selected for review. Search results are shown in Figure 1.

Features of the included studies

A total of 17 studies were analysed in two separate analyses: direct comparison of the cupping (sole) and control groups; and an add-on analysis comparing the cupping with control group with the control group. Two studies used three groups; 11 studies were included in the sole analysis while eight studies were included in the add-on analysis.

Seven of the 17 studies used wet cupping while nine used dry cupping; the remaining study mainly used dry cupping but also used wet cupping. The frequency of cupping therapy varied greatly. Two studies performed only one round of therapy, and four performed two to three rounds. The majority of studies performed >10 rounds of therapy because most treated patients had neck pain with radiculopathy or chronic neck pain. The site of therapy was mostly the upper shoulder and neck area, primarily on the ashi acupoint or other acupoints in proximity. Because these studies treated pain, most presented pain scores in the form of a VAS; disability was presented in NDI, while QoL was mostly reflected in the responses to the EQ-5D and SF-36 questionnaires. The features of each study are presented in Table 1.

Risk for bias assessment

Random sequence: Seven of the 17 studies[15-21] were assessed to have a low risk for bias because they randomly allocated the subjects using a table of random numbers. The remaining 10 studies, however, only mentioned randomly assigning subjects without specifying the method used for randomization; thus, these studies were assessed to have an unclear risk for bias. The results are shown in Figure 2.

Allocation concealment: Eight studies[15 17-19 21-24] concealed allocation using a sealed envelope and, thus, were

assessed to have a low risk for bias. The remaining studies were determined to be unclear because they did not describe the method of allocation concealment used.

Blinding: Control groups were either wait control or active controls. There was one study that included sham cupping;[25] however, blinding is practically difficult, given that sham cupping is generally not used. Chi et al[22] described single blinding; however, it was difficult to conclude whether blinding was actually implemented. Hence, all studies were considered to not have blinded their investigators and/or participants. With regard to the blinding of participants and personnel, all studies were assessed to have a high risk for bias. Similarly, blinding of outcome assessment was not performed in most studies because many used VAS for pain measurement and used patient-reported outcomes. Blinding could have been feasible if the studies used an outcome variable measured by the examiner; however, such studies were lacking. Therefore, all studies were assessed to have high risk for bias.

Incomplete outcome data: Five studies[15 17 18 23 24] reported the number of excluded and withdrawn participants, and the number of participants included in the final analysis. It was decided that the number of withdrawn participants and the reason for withdrawal were not a cause of bias; therefore, these studies were assessed to have low risk for bias. The remaining studies were determined to be unclear for not mentioning the number of participants who withdrew or were excluded.

Selective reporting: Ten of the 17 studies were determined to have an unclear risk for bias due to selective reporting because they did not describe adverse events and did not registered their protocols. The remaining seven studies[15 17 18 20 22-24] were found to have reported all of the outcome variables they initially had attempted to investigate and, thus, were determined to have a low risk for bias.

Other biases: All studies were assessed to have low risk for other biases.

Analysis

Cupping versus no treatment

Pain: Four studies[22-24 26] were included in the meta-analysis. Compared with the no intervention group, the cupping group reported a significant reduction in pain, with an SMD of -1.57 (95% CI -2.41 to -0.73). Notable heterogeneity was observed (I^2=84%; P=0.0002 [chi-square test]); however, the direction of efficacy of was consistent.

Disability: Two studies were included in the analysis. The results revealed that the cupping group reported significant functional improvement compared with the no intervention group, with an SMD of -0.59 (95% CI -1.01 to -0.17; I^2=0%; P=0.006).

QoL: Two studies were included in the analysis, and results revealed that the cupping group reported a significant improvement in QoL, with an SMD of 0.53 (95% CI 0.11 to 0.95; I^2=0%; P=0.01) (Figure 3).

Cupping versus active control

Pain: Seven studies were included in the analysis. Compared with the control group, the cupping group exhibited a significant reduction in pain, with an SMD of -0.42 (95% CI -0.66 to -0.18; P=0.0007). A chi-square test, however, revealed some heterogeneity (p=0.09; I^2 =46%), but not to a notable degree.

Disability: Four studies were included in the analysis. Compared with control, the cupping group demonstrated functional improvement, with an SMD of -0.50 (95% CI -1.06 to 0.06; P=0.08), but not to a statistically significant degree, and heterogeneity was high (I^2=75%; P=0.007).

QoL: Two studies were included in this analysis. Compared with control, the cupping group reported a significant improvement in quality of life, with an SMD of 0.61 (95% CI 0.15 to 1.07; P=0.009) (Figure 4).

Cupping with active control versus active control (add-on)

Pain: Eight studies were included in the analysis. When analysed comprehensively, adding cupping therapy to the treatment given to the control group led to a significant reduction in pain, with an SMD of -0.78 (95% CI -1.21 to -0.34; P=0.0004). However, notable heterogeneity was observed; therefore, a subgroup analysis was performed for each type of cupping therapy. For dry cupping therapy, efficacy demonstrated an SMD -0.61 (95% CI -0.79 to -0.43, P<0.00001), with a heterogeneity of I^2=0%, P=0.92. On the other hand, wet cupping therapy led to a significant reduction in pain, with an SMD of -0.96 (95% CI -1.84 to -0.08, P=0.03); however, heterogeneity was persistent in the wet cupping group (I^2=93%; P<0.00001).

Disability: Only one study reported a disability-related outcome, and the effect on disability was not significant, with an SMD of 0.25 (95% CI -0.28 to 0.77; P=0.36) (Figure 5).

Safety of cupping

Ten of the 17 studies included in the final analysis did not address safety, while seven studies did. First, Kim et al[17] reported one case of skin laceration, one case of whole body itching, one case of pain at the cupping sites, and one case of generalized body ache in four patients in the cupping group; however, the study reported that the symptoms were mild and resolved within a few days. Lauche et al (2012)[24] reported one case of pain during the procedure itself in addition to tension headache, migraine, tinnitus, and wound healing itches; however, all side effects were mild and temporary. Chi et al[22] reported two cases of mild low back pain due to the seated position in the cupping group. Lauche et al (2013)[18] reported one case of muscular tension, one case of increased pain, and one case of prolapsed intervertebral disc, while Lauche et al (2011)[23] reported one case of tingling sensation in the hands and arms, two cases of strain/pain at the treated area, one case of strain/pain in their general neck region, one case of slight headache, one case of tiredness, one case of shivering attack, and one case of blurred vision. Yin et al[20] reported one case of delayed wound healing due to wet cupping. Cramer et al[15] reported two cases of muscle soreness, one case of minor hematoma, and two cases of increased neck pain for 1 h to 5 h. None of the reported side effects caused by cupping were serious in nature.

Levels of evidence

The quality of evidence in each analysis is shown in Table 2. In the waitlist comparison, the quality of evidence for the outcomes of pain, QoL, and disability was assessed to be low due to concerns over risk for bias and imprecision domain. In the active control comparison, the quality of evidence for the outcomes of pain and QoL was low in consideration of a risk for bias and imprecision, and that for disability was assessed to be very low due to a risk for bias, imprecision, and unexplained heterogeneity. In the add-on comparison between the active control group and active control with cupping group, the quality of evidence for pain for the dry cupping add-on group was low due to a risk for bias and unexplained heterogeneity. The quality of evidence for pain outcomes for the wet cupping add-on group was very low. The quality of evidence for disability outcomes for the add-on groups was low due to a risk for bias and imprecision (Table 2).

DISCUSSION

The present study aimed to reveal evidence supporting the efficacy of cupping on neck pain through a systematic literature review. We performed a systematic and wide search in non-Asian as well as Asian databases, including those from China, Korea, and Japan, where cupping is popular. Seventeen articles were selected and were analysed according to the type of control group(s) used. When compared with an inactive control, cupping significantly reduced pain, improved function(s), and improved QoL. Although heterogeneity was quite high in terms of pain reduction, we did not lower the quality of evidence because the direction of effects was consistent across all studies. When compared with an active control, the cupping group exhibited a significant reduction in pain but no significant differences in functional improvement. The quality of evidence was found to be low or very low in most studies; however, the marked reduction in pain, functional improvement, and improvement in QoL associated with cupping compared with no intervention may be clinically relevant. Notable heterogeneity was observed for pain outcomes in the comparison between the cupping and no intervention groups. The direction of effects was consistent, which suggests that the heterogeneity was a result of the size of the effect, which we speculate to be caused by differences in operator cupping proficiency and patients' pain severity. When compared with an active control group receiving various therapies, cupping significantly reduced pain but did not demonstrate significant differences in functional improvement. When added on to existing treatment, cupping significantly reduced pain, with an SMD of -0.78 (95% CI -1.21 to -0.34). However, heterogeneity was high; therefore, we performed a subgroup analysis. Effect sizes were similar across studies using dry cupping; however, effect sizes varied greatly across studies using wet cupping. Additional analysis is needed to substantiate whether the differences are caused by differences in various types of wet cupping procedures or whether other factors are in play. Wet cupping involves drawing blood before cupping, and may be well accepted by some cultures, but cause fear in others. Furthermore, the intensity of the procedure and the amount of bleeding may also affect outcome, which may have contributed to the varying effect sizes. However, the type and frequency of the procedure, and patients' pain severity may have also led to the varying effect sizes.

This study had several limitations. One significant shortcoming was that only some studies reported issues related to safety. Although severe adverse events were not found in association with cupping in the studies that reported side effects, there were a greater number of studies that did not report side effects, which should prompt well-designed, large-scale study to investigate the side effects of cupping. A systematic review investigating the side effects of cupping reported that the most common side effect was scar formation and there were some cases of severe side effects.[27] However, adverse reactions to cupping may vary according to the proficiency of the practitioner, type of procedure, and disinfection and sterilization during the procedure.[27] Another limitation was that the quality of evidence was either low or very low for all outcomes. The primary causes of the low quality of evidence were risk for bias and unexplained heterogeneity. The quality of evidence for random sequence and allocation concealment could have not been lowered if the studies were performed correctly; however, the selected studies did not maintain meticulous procedures regarding these issues. Nevertheless, cupping is an invaluable therapy that anyone properly trained can use easily. Lauche et al (2013)[18] performed a clinical trial on home-based cupping. Due to the growing use of computers and smartphones, neck pain has become quite common[28] and readily becomes chronic. The findings of our study are meaningful because it represents a non-

invasive, simple, and effective treatment modality for patients with chronic pain.

In traditional Chinese medicine, cupping has been popularly used to eliminate stagnated qi and blood, and to facilitate circulation.[29] Since ancient times, cupping has been deemed to be effective on local areas of inflammation.[30] A review of various studies related to the mechanism of cupping reveals that cupping exerts its effects via a haemodynamic mechanism that facilitates muscle function, as demonstrated by the reduction of deoxy-haemoglobin and elevated oxy-haemoglobin levels in muscle areas treated with cupping.[31] In other studies, cupping was reported to be involved in a mechanism for removing oxidative stress,[32] and that cupping produces therapeutic effects through diffuse noxious inhibitory control,[33] which would have contributed to the elimination of pain.

For these reasons, a growing number of clinical trials are investigating the effects of cupping on pain and disease. In a systematic literature review of the efficacy of cupping in lower back pain, cupping led to significant reductions in pain and improvement of function.[12] A recent systematic review investigated cupping in relation to overall disease;[34] however, the review only included some articles about neck pain and did not specifically discuss neck pain. Furthermore, there was a study that examined the effect of cupping on neck pain, but the study was published in 2013[12]. In this context, our study, which analysed more recent evidence of the effects of cupping on neck pain without a language restriction, is meaningful.

A new clinical trial that was not included in the present analysis was published recently.[35] Due to the publication date settings in our search, the results of our analysis including this particular study[35] were not presented in our results. However, when the study was included in our analysis, the statistical significance of the pain and functional improvement in the cupping group against the no intervention group were not altered (pain: SMD -1.37 [95% CI -2.11 to -0.62], disability: SMD -0.63 [95% CI -0.97 to -0.28]), and only the QoL outcome became statistically insignificant (SMD 0.33 [95% CI -0.08 to 0.73]).

Cupping has been found to be effective compared with no treatment and to conventional treatment. In particular, adding cupping therapy to conventional treatment led to a more significant reduction in pain, suggesting that adjunctive cupping therapy would produce the best outcome. Although we did not find notable adverse events in the articles we reviewed in this study, cupping is not without side effects, and a large-scale study is needed to thoroughly examine cupping side effects. Furthermore, wet cupping requires thorough hygiene education and precautions during the procedure because it induces bleeding during the procedure. A well designed large-scale clinical trial using a standardized procedure is still needed. Nevertheless, our study is meaningful in that it sheds light on the promising nature of cupping as a safe and effective treatment for neck pain.

CONCLUSION

Cupping was found to significantly reduce neck pain compared with an inactive control group and active control group receiving standard medical care. Cupping may be an effective non-invasive treatment for neck pain, which is becoming more prevalent among younger patients and may induce disability when it becomes chronic. However, additional well-designed studies are needed to draw definitive conclusions.

FOOTNOTES

Contributors: SK, MRK, IHH, and YJL designed the study. SK and YJL conducted the systematic search. SK, MRK, and YJL assessed the literatures for inclusion and extracted the data. JL, JSS, and IHH monitored data collection. EJK, DSH, JL, JSS, and IHH interpreted the data. SK, MRK, IHH, and YJL wrote the draft; EJK, DSH, JL, and JSS critically revised the manuscript. All authors have read and approved the final version.

Funding: This study was supported by the Traditional Korean Medicine R&D Program funded by the Ministry of Health & Welfare through the Korea Health Industry Development Institute (KHIDI) (HB16C0035).

Competing Interests: None declared

Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: No additional data are available.

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Table 1. Characteristics of the included studies

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relavent Outcomes (Primary/secondary)
Cupping vs Control (Sole)										
Vs waitlist (no intervention)										
Arslan 2015	Turkey	computer users diagnosed minimum 3 neck pain	EG: 20, CG: 20	EG: 26.0±3.5, CG: 26.0±3.8	Dry cupping (moving)	no intervention	upper shoulder and neck region	10	After treatment	VAS
Chi 2016	Taiwan	work-related chronic neck shoulder pain	EG: 30, CG: 30	EG: 43.6±6.3, CG: 42.5±5.8	Dry cupping	no intervention	SI15, GB21, LI15	1	After treatment	VAS
Lauche 2011	Germany	chronic nonspecific neck pain	EG: 22, CG: 24	EG: 26.1±4.2 CG: 25.1±3.0	Dry cupping	Waiting list control group	descending and transverse parts of the trapezius muscle	5	After treatment	VAS, NDI, SF-36
Lauche 2012	Germany	chronic nonspecific neck pain	EG: 22, CG: 23	EG: 54.8±3.2 CG: 29.3±2.9	Wet cupping	Waiting list control group	descending parts of the trapezius muscle	1	Post-cupping after 3 days	VAS, NDI, SF-36
Vs active control										
Liu 2016	China	cervical spondylosis	EG: 20, CG: 20	NR	Wet cupping	Tuina	GV14, Ashi points	3	After treatment	VAS, effective rate, tenderness
Mou 2015*	China (Multi center)	cervical radiculopathy	EG: 68, CG: 56	EG: 46.4±11.6 CG: 47.8±11.9	Wet cupping	MA	GV14, GB21	4-12	After treatment	VAS, NDI, CAS
Yin 2009	China	cervical spondylosis	EG: 56 CG: 55	EG: 32.13±7.87 CG: 35.24±6.67	Wet cupping	MA	EX-B2,BL11, GB21, Ashi points	10	After treatment	VAS, effective rate
Cramer 2011	Germany	nonspecific neck pain for at least the previous 3 months	EG: 24 CG: 24	EG: 44.46 CG: 47.88	Dry cupping	Standard Medical Care	Neck and shoulder lesion	3-4	After treatment	VAS, NDI, SF-36
Kim 2012	Korea	VDT workers with neck pain	EG: 20 CG: 20	EG : 25.5 (median) CG : 28 (median)	Dry and wet cupping	Heating pad group	GV14, GV16, GV15, GV12, GB20, GB21, LI17, SI11, SI12, SI13, SI14, SI15, BL10, BL11, BL12, BL13, BL14, BL15, BL16, BL17, BL41, BL42, BL43, BL44, EX-HN15	6	7 weeks	NRS, NDI, EQ-5D
Lauche 2013	Germany	chronic nonspecific neck pain	EG: 30 CG: 31	EG: 54.5±12.3 CG: 53.7±13.4	Dry cupping	progressive muscle relaxation(PMR)	NR	24	12 weeks	VAS, NDI, SF-36

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relavent Outcomes (Primary/secondary)
Sui 2008*	China	cervical radiculopathy	EG: 120, CG: 120	NR	Dry cupping (moving)	traction	Acupoints at Bladder Meridian and Governor Vessel	20	After treatment	VAS
Cupping with usual care vs usual care (Add-on)										
Dry cupping										
Cai 2015	China	Chronic neck pain	EG: 60 CG: 60	EG: 45.48±10.9 CG: 45.7±11.1	Dry cupping	MA	EX-B2	12	After treatment	SF-MPQ
Su 2016	China	Neck pain after sleeping	EG:29 CG:29	EG: 30.72±6.69 CG: 31.76±7.16	Dry cupping	MA	upper shoulder and neck region	3	After treatment	VAS, effective rate
Sui 2008*	China	cervical radiculopathy	EG: 120, CG: 120	NR	Dry cupping (moving)+traction	traction	Acupoints at Bladder Meridian and Governor Vessel	20	After treatment	VAS
Yang 2011	China	cervical radiculopathy	EG: 30 CG: 30	NR	dry cupping+MA	MA	Ashi points, GV14, GB21, SI14, SI11, LI15	10	After treatment	VAS, effective rate
Wet cupping										
Cheng 2012	China	cervical spondylosis	EG: 30 CG: 30	NR	wet cupping+EA	EA	Ashi points nearby GV14	2-3	After treatment	VAS, effective rate
Jin 2014	China	neck type cervical spondylosis	EG: 33 CG: 33	EG: 31.81±8.30 CG: 30.48±9.74	wet cupping+MA	MA	upper shoulder and neck region	5	After treatment	VAS, NPQ, effective rate
Mou 2015*	China (Multicenter)	cervical radiculopathy	EG: 59, CG: 56	EG: 45.4±11.6 CG: 47.8±11.9	wet cupping+MA	MA	EX-B2, BL11, GB21, Ashi points	10	After treatment	VAS, NDI, CAS
Zhou 2014	China	Cervical Spondylopathy	EG:100 CG:100	NR	Wet cupping+MA	MA	Ashi points, EX-B2, GB21	10	After treatment	VAS , effective rate

EG: experimental group, CG: control group, EA: electroacupuncture, MA: manual acupuncture, NR: not reported, VAS: Visual Analogue Scale, NDI: Neck Disability Index, EQ-5D: Euroqol5-D health utility, SF-36: 36-Item Short Form Health Survey, SF-MPQ: Short Form McGill Pain Questionnaire, NPQ: Neck Pain Questionnaire, CAS: Clinical assessment scale, VDT: Video Display Terminal, SD: Standard deviation

*The study is a three-armed study, i.e. cupping group, control group, cupping plus control group.

Table 2. Meta-analysis of outcomes and level of evidence

Variable	Overall effect						Studies (N)	Sample size (N)	Level of evidence
	SMD	95% CI	*P*	I^2	P	Statistical method			
Cupping versus Waitlist (Sole)									
Pain (VAS)	-1.57	-2.41, -0.73	0.0002	84	0.0003	Random Inverse Variance	4	191	Low
Disability (NDI)	-0.59	-1.01, -0.17	0.005	0	0.32	Random Inverse Variance	2	91	Low
QoL (SF-36)	0.53	0.11, 0.95	0.01	0	0.99	Random Inverse Variance	2	91	Low
Cupping versus Active control (Sole)									
Pain (VAS)	-0.42	-0.66, -0.18	0.0007	46	0.09	Random Inverse Variance	7	604	Low
Disability (NDI)	-0.50	-1.06, 0.06	0.08	75	0.007	Random Inverse Variance	4	213	Very low
QoL (SF-36)	0.61	0.15, 1.07	0.009	109	0.23	Random Inverse Variance	2	109	Low
Cupping with active control vs control (addon)									
Pain (VAS) with dry cupping	-0.61	-0.79, -0.43	<0.00001	0	0.92	Random Inverse Variance	4	478	Low
Pain (VAS) With wet cupping	-0.96	-1.84, -0.08	0.03	93	<0.00001	Random Inverse Variance	4	382	Very low
Disability (NDI)	0.25	-0.28, 0.77	0.36	-	-	Random Inverse Variance	1	56	Low

VAS: Visual analogue scale, NDI: Neck disability index, QoL: Quality of life, SMD: Standardized mean difference

FIGURE LEGENDS

Figure 1. PRISMA flow diagram of the literature search

Figure 2. Risk of bias in the included studies, as assessed using the Cochrane Collaboration's risk of bias tool

+: high risk of bias, ?: unclear risk of bias, -: low risk of bias

Figure 3. Forest plots demonstrating the effect of cupping as the sole intervention vs no treatment on neck pain

CI: confidence interval

Figure 4. Forest plots demonstrating the effect of cupping as the sole intervention vs active control on neck pain

CI: confidence interval

Figure 5. Forest plots demonstrating the effect of cupping as the add-on intervention on neck pain

CI: confidence interval

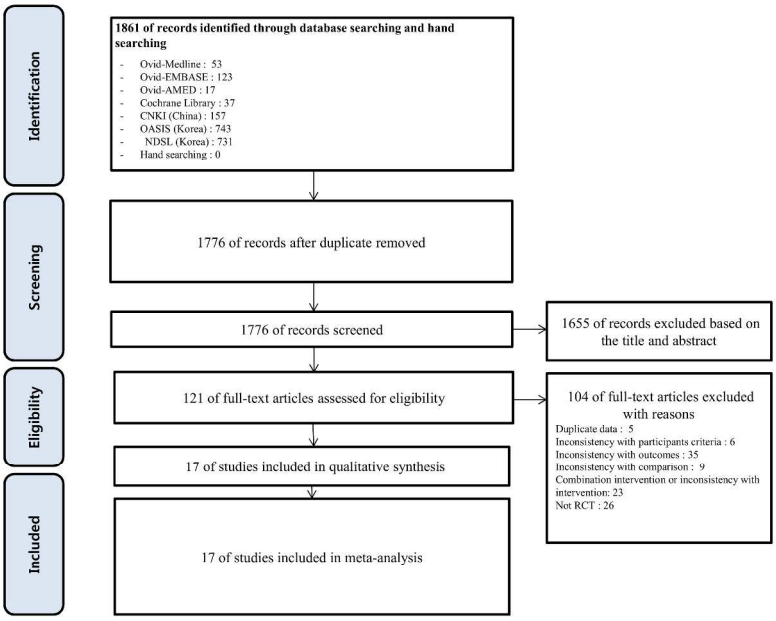

Figure 1. PRISMA flow diagram of the literature search

297x209mm (300 x 300 DPI)

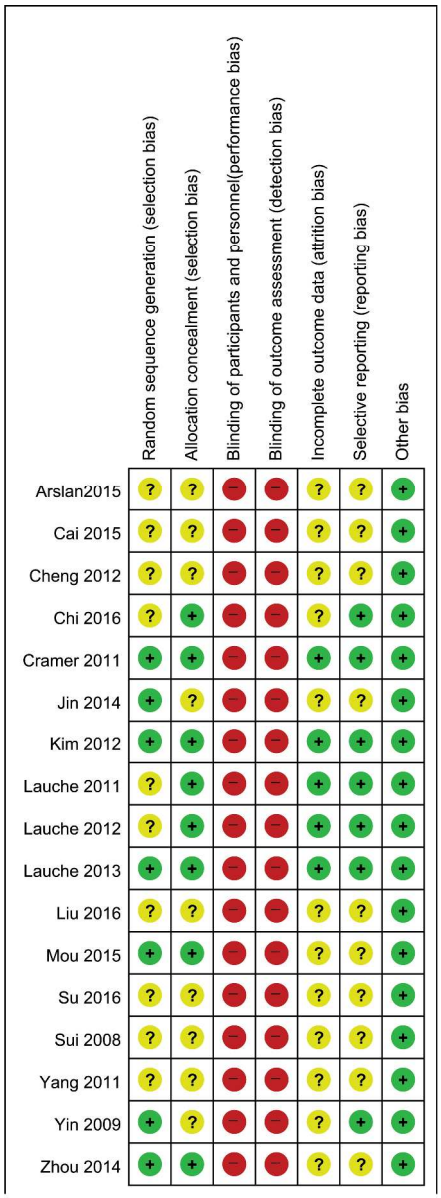

Figure 2. Risk of bias in the included studies, as assessed using the Cochrane Collaboration's risk of bias tool
+: high risk of bias, ?: unclear risk of bias, -: low risk of bias

266x738mm (300 x 300 DPI)

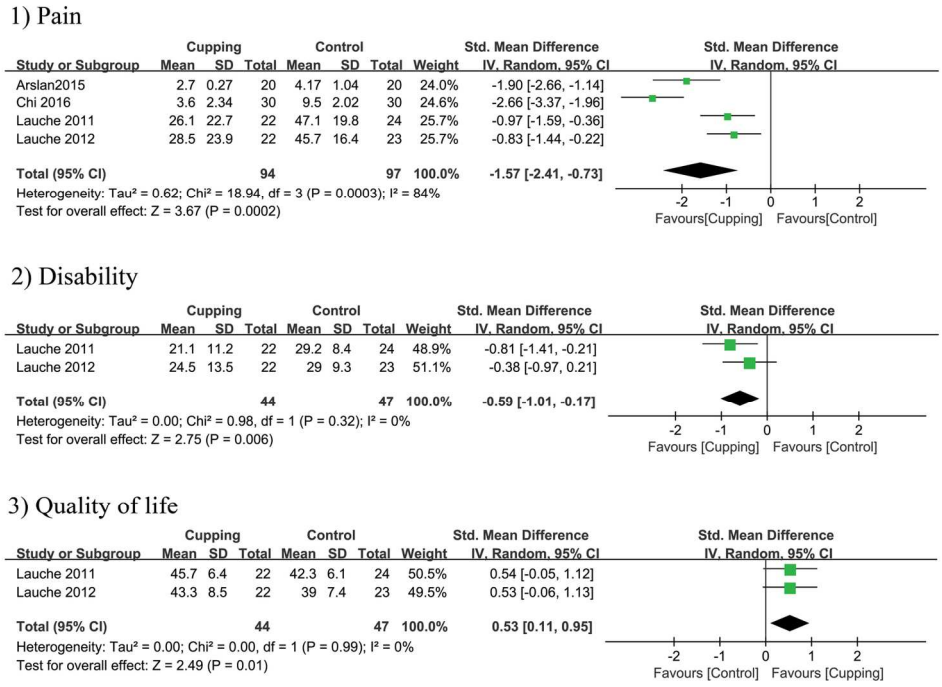

Figure 3. Forest plots demonstrating the effect of cupping as the sole intervention vs no treatment on neck pain
CI: confidence interval

151x109mm (300 x 300 DPI)

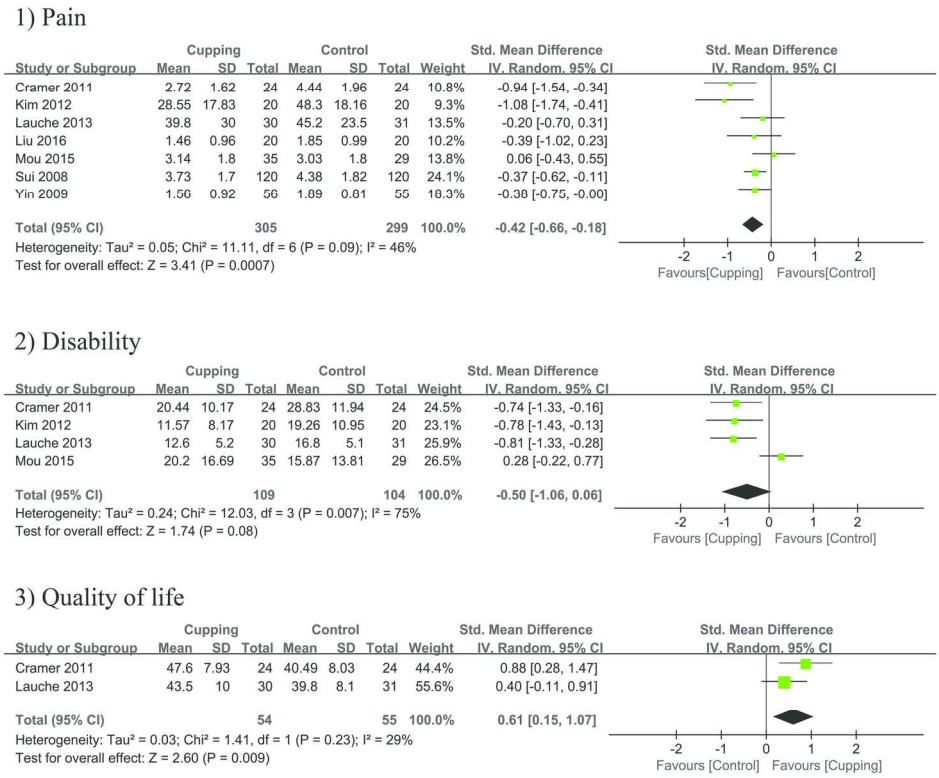

Figure 4. Forest plots demonstrating the effect of cupping as the sole intervention vs active control on neck pain
CI: confidence interval

173x143mm (300 x 300 DPI)

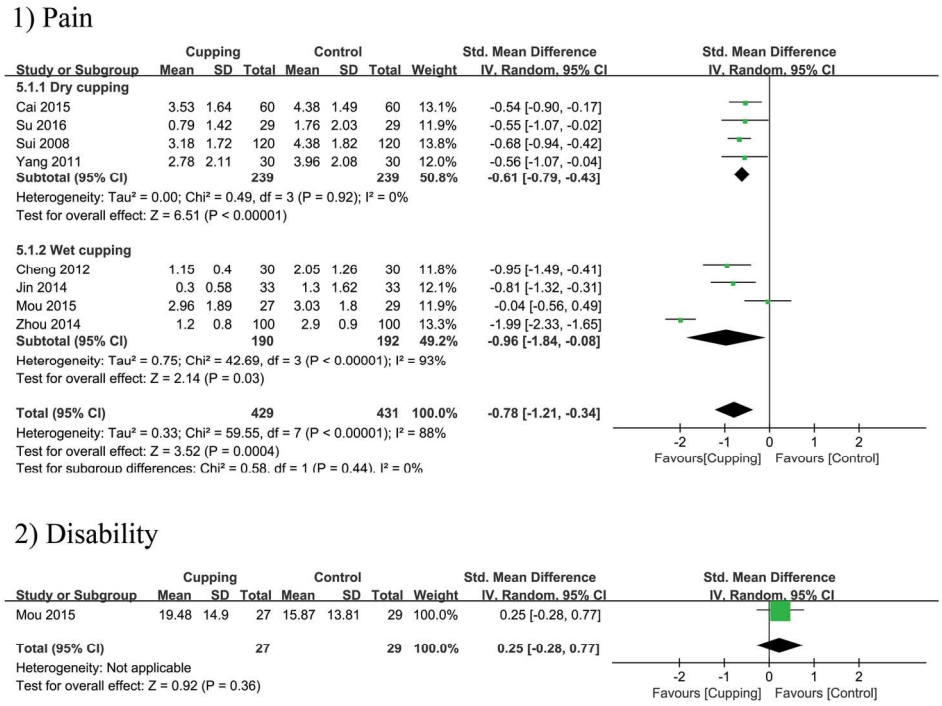

Figure 5. Forest plots demonstrating the effect of cupping as the add-on intervention on neck pain
CI: confidence interval

158x118mm (300 x 300 DPI)

Appendix 1. Search strategy

Ovid MEDLINE(R) 1946 to July Week 2 2016		Date : July 21. 2016
	Searches	Results
1	Neck Pain/	5341
2	exp Brachial Plexus Neuropathies/	3293
3	cervical pain.mp.	696
4	neckache.mp.	14
5	cervicodynia.mp.	9
6	cervicalgia.mp.	78
7	brachialgia.mp.	156
8	brachial neuritis.mp.	136
9	brachial neuralgia.mp.	113
10	neck pain.mp.	8419
11	neck injur*.mp.	5039
12	brachial plexus neuropath*.mp.	2057
13	brachial plexus neuritis.mp.	1420
14	thoracic outlet syndrome/ or cervical rib syndrome/	2063
15	Torticollis/	3295
16	exp brachial plexus neuropathies/ or exp brachial plexus neuritis/	3293
17	cervico brachial neuralgia.ti,ab.	41
18	cervicobrachial neuralgia.ti,ab.	63
19	(monoradicul* or monoradicl*).tw.	123
20	or/1-19	22501
21	neck/	26649
22	neck muscles/	5273
23	exp cervical plexus/	7338
24	exp cervical vertebrae/	34135
25	atlanto-axial joint/	2735
26	atlanto-occipital joint/	1519
27	Cervical Atlas/	2356
28	spinal nerve roots/	9829
29	exp brachial plexus/	22673
30	(odontoid* or cervical or occip* or atlant*).tw.	218433
31	axis/ or odontoid process/	1567

32	Thoracic Vertebrae/	17626
33	cervical vertebrae.mp.	31224
34	cervical plexus.mp.	1269
35	cervical spine.mp.	16170
36	(neck adj3 muscles).mp.	6243
37	(brachial adj3 plexus).mp.	12284
38	(thoracic adj3 vertebrae).mp.	18287
39	neck.mp.	189378
40	(thoracic adj3 spine).mp.	5119
41	(thoracic adj3 outlet).mp.	2364
42	trapezius.mp.	2799
43	or/21-42	445033
44	exp pain/	335410
45	exp injuries/	792763
46	pain.mp.	507456
47	ache.mp.	11686
48	sore.mp.	5787
49	stiff.mp.	6463
50	discomfort.mp.	31068
51	injur*.mp.	838096
52	neuropath*.mp.	107269
53	or/44-52	1807004
54	43 and 53	110046
55	Radiculopathy/	4242
56	exp temporomandibular joint disorders/ or exp temporomandibular joint dysfunction syndrome/	15244
57	myofascial pain syndromes/	1358
58	exp "Sprains and Strains"/	16868
59	exp Spinal Osteophytosis/	3865
60	exp Neuritis/	6804
61	Polyradiculopathy/	2472
62	exp Arthritis/	225889
63	Fibromyalgia/	7136
64	spondylitis/ or discitis/	5978
65	spondylosis/ or spondylolysis/ or spondylolisthesis/	6193
66	radiculopathy.mp.	6615
67	radiculitis.mp.	709

68	temporomandibular.mp.	23695
69	myofascial pain syndrome*.mp.	1513
70	thoracic outlet syndrome*.mp.	2200
71	spinal osteophytosis.mp.	3349
72	neuritis.mp.	14620
73	spondylosis.mp.	3480
74	spondylitis.mp.	19102
75	spondylolisthesis.mp.	5006
76	or/55-75	311063
77	43 and 76	24187
78	exp neck/	26656
79	exp cervical vertebrae/	34135
80	Thoracic Vertebrae/	17626
81	neck.mp.	189378
82	(thoracic adj3 vertebrae).mp.	18287
83	(thoracic adj3 spine).mp.	5119
84	cervical spine.mp.	16170
85	78 or 79 or 80 or 81 or 82 or 83 or 84	237596
86	Intervertebral Disk/	12624
87	(disc or discs).mp.	78491
88	(disk or disks).mp.	39655
89	86 or 87 or 88	105850
90	85 and 89	7657
91	herniat*.mp.	16266
92	slipped.mp.	3701
93	prolapse*.mp.	25552
94	displace*.mp.	113739
95	degenerat*.mp.	184631
96	(bulge or bulged or bulging).mp.	7023
97	or/91-96	335815
98	90 and 97	4888
99	intervertebral disk degeneration/ or intervertebral disk displacement/	19139
100	intervertebral disk displacement.mp.	1714
101	intervertebral disc displacement.mp.	17001
102	intervertebral disk degeneration.mp.	98
103	intervertebral disc degeneration.mp.	3296
104	or/99-103	19468

105	85 and 104	3566
106	20 or 54 or 77 or 98 or 105	124557
107	cupping.mp.	1298
108	ventouse.tw.	182
109	exp Bloodletting/	2596
110	bloodletting.mp.	2776
111	blood letting.mp.	302
112	blood-letting.mp.	302
113	spilled blood.mp.	10
114	venesection.mp.	569
115	107 or 108 or 109 or 110 or 111 or 112 or 113 or 114	4788
116	106 and 115	53

	Ovid EMBASE 1980 to 2016 July 21	**Date : July 22. 2016**
	Searches	Results
1	Neck Pain/	16361
2	brachial plexus neuropathy/	1638
3	cervical pain.mp.	1194
4	neckache.mp.	24
5	cervicodynia.mp.	18
6	cervicalgia.mp.	158
7	brachialgia/	252
8	brachialgia.mp.	380
9	brachial neuritis.mp.	197
10	brachial neuralgia.mp.	72
11	neck pain.mp.	18504
12	neck injur*.mp.	6901
13	brachial plexus neuropath*.mp.	1887
14	brachial plexus neuritis.mp.	95
15	thoracic outlet syndrome/	1953
16	Torticollis/	4007
17	exp brachial plexus neuropathies/ or exp brachial plexus neuritis/	1638
18	cervico brachial neuralgia.ti,ab.	43
19	cervicobrachial neuralgia.ti,ab.	82
20	(monoradicul* or monoradicl*).tw.	139
21	or/1-20	33843

22	neck/	44189
23	neck muscles/	4905
24	cervical plexus/	1099
25	cervical spine/	30009
26	atlantoaxial joint/	1640
27	atlantooccipital joint/	2036
28	atlas/	1842
29	spinal root/	4476
30	brachial plexus/	7512
31	(odontoid* or cervical or occip* or atlant*).tw.	287940
32	odontoid process/	2216
33	cervical vertebra.mp.	2342
34	cervical vertebrae.mp.	2846
35	cervical plexus.mp.	1355
36	cervical spine.mp.	45628
37	(neck adj3 muscles).mp.	2411
38	(brachial adj3 plexus).mp.	16727
39	(thoracic adj3 vertebrae).mp.	1961
40	neck.mp.	273953
41	(thoracic adj3 spine).mp.	12633
42	(thoracic adj3 outlet).mp.	2309
43	trapezius.mp.	4700
44	or/22-43	571079
45	exp pain/	980950
46	exp injuries/	1694977
47	pain.mp.	926638
48	ache.mp.	15335
49	sore.mp.	16755
50	stiff.mp.	10024
51	discomfort.mp.	57435
52	injur*.mp.	1289699
53	neuropath*.mp.	245028
54	or/45-53	3161489
55	44 and 54	171039
56	Radiculopathy/	8123
57	temporomandibular joint disorder/	11500
58	myofascial pain/	6940

59	spondylosis/ or cervical spondylosis/	6531
60	Neuritis/	6092
61	exp Arthritis/	381726
62	Fibromyalgia/	15823
63	exp spondylitis/	32769
64	diskitis/	1914
65	spondylolisthesis/	6558
66	radiculopathy.mp.	10970
67	radiculitis.mp.	1246
68	temporomandibular.mp.	24975
69	myofascial pain syndrome*.mp.	1068
70	spinal osteophytosis.mp.	63
71	neuritis.mp.	18454
72	spondylosis.mp.	7663
73	spondylitis.mp.	33467
74	spondylolisthesis.mp.	7282
75	or/56-74	457219
76	44 and 75	25812
77	neck/	44189
78	cervical spine/	30009
79	neck.mp.	273953
80	(thoracic adj3 vertebrae).mp.	1961
81	(thoracic adj3 spine).mp.	12633
82	cervical spine.mp.	45628
83	or/77-82	319795
84	Intervertebral Disk/	10857
85	(disc or discs).mp.	76993
86	(disk or disks).mp.	89287
87	or/84-86	134067
88	83 and 87	8827
89	herniat*.mp.	22785
90	slipped.mp.	3494
91	prolapse*.mp.	39404
92	displace*.mp.	119055
93	degenerat*.mp.	290515
94	(bulge or bulged or bulging).mp.	9633
95	or/89-94	475220

96	88 and 95	4658
97	intervertebral disk hernia/	15184
98	intervertebral disk degeneration/	7340
99	intervertebral disk displacement.mp.	1030
100	intervertebral disc displacement.mp.	494
101	intervertebral disk degeneration.mp.	7386
102	intervertebral disc degeneration.mp.	1643
103	or/97-102	22767
104	83 and 103	3864
105	21 or 55 or 76 or 96 or 104	184666
106	cupping.mp.	1702
107	ventouse.tw.	396
108	exp phlebotomy/	8690
109	bloodletting.mp.	627
110	blood letting.mp.	335
111	bloodletting.mp.	627
112	spilled blood.mp.	13
113	venesection.mp.	699
114	106 or 107 or 108 or 109 or 110 or 111 or 112 or 113	11385
115	105 and 114	123

	Ovid AMED (Allied and Complementary Medicine) 1985 to July 2016	**Date : July. 22. 2016**
	Searches	Results
1	Neck Pain/	983
2	exp Brachial plexus/	282
3	cervical pain.mp.	74
4	neckache.mp.	0
5	cervicodynia.mp.	2
6	cervicalgia.mp.	13
7	brachialgia.mp.	6
8	brachial neuritis.mp.	1
9	brachial neuralgia.mp.	5
10	neck pain.mp.	1327
11	neck injur*.mp.	134
12	brachial plexus neuropath*.mp.	8
13	brachial plexus neuritis.mp.	1

14	thoracic outlet syndrome/ or cervical rib syndrome/	43
15	Torticollis/	68
16	cervico brachial neuralgia.ti,ab.	0
17	cervicobrachial neuralgia.ti,ab.	2
18	(monoradicul* or monoradicl*).tw.	0
19	or/1-18	1875
20	neck/	653
21	neck muscles/	137
22	exp cervical plexus/	30
23	exp cervical vertebrae/	1618
24	Atlanto axial joint/	32
25	Atlanto occipital joint/	17
26	spinal nerve roots/	90
27	(odontoid* or cervical or occip* or atlant*).tw.	3845
28	Axis/	8
29	Odontoid process/	8
30	Thoracic Vertebrae/	293
31	cervical vertebrae.mp.	1650
32	cervical plexus.mp.	11
33	cervical spine.mp.	1152
34	(neck adj3 muscles).mp.	295
35	(brachial adj3 plexus).mp.	200
36	(thoracic adj3 vertebrae).mp.	322
37	neck.mp.	3669
38	(thoracic adj3 spine).mp.	350
39	(thoracic adj3 outlet).mp.	83
40	trapezius.mp.	491
41	or/20-40	7438
42	exp pain/	19753
43	exp injuries/	2719
44	pain.mp.	28582
45	ache.mp.	113
46	sore.mp.	163
47	stiff.mp.	218
48	discomfort.mp.	969
49	injur*.mp.	27054
50	neuropath*.mp.	1728

51	or/42-50	55282
52	41 and 51	3984
53	myofascial pain syndromes/	330
54	exp "Sprains and Strains"/	902
55	exp Spinal Osteophytosis/	35
56	exp Neuritis/	61
57	exp Arthritis/	5226
58	Fibromyalgia/	1612
59	spondylitis/ or discitis/	72
60	spondylosis/ or spondylolysis/ or spondylolisthesis/	139
61	radiculopathy.mp.	282
62	radiculitis.mp.	10
63	temporomandibular.mp.	551
64	myofascial pain syndrome*.mp.	402
65	thoracic outlet syndrome*.mp.	80
66	spinal osteophytosis.mp.	41
67	neuritis.mp.	75
68	spondylosis.mp.	129
69	spondylitis.mp.	346
70	spondylolisthesis.mp.	153
71	or/53-70	9340
72	41 and 71	781
73	exp neck/	697
74	exp cervical vertebrae/	1618
75	Thoracic Vertebrae/	293
76	neck.mp.	3669
77	(thoracic adj3 vertebrae).mp.	322
78	(thoracic adj3 spine).mp.	350
79	cervical spine.mp.	1152
80	73 or 74 or 75 or 76 or 77 or 78 or 79	5606
81	Intervertebral Disk/	325
82	(disc or discs).mp.	1189
83	(disk or disks).mp.	972
84	81 or 82 or 83	1665
85	80 and 84	224
86	herniat*.mp.	384
87	slipped.mp.	27

88	prolapse*.mp.	120
89	displace*.mp.	2488
90	degenerat*.mp.	1631
91	(bulge or bulged or bulging).mp.	63
92	or/86-91	4359
93	85 and 92	140
94	intervertebral disk degeneration/ or intervertebral disk displacement/	333
95	intervertebral disk displacement.mp.	370
96	intervertebral disc displacement.mp.	1
97	intervertebral disk degeneration.mp.	25
98	intervertebral disc degeneration.mp.	20
99	94 or 95 or 96 or 97 or 98	404
100	80 and 99	54
101	19 or 52 or 72 or 93 or 100	4612
102	cupping.mp.	161
103	ventouse.tw.	2
104	exp Bloodletting/	43
105	exp Cupping/	91
106	bloodletting.mp.	68
107	blood letting.mp.	29
108	bloodletting.mp.	68
109	spilled blood.mp.	0
110	venesection.mp.	0
111	102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110	221
112	101 and 111	17

Cochrane Central Register of Controlled Trials : July 2016	**Date : July. 22. 2016**	
	Searches	Results
1	[mh ^"Neck pain"]	719
2	[mh "Brachial Plexus Neuropathies"]	50
3	cervical pain:ti,ab,kw	2541
4	neckache:ti,ab,kw	1
5	cervicodynia:ti,ab,kw	1
6	cervicalgia:ti,ab,kw	7
7	brachialgia:ti,ab,kw	9
8	brachial neuritis:ti,ab,kw	27

9	brachial neuralgia:ti,ab,kw	15
10	neck pain:ti,ab,kw	3706
11	neck injur*:ti,ab,kw	1082
12	brachial plexus neuropath*:ti,ab,kw	49
13	brachial plexus neuritis:ti,ab,kw	27
14	[mh ^"thoracic outlet syndrome"]	17
15	[mh ^"cervical rib syndrome"]	1
16	[mh ^Torticollis]	90
17	[mh "brachial plexus neuropathies"]	50
18	[mh "brachial plexus neuritis"]	25
19	cervico brachial neuralgia:ti,ab,kw	3
20	cervicobrachial neuralgia:ti,ab,kw	58
21	monoradicul* or monoradicl*;ti,ab,kw	27
22	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21	6147
23	[mh ^neck]	445
24	[mh ^"neck muscles"]	189
25	[mh "cervical plexus"]	97
26	[mh "cervical vertebrae"]	876
27	[mh ^"atlanto-axial joint"]	20
28	[mh ^"atlanto-occipital joint"]	6
29	[mh ^"Cervical Atlas"]	3
30	[mh ^"spinal nerve roots"]	145
31	[mh "brachial plexus"]	900
32	odontoid* or cervical or occip* or atlant*:ti,ab,kw	14562
33	[mh ^"odontoid process"]	10
34	[mh ^"Thoracic Vertebrae"]	400
35	cervical vertebrae:ti,ab,kw	1028
36	cervical plexus:ti,ab,kw	180
37	cervical spine:ti,ab,kw	1202
38	neck muscles:ti,ab,kw	579
39	brachial plexus:ti,ab,kw	1007
40	thoracic vertebrae:ti,ab,kw	490
41	neck:ti,ab,kw	12448
42	thoracic spine:ti,ab,kw	531
43	thoracic outlet:ti,ab,kw	32
44	trapezius:ti,ab,kw	386

45	#23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44	27955
46	[mh pain]	35540
47	[mh injuries]	17847
48	pain:ti,ab,kw	89051
49	ache:ti,ab,kw	269
50	sore:ti,ab,kw	1723
51	stiff:ti,ab,kw	260
52	discomfort:ti,ab,kw	7614
53	injur*:ti,ab,kw	28417
54	neuropath*:ti,ab,kw	6367
55	#46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54	133237
56	#45 and #55	8163
57	[mh ^Radiculopathy]	251
58	[mh "temporomandibular joint disorders"]	554
59	[mh "temporomandibular joint dysfunction syndrome"]	169
60	[mh "myofascial pain syndromes"]	401
61	[mh "Sprains and Strains"]	911
62	[mh "Spinal Osteophytosis"]	90
63	[mh Neuritis]	68
64	[mh ^polyradiculopathy]	13
65	[mh arthritis]	9924
66	[mh ^Fibromyalgia]	756
67	[mh ^spondylitis]	19
68	[mh ^discitis]	8
69	[mh ^spondylosis]	108
70	[mh ^spondylolysis]	11
71	[mh ^spondylolisthesis]	134
72	radiculopathy:ti,ab,kw	561
73	radiculitis:ti,ab,kw	34
74	temporomandibular:ti,ab,kw	958
75	myofascial pain syndrome*:ti,ab,kw	486
76	thoracic outlet syndrome*:ti,ab,kw	27
77	spinal osteophytosis:ti,ab,kw	94
78	neuritis:ti,ab,kw	452
79	spondylosis:ti,ab,kw	339

80	spondylitis:ti,ab,kw	1023
81	spondylolisthesis:ti,ab,kw	335
82	#57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81	14999
83	#45 and #82	1279
84	[mh neck]	445
85	[mh "cervical vertebrae"]	876
86	[mh ^"thoracic vertebrae"]	400
87	neck:ti,ab,kw	12448
88	thoracic vertebrae:ti,ab,kw	490
89	thoracic spine:ti,ab,kw	531
90	cervical spine:ti,ab,kw	1202
91	#84 or #85 or #86 or #87 or #88 or #89 or #90	14136
92	[mh ^"Intervertebral Disk"]	271
93	disc$:ti,ab,kw	3158
94	#92 or #93	3158
95	#91 and #94	409
96	herniat*:ti,ab,kw	1002
97	slipped:ti,ab,kw	34
98	prolapse*:ti,ab,kw	1605
99	displace*:ti,ab,kw	3532
100	degenerat*:ti,ab,kw	4479
101	bulge or bulged or bulging:ti,ab,kw	224
102	#96 or #97 or #98 or #99 or #100 or #101	10133
103	#95 and #102	271
104	[mh ^"intervertebral disk degeneration"]	151
105	[mh ^"intervertebral disk displacement"]	683
106	intervertebral disk displacement:ti,ab,kw	215
107	intervertebral disc displacement:ti,ab,kw	750
108	intervertebral disk degeneration:ti,ab,kw	119
109	intervertebral disc degeneration:ti,ab,kw	276
110	#104 or #105 or #106 or #107 or #108 or #109	1023
111	#91 and #110	181
112	#111 or #103 or #83 or #56 or #22	9416
113	cupping:ti,ab,kw	313
114	ventouse:ti,ab,kw	47

115	MeSH descriptor: [Bloodletting] explode all trees	94
116	bloodletting:ti,ab,kw	146
117	blood letting:ti,ab,kw	74
118	blood-letting:ti,ab,kw	70
119	spilled blood:ti,ab,kw	4
120	venesection:ti,ab,kw	57
121	#113 or #114 or #115 or #116 or #117 or #118 or #119 or #120	546
122	#112 and #121	37

	CNKI	**Date : : July. 30. 2016**
	Searches	Results
#1	(SU='颈痛'OR SU='颈肩痛'OR SU='颈椎病' OR SU='颈肩部'OR SU='颈椎间盘突出症' OR SU='颈部'OR SU='神经根型颈椎病') AND (SU='罐' OR SU='cupping') AND (SU='随机' or SU='对照')	157

	J-Stage	**Date: Sep. 10. 2016**
	Searches	Results
#1	Full text : acupuncture AND neck pain AND random	19
#2	Full text : 漢方薬 AND neck AND random	5

	ICHUSHI	**Date: Sep. 10. 2016**
	Searches	Results
#1	(頸椎症性脊髄症/TH or 頸椎症/AL)	9,793
#2	頸椎椎間板ヘルニア/AL	1,044
#3	((@頸椎/TH and @脊椎損傷/TH and @捻挫/TH) or 頸椎捻挫/AL)	310
#4	(頸部痛/TH or 頸部疼痛/AL)	1,889
#5	頸肩部痛/AL	3,584
#6	頸肩部痛/AL	56
#7	#1 or #2 or #3 or #4 or #5 or #6	14,181
#8	(鍼療法/TH or 鍼/AL)	32,246
#9	(漢方医学/TH or 漢方医学/AL)	7,387
#10	(灸療法/TH or 灸/AL)	27,270
#11	cupping/AL	27
#12	吸角/AL	22
#13	(漢方薬/TH or 漢方薬/AL)	58,323

#14	(漢方薬/TH or 漢方/AL)	66,206
#15	湯/AL	73,638
#16	散/AL	90,826
#17	丸/AL	158,762
#18	(ランダム化比較試験/TH or RCT/AL)	47,588
#19	(ランダム化比較試験/TH or ランダム化比較試験/AL)	45,866
#20	random/AL	4,268
#21	(電気鍼療法/TH or electroacupuncture/AL)	1,454
#22	(電気鍼療法/TH or 電気鍼療法/AL)	1,459
#23	#8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #22 or #23	373,585
#24	#7 and #21 and #24	34
#25	(#25) and (PT=会議録除く)	17

	OASIS (Korea)	**Date : July. 20. 2016**
	Searches	Results
#1	경항통 OR 경추 OR 頸 OR 項	743

	NDSL (Korea)	**Date : July. 20. 2016**
	Searches	Results
#1	TI : (경항통 or 경추 or 頸 or 項 or "Neck pain") or AB : (경항통 or 경추 or 頸 or 項 or "Neck pain")	731

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4-5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4-5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6, 9
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	6, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	6-7, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	7 Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	7-9
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	7-9
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	7-9 Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	7-9
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	9
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	10
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	11
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	11

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

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BMJ Open

Is cupping therapy effective in neck pain patients? A systematic review and meta-analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021070.R1
Article Type:	Research
Date Submitted by the Author:	16-May-2018
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Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Neck pain, Complementary Therapies, Meta-Analysis, Systematic Review

Is cupping therapy effective in neck pain patients? A systematic review and meta-analysis

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ABSTRACT

Objectives: Neck pain is a significant condition that is second only to depression as a cause of years lived with disability worldwide, and this should be sufficient reason to precipitate the search for effective treatment modalities. This systematic literature review aimed to investigate the effects of cupping on neck pain from current evidence.

Design: Systematic review and meta-analysis of randomised controlled trials (RCTs)

Setting: Nine databases, including Chinese, Korean and Japanese databases, through to January 2018

Participants: Neck pain patients

Interventions: Cupping therapy as the sole or add-on intervention compared with no treatment or active controls

Primary and secondary outcome measures: Pain severity, functional disability, and quality of life

Results: Eighteen RCTs were selected. Compared with the no intervention group, the cupping group exhibited significant reduction in pain (mean difference [MD] -2.42 [95% CI -3.98 to -0.86]) and improvement in function (MD -4.34 [95% CI -6.77 to -1.19]). Compared with the active control, the cupping group reported significant reduction in pain (P=0.0009) and significantly improved quality of life (P=0.001). The group that received control treatment with cupping therapy (add-on group) displayed significant pain reduction compared to the active control group (P=0.001). Of all eighteen studies, only eight studies reported occurrence of adverse events (AEs), which were mild of nature. The selected studies described mild side effects of cupping, and none were serious.

Conclusions: Compared to no intervention or active controls, or as an add-on treatment, cupping was found to decrease pain in neck pain patients. Depending on the type of control group, cupping was also associated with significant improvement in terms of function and quality of life; however, it is difficult to draw definitive conclusions due to the low to very low quality of evidence. Future well-designed studies are warranted to substantiate the effectiveness of cupping on neck pain.

Keywords: Neck pain, Complementary Therapies, Meta-Analysis, Systematic Review

ARTICLE SUMMARY

Strengths and limitations of this study

- This systematic review investigated the effectiveness of cupping in treating pain, and placed no restrictions on publication language.
- This study employed stringent inclusion and exclusion criteria, and nine databases were accordingly searched for randomised controlled trials.
- The analysis also addressed functional improvement and quality of life, safety of cupping, risk of bias, and levels of evidence.
- The results of data synthesis may be limited due to the heterogeneity across selected studies, and low quality of evidence.

INTRODUCTION

Studies analysing the 20 major causes of years lived with disability (YLD) from 2000 to 2012 worldwide reported that neck pain is the second leading cause of YLD following depression.[1] A Dutch study revealed that neck pain was associated with 1% of total medical expenditure and 0.1% of gross domestic product (GDP), 77% of which were indirect medical expenses associated with absence from work or disability expenses.[2] As reported in the present review, neck pain is an important condition whose prevalence is directly associated with escalated medical costs and negative impact on productivity, potentially increasing long-term absence from work.

Neck pain is a common disorder with a lifelong prevalence of 14.2% to 71% in adults, although these figures vary greatly across studies.[3] The disorder easily progresses to chronic conditions, with approximately 25% to 60% of patients developing chronic back or neck pain within the first year.[4] Furthermore, neck pain is reported to be most prevalent in high activity age groups, particularly individuals aged 35 to 49 years.[5] It is also more common in women.[3]

Standard first-line therapy for neck pain can be largely divided into pharmacological and non-pharmacological therapies. Pharmacological treatment frequently involves use of acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). However, acetaminophen and NSAIDs are known to increase risk of reduced liver function, liver failure, and haemorrhagic gastritis,[6] and side effects may be more common when these drugs are used in the long-term for chronic neck pain, which is often the case due to pain chronicity. For these reasons, many studies have investigated the clinical effectiveness of complementary and alternative medicine therapies, including acupuncture for chronic pain conditions such as pain of spinal origin.[7]

Cupping has been used globally across various countries such as Egypt and China, and its use dates back several thousand years.[8] Cupping is a physical treatment mainly employed by acupuncturists and other complementary and alternative medicine therapists that utilizes glass or plastic cups to create negative pressure on the skin over a painful area or acupuncture point through suction. The rationale for use of cupping is not yet fully explained; it is purported to be a detoxification process by which waste matter and toxins are removed, and as a harmonization process of Qi imbalance.[8] From a holistic perspective, cupping is widely used in Europe for inpatient care and the prevention and treatment of various disorders, as well as promotion of general health.[9] There are two types of cupping: dry and wet. Dry cupping is a technique in which cups are applied to the skin to create a vacuum for suction without drawing blood, whereas in wet cupping, blood is drawn with scarification before applying the cups for blood-letting. Cupping therapy is used for post-stroke rehabilitation and hypertension, and has been reported to be effective for treating pain and musculoskeletal disorders.[10 11] Cupping is particularly popular in South Korea and is covered by national health insurance; insurance claims for cupping reached a total 215,079,729,000 Korean won in 2013 alone.[12] Studies on the effects of cupping on neck pain include a systematic literature review published by Yuan et al., which reported that cupping is effective for reducing pain and improving function in chronic neck pain.[13] However, this 2015 systematic review covered articles published up to 2013, and as new clinical trials investigating cupping for neck pain have since been published, an updated systematic review on the topic is needed. Moreover, Yuan et al.[13] restricted the publication language in inclusion of study articles. The present review holds the advantage of not placing any restrictions on

publication language in an attempt to conduct a more extensive and inclusive review before drawing any definite conclusions. This systematic review of randomised controlled trials (RCTs) was conducted in order to comprehensively assess the current evidence of cupping for neck pain as evaluated using pain, function, quality of life, and safety measures.

METHODS

The protocol of this systematic literature review was registered in the PROSPERO International prospective register of systematic reviews (CRD42016047218). This review was performed and reported in adherence with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA).[14]

Literature search

Studies that used cupping as an intervention for neck pain were searched in the Ovid-Medline (1946 to Jan 2018), Ovid-EMBASE (1980 to Jan 2018), Ovid-AMED (1985 to Dec 2017), and the Cochrane Central Register of Controlled Trials (CENTRAL) up to January 9, 2018. The Chinese database China National Knowledge Infrastructure (CNKI), Korean databases Oriental Medicine Advanced Searching Integrated System (OASIS) and National Discovery for Science Leader (NDSL), and Japanese databases J-stage and ISHUSHI were also used. Search terms included a combination of Medical Subject Headings (MeSH) terms such as neck pain (e.g., neck pain, cervical spondylosis, cervical radiculopathy, cervical disc herniation, and myofascial pain syndrome) and cupping. Details of the search strategy are presented in Appendix 1. No language restrictions were emplaced.

Study inclusion and exclusion

Two or more investigators (YJL, SYK, and/or SHL) independently selected articles for analysis from the searched articles. After excluding duplicate publications, titles and abstracts were reviewed to primarily screen for articles according to the inclusion and exclusion criteria. The full texts of these articles were then reviewed for secondary screening of articles per inclusion and exclusion criteria. Only RCTs were considered. Any disagreement in the study selection process was resolved by discussion, and when an agreement was not reached, a third investigator intervened to reach consensus. The publication language of study articles was not restricted. Subjects encompassed adult patients with neck pain, including neck pain with neuropathy, and did not discriminate between acute and chronic phases. However, post-traumatic pain caused by whiplash or sports injuries was excluded as the natural history of neck pain may differ in such cases. Furthermore, patients with myelopathy or cervical headache/vertigo without neck pain were also excluded. All types of cupping therapies were included without restrictions regarding dry or wet cupping, and the type of cupping device was also not limited. Control groups included patients who underwent usual care for neck pain, such as physical therapy, NSAIDs, heat pack therapy, and acupuncture,[15-17] as well as inactive controls such as waiting lists or no intervention groups. The outcome variables assessing the effectiveness of cupping included pain intensity, neck disability indexes, and quality of life (QoL). Pain intensity was measured using visual analogue scale (VAS), the McGill Pain Questionnaire, and the Northwick Park Neck Pain Questionnaire (NPQ). The Neck Disability Index

(NDI) was generally used to evaluate neck function disability. QoL was assessed using the 36-item Short-form (SF-36) and EQ-5D questionnaires. However, studies that did not use objective instruments and only reported outcomes in terms of improvement rates without standards or investigations that used instruments without confirmation of reliability and validity were excluded.

Risk of bias evaluation and data extraction

Risk of bias in the RCTs was assessed by seven categories according to the Cochrane Risk of Bias. Studies that used appropriate methods for each item and specified the methods in the text were considered to have low risk of bias; studies that did not perform or used inappropriate methods were considered to have high risk of bias; and studies that did not mention or used ambiguous expressions were considered to have an unclear risk of bias. Two or more investigators independently assessed all research data, and disagreements were resolved through discussion. When an agreement could not be reached, a third investigator intervened to reach consensus. Two reviewers independently read the full text of all articles and extracted data according to a pre-determined format. Any disagreements were resolved by discussion between the two reviewers.

Data analysis

A meta-analysis was performed using quantitative data from each study to assess the effectiveness of cupping. The mean difference (MD) and 95% confidence interval (CI) were calculated using the Cochrane Collaboration software (Review Manager [RevMan] version 5.3, Copenhagen: The Nordic Cochrane Centre) for Windows (Microsoft Corporation, Redmond, WA, USA). Heterogeneity across studies was assessed using the χ^2 (chi-squared) test with a significance level of $P<0.10$ and the I^2 statistic. When heterogeneity was statistically significant, the cause of heterogeneity was analysed through subgroup analysis. We also conducted sensitivity analyses to test the robustness of the impact of a single study on the overall results. If we found statistical heterogeneity, the sensitivity analyses (by eliminating 1 study at a time) were performed to explore the possible reasons for this heterogeneity. A random effect model was applied, and publication bias was not assessed when the number of studies in the group was < 10.

Quality of evidence

The quality of evidence for each outcome was assessed in accordance with the Grading of Recommendations, Assessment, Development and Evaluation (GRADE). Quality of evidence was classified into high, moderate, low, and very low. To determine the quality of evidence, the following domains were assessed according to the standards suggested by the GRADE group: risk of bias; imprecision; inconsistency; indirectness; publication bias; large magnitude of effect; dose-response; and confounding.[18]

Patient and Public Involvement

Patients and public were not involved in development of the research question and outcome measures, design of this study, or recruitment to and conduct of the study as a systematic review and meta analysis. There are no

plans for the results to be disseminated directly to study participants.

RESULTS

Search results

A total of 541 articles were retrieved, including 86 from Ovid-Medline, 137 from Ovid-EMBASE, 19 from Ovid-AMED, 43 from the Cochrane Library, 193 from a Chinese database, 47 from Korean databases and 16 from Japanese databases. Following the first and second rounds of screening, a total of 18 articles were selected for review. Search results are shown in Figure 1.

Features of the included studies

A total of 18 studies were analysed in two separate analyses[19-36]: direct comparison of the cupping (sole) and control groups; and an add-on analysis comparing the control with cupping group with the control only group. Two studies used three groups; 15 studies were included in the sole analysis while five studies were included in the add-on analysis.

Seven[19 21 23 26-28 34] of the 18 studies used wet cupping while eleven studies used dry cupping. The frequency of cupping therapy varied greatly. Two studies performed only one round of therapy, and four conducted two to four rounds. The majority of studies conducted >10 rounds of therapy because most treated patients had neck pain with radiculopathy or were chronic neck pain cases. The region of administration was mostly the upper shoulder and neck area, and primarily Ashi or other proximal acupoints. As these studies mainly treated pain, most presented pain scores in the form of VAS scores; disability was presented in NDI scores, while QoL was mostly reflected in the responses to the EQ-5D and SF-36 questionnaires. The features of each study are presented in Table 1.

Table 1. Characteristics of the included studies

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relavent Outcomes (Primary/secondary)
Cupping vs Control (Sole)										
Vs waitlist (no intervention)										
Arslan 2015	Turkey	computer users diagnosed minimum 3 neck pain	EG: 20, CG: 20	EG: 26.0±3.5, CG: 26.0±3.8	Dry cupping (moving)	no intervention	upper shoulder and neck region	10	After treatment	VAS
Chi 2016	Taiwan	work-related chronic neck shoulder pain	EG: 30, CG: 30	EG: 43.6±6.3, CG: 42.5±5.8	Dry cupping	no intervention	SI15, GB21, LI15	1	After treatment	VAS
Lauche 2011	Germany	chronic nonspecific neck pain	EG: 22, CG: 24	EG: 26.1±4.2 CG: 25.1±3.0	Dry cupping	Waiting list control group	descending and transverse parts of the trapezius muscle	5	After treatment	VAS, NDI, SF-36
Saha 2017	Germany	Chronic neck pain	EG: 25, CG: 25	EG: 54.3 ± 8.6 CG: 53.3 ± 11.1	Dry cupping	Waiting list control group	from the occiput towards the mid-level thoracic spine as well as over the upper trapezius muscle	5	Post-cupping after 3 weeks	VAS, POM, NDI, SF-36
Lauche 2012	Germany	chronic nonspecific neck pain	EG: 22, CG: 23	EG: 54.8±3.2 CG: 29.3±2.9	Wet cupping	Waiting list control group	descending parts of the trapezius muscle	1	Post-cupping after 3 days	VAS, NDI, SF-36
Vs active control (dry cupping)										
Sui 2008*	China	cervical radiculopathy	EG: 120, CG: 120	NR	Dry cupping (moving)	traction	Acupoints at Bladder Meridian and Governor Vessel	20	After treatment	VAS, POM, NDI, SF-36
Cramer 2011	Germany	nonspecific neck pain for at least the previous 3 months	EG: 24 CG: 24	EG: 44.46 CG: 47.88	Dry cupping	Standard Medical Care	Neck and shoulder lesion	3-4	After treatment	VAS, NDI, SF-36

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relavent Outcomes (Primary/secondary)
Kim 2012	Korea	VDT workers with neck pain	EG: 20 CG: 20	EG : 25.5 (median) CG : 28 (median)	Dry cupping	Heating pad group	GV14, GV16, GV15, GV12, GB20, GB21, LI17, SI11, SI12, SI13, SI14, SI15, BL10, BL11, BL12, BL13, BL14, BL15, BL16, BL17, BL41, BL42, BL43, BL44, EX-HN15	6	7 weeks	NRS, NDI, EQ-5D
Lauche 2013	Germany	chronic nonspecific neck pain	EG: 30 CG: 31	EG: 54.5±12.3 CG: 53.7±13.4	Dry cupping	progressive muscle relaxation(PMR)	NR	24	12 weeks	VAS, NDI, SF-36
Vs active control (wet cupping)										
Liu 2016	China	cervical spondylosis	EG: 20, CG: 20	NR	Wet cupping	Tuina	GV14, Ashi points	3	After treatment	VAS, effective rate, tenderness
Mou 2015*	China (Multi center)	cervical radiculopathy	EG: 68, CG: 56	EG: 46.4±11.6 CG: 47.8±11.9	Wet cupping	MA	GV14, GB21	4-12	After treatment	VAS, NDI, CAS
Yin 2009	China	cervical spondylosis	EG: 56 CG: 55	EG: 32.13±7.87 CG: 35.24±6.67	Wet cupping	MA	EX-B2,BL11, GB21, Ashi points	10	After treatment	VAS, effective rate
Zhou 2014	China	Cervical Spondylopathy	EG:100 CG:100	NR	Wet cupping	MA	Ashi points, EX-B2, GB21	10	After treatment	VAS , effective rate
Jin 2014	China	neck type cervical spondylosis	EG: 33 CG: 33	EG: 31.81±8.30 CG: 30.48±9.74	Wet cupping	MA	upper shoulder and neck region	5	After treatment	VAS, NPQ, effective rate
Yin 2016	China	Cervical Spondylosis	EG: 47, CG: 48	EG: 45. 68 ± 10. 46, CG: 47. 29 ± 8.03	Wet cupping	acupuncture	EX - B2, SI15, GB21, SJ5	4	After treatment	NPQ
Cupping with usual care vs usual care (Add-on)										
Dry cupping										
Cai 2015	China	Chronic neck pain	EG: 60 CG: 60	EG: 45.48±10.9 CG: 45.7±11.1	Dry cupping	MA	EX-B2	12	After treatment	SF-MPQ
Su 2016	China	Neck pain after sleeping	EG:29 CG:29	EG: 30.72±6.69 CG: 31.76±7.16	Dry cupping	MA	upper shoulder and neck region	3	After treatment	VAS, effective rate
Sui 2008*	China	cervical radiculopathy	EG: 120, CG: 120	NR	Dry cupping (moving)+traction	traction	Acupoints at Bladder Meridian and Governor Vessel	20	After treatment	VAS
Wet cupping										

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relavent Outcomes (Primary/secondary)
Mou 2015*	China (Multicenter)	cervical radiculopathy	EG: 59, CG: 56	EG: 45.4±11.6 CG: 47.8±11.9	Wet cupping+MA	MA	EX-B2, BL11, GB21, Ashi points	10	After treatment	VAS, NDI, CAS
Jiang 2017	China	Myofascial Pain Syndrome of Neck and Shoulder	EG:30 CG:30	EG: 21±3 CG: 22±3	Wet cupping+MA	MA	Ashi points	5	After treatment	VAS , effective rate

CAS: Clinical assessment scale, CG: control group, EA: electroacupuncture, EG: experimental group, EQ-5D: Euroqol5-D health utility, MA: manual acupuncture, NDI: Neck Disability Index, NPQ: Neck Pain Questionnaire, NR: not reported, SD: Standard deviation, SF-MPQ: Short Form McGill Pain Questionnaire, SF-36: 36-Item Short Form Health Survey, VAS: Visual Analogue Scale, VDT: Video Display Terminal, POM: Pain on movement

*The study is a three-armed study, i.e. cupping group, control group, cupping plus control group.

Risk of bias assessment

Random sequence: Seven of the 18 studies[20 22-25 27 28] were assessed to have low risk of bias as they randomly allocated the subjects using a table of random numbers. One study did not specify the randomization method, and the group size notably varied, i.e. 68, 56, and 59; this study was thus assessed to have high risk of bias.[26] The remaining 10 studies, however, only mentioned randomly assigning subjects without specifying the method used for randomization; thus, these studies were assessed to have an unclear risk of bias. The results are shown in Figure 2.

Allocation concealment: Nine[20 22 24-26 28-31] studies concealed allocation using a sealed envelope, and thus were considered to have low risk of bias. The remaining studies were determined to be unclear because they did not describe the method of allocation concealment used.

Blinding: Control groups were either waiting list controls or active controls. Although efforts have been made to develop a sham version of cupping[37], blinding is difficult given that sham cupping is not often used. Chi et al.[29] described single blinding; however, it was difficult to assess whether blinding was actually implemented. Hence, all studies were considered to not have blinded their investigators and participants. With regard to the blinding of participants and personnel, all studies were considered to have high risk of bias. Similarly, blinding of outcome assessors was not performed in most studies as many used VAS for pain measurement and patient-reported outcomes. Blinding of outcome assessors would have been made feasible if the studies had used physician-reported outcomes or other outcome variables measured by the examiner; however, such studies were found lacking. Therefore, all studies were assessed to have high risk of bias.

Incomplete outcome data: Seven[20 22 24 25 27 30 31] studies reported the number of excluded and withdrawn participants, and the number of participants included for final analysis. It was decided that the number of withdrawn participants and the reason for withdrawal were not a cause of bias; therefore, these studies were considered to have low risk of bias. One study was regarded to possess high risk of bias as 33 participants from the intervention group and 27 from the control group dropped out after only one session of treatment.[26] The remaining studies were determined to be unclear for not mentioning the number of participants who withdrew or were excluded.

Selective reporting: Ten[20 22 24 25 27 29-31] of the 18 studies were determined to have unclear risk of bias regarding selective reporting as they did not describe adverse events nor did they register the trial protocols. The remaining eight studies were found to have reported all outcome variables initially planned to be investigated, and thus were determined to have low risk of bias.

Other biases: All studies were assessed to have low risk of other biases.

Analysis

Cupping versus no treatment

Pain: Five studies were included in the meta-analysis.[20 29-32] Compared with the no intervention group, the cupping group reported significant reduction in pain with an MD of -2.42 (95% CI -3.98 to -0.86). Considerable heterogeneity was observed (I^2=93%; P<0.00001 [chi-square test]); however, the study by Chi 2016[29] showed a

statistically outlying effect size; a sensitivity analysis was conducted with the study omitted, and resulted in an MD of -1.48 (95% CI -1.86, -1.10; I2=0%; P=0.57)) with the heterogeneity resolved.

Disability: Three studies were included in the analysis.[20 30 31] The results revealed that the cupping group reported significant functional improvement compared with the no intervention group with an MD of -4.34 (95% CI -6.77 to -1.91; I^2=6%; P=0.35).

QoL: Three studies were included in the analysis,[20 30 31] and results showed that the cupping group indicated significant improvement in the mental component summary of SF-36, with an MD of 5.32 (95% CI 0.83 to 9.80; I^2=32%; P=0.23). No statistical significance was found in terms of the physical component summary of SF-36 with an MD of 2.46 (95% CI -0.36, 5.29) (Figure 3).

Cupping versus active control

Pain: Ten studies were included in the analysis.[21-28 34 35] Of these 10 studies, nine reported the outcome in VAS, while one study reported NPQ scores.[21] In analysis of the nine studies, the cupping group exhibited significant reduction in pain with an MD of -0.89 (95% CI -1.42 to -0.37; P=0.0009) compared with the control group. The chi-square test, however, revealed some heterogeneity (p<0.00001; I^2 =88%). In order to resolve the heterogeneity, studies were separately analysed depending on the type of cupping: either wet (with scarification) or dry. Meta-analysis of three studies conducted with dry cupping indicated an MD of -1.50 (95% CI -2.28 to -0.72 ; I^2=28%; P=0.25). On the other hand, analysis of studies with wet cupping showed an MD of -0.70 (95% CI -1.32 to -0.07 ; I2=92%; P<0.00001) with unresolved heterogeneity. Omission of the study by Zhou 2014[28] – the effect size of which was notably large – resulted in an MD of -0.49 (95% CI -0.78 to -0.20) with I^2=-35%, P=0.19, implying that the heterogeneity was considerably resolved. The one study that reported outcomes with NPQ indicated an MD of 3.59 (95% CI 2.02, 5.16), suggesting that cupping significantly decreased pain compared to the control.

Disability: Four studies were included in the analysis.[22 24-26] Compared with the control, the cupping group demonstrated functional improvement, with an MD of -4.36 (95% CI -8.67 to -0.04; P=0.05), but not to a statistically significant degree, and substantial heterogeneity was identified (I^2=62%; P=0.05).

QoL: Two studies were included in this analysis.[22 25] Compared with the control, the cupping group reported significant improvement in the physical component summary of SF-36, with an MD of 5.44 (95% CI 2.09 to 8.78; P=0.001). However, statistically significant differences were not found for the mental component summary of SF-36 with an MD of 0.44 (95% CI -4.05, 4.93) (Figure 4). The study by Kim et al. reported EQ-5D outcomes as median values, and therefore inclusion for meta-analysis was not feasible. In this study, the cupping group and control reported identical median values of 0.91, suggesting no statistical difference.

Cupping with active control versus active control (add-on)

Pain: Five studies were included in the analysis.[19 26 33 35 36] Adding cupping therapy to the treatment administered in the control group led to significant reduction in pain, with an MD of -0.87 (95% CI -1.14 to -0.61; P<0.00001).

Disability: Only one study reported a disability-related outcome,[26] and the effect on disability was not significant, with an MD of 3.61 (95% CI -3.93 to 11.15; P=0.35). Heterogeneity was not identified (I^2=19%;

P=0.29) (Figure 5).

Safety of cupping

Ten of the 18 studies included in the final analysis did not address safety, while eight studies did. First, Kim et al.[24] reported skin laceration (n=1), whole body itching (n=1), pain at the cupping sites (n=1), and generalized body ache (n=1) in four patients in the cupping group; however, the study reported that the symptoms were mild and resolved within a few days. Lauche et al. (2012)[31] reported one case of pain during the procedure itself in addition to tension headache, migraine, tinnitus, and wound healing itches; however, all side effects were mild and temporary. Chi et al.[29] reported two cases of mild low back pain due to the seated position in the cupping group. Lauche et al. (2013)[25] reported muscular tension (n=1), increased pain (n=1), and prolapsed intervertebral disc (n=1), while prolapsed intervertebral disc should be regarded to be a severe event, the original authors stated that a causal relationship was unlikely. Lauche et al. (2011)[30] reported tingling sensation in the hands and arms (n=1), strain/pain at the treated area (n=2), strain/pain in their general neck region (n=1), slight headache (n=1), tiredness (n=1), shivering attack (n=1), and blurred vision (n=1). Lauche et al. (2011) reported that all symptoms subsided within four hours, and that the causal relationship with cupping was unclear. Yin et al.[27] reported one case of delayed wound healing due to wet cupping. Cramer et al.[22] reported muscle soreness (n=2), minor hematoma (n=1), and increased neck pain for 1 hour to 5 hours (n=2). In the study by Saha et al.,[20] two participants complained of headache that resolved within one hour. One participant suffered upper back pain, which subsided within days, and one participant reported slight dizziness. Although one case of lipoma was identified during the trial, it did not have any causal relationship with cupping, as reported by the authors.

Levels of evidence

The quality of evidence for each analysis is shown in Table 2. In the waiting list comparison, the quality of evidence for the outcomes of pain, QoL, and disability was assessed to be low to very low due to concerns regarding risk of bias, imprecision and inconsistency. In the active control comparison, the quality of evidence for the outcomes of pain and QoL was low in consideration of the risk of bias and imprecision, and that for disability was assessed to be very low due to risk of bias, imprecision, and unexplained heterogeneity. In the add-on comparison between the active control, and active control with cupping groups, the quality of evidence for pain in the dry cupping add-on group was low due to risk of bias and unexplained heterogeneity. The quality of evidence for pain outcomes was very low. The quality of evidence for disability outcomes in the add-on groups was low due to risk of bias and imprecision (Table 2).

Table 2. Meta-analysis of outcomes and level of evidence

Variable	Overall effect						Studies (N)	Sample size (N)	Level of evidence
	MD	95% CI	*P*	I^2	P	Statistical method			
Cupping versus Waitlist (Sole)									
Pain (VAS)	-2.42	-3.98, -0.86	0.002	93	<0.00001	Random Inverse Variance	5	241	Very low
Pain (VAS) omitted 1 studies	-1.48	-1.86, -1.10	<0.00001	0	0.57	Random Inverse Variance	4	181	-
Disability (NDI)	-4.34	-6.77, -1.91	0.0005	6	0.35	Random Inverse Variance	3	141	Low
QoL (Physical component of SF-36)	2.46	-0.36,5.29	0.09	24	0.27	Random Inverse Variance	3	141	Low
QoL (Mental component of SF-36)	5.32	0.83, 9.80	0.02	32	0.23	Random Inverse Variance	3	141	Low
Cupping versus Active control (Sole)									
Pain (VAS)	-0.89	-1.42, -0.37	0.0009	88	<0.00001	Random Inverse Variance	9	870	Low
Pain (VAS) of dry cupping	-1.48	-1.86, -1.10	<0.00001	0	0.57	Random Inverse Variance	3	149	-
Pain (VAS) of wet cupping	-0.70	-1.32, -0.07	0.03	92	<0.00001	Random Inverse Variance	6	721	-
Pain (VAS) of wet cupping omitted 1 studies	-0.49	-0.78, -0.20	0.0008	35	0.19	Random Inverse Variance	5	521	-
Disability (NDI)	-4.36	-8.67, -0.04	0.05	62	0.05	Random Inverse Variance	4	213	Very low
QoL (SF-36) (Physical component of SF-36)	5.44	2.09, 8.78	0.001	7	0.30	Random Inverse Variance	2	109	Low
QoL (SF-36) (Mental component of SF-36)	0.44	-4.05, 4.93	0.85	0	0.59	Random Inverse Variance	2	109	Low
Cupping with active control vs control (addon)									
Pain (VAS)	-0.87	-1.14, -0.61	<0.00001	19	0.29	Random Inverse Variance	5	534	Low
Disability (NDI)	3.61	-3.93, 11.15	0.35	-	-	Random Inverse Variance	1	56	Low

VAS: Visual analogue scale, NDI: Neck disability index, QoL: Quality of life, MD: Mean difference

DISCUSSION

The present study aimed to assess the evidence supporting the effectiveness of cupping on neck pain through a comprehensive systematic literature review. We performed a systematic and inclusive search in non-Asian as well as Asian databases, including those from China, Korea, and Japan, where cupping is popular and widely used. Eighteen articles were selected and analysed according to the type of control group used. When compared with inactive controls, cupping significantly reduced pain and improved function and QoL. The heterogeneity was quite high in terms of pain reduction, and the quality of evidence was lowered as a consequence. As the study by Chi reported a considerably large effect size, the heterogeneity was resolved upon omission of this study in sensitivity analysis. The quality of evidence was found to be low to very low in most studies; however, the marked reduction in pain, functional improvement, and improvement in QoL associated with cupping compared with no interventions may be construed to be clinically relevant. When compared with active controls, the cupping group exhibited significant reduction in pain but no significant differences for functional improvement. Analysis in pain outcomes found an MD of -0.89 (95% CI -1.42, -0.37). However, heterogeneity was high and subgroup analysis was therefore performed. Effect sizes were similar across studies using dry cupping; however, effect sizes varied greatly across studies using wet cupping. Omission of the study by Zhou 2014[28] resolved the heterogeneity. Additional analyses are needed to substantiate whether the differences may be attributed to the difference in types of wet cupping procedures or whether other factors are at play. Wet cupping involves drawing blood before cupping, and may be well accepted in some cultures, but otherwise incur fear and aversion in others. Furthermore, the intensity of the procedure and amount of bleeding may also have affected outcomes, which may have further contributed to the varying effect sizes. However, the type and frequency of procedures, and patient pain severity may also have contributed to the varying effect sizes. When added on to existing treatments, cupping significantly reduced pain, with an MD of -0.87 (95% CI -1.14 to -0.61). In addition to statistical significance, the effect size must be assessed in terms of clinical significance. Based on four studies of cupping, Lauche et al.[38] proposed the minimal clinically important difference (MCID) of VAS to be -8 (-0.8 of a ten point scale), the NDI to be -3, and the physical component summary of SF-36 to be +5.1. From the current meta-analysis, cupping exhibited an MD of -2.42 compared to the waiting list control, -0.89 compared to the active control, and -0.87 as an add-on treatment, which all surpasses the above criteria for the MCID of VAS. With regard to NDI, cupping indicated an MD of between -4.34 and -4.36, depending on the type of control, which again sufficed the MCID criteria. For the physical component summary, however, cupping failed to display a treatment effect larger than MCID; Yet, when compared to the active control, cupping showed an effect size exceeding MCID, which calls for further investigation.

Records of cupping, also known as hijama, document how its use dates back several thousand years, and how it originated and has been employed in such diverse regions as early Egypt and China.[8] In traditional Chinese medicine, cupping is widely used to eliminate stagnated Qi and Blood, and facilitate circulation.[39] Since ancient times, cupping has been considered to be effective for local areas of inflammation.[40] A review of various studies concerning the mechanism of cupping suggested that cupping exerts its effects by means of a haemodynamic mechanism that facilitates muscle function, as demonstrated by the reduction of deoxy-haemoglobin and

elevated oxy-haemoglobin levels in muscle areas treated with cupping.[41] In other studies, cupping was purported to involve a mechanism for removing oxidative stress,[42] and to produce therapeutic effects through diffuse noxious inhibitory control,[43] which would contribute to alleviation of pain.

For these reasons, a growing number of clinical trials are investigating the effects of cupping on pain and various disease symptoms. Through analysis of 135 RCTs on cupping, Cao 2012[44] reported that clinical trials of wet cupping have been conducted in association with such disorders as herpes zoster, facial paralysis, cough/dyspnea, and acne. There is also a more recent systematic review that investigated cupping in relation to overall disease;[45] however, the review only included some articles pertaining to neck pain and did not focus on the condition. In another systematic literature review on the efficacy of cupping for lower back pain, cupping led to significant reductions in pain and improvement of function.[13 46] There was also a study that specifically evaluated the effect of cupping on neck pain, but the study was published in 2013.[13] This previous study only analysed five trials whereas the present review was conducted with 18 RCTs. The results of this study, therefore, are hoped to hold and convey stronger evidence as well as greater clinical relevance and implications. In this context, the present study is considered to hold heightened significance in that it analysed more recent evidence on the effects of cupping for neck pain without language restrictions.

However, this study also holds several limitations. One significant shortcoming is that only some studies reported issues related to safety. Although severe adverse events were not found in association with cupping in the studies that reported side effects, there were a greater number of studies that did not report side effects, and this calls for more well-designed, large-scale studies investigating the potential side effects of cupping. A systematic review investigating the side effects of cupping reported that the most common side effect was scar formation, and there were also some cases of severe side effects.[47] However, adverse reactions to cupping may vary according to the proficiency of the practitioner, type of procedure, and disinfection and sterilization processes implemented during the treatment procedure.[47] Certain severe AEs such as infection may be pre-emptively avoided as its occurrence is directly associated with the education and training, and experience and proficiency of therapists. Another limitation was that the quality of evidence was either low or very low for all outcomes. The primary causes of the low quality of evidence were risk of bias and unexplained heterogeneity. The quality of evidence for random sequence and allocation concealment would not have been lowered if the studies had been performed correctly; however, the selected studies did not maintain rigorous standards and procedures regarding these issues. In addition, most of the included studies, except for the one by Su 2016,[33] were conducted only in chronic neck pain patients. Whether the therapeutic effect of cupping is dependent on the clinical characteristics (acute vs. chronic) of neck pain remains to be elucidated. Nevertheless, cupping is an invaluable therapy that persons who have received proper training can use easily. Lauche et al. (2013)[25] performed a clinical trial on home-based cupping. Due to the increase of computer and smartphone use, the prevalence of neck pain is rising steadily,[48] and neck pain is also notorious for its high percentage of chronicity. The findings of this study are meaningful in that it represents a non-invasive, simple, and effective treatment modality for patients with chronic pain.

Cupping was shown to be effective for neck pain in this review. However, the current review on the effect of

cupping was unable to find conclusive evidence, and this suggests the need for more high-quality RCTs. Study designs should implement standardized randomization and allocation procedures, and appropriate blinding of outcome assessors where possible. To obtain more conclusive evidence regarding the effectiveness and safety of cupping, such well-designed clinical trials are warranted. Similarly, the safety and risks of cupping could not be sufficiently assessed due to the lack of studies reporting AEs. Although no serious AEs have been reported so far in the analyzed trials, the majority of trials failed to given any mention of AE occurrence. Further investigations are required to draw solid conclusions regarding the safety of cupping therapy. Firm conclusions on clinical use of cupping for pain disorders shall be made possible only through such rigorous assessments of safety and effectiveness.

CONCLUSION

The current results suggest that cupping may be effective for neck pain patients in terms of pain, function, and quality of life compared to no treatment or active controls. The level of evidence for the findings, however, was found to be low or very low, which prevented the study from drawing firm conclusions. Although this study did not identify notable adverse events in the articles reviewed for this study, cupping is not without side effects, and further well-designed large-scale studies employing standardized procedures are needed for thorough examination of its potential side effects. Furthermore, wet cupping requires rigorous education and training on hygiene and precautions as it entails a blood-letting process. Although this study was unable to draw any definite conclusions, it holds significance in that it showcased the possibility of cupping use as an effective and safe therapy for neck pain.

FOOTNOTES

Contributors: SK, MRK, IHH, and YJL designed the study. SK, SHL and YJL conducted the systematic search. SK, MRK, and YJL assessed the literatures for inclusion and extracted the data. JL, JSS, and IHH monitored data collection. EJK, DSH, JL, JSS, and IHH interpreted the data. SK, MRK, IHH, and YJL wrote the draft; SHL, EJK, DSH, JL, and JSS critically revised the manuscript. All authors have read and approved the final version.

Funding: This study was supported by the Traditional Korean Medicine R&D Program funded by the Ministry of Health & Welfare through the Korea Health Industry Development Institute (KHIDI) (HB16C0035).

Competing Interests: None declared

Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: No additional data are available.

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FIGURE LEGENDS

Figure 1. PRISMA flow diagram of the literature search

PRISMA : Preferred Reporting Items for Systematic Reviews and Meta Analyses

Figure 2. Risk of bias in the included studies, as assessed using the Cochrane Collaboration's risk of bias tool

+: high risk of bias, ?: unclear risk of bias, -: low risk of bias

Figure 3. Forest plots demonstrating the effect of cupping as the sole intervention vs no treatment on neck pain

CI: confidence interval

Figure 4. Forest plots demonstrating the effect of cupping as the sole intervention vs active control on neck pain

CI: confidence interval

Figure 5. Forest plots demonstrating the effect of cupping as the add-on intervention on neck pain

CI: confidence interval

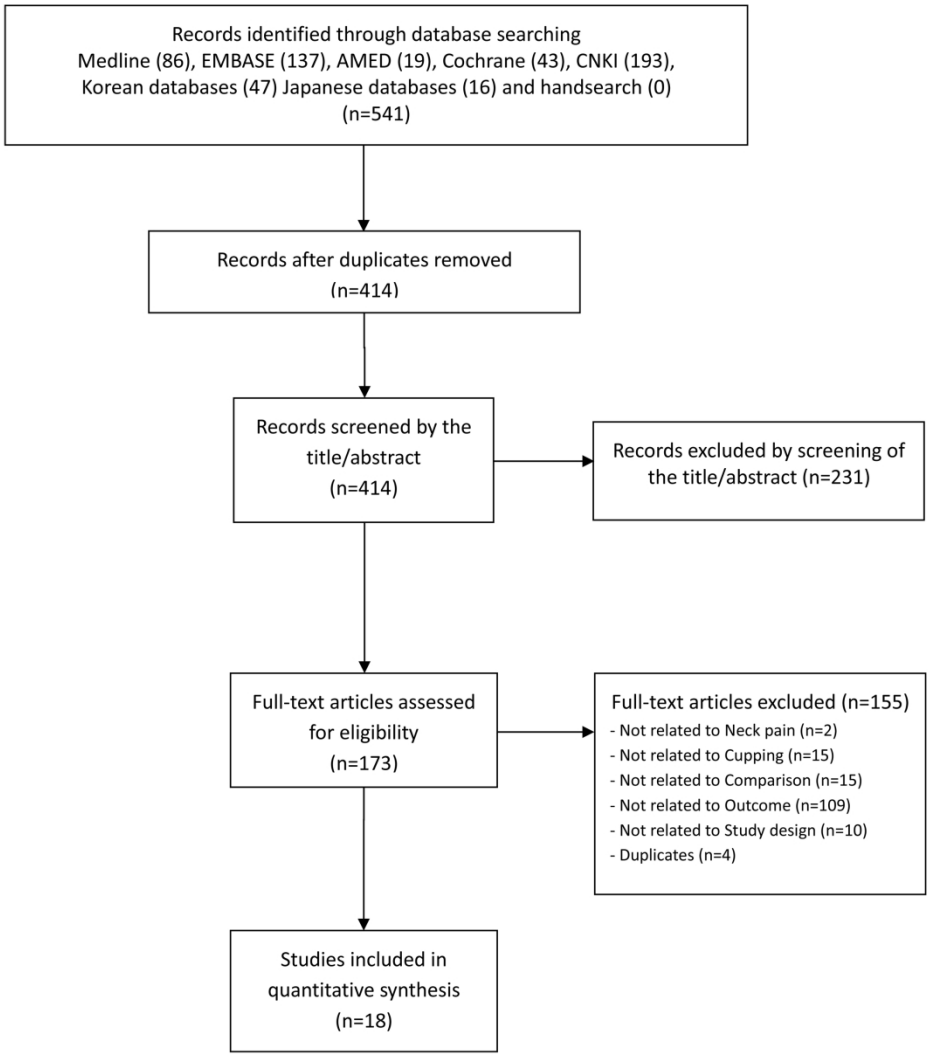

Figure 1. PRISMA flow diagram of the literature search

PRISMA : Preferred Reporting Items for Systematic Reviews and Meta Analyses

Figure 1. PRISMA flow diagram of the literature search
PRISMA : Preferred Reporting Items for Systematic Reviews and Meta Analysis

214x256mm (300 x 300 DPI)

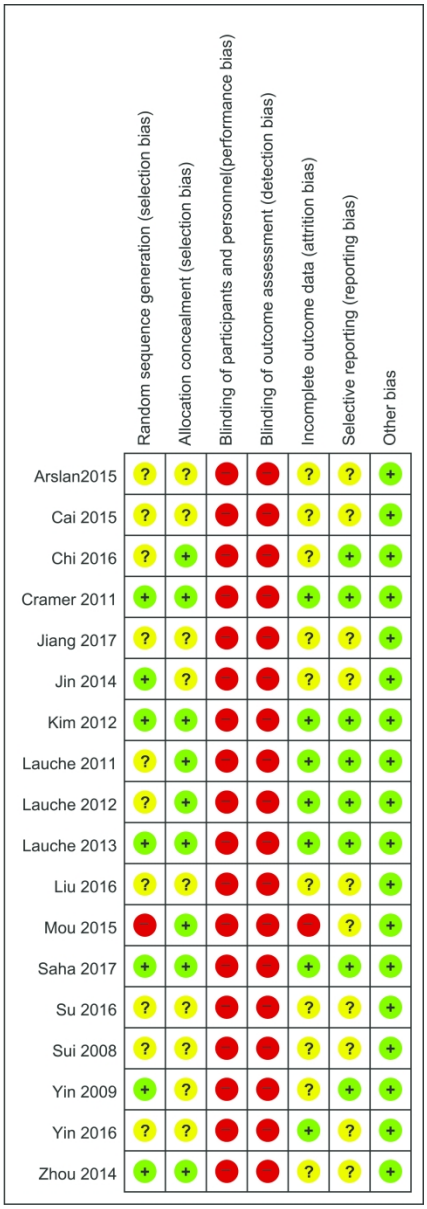

Figure 2. Risk of bias in the included studies, as assessed using the Cochrane Collaboration's risk of bias tool
+ : high risk of bias, ? : unclear risk of bias, - : low risk of bias

264x731mm (300 x 300 DPI)

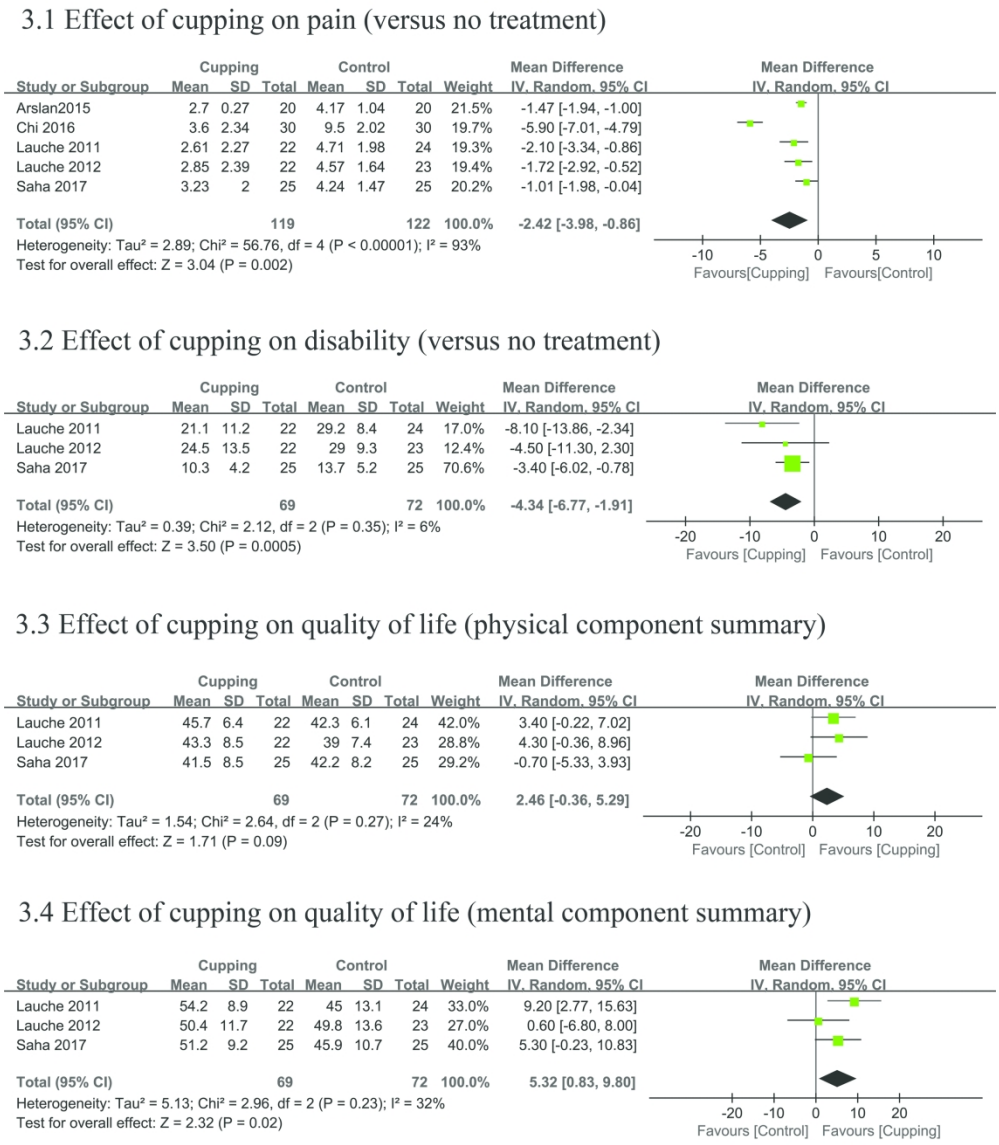

Figure 3. Forest plots demonstrating the effect of cupping as the sole intervention vs no treatment on neck pain
CI : confidence interval

236x285mm (300 x 300 DPI)

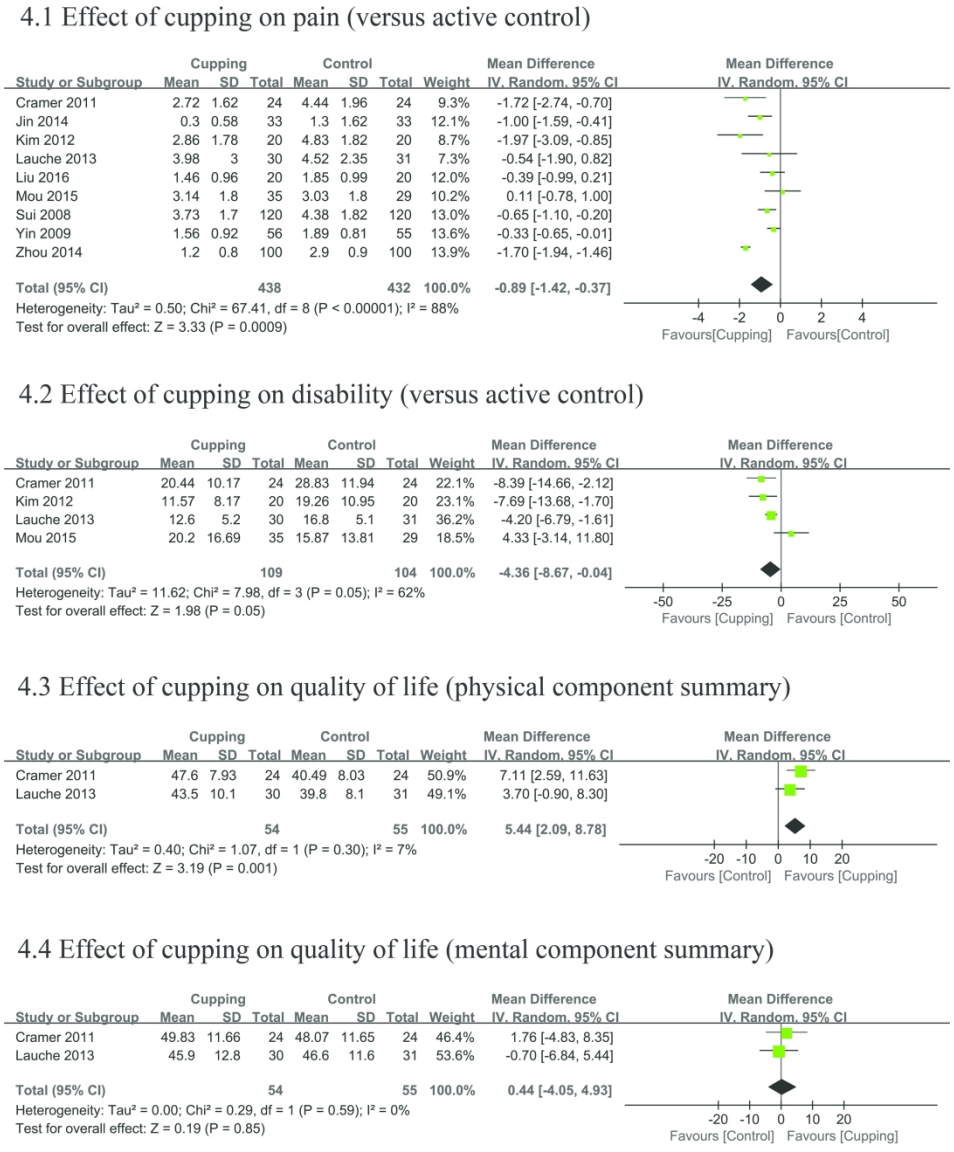

Figure 4. Forest plots demonstrating the effect of cupping as the sole intervention vs active control on neck pain
CI : confidence interval

247x313mm (300 x 300 DPI)

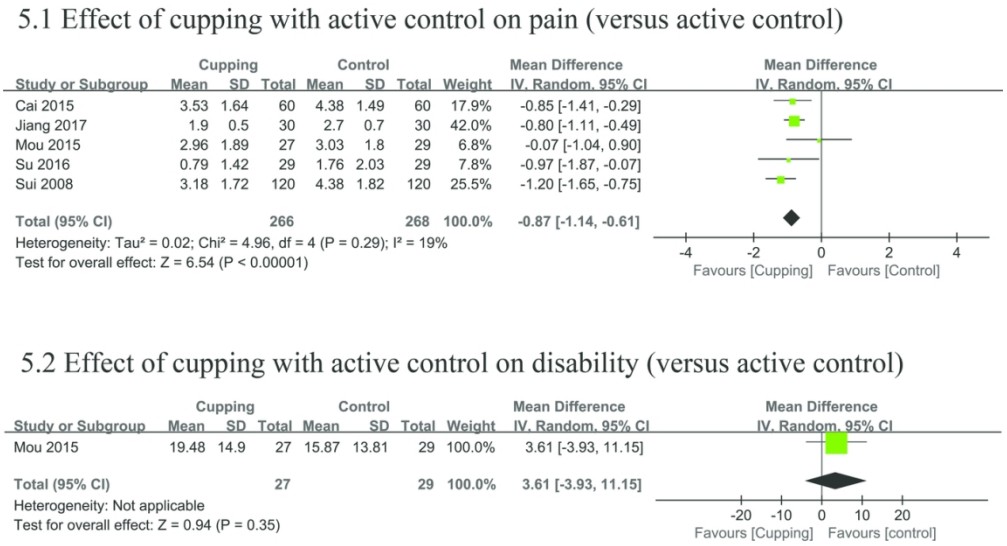

Figure 5. Forest plots demonstrating the effect of cupping as the add-on intervention on neck pain
CI : confidence interval

119x72mm (300 x 300 DPI)

Appendix S1 Search strategy

Ovid-Medline 1946 to Jan Week 1 2018 Date: 2018.01.08		
	Searches	**Results**
1	Neck Pain/	6385
2	exp Brachial Plexus Neuropathies/	3563
3	cervical pain.mp.	961
4	neckache.mp.	20
5	cervicodynia.mp.	9
6	cervicalgia.mp.	114
7	brachialgia.mp.	165
8	brachial neuritis.mp.	174
9	brachial neuralgia.mp.	122
10	neck pain.mp.	14709
11	neck injur*.mp.	5953
12	brachial plexus neuropath*.mp.	2277
13	brachial plexus neuritis.mp.	1527
14	thoracic outlet syndrome/ or cervical rib syndrome/	2228
15	Torticollis/	3691
16	exp brachial plexus neuropathies/ or exp brachial plexus neuritis/	3563
17	cervico brachial neuralgia.ti,ab.	43
18	cervicobrachial neuralgia.ti,ab.	68
19	(monoradicul* or monoradicl*).tw.	143
20	or/1-19	33193
21	neck/	30018
22	neck muscles/	6076
23	exp cervical plexus/	8027
24	exp cervical vertebrae/	38618
25	atlanto axial joint	1767
26	atlanto occipital joint	3372
27	Cervical Atlas/	2539

28	spinal nerve roots/	10,825
29	exp brachial plexus/	24658
30	(odontoid* or cervical or occip* or atlant*).tw.	282283
31	axis/ or odontoid process/	1777
32	Thoracic Vertebrae/	20133
33	cervical vertebrae.mp.	35831
34	cervical plexus.mp.	1465
35	cervical spine.mp.	21326
36	(neck adj3 muscles).mp.	7410
37	(brachial adj3 plexus).mp.	13431
38	(thoracic adj3 vertebrae).mp.	21124
39	neck.mp.	244594
40	(thoracic adj3 spine).mp.	7024
41	(thoracic adj3 outlet).mp.	2763
42	trapezius.mp.	3985
43	or/21-42	566354
44	exp pain/	387369
45	exp injuries/	891764
46	pain.mp.	672242
47	ache.mp.	15382
48	sore.mp.	7757
49	stiff.mp.	9236
50	discomfort.mp.	42264
51	injur*.mp.	1050876
52	neuropath*.mp.	140510
53	or/44-52	2242467
54	43 and 53	135447
55	Radiculopathy/	4853
56	exp temporomandibular joint disorders/ or exp temporomandibular joint dysfunction syndrome/	16566

57	myofascial pain syndromes/	1627
58	exp "Sprains and Strains"/	18830
59	exp Spinal Osteophytosis/	4196
60	exp Neuritis/	7282
61	Polyradiculopathy/	2656
62	exp Arthritis/	259875
63	Fibromyalgia/	8641
64	spondylitis/ or discitis/	6486
65	spondylosis/ or spondylolysis/ or spondylolisthesis/	7014
66	radiculopathy.mp.	8529
67	radiculitis.mp.	821
68	temporomandibular.mp.	27614
69	myofascial pain syndrome*.mp.	1967
70	thoracic outlet syndrome*.mp.	2552
71	spinal osteophytosis.mp.	3575
72	neuritis.mp.	17471
73	spondylosis.mp.	4358
74	spondylitis.mp.	23814
75	spondylolisthesis.mp.	6178
76	or/55-75	361804
77	43 and 76	28356
78	exp neck/	30044
79	exp cervical vertebrae/	38618
80	Thoracic Vertebrae/	20133
81	neck.mp.	244594
82	(thoracic adj3 vertebrae).mp.	21124
83	(thoracic adj3 spine).mp.	7024
84	cervical spine.mp.	21326
85	or/78-84	302173
86	Intervertebral Disk/	13804
87	(disc or discs).mp.	99973
88	(disk or disks).mp.	53273

89	or/86-88	139200
90	85 and 89	9454
91	herniat*.mp.	21849
92	slipped.mp.	4540
93	prolapse*.mp.	32528
94	displace*.mp.	149806
95	degenerat*.mp.	237832
96	(bulge or bulged or bulging).mp.	9191
97	or/91-96	437364
98	90 and 97	6049
99	intervertebral disk degeneration/ or intervertebral disk displacement/	21747
100	intervertebral disk displacement.mp.	1741
101	intervertebral disc displacement.mp.	18641
102	intervertebral disk degeneration.mp.	152
103	intervertebral disc degeneration.mp.	4850
104	intervertebral disk hernia.mp.	222
105	or/99-104	22513
106	85 and 105	4166
107	20 or 54 or 77 or 98 or 106	156956
108	cupping.mp.	1754
109	ventouse.tw.	237
110	exp phlebotomy/	5704
111	bloodletting.mp.	2994
112	blood letting.mp.	349
113	bloodletting.mp.	2994
114	spilled blood.mp.	13
115	venesection.mp.	686
116	or/108-115	8424
117	107 and 116	86

Ovid-EMBASE 1980 to 2018 Jan **DATE: 2018.01.08**

	Searches	Results
1	Neck Pain/	18952
2	brachial plexus neuropathy/	1779
3	cervical pain.mp.	1285
4	neckache.mp.	23
5	cervicodynia.mp.	17
6	cervicalgia.mp.	176
7	brachialgia/	262
8	brachialgia.mp.	368
9	brachial neuritis.mp.	204
10	brachial neuralgia.mp.	67
11	neck pain.mp.	21299
12	neck injur*.mp.	7234
13	brachial plexus neuropath*.mp.	1944
14	brachial plexus neuritis.mp.	85
15	thoracic outlet syndrome/	2075
16	Torticollis/	4014
17	exp brachial plexus neuropathies/ or exp brachial plexus neuritis/	1779
18	cervico brachial neuralgia.ti,ab.	36
19	cervicobrachial neuralgia.ti,ab.	75
20	(monoradicul* or monoradicl*).tw.	150
21	or/1-20	37046
22	neck/	50115
23	neck muscles/	5295
24	cervical plexus/	1090
25	cervical spine/	31073
26	atlantoaxial joint/	1743
27	atlantooccipital joint/	2016
28	atlas/	1765
29	spinal root/	4655
30	brachial plexus/	7832
31	(odontoid* or cervical or occip* or atlant*).tw.	313982

32	odontoid process/	2481
33	cervical vertebra.mp.	3529
34	cervical vertebrae.mp.	3134
35	cervical plexus.mp.	1403
36	cervical spine.mp.	48597
37	(neck adj3 muscles).mp.	2581
38	(brachial adj3 plexus).mp.	17831
39	(thoracic adj3 vertebrae).mp.	2227
40	neck.mp.	300025
41	(thoracic adj3 spine).mp.	13953
42	(thoracic adj3 outlet).mp.	2435
43	trapezius.mp.	5264
44	or/22-43	622696
45	exp pain/	1091658
46	exp injuries/	66466
47	pain.mp.	1032154
48	ache.mp.	16783
49	sore.mp.	18614
50	stiff.mp.	11265
51	discomfort.mp.	64832
52	injur*.mp.	1377870
53	neuropath*.mp.	267008
54	or/45-53	2799546
55	44 and 54	151698
56	Radiculopathy/	8801
57	temporomandibular joint disorder/	11910
58	myofascial pain/	7225
59	spondylosis/ or cervical spondylosis/	6895
60	Neuritis/	5803
61	exp Arthritis/	395884
62	Fibromyalgia/	17215
63	exp spondylitis/	34738

64	diskitis/	2171
65	spondylolisthesis/	7164
66	radiculopathy.mp.	11998
67	radiculitis.mp.	1260
68	temporomandibular.mp.	25840
69	myofascial pain syndrome*.mp.	1158
70	spinal osteophytosis.mp.	36
71	neuritis.mp.	19219
72	spondylosis.mp.	8026
73	spondylitis.mp.	35047
74	spondylolisthesis.mp.	7954
75	or/56-74	476180
76	44 and 75	27829
77	neck/	50115
78	cervical spine/	31073
79	neck.mp.	300025
80	(thoracic adj3 vertebrae).mp.	2227
81	(thoracic adj3 spine).mp.	13953
82	cervical spine.mp.	48597
83	or/77-82	348878
84	Intervertebral Disk/	11331
85	(disc or discs).mp.	85296
86	(disk or disks).mp.	97488
87	or/84-86	146518
88	83 and 87	9652
89	herniat*.mp.	25041
90	slipped.mp.	3710
91	prolapse*.mp.	41853
92	displace*.mp.	127797
93	degenerat*.mp.	321664
94	(bulge or bulged or bulging).mp.	10599
95	or/89-94	520028

96	88 and 95	5203
97	intervertebral disk hernia/	15253
98	intervertebral disk degeneration/	8780
99	intervertebral disk displacement.mp.	533
100	intervertebral disc displacement.mp.	131
101	intervertebral disk degeneration.mp.	8836
102	intervertebral disc degeneration.mp.	1880
103	or/97-102	23812
104	83 and 103	4121
105	21 or 55 or 76 or 96 or 104	169900
106	cupping.mp.	1908
107	ventouse.tw.	411
108	exp phlebotomy/	9427
109	bloodletting.mp.	672
110	blood letting.mp.	315
111	blood-letting.mp.	315
112	spilled blood.mp.	14
113	venesection.mp.	743
114	106 or 107 or 108 or 109 or 110 or 111 or 112 or 113	12343
115	105 and 114	137

Ovid-AMED 1985 to December 2017		**Date: 2018.01.08.**
	Searches	**Results**
1	Neck Pain/	1031
2	exp Brachial plexus/	282
3	cervical pain.mp.	75
4	neckache.mp.	0
5	cervicodynia.mp.	2
6	cervicalgia.mp.	13
7	brachialgia.mp.	6
8	brachial neuritis.mp.	1

9	brachial neuralgia.mp.	5
10	neck pain.mp.	1380
11	neck injur*.mp.	139
12	brachial plexus neuropath*.mp.	8
13	brachial plexus neuritis.mp.	1
14	thoracic outlet syndrome/ or cervical rib syndrome/	43
15	Torticollis/	70
16	cervico brachial neuralgia.ti,ab.	0
17	cervicobrachial neuralgia.ti,ab.	2
18	(monoradicul* or monoradicl*).tw.	0
19	or/1-18	1941
20	neck/	663
21	neck muscles/	150
22	exp cervical plexus/	30
23	exp cervical vertebrae/	1647
24	Atlanto axial joint/	32
25	Atlanto occipital joint/	17
26	spinal nerve roots/	92
27	(odontoid* or cervical or occip* or atlant*).tw.	3929
28	Axis/	9
29	Odontoid process/	8
30	Thoracic Vertebrae/	302
31	cervical vertebrae.mp.	1678
32	cervical plexus.mp.	11
33	cervical spine.mp.	1163
34	(neck adj3 muscles).mp.	311
35	(brachial adj3 plexus).mp.	203
36	(thoracic adj3 vertebrae).mp.	331
37	neck.mp.	3781
38	(thoracic adj3 spine).mp.	355
39	(thoracic adj3 outlet).mp.	83
40	trapezius.mp.	502
41	or/20-40	7636

42	exp pain/	20488
43	exp injuries/	3007
44	pain.mp.	29672
45	ache.mp.	124
46	sore.mp.	167
47	stiff.mp.	228
48	discomfort.mp.	991
49	injur*.mp.	28051
50	neuropath*.mp.	1781
51	or/42-50	57325
52	41 and 51	4097
53	myofascial pain syndromes/	352
54	exp "Sprains and Strains"/	949
55	exp Spinal Osteophytosis/	35
56	exp Neuritis/	62
57	exp Arthritis/	5513
58	Fibromyalgia/	1647
59	spondylitis/ or discitis/	77
60	spondylosis/ or spondylolysis/ or spondylolisthesis/	140
61	radiculopathy.mp.	285
62	radiculitis.mp.	10
63	temporomandibular.mp.	582
64	myofascial pain syndrome*.mp.	424
65	thoracic outlet syndrome*.mp.	80
66	spinal osteophytosis.mp.	41
67	neuritis.mp.	78
68	spondylosis.mp.	130
69	spondylitis.mp.	358
70	spondylolisthesis.mp.	154
71	or/53-70	9763
72	41 and 71	794
73	exp neck/	710

74	exp cervical vertebrae/	1647
75	Thoracic Vertebrae/	302
76	neck.mp.	3781
77	(thoracic adj3 vertebrae).mp.	331
78	(thoracic adj3 spine).mp.	355
79	cervical spine.mp.	1163
80	or/73-79	5755
81	Intervertebral Disk/	327
82	(disc or discs).mp.	1209
83	(disk or disks).mp.	985
84	or/81-83	1693
85	80 and 84	225
86	herniat*.mp.	390
87	slipped.mp.	27
88	prolapse*.mp.	122
89	displace*.mp.	2548
90	degenerat*.mp.	1676
91	(bulge or bulged or bulging).mp.	63
92	or/86-91	4467
93	85 and 92	141
94	intervertebral disk degeneration/ or intervertebral disk displacement/	342
95	intervertebral disk displacement.mp.	376
96	intervertebral disc displacement.mp.	1
97	intervertebral disk degeneration.mp.	29
98	intervertebral disc degeneration.mp.	22
99	intervertebral disk hernia/	0
100	or/94-99	414
101	80 and 100	54
102	19 or 52 or 72 or 93 or 101	4732
103	cupping.mp.	173
104	ventouse.tw.	2
105	exp Bloodletting/	43

106	exp Cupping/	101
107	bloodletting.mp.	69
108	blood letting.mp.	30
109	bloodletting.mp.	69
110	spilled blood.mp.	0
111	venesection.mp.	0
112	or/103-111	235
113	102 and 112	19

Cochrane Library		**Date: 2018.01.09**
	Searches	**Results**
1	[mh ^"Neck pain"]	845
2	[mh "Brachial Plexus Neuropathies"]	53
3	cervical pain:ti,ab,kw	3071
4	neckache:ti,ab,kw	1
5	cervicodynia:ti,ab,kw	1
6	cervicalgia:ti,ab,kw	11
7	brachialgia:ti,ab,kw	12
8	brachial neuritis:ti,ab,kw	28
9	brachial neuralgia:ti,ab,kw	17
10	neck pain:ti,ab,kw	4667
11	neck injur*:ti,ab,kw	1417
12	brachial plexus neuropath*:ti,ab,kw	75
13	brachial plexus neuritis:ti,ab,kw	28
14	[mh ^"thoracic outlet syndrome"]	18
15	[mh ^"cervical rib syndrome"]	1
16	[mh ^Torticollis]	98
17	[mh "brachial plexus neuropathies"]	53
18	[mh "brachial plexus neuritis"]	25
19	cervico brachial neuralgia:ti,ab,kw	5
20	cervicobrachial neuralgia:ti,ab,kw	115

21	monoradicul* or monoradicl*;ti,ab,kw	26
22	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21	7525
23	[mh ^neck]	486
24	[mh ^"neck muscles"]	216
25	[mh "cervical plexus"]	111
26	[mh "cervical vertebrae"]	994
27	[mh ^"atlanto-axial joint"]	23
28	[mh ^"atlanto-occipital joint"]	8
29	[mh ^"Cervical Atlas"]	4
30	[mh ^"spinal nerve roots"]	150
31	[mh "brachial plexus"]	949
32	odontoid* or cervical or occip* or atlant*:ti,ab,kw	16822
33	[mh ^"odontoid process"]	11
34	[mh ^"Thoracic Vertebrae"]	469
35	cervical vertebrae:ti,ab,kw	1086
36	cervical plexus:ti,ab,kw	217
37	cervical spine:ti,ab,kw	1609
38	neck muscles:ti,ab,kw	704
39	brachial plexus:ti,ab,kw	1237
40	thoracic vertebrae:ti,ab,kw	584
41	neck:ti,ab,kw	15234
42	thoracic spine:ti,ab,kw	741
43	thoracic outlet:ti,ab,kw	41
44	trapezius:ti,ab,kw	530
45	#23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44	33047
46	[mh pain]	39333
47	[mh injuries]	19901
48	pain:ti,ab,kw	107702
49	ache:ti,ab,kw	298
50	sore:ti,ab,kw	2106
51	stiff:ti,ab,kw	296

52	discomfort:ti,ab,kw	9125
53	injur*:ti,ab,kw	39318
54	neuropath*:ti,ab,kw	8396
55	#46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54	161760
56	#45 and #55	10128
57	[mh ^Radiculopathy]	293
58	[mh "temporomandibular joint disorders"]	614
59	[mh "temporomandibular joint dysfunction syndrome"]	179
60	[mh "myofascial pain syndromes"]	451
61	[mh "Sprains and Strains"]	999
62	[mh "Spinal Osteophytosis"]	91
63	[mh Neuritis]	70
64	[mh ^polyradiculopathy]	13
65	[mh arthritis]	10946
66	[mh ^Fibromyalgia]	842
67	[mh ^spondylitis]	20
68	[mh ^discitis]	9
69	[mh ^spondylosis]	126
70	[mh ^spondylolysis]	11
71	[mh ^spondylolisthesis]	155
72	radiculopathy:ti,ab,kw	725
73	radiculitis:ti,ab,kw	38
74	temporomandibular:ti,ab,kw	1111
75	myofascial pain syndrome*:ti,ab,kw	569
76	thoracic outlet syndrome*:ti,ab,kw	35
77	spinal osteophytosis:ti,ab,kw	95
78	neuritis:ti,ab,kw	550
79	spondylosis:ti,ab,kw	411
80	spondylitis:ti,ab,kw	1395
81	spondylolisthesis:ti,ab,kw	460
82	#57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81	17164

83	#45 and #82	1519
84	[mh neck]	486
85	[mh "cervical vertebrae"]	994
86	[mh ^"thoracic vertebrae"]	469
87	neck:ti,ab,kw	15234
88	thoracic vertebrae:ti,ab,kw	584
89	thoracic spine:ti,ab,kw	741
90	cervical spine:ti,ab,kw	1609
91	#84 or #85 or #86 or #87 or #88 or #89 or #90	14188
92	[mh ^"Intervertebral Disk"]	271
93	disc$:ti,ab,kw	3867
94	#92 or #93	3867
95	#91 and #94	541
96	herniat*:ti,ab,kw	1225
97	slipped:ti,ab,kw	49
98	prolapse*:ti,ab,kw	1996
99	displace*:ti,ab,kw	4124
100	degenerat*:ti,ab,kw	5989
101	bulge or bulged or bulging:ti,ab,kw	279
102	#96 or #97 or #98 or #99 or #100 or #101	12784
103	#95 and #102	372
104	[mh ^"intervertebral disk degeneration"]	205
105	[mh ^"intervertebral disk displacement"]	746
106	intervertebral disk displacement:ti,ab,kw	247
107	intervertebral disc displacement:ti,ab,kw	812
108	intervertebral disk degeneration:ti,ab,kw	238
109	intervertebral disc degeneration:ti,ab,kw	416
110	intervertebral disk hernia	419
111	#104 or #105 or #106 or #107 or #108 or #109 or #110	1529
112	#91 and #111	277
113	#112 or #103 or #83 or #56 or #22	11540
114	cupping:ti,ab,kw	340
115	ventouse:ti,ab,kw	56

116	MeSH descriptor: [Bloodletting] explode all trees	100
117	bloodletting:ti,ab,kw	159
118	blood letting:ti,ab,kw	77
119	blood-letting:ti,ab,kw	72
120	spilled blood:ti,ab,kw	6
121	venesection:ti,ab,kw	60
122	#114 or #115 or #116 or #117 or #118 or #119 or #120 or #121	596
123	#113 and #122	43

CHINA Academic Journals Full-text Database

(SU='颈痛'OR SU='颈肩痛'OR SU='颈椎病' OR SU='颈肩部'OR SU='颈椎间盘突出症' OR SU='颈部'OR SU='神经根型颈椎病') AND (SU='罐' OR SU='cupping') AND (SU='随机' or SU='对照') 193

Korean databases

KoreaMed (Date：2018.01.11)		
1	경항통 and 부항	0
2	neck pain and cupping	0
3	頸項痛 and 罐	0

KMBASE (Date：2018.01.11)		
1	경항통 and 부항	0
2	neck pain and cupping	0

3	頸項痛 and 罐	0

OASIS (Date : 2018.01.11)		
1	경항통 and 부항	0
2	neck pain and cupping	0
3	頸項痛 and 罐	0

NDSL (Date : 2018.1.11)		
1	경항통 and 부항	0
2	neck pain and cupping	37
3	頸項痛 and 罐	0

KISS (Date : 2018. 01. 11)		
1	경항통 and 부항	0
2	neck pain and cupping	5
3	頸項痛 and 罐	5

Japan database

J-stage (Date : 2018. 01. 11)		
1	neck pain cupping	15

医学中央雑誌刊行会(Ichushi)(Date : 2018. 01. 11)		
#1	(頸椎症性脊髄症/TH or 頸椎症/AL)	10,553
#2	頸椎椎間板ヘルニア/AL	1,077
#3	((@頸椎/TH and @脊椎損傷/TH and @捻挫/TH) or 頸椎捻挫/AL)	327
#4	(頸部痛/TH or 頸部疼痛/AL)	2,188
#6	頸肩部痛/AL	64
#7	#1 or #2 or #3 or #4 or #5 or #6	13,698
#8	cupping/AL	38
#9	吸角/AL	30
#10	#8 or #9	66
#11	#7 AND #10	1

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6, 11
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11 Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-13
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11 Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16-17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

For more information, visit: **www.prisma-statement.org**.

BMJ Open

Is cupping therapy effective in neck pain patients? A systematic review and meta-analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2017-021070.R2
Article Type:	Research
Date Submitted by the Author:	06-Jul-2018
Complete List of Authors:	Kim, Seoyoun; Jaseng Medical Foundation, Jaseng Spine and Joint Research Institute; Korea University, Graduate school of Public Health Lee, Sook-Hyun; Jaseng Medical Foundation, Jaseng Spine and Joint Research Institute Kim, Me-riong; Kyung Hee University, Department of Preventive Medicine, College of Korean Medicine Kim, Eun-jung; Dongguk University, Dept. of Acupuncture & Moxibustion, College of Korean Medicine Hwang, Deok-Sang; Kyung Hee University, Department of Korean Medicine Obstetrics & Gynecology, College of Korean Medicine Lee, Jinho; Jaseng Medical Foundation, Jaseng Spine and Joint Research Institute Shin, Joon-Shik; Jaseng Medical Foundation, Jaseng Spine and Joint Research Institute Ha, In-Hyuk; Kyung Hee University, Department of Preventive Medicine, College of Korean Medicine Lee, Yoon Jae; Jaseng Medical Foundation, Jaseng Spine and Joint Research Institute
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Rehabilitation medicine
Keywords:	Neck pain, Complementary Therapies, Meta-Analysis, Systematic Review

Is cupping therapy effective in neck pain patients? A systematic review and meta-analysis

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ABSTRACT

Objectives: Neck pain is a significant condition that is second only to depression as a cause of years lived with disability worldwide. Thus, identifying and understanding effective treatment modalities for neck pain is of heightened importance. This systematic review aimed to investigate the effects of cupping on neck pain from the current literature.

Design: Systematic review and meta-analysis of randomised controlled trials (RCTs)

Setting: Nine databases, including Chinese, Korean, and Japanese databases, were searched for data up to January 2018 with no restrictions on publication language

Participants: Neck pain patients

Interventions: Cupping therapy as the sole or add-on intervention compared with no treatment or active controls

Primary and secondary outcome measures: Pain severity, functional disability, and quality of life

Results: Eighteen RCTs were selected. Compared with the no intervention group, the cupping group exhibited significant reduction in pain (mean difference [MD] -2.42 [95% CI -3.98 to -0.86]) and improvement in function (MD -4.34 [95% CI -6.77 to -1.19]). Compared with the active control, the cupping group reported significant reduction in pain (P=0.0009) and significantly improved quality of life (P=0.001). The group that received control treatment with cupping therapy (add-on group) displayed significant pain reduction compared to the active control group (P=0.001). Of the eighteen studies, only eight reported occurrence of adverse events, which were mostly mild and temporary.

Conclusions: Cupping was found to reduce neck pain in patients compared to no intervention or active control groups, or as an add-on treatment. Depending on the type of control group, cupping was also associated with significant improvement in terms of function and quality of life; however, due to the low quality of evidence of the included studies, definitive conclusions could not be drawn from this review. Future well-designed studies are needed to substantiate the effectiveness of cupping on neck pain.

Keywords: Neck Pain, Complementary Therapies, Meta-Analysis, Systematic Review

ARTICLE SUMMARY

Strengths and limitations of this study

- This systematic review investigated the effectiveness of cupping in treating pain, and placed no restrictions on publication language.
- This study employed stringent inclusion and exclusion criteria, and nine databases were accordingly searched for randomised controlled trials.
- The analysis addressed functional improvement, quality of life and safety of cupping, and risk of bias and levels of evidence.
- The results of data synthesis may be limited due to the heterogeneity and low quality of evidence of selected studies.

INTRODUCTION

A recent World Health Organization study of the 20 major causes of years lived with disability (YLD) from 2000 to 2012 worldwide reported that neck pain is the second leading cause of YLD.[1] One study of patients in the Netherlands showed that neck pain was associated with 1% of total medical expenditure and 0.1% of gross domestic product (GDP), 77% of which was comprised of indirect medical expenses associated with absence from work or disability expenses.[2] Prevalence of neck pain is directly associated with escalated medical costs and negative impact on productivity, potentially increasing long-term absences from work. The lifelong prevalence of neck pain in adults ranges from 14.2% to 71%, although this rate varies greatly across studies.[3] Neck pain can easily progress to chronic conditions, with approximately 25% to 60% of patients developing chronic back or neck pain within the first year.[4] Additionally, neck pain is reported to be most prevalent in high activity age groups, particularly individuals aged 35 to 49 years,[5] and is also more common in women.[3]

Standard first-line therapy for neck pain can be largely divided into pharmacological and non-pharmacological therapies. Pharmacological treatment frequently involves use of acetaminophen and nonsteroidal anti-inflammatory drugs (NSAIDs). However, acetaminophen and NSAIDs are known to increase risk of reduced liver function, liver failure, and haemorrhagic gastritis,[6] and side effects may be more common when these drugs are used long-term for chronic neck pain. For these reasons, many studies have investigated the clinical effectiveness of complementary and alternative medicine therapies, including acupuncture for chronic pain conditions.[7]

One type of complementary therapy that can be used for neck pain is cupping. Cupping is a physical treatment, typically used by acupuncturists and other complementary and alternative medicine therapists, that utilizes glass or plastic cups placed on the skin over a painful area or acupuncture point to create negative pressure through suction. The rationale for use of cupping is not yet fully understood; it is described as a detoxification process by which waste matter and toxins are removed, and as a harmonization process for the imbalance of Qi, a traditional Chinese medicine term for "vital energy".[8] Cupping has been used globally for several thousand years, particularly in countries such as Egypt and China.[8] Today, cupping is widely used as a holistic treatment in Europe for inpatient care and the prevention and treatment of various disorders, as well as for promotion of general health.[9] In South Korea, cupping is a popular treatment, and is covered by national health insurance; in 2013 alone, insurance claims for cupping reached a total 215 billion Korean won.[10]

There are two types of cupping: dry and wet. Dry cupping is a technique in which cups are applied to the skin to create a vacuum for suction without drawing blood, whereas in wet cupping, blood is drawn with scarification before applying the cups for blood-letting. Cupping therapy is used for post-stroke rehabilitation and hypertension, and has been reported to be effective for treating pain and musculoskeletal disorders.[11 12] A systematic literature review published by Yuan et al. in 2015 reviewed the effects of cupping on neck pain, reporting that cupping is effective for reducing pain and improving function.[13] However, only articles published up to 2013 were included in that review, and as new clinical trials investigating cupping for neck pain have since been published, an updated systematic review on the topic is needed. Moreover, Yuan et al.[13] restricted the publication language to include only English and Chinese language articles.

Therefore, the aim of this study was to assess current evidence of cupping for neck pain and better understand its effects on pain, function, quality of life (QoL), and safety through the review of randomised control trials (RCTs). To conduct a more extensive review, no restrictions were placed on publication language, and studies in English, Korean, Japanese, and Chinese were included.

METHODS

The protocol of this systematic literature review was registered in the PROSPERO international prospective register of systematic reviews (CRD42016047218). This review was performed and reported in adherence with the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA).[14]

Literature search

Studies that used cupping as an intervention for neck pain were searched in the Ovid-Medline (1946 to Jan 2018), Ovid-EMBASE (1980 to Jan 2018), Ovid-AMED (1985 to Dec 2017), and the Cochrane Central Register of Controlled Trials (CENTRAL) up to January 9, 2018. The Chinese database China National Knowledge Infrastructure (CNKI), Korean databases Oriental Medicine Advanced Searching Integrated System (OASIS) and National Discovery for Science Leaders (NDSL), and Japanese databases J-stage and ISHUSHI were also used. Search terms included a combination of Medical Subject Headings (MeSH) terms such as neck pain (e.g., neck pain, cervical spondylosis, cervical radiculopathy, cervical disc herniation, and myofascial pain syndrome) and cupping. Details of the search strategy are presented in Appendix 1. The publication language of study articles was not restricted.

Study inclusion and exclusion

Two or more investigators (YJL, SYK, and/or SHL) independently selected articles for analysis from the searched articles. After excluding duplicate publications, titles and abstracts were reviewed to primarily screen for articles according to the inclusion and exclusion criteria. The full texts of these articles were then reviewed for secondary screening of articles per inclusion and exclusion criteria. Only RCTs were considered. Any disagreement in the study selection process was resolved by discussion, and when an agreement was not reached, a third investigator intervened to reach consensus. Study subjects included adult patients with neck pain, including neck pain with neuropathy, and the authors did not discriminate between acute and chronic phases of neck pain. However, post-traumatic pain caused by whiplash or sports injuries was excluded as the natural history of neck pain may differ in such cases. Furthermore, patients with myelopathy or cervical headache/vertigo without neck pain were also excluded. All types of cupping therapies were included without restriction regarding dry or wet cupping, and the type of cupping device was not limited. Control groups included patients who underwent usual care for neck pain, such as physical therapy, NSAIDs, heat pack therapy, and acupuncture,[15-17] as well as inactive controls, such as waiting lists or no intervention groups. The outcome variables assessing the effectiveness of cupping included pain intensity, neck disability indexes, and quality of life. Pain intensity was measured using the visual analogue scale (VAS), the McGill Pain Questionnaire, and the

Northwick Park Neck Pain Questionnaire (NPQ). The Neck Disability Index (NDI) was generally used to evaluate neck function disability. QoL was assessed using the 36-item Short-form (SF-36) and EuroQol-5 Dimension (EQ-5D) questionnaires. However, studies that did not use objective instruments and reported outcomes in terms of improvement rates without standards, and investigations that used instruments without confirmation of reliability and validity were excluded.

Risk of bias evaluation and data extraction

Risk of bias in the RCTs was assessed by seven categories according to the Cochrane Risk of Bias. Studies that used appropriate methods for each item and specified the methods in the text were considered to have low risk of bias; studies that did not perform the relevant item or used inappropriate methods were considered to have high risk of bias; and studies that did not mention specific methods or used ambiguous expressions to describe the methods for each item were considered to have an unclear risk of bias. Two or more investigators independently assessed all research data, and disagreements were resolved through discussion. When an agreement could not be reached, a third investigator intervened to reach consensus. Two reviewers independently read the full text of all articles and extracted data according to a pre-determined format. Any disagreements were resolved by discussion between the two reviewers.

Data analysis

A meta-analysis was performed using quantitative data from each study to assess the effectiveness of cupping. The mean difference (MD) and 95% confidence intervals (CIs) were calculated using the Cochrane Collaboration software (Review Manager [RevMan] version 5.3, Copenhagen: The Nordic Cochrane Centre) for Windows (Microsoft Corporation, Redmond, WA, USA). Heterogeneity across studies was assessed using the χ^2 (chi-squared) test with a significance level of $P<0.10$ and I^2 statistics. When heterogeneity was statistically significant, the cause of heterogeneity was analysed through subgroup analysis. Sensitivity analyses were also conducted to test the robustness of results by determining the impact of a single study on overall results. If statistical heterogeneity was found, sensitivity analyses (by eliminating one study at a time) were performed to explore possible reasons for the heterogeneity. A random effect model was applied, and publication bias was not assessed when the number of studies in the group was <10.

Quality of evidence

The quality of evidence for each outcome was assessed in accordance with the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE). Quality of evidence was classified into high, moderate, low, and very low. To determine the quality of evidence, the following domains were assessed according to the standards suggested by the GRADE group: risk of bias, imprecision, inconsistency, indirectness, publication bias, large magnitude of effect, dose-response, and confounding.[18]

Patient and Public Involvement

Patients and public were not involved in the development of the research question and outcome measures or design of this study, or recruitment to and conduct of the study as a systematic review and meta-analysis. There are no plans for the results to be disseminated directly to study participants.

RESULTS

Search results

A total of 541 articles were retrieved, including 86 from Ovid-Medline, 137 from Ovid-EMBASE, 19 from Ovid-AMED, 43 from the Cochrane Library, 193 from a Chinese database, 47 from Korean databases and 16 from Japanese databases. Following the first and second rounds of screening, a total of 18 articles were selected for review. The search results are shown in Figure 1.

Features of the included studies

A total of 18 studies were analysed in two separate analyses[19-36]: direct comparison of the cupping (sole) and control groups; and an add-on analysis comparing the control with cupping group with the control only group. Two studies used three groups; 15 studies were included in the sole analysis while five studies were included in the add-on analysis.

Seven[19 21 23 26-28 34] of the 18 studies used wet cupping while eleven studies used dry cupping. The frequency of cupping therapy varied greatly. Two studies performed only one round of therapy, and four conducted two to four rounds. The majority of studies conducted >10 rounds of therapy because most patients who were treated had neck pain with radiculopathy or chronic neck pain. The region of administration was typically the upper shoulder and neck area, and cupping was primarily administered to Ashi or other proximal acupoints. As these studies mainly treated pain, most presented pain scores in the form of VAS scores; disability was presented in NDI scores, while QoL was mostly reflected in responses to the EQ-5D and SF-36 questionnaires. The features of each study are presented in Table 1.

Table 1. Characteristics of the included studies

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relevant
Cupping vs. Control (Sole)										
vs. ***waitlist (no intervention)***										
Arslan 2015	Turkey	computer users diagnosed minimum 3 neck pain	EG: 20, CG: 20	EG: 26.0±3.5, CG: 26.0±3.8	Dry cupping (moving)	no intervention	upper shoulder and neck region	10	After treatment	VAS
Chi 2016	Taiwan	work-related chronic neck shoulder pain	EG: 30, CG: 30	EG: 43.6±6.3, CG: 42.5±5.8	Dry cupping	no intervention	SI15, GB21, LI15	1	After treatment	VAS
Lauche 2011	Germany	chronic nonspecific neck pain	EG: 22, CG: 24	EG: 26.1±4.2 CG: 25.1±3.0	Dry cupping	Waiting list control group	descending and transverse parts of the trapezius muscle	5	After treatment	VAS, NDI, SF-36
Saha 2017	Germany	Chronic neck pain	EG: 25, CG: 25	EG: 54.3 ± 8.6 CG: 53.3 ± 11.1	Dry cupping	Waiting list control group	from the occiput towards the mid-level thoracic spine as well as over the upper trapezius muscle	5	Post-cupping after 3 weeks	VAS, POM, NDI, SF-36
Lauche 2012	Germany	chronic nonspecific neck pain	EG: 22, CG: 23	EG: 54.8±3.2 CG: 29.3±2.9	Wet cupping	Waiting list control group	descending parts of the trapezius muscle	1	Post-cupping after 3 days	VAS, NDI, SF-36
vs. ***active control (dry cupping)***										
Sui 2008*	China	cervical radiculopathy	EG: 120, CG: 120	NR	Dry cupping (moving)	traction	Acupoints at Bladder Meridian and Governor Vessel	20	After treatment	VAS, POM, NDI, SF-36
Cramer 2011	Germany	nonspecific neck pain for at least the previous 3 months	EG: 24 CG: 24	EG: 44.46 CG: 47.88	Dry cupping	Standard Medical Care	Neck and shoulder lesion	3-4	After treatment	VAS, NDI, SF-36

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relevant
Kim 2012	Korea	VDT workers with neck pain	EG: 20 CG: 20	EG : 25.5 (median) CG : 28 (median)	Dry cupping	Heating pad group	GV14, GV16, GV15, GV12, GB20, GB21, LI17, SI11, SI12, SI13, SI14, SI15, BL10, BL11, BL12, BL13, BL14, BL15, BL16, BL17, BL41, BL42, BL43, BL44, EX-HN15	6	7 weeks	NRS, NDI, EQ-5D
Lauche 2013	Germany	chronic nonspecific neck pain	EG: 30 CG: 31	EG: 54.5±12.3 CG: 53.7±13.4	Dry cupping	progressive muscle relaxation(PMR)	NR	24	12 weeks	VAS, NDI, SF-36
vs ***active control (wet cupping)***										
Liu 2016	China	cervical spondylosis	EG: 20, CG: 20	NR	Wet cupping	Tuina	GV14, Ashi points	3	After treatment	VAS, effective rate, tenderness
Mou 2015[*]	China (Multi center)	cervical radiculopathy	EG: 68, CG: 56	EG: 46.4±11.6 CG: 47.8±11.9	Wet cupping	MA	GV14, GB21	4-12	After treatment	VAS, NDI, CAS
Yin 2009	China	cervical spondylosis	EG: 56 CG: 55	EG: 32.13±7.87 CG: 35.24±6.67	Wet cupping	MA	EX-B2,BL11, GB21, Ashi points	10	After treatment	VAS, effective rate
Zhou 2014	China	Cervical Spondylopathy	EG:100 CG:100	NR	Wet cupping	MA	Ashi points, EX-B2, GB21	10	After treatment	VAS , effective rate
Jin 2014	China	neck type cervical spondylosis	EG: 33 CG: 33	EG: 31.81±8.30 CG: 30.48±9.74	Wet cupping	MA	upper shoulder and neck region	5	After treatment	VAS, NPQ, effective rate
Yin 2016	China	Cervical Spondylosis	EG: 47, CG: 48	EG: 45. 68 ± 10. 46, CG: 47. 29 ± 8.03	Wet cupping	acupuncture	EX - B2, SI15, GB21, SJ5	4	After treatment	NPQ
Cupping with usual care vs. usual care (Add-on)										
Dry cupping										
Cai 2015	China	Chronic neck pain	EG: 60 CG: 60	EG: 45.48±10.9 CG: 45.7±11.1	Dry cupping	MA	EX-B2	12	After treatment	SF-MPQ
Su 2016	China	Neck pain after sleeping	EG:29 CG:29	EG: 30.72±6.69 CG: 31.76±7.16	Dry cupping	MA	upper shoulder and neck region	3	After treatment	VAS, effective rate
Sui 2008[*]	China	cervical radiculopathy	EG: 120, CG: 120	NR	Dry cupping (moving)+traction	traction	Acupoints at Bladder Meridian and Governor Vessel	20	After treatment	VAS
Wet cupping										

Study ID	Country	Disease	Number of participants	Age (years, mean±SD)	Methods of Intervention	Comparison	Cupping sites	Number of cupping	Follow up period	Relevant
Mou 2015*	China (Multicentre)	cervical radiculopathy	EG: 59, CG: 56	EG: 45.4±11.6 CG: 47.8±11.9	Wet cupping+MA	MA	EX-B2, BL11, GB21, Ashi points	10	After treatment	VAS, NDI, CAS
Jiang 2017	China	Myofascial Pain Syndrome of Neck and Shoulder	EG:30 CG:30	EG: 21±3 CG: 22±3	Wet cupping+MA	MA	Ashi points	5	After treatment	VAS , effective rate

CAS: Clinical assessment scale, CG: control group, EA: electroacupuncture, EG: experimental group, EQ-5D: EuroQol 5-Dimension, MA: manual acupuncture, NDI: Neck Disability Index, NPQ: Neck Pain Questionnaire, NR: not reported, SD: Standard deviation, SF-MPQ: Short Form McGill Pain Questionnaire, SF-36: 36-Item Short Form Health Survey, VAS: Visual Analogue Scale, VDT: Video Display Terminal, POM: Pain on movement

*Is a three-armed study, i.e. cupping group, control group, cupping plus control group.

Risk of bias assessment

Random sequence

Seven of the 18 studies[20 22-25 27 28] were assessed to have low risk of bias as they randomly allocated the subjects using a table of random numbers. One study did not specify the randomization method, and the group sizes notably varied, i.e. 68, 56, and 59; this study was thus assessed to have high risk of bias.[26] The remaining 10 studies, however, only mentioned randomly assigning subjects without specifying the method used for randomization; thus, these studies were assessed to have an unclear risk of bias. The results are shown in Figure 2.

Allocation concealment

Nine[20 22 24-26 28-31] studies concealed allocation using a sealed envelope, and thus were considered to have low risk of bias. The remaining studies were determined to be unclear as they did not describe the method of allocation concealment used.

Blinding

Control groups were either waiting list controls or active controls. Although efforts have been made to develop a sham version of cupping[37], blinding is difficult given that sham cupping is not often used. Chi et al.[29] described single blinding; however, it was difficult to assess whether blinding was actually implemented. Hence, all studies were considered to not have blinded their investigators and participants. With regard to the blinding of participants and medical personnel, all studies were considered to have high risk of bias. Similarly, blinding of outcome assessors could not be performed in most studies as many used VAS for pain measurement and patient-reported outcomes. Blinding of outcome assessors would have been made feasible if the studies had used physician-reported outcomes or other outcome variables measured by the examiner; however, such studies were found lacking. Therefore, all studies were considered to have high risk of bias.

Incomplete outcome data

Seven[20 22 24 25 27 30 31] studies reported the number of excluded and withdrawn participants, and the number of participants included for final analysis. It was decided that the number of withdrawn participants and the reasons for withdrawal were not a cause of bias; therefore, these studies were considered to have low risk of bias. One study was regarded to possess a high risk of bias as 33 participants from the intervention group and 27 from the control group dropped out after only one session of treatment.[26] The remaining studies were determined to be unclear for not mentioning the number of participants who withdrew or were excluded.

Selective reporting

Ten[20 22 24 25 27 29-31] of the 18 studies were determined to have unclear risk of bias regarding selective reporting as they did not describe adverse events (AEs) nor did they register the trial protocols. The remaining eight studies were found to have reported all outcome variables initially planned to be investigated, and thus were determined to have low risk of bias.

Other biases

All studies were assessed to have low risk of other biases.

Analysis

Cupping versus no treatment

Pain: Five studies were included in the meta-analysis.[20 29-32] Compared with the no intervention group, the cupping group reported significant reduction in pain with an MD of -2.42 (95% CI -3.98 to -0.86). Considerable heterogeneity was observed (I^2=93%; P<0.00001 [chi-square test]); however, the study by Chi et al.[29] showed a statistically outlying effect size; a sensitivity analysis was conducted with the study omitted, and resulted in an MD of -1.48 (95% CI -1.86, -1.10; I2=0%; P=0.57)) with the heterogeneity resolved.

Disability: Three studies were included in the analysis.[20 30 31] Results revealed that the cupping group reported significant functional improvement compared to the no intervention group with an MD of -4.34 (95% CI -6.77 to -1.91; I^2=6%; P=0.35).

QoL: Three studies were included in the analysis,[20 30 31] and results showed that the cupping group indicated significant improvement in the mental component summary of SF-36, with an MD of 5.32 (95% CI 0.83 to 9.80; I^2=32%; P=0.23). No statistical significance was found in terms of the physical component summary of SF-36 with an MD of 2.46 (95% CI -0.36, 5.29) (Figure 3).

Cupping versus active control

Pain: Ten studies were included in the analysis.[21-28 34 35] Of these 10 studies, nine reported the outcome in VAS, while one study reported NPQ scores.[21] In analysis of the nine studies, the cupping group exhibited significant reduction in pain with an MD of -0.89 (95% CI -1.42 to -0.37; P=0.0009) compared with the control group. The chi-square test, however, revealed some heterogeneity (p<0.00001; I^2=88%). In order to resolve the heterogeneity, studies were analysed separately depending on the type of cupping: either wet (with scarification) or dry. Meta-analysis of three studies conducted with dry cupping indicated an MD of -1.50 (95% CI -2.28 to -0.72 ; I^2=28%; P=0.25). On the other hand, analysis of studies with wet cupping showed an MD of -0.70 (95% CI -1.32 to -0.07 ; I2=92%; P<0.00001) with unresolved heterogeneity. Omission of the study by Zhou 2014[28] – which had a notably large effect size – resulted in an MD of -0.49 (95% CI -0.78 to -0.20) with I^2=-35%, P=0.19, implying that the heterogeneity was considerably resolved. The single study that reported outcomes with NPQ indicated an MD of 3.59 (95% CI 2.02 to 5.16), suggesting that cupping significantly decreased pain compared to the control.

Disability: Four studies were included in the analysis.[22 24-26] Compared with the control, the cupping group demonstrated functional improvement, with an MD of -4.36 (95% CI -8.67 to -0.04; P=0.05), but not to a statistically significant degree, and substantial heterogeneity was identified (I^2=62%; P=0.05).

QoL: Two studies were included in this analysis.[22 25] Compared with the control, the cupping group reported significant improvement in the physical component summary of SF-36, with an MD of 5.44 (95% CI 2.09 to 8.78; P=0.001). However, statistically significant differences were not found for the mental component summary of SF-36 with an MD of 0.44 (95% CI -4.05 to 4.93) (Figure 4). The study by Kim et al. reported EQ-5D outcomes as median values, and therefore inclusion for meta-analysis was not feasible. In this study, the cupping group and control reported identical median values of 0.91, suggesting no statistical difference.

Cupping with active control versus active control (add-on)

Pain: Five studies were included in the analysis.[19 26 33 35 36] Adding cupping therapy to the treatment administered in the control group led to significant reduction in pain, with an MD of -0.87 (95% CI -1.14 to -0.61; P<0.00001).

Disability: Only one study reported a disability-related outcome,[26] and the effect on disability was not significant, with an MD of 3.61 (95% CI -3.93 to 11.15; P=0.35). Heterogeneity was not identified (I^2=19%; P=0.29) (Figure 5).

Safety of cupping

Ten of the 18 studies included in the final analysis did not address safety, while eight studies did. First, Kim et al.[24] reported skin laceration (n=1), whole body itching (n=1), pain at the cupping sites (n=1), and generalized body ache (n=1) in four patients in the cupping group; however, the study reported that the symptoms were mild and resolved within a few days. Lauche et al. (2012)[31] reported one case of pain during the procedure itself in addition to tension headache, migraine, tinnitus, and wound healing itches; however, all side effects were mild and temporary. Chi et al.[29] reported two cases of mild low back pain due to the seated position in the cupping group. Lauche et al. (2013)[25] reported muscular tension (n=1), increased pain (n=1), and prolapsed intervertebral disc (n=1). While prolapsed intervertebral disc should be regarded as a severe event, the original authors stated that a causal relationship was unlikely. Lauche et al. (2011)[30] reported tingling sensation in the hands and arms (n=1), strain/pain at the treated area (n=2), strain/pain in the general neck region (n=1), slight headache (n=1), tiredness (n=1), shivering attack (n=1), and blurred vision (n=1). Lauche et al. (2011)[30] reported that all symptoms subsided within four hours, and that the causal relationship with cupping was unclear. Yin et al.[27] reported one case of delayed wound healing due to wet cupping. Cramer et al.[22] reported muscle soreness (n=2), minor hematoma (n=1), and increased neck pain for 1 hour to 5 hours (n=2). In the study by Saha et al.,[20] two participants complained of headache that resolved within one hour. One participant suffered upper back pain, which subsided within days, and one participant reported slight dizziness. Although one case of lipoma was identified during the trial, it did not have any causal relationship with cupping, as reported by the authors.

Levels of evidence

The quality of evidence for each analysis is shown in Table 2. In the waiting list comparison, the quality of evidence for the outcomes of pain, QoL, and disability was assessed to be low to very low due to concerns regarding risk of bias, imprecision and inconsistency. In the active control comparison, the quality of evidence for pain and QoL was low due to risk of bias and imprecision, and that for disability was assessed to be very low due to risk of bias, imprecision, and unexplained heterogeneity. In the add-on comparison between the active control and active control with cupping groups, the quality of evidence for pain in the dry cupping add-on group was low due to risk of bias and unexplained heterogeneity. The quality of evidence for pain outcomes was very low. The quality of evidence for disability outcomes in the add-on groups was low due to risk of bias and imprecision (Table 2).

Table 2. Meta-analysis of outcomes and level of evidence

Variable	Overall effect						Studies (N)	Sample size (N)	Level of evidence
	MD	95% CI	*P*	I^2	P	Statistical method			
Cupping vs. Waitlist (Sole)									
Pain (VAS)	-2.42	-3.98, -0.86	0.002	93	<0.00001	Random Inverse Variance	5	241	Very low
Pain (VAS) omitting 1 study	-1.48	-1.86, -1.10	<0.00001	0	0.57	Random Inverse Variance	4	181	-
Disability (NDI)	-4.34	-6.77, -1.91	0.0005	6	0.35	Random Inverse Variance	3	141	Low
QoL (Physical component of SF-36)	2.46	-0.36,5.29	0.09	24	0.27	Random Inverse Variance	3	141	Low
QoL (Mental component of SF-36)	5.32	0.83, 9.80	0.02	32	0.23	Random Inverse Variance	3	141	Low
Cupping vs. Active control (Sole)									
Pain (VAS)	-0.89	-1.42, -0.37	0.0009	88	<0.00001	Random Inverse Variance	9	870	Low
Pain (VAS) of dry cupping	-1.48	-1.86, -1.10	<0.00001	0	0.57	Random Inverse Variance	3	149	-
Pain (VAS) of wet cupping	-0.70	-1.32, -0.07	0.03	92	<0.00001	Random Inverse Variance	6	721	-
Pain (VAS) of wet cupping omitting 1 study	-0.49	-0.78, -0.20	0.0008	35	0.19	Random Inverse Variance	5	521	-
Disability (NDI)	-4.36	-8.67, -0.04	0.05	62	0.05	Random Inverse Variance	4	213	Very low
QoL (SF-36) (Physical component of SF-36)	5.44	2.09, 8.78	0.001	7	0.30	Random Inverse Variance	2	109	Low
QoL (SF-36) (Mental component of SF-36)	0.44	-4.05, 4.93	0.85	0	0.59	Random Inverse Variance	2	109	Low
Cupping with active control vs. control (add-on)									
Pain (VAS)	-0.87	-1.14, -0.61	<0.00001	19	0.29	Random Inverse Variance	5	534	Low
Disability (NDI)	3.61	-3.93, 11.15	0.35	-	-	Random Inverse Variance	1	56	Low

VAS: Visual analogue scale, NDI: Neck disability index, QoL: Quality of life, MD: Mean difference

DISCUSSION

The present study aimed to assess the evidence supporting the effectiveness of cupping for neck pain through a comprehensive systematic literature review. We performed a systematic and inclusive search in non-Asian and Asian databases, including those based in China, Korea, and Japan, where cupping is popular and widely used. Eighteen articles were selected and analysed according to the type of control group used. When compared with inactive controls, cupping significantly reduced pain, and improved function and QoL. However, the heterogeneity between studies was quite high in terms of pain reduction, and the quality of evidence was lowered as a consequence. As one study, by Chi et al.,[29] reported a considerably large effect size, the heterogeneity was resolved when this study was omitted in the sensitivity analysis. Although in most studies the quality of evidence was found to be low to very low, the marked pain reduction and improvement in function and QoL found to be associated with cupping may be clinically relevant. When compared with active controls, the cupping group exhibited significant reduction in pain but no significant differences in functional improvement. Analysis in pain outcomes found an MD of -0.89 (95% CI -1.42 to -0.37); however, heterogeneity was high and subgroup analysis was thus performed. Effect sizes were similar across studies using dry cupping but varied greatly across studies using wet cupping; omission of the study by Zhou et al.[28] resolved the heterogeneity. Additional analyses are needed to clarify whether the differences between studies can be attributed to different types of wet cupping procedures or whether other sociopsychological factors were involved. Wet cupping involves drawing blood before cupping, and, despite being accepted in some cultures, may not be tolerated in others. Furthermore, the intensity of the procedure and amount of bleeding may also have affected study outcomes, which may have further contributed to the varying effect sizes. Alternatively, the type and frequency of procedures and patient pain severity could contribute to varying effect sizes.

When used to compliment existing treatments, cupping was found to significantly reduce pain, with an MD of -0.87 (95% CI -1.14 to -0.61). However, in addition to statistical significance, the effect size of a treatment should be assessed for clinical significance. Based on four studies of cupping, Lauche et al. (2013)[38] proposed the minimal clinically important difference (MCID) of VAS to be -8 (-0.8 of a ten point scale), the NDI to be -3, and the physical component summary of SF-36 to be +5.1. From the current meta-analysis, cupping exhibited an MD of -2.42 compared to the waiting list control, -0.89 compared to the active control, and -0.87 as an add-on treatment, which all surpasses the above criteria for the MCID of VAS. With regard to NDI, cupping indicated an MD of between -4.34 and -4.36, depending on the type of control, which also meets the MCID criteria. For the physical component summary, however, cupping failed to display a treatment effect larger than MCID. In contrast, cupping showed an effect size exceeding MCID when compared to the active control, which calls for further investigation.

Cupping has been used for several thousand years in such diverse regions as early Egypt and China.[8] In traditional Chinese medicine, cupping is widely used to eliminate stagnated Qi and Blood, and facilitate circulation.[39] Since ancient times, cupping has been considered to be effective in the local treatment of areas of inflammation.[40] A previous review analysing the reported mechanism of cupping suggested that the positive effects of cupping are the result of a haemodynamic mechanism facilitating muscle function, as demonstrated by

the reduction of deoxy-haemoglobin and elevated oxy-haemoglobin levels in muscle areas treated with cupping.[41] Other studies have suggested that cupping involves a mechanism for removing oxidative stress,[42] and produces therapeutic effects through diffuse noxious inhibitory control;[43] this would contribute to the alleviation of pain.

For these reasons, a growing number of clinical trials are investigating the effects of cupping on pain and various disease symptoms. Through the analysis of 135 RCTs on cupping, Cao et al.[44] reported that clinical trials of wet cupping have been conducted in association with various disorders such as herpes zoster, facial paralysis, cough/dyspnea, and acne. A more recent systematic review investigated cupping in relation to overall disease;[45] however, although the analysis included some articles pertaining to neck pain, it did not focus on the condition. In another systematic literature review on the efficacy of cupping for lower back pain, cupping was found to lead to significant reductions in pain and improvement of function.[13 46] Only one previous review has specifically evaluated the effect of cupping on neck pain, but that review was published in 2013 and analysed only five trials.[13] Therefore, the results of the present study, which included 18 RCTs and did not limit inclusion by language, provide greater clinical relevance and implications.

However, this study has several limitations. One significant shortcoming is that only some studies reported issues related to safety. Although severe AEs were not found in association with cupping in the studies that reported side effects, many studies did not report side effects at all. A systematic review investigating the side effects of cupping reported that the most common side effect was scar formation, and there have been some previously reported cases of severe side effects.[47] However, adverse reactions to cupping may vary according to the proficiency of the practitioner, type of procedure, and disinfection and sterilization processes implemented during the treatment procedure.[47] Certain severe AEs, such as infection, may be preventable as their occurrence can be directly associated with the education, training, experience, and proficiency of therapists. Another limitation was the low or very low quality of evidence for all outcomes; this low quality of evidence was primarily caused by risk of bias and unexplained heterogeneity between studies. Additionally, many selected studies did not maintain rigorous standards or procedures regarding allocation and blinding. Furthermore, the outcomes included for analysis in this study were all patient-reported outcomes (i.e., pain, disability, QoL), and none of the included studies were designed to assess the placebo effect of cupping. It is possible that the results may have been influenced by the fact that all outcome measures were patient-reported and the lack of blinding. Moreover, all of the included studies, with the exception of a study published by Su et al. in 2016,[33] were conducted only in patients with chronic neck pain. Whether the therapeutic effect of cupping is dependent on the clinical characteristics (acute vs. chronic) of neck pain remains to be elucidated. Finally, many of the included studies had small sample sizes.

Nevertheless, cupping may be an important and cost-effective therapy for the treatment of neck pain. For example, Lauche et al. (2013)[25] performed a clinical trial on home-based cupping. Due to the increased use of computers and smartphones around the world, the prevalence of neck pain is rising steadily,[48] and this type of pain can often develop into chronic pain. Thus, this study is meaningful in that it evaluates a non-invasive, simple, and effective treatment modality for patients with chronic pain.

CONCLUSION

The current results suggest that cupping may be effective for neck pain patients in terms of reducing pain and improving function and quality of life, when compared to no treatment or active controls. The level of evidence for the findings of the included studies, however, was found to be low or very low, thus preventing strong conclusions from being drawn for the effectiveness of this treatment. Although this study did not identify notable AEs in the articles reviewed, cupping is not without side effects, and further well-designed, large-scale studies employing standardized procedures are needed to thoroughly examine potential adverse effects. Furthermore, wet cupping requires rigorous education and training on hygiene and precautions, as it entails a blood-letting process. Although definite conclusions cannot be drawn from this study, cupping appears to be a potentially effective and safe therapy for neck pain.

FOOTNOTES

Contributors: SK, MRK, IHH, and YJL designed the study. SK, SHL and YJL conducted the systematic search. SK, MRK, and YJL assessed the literature for inclusion and extracted the data. JL, JSS, and IHH monitored data collection. EJK, DSH, JL, JSS, and IHH interpreted the data. SK, MRK, IHH, and YJL wrote the draft; SHL, EJK, DSH, JL, and JSS critically revised the manuscript. All authors have read and approved the final version.

Funding: This study was supported by the Traditional Korean Medicine R&D Program funded by the Ministry of Health & Welfare through the Korea Health Industry Development Institute (KHIDI) (HB16C0035).

Competing Interests: None declared

Provenance and peer review: Not commissioned; externally peer reviewed.

Data sharing statement: No additional data are available.

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FIGURE LEGENDS

Figure 1. PRISMA flow diagram of the literature search

PRISMA : Preferred Reporting Items for Systematic Reviews and Meta Analyses

Figure 2. Risk of bias in the included studies, as assessed using the Cochrane Collaboration's risk of bias tool

+: high risk of bias, ?: unclear risk of bias, -: low risk of bias

Figure 3. Forest plots demonstrating the effect of cupping as the sole intervention vs. no treatment on neck pain

CI: confidence interval

Figure 4. Forest plots demonstrating the effect of cupping as the sole intervention vs. active control on neck pain

CI: confidence interval

Figure 5. Forest plots demonstrating the effect of cupping as the add-on intervention on neck pain

CI: confidence interval

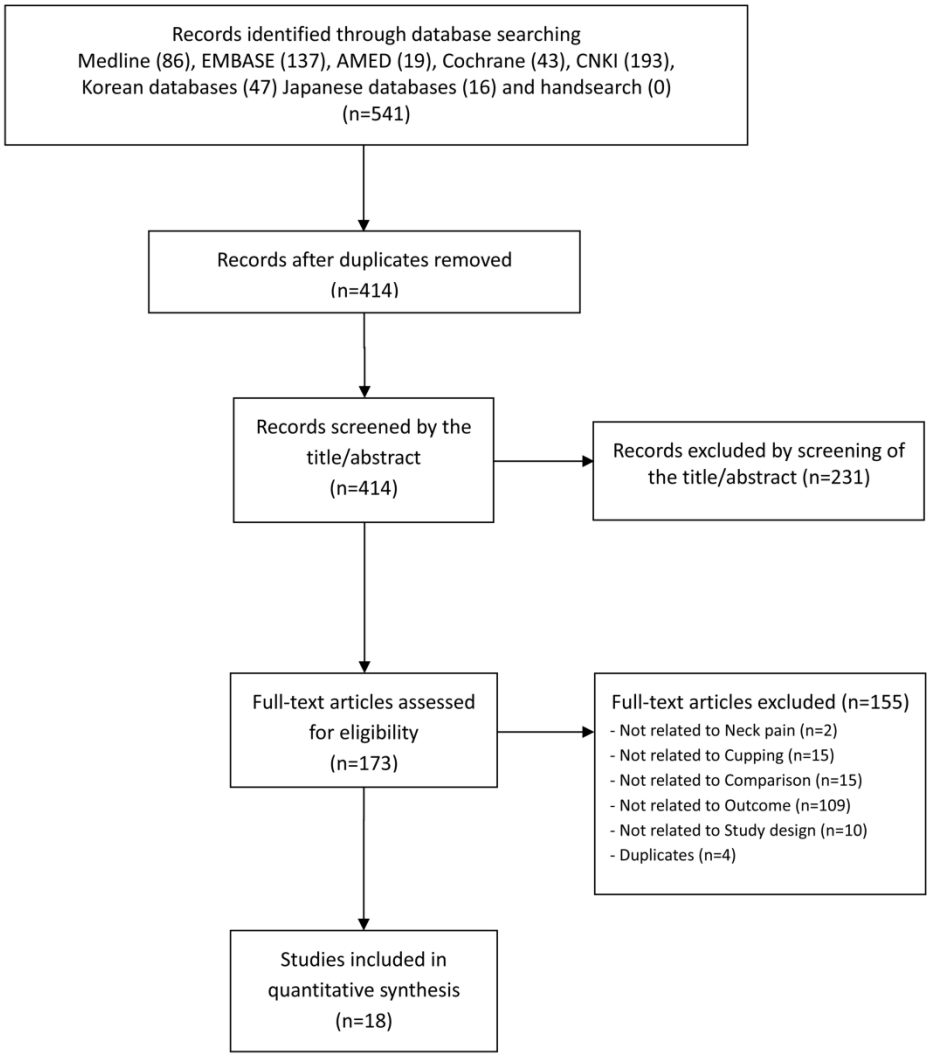

Figure 1. PRISMA flow diagram of the literature search

PRISMA : Preferred Reporting Items for Systematic Reviews and Meta Analyses

Figure 1. PRISMA flow diagram of the literature search
PRISMA : Preferred Reporting Items for Systematic Reviews and Meta Analysis

214x256mm (300 x 300 DPI)

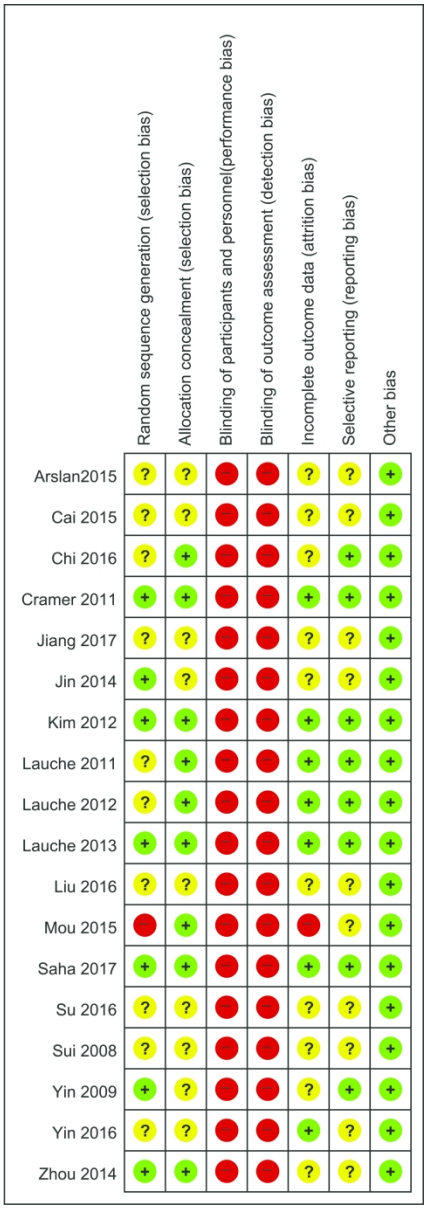

Figure 2. Risk of bias in the included studies, as assessed using the Cochrane Collaboration's risk of bias tool
+ : high risk of bias, ? : unclear risk of bias, - : low risk of bias

264x731mm (300 x 300 DPI)

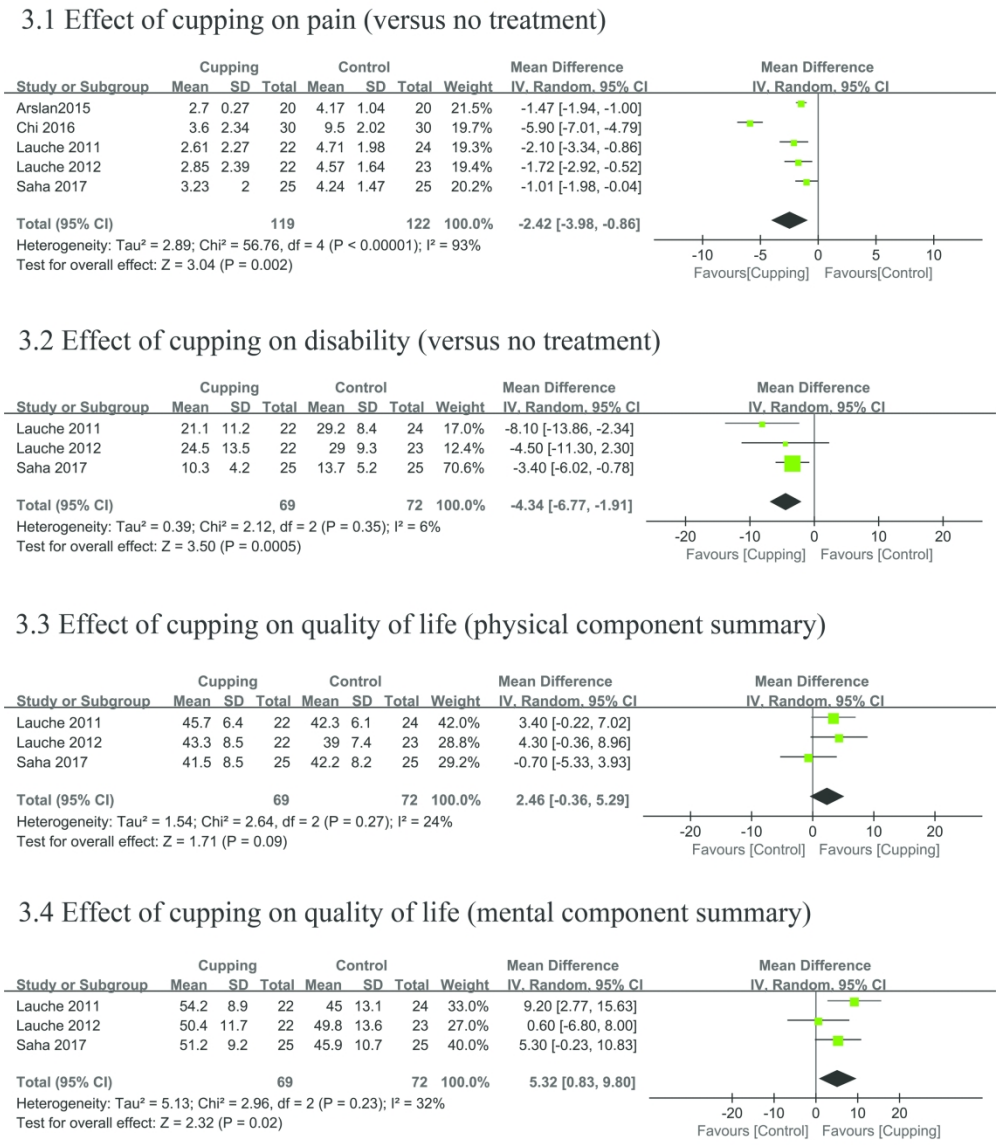

Figure 3. Forest plots demonstrating the effect of cupping as the sole intervention vs no treatment on neck pain
CI : confidence interval

236x285mm (300 x 300 DPI)

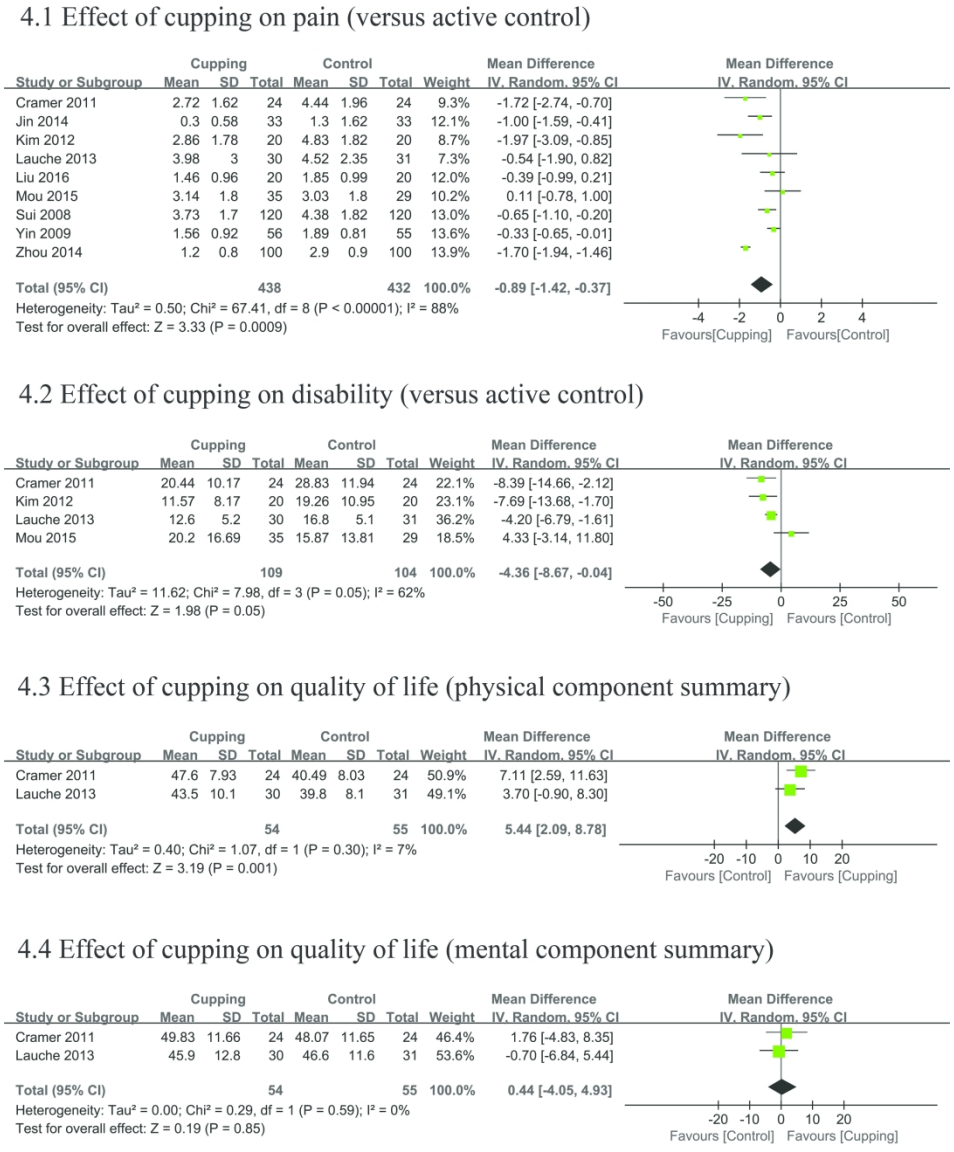

Figure 4. Forest plots demonstrating the effect of cupping as the sole intervention vs active control on neck pain
CI : confidence interval

247x313mm (300 x 300 DPI)

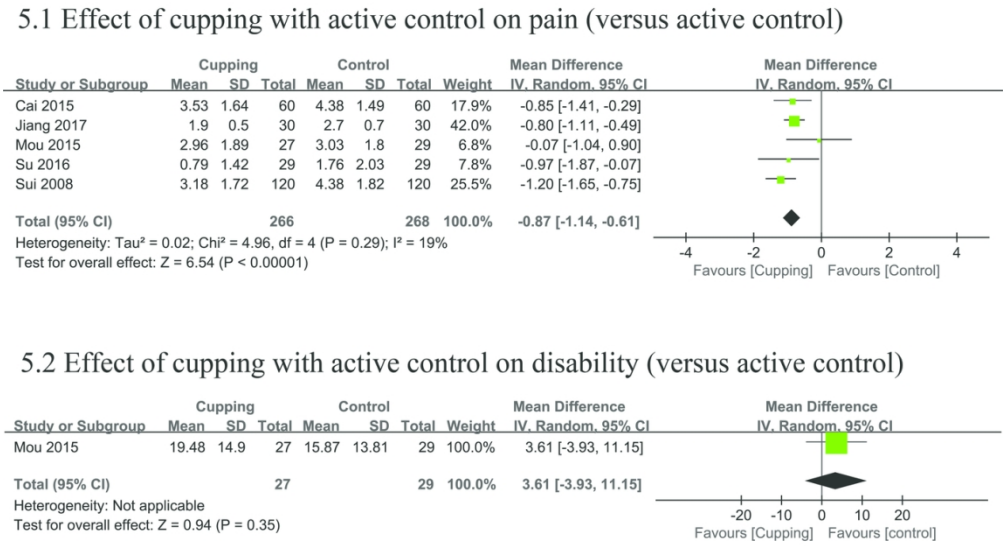

Figure 5. Forest plots demonstrating the effect of cupping as the add-on intervention on neck pain
CI : confidence interval

119x72mm (300 x 300 DPI)

Appendix S1 Search strategy

Ovid-Medline 1946 to Jan Week 1 2018 Date: 2018.01.08		
	Searches	**Results**
1	Neck Pain/	6385
2	exp Brachial Plexus Neuropathies/	3563
3	cervical pain.mp.	961
4	neckache.mp.	20
5	cervicodynia.mp.	9
6	cervicalgia.mp.	114
7	brachialgia.mp.	165
8	brachial neuritis.mp.	174
9	brachial neuralgia.mp.	122
10	neck pain.mp.	14709
11	neck injur*.mp.	5953
12	brachial plexus neuropath*.mp.	2277
13	brachial plexus neuritis.mp.	1527
14	thoracic outlet syndrome/ or cervical rib syndrome/	2228
15	Torticollis/	3691
16	exp brachial plexus neuropathies/ or exp brachial plexus neuritis/	3563
17	cervico brachial neuralgia.ti,ab.	43
18	cervicobrachial neuralgia.ti,ab.	68
19	(monoradicul* or monoradicl*).tw.	143
20	or/1-19	33193
21	neck/	30018
22	neck muscles/	6076
23	exp cervical plexus/	8027
24	exp cervical vertebrae/	38618
25	atlanto axial joint	1767
26	atlanto occipital joint	3372
27	Cervical Atlas/	2539

28	spinal nerve roots/	10,825
29	exp brachial plexus/	24658
30	(odontoid* or cervical or occip* or atlant*).tw.	282283
31	axis/ or odontoid process/	1777
32	Thoracic Vertebrae/	20133
33	cervical vertebrae.mp.	35831
34	cervical plexus.mp.	1465
35	cervical spine.mp.	21326
36	(neck adj3 muscles).mp.	7410
37	(brachial adj3 plexus).mp.	13431
38	(thoracic adj3 vertebrae).mp.	21124
39	neck.mp.	244594
40	(thoracic adj3 spine).mp.	7024
41	(thoracic adj3 outlet).mp.	2763
42	trapezius.mp.	3985
43	or/21-42	566354
44	exp pain/	387369
45	exp injuries/	891764
46	pain.mp.	672242
47	ache.mp.	15382
48	sore.mp.	7757
49	stiff.mp.	9236
50	discomfort.mp.	42264
51	injur*.mp.	1050876
52	neuropath*.mp.	140510
53	or/44-52	2242467
54	43 and 53	135447
55	Radiculopathy/	4853
56	exp temporomandibular joint disorders/ or exp temporomandibular joint dysfunction syndrome/	16566

57	myofascial pain syndromes/	1627
58	exp "Sprains and Strains"/	18830
59	exp Spinal Osteophytosis/	4196
60	exp Neuritis/	7282
61	Polyradiculopathy/	2656
62	exp Arthritis/	259875
63	Fibromyalgia/	8641
64	spondylitis/ or discitis/	6486
65	spondylosis/ or spondylolysis/ or spondylolisthesis/	7014
66	radiculopathy.mp.	8529
67	radiculitis.mp.	821
68	temporomandibular.mp.	27614
69	myofascial pain syndrome*.mp.	1967
70	thoracic outlet syndrome*.mp.	2552
71	spinal osteophytosis.mp.	3575
72	neuritis.mp.	17471
73	spondylosis.mp.	4358
74	spondylitis.mp.	23814
75	spondylolisthesis.mp.	6178
76	or/55-75	361804
77	43 and 76	28356
78	exp neck/	30044
79	exp cervical vertebrae/	38618
80	Thoracic Vertebrae/	20133
81	neck.mp.	244594
82	(thoracic adj3 vertebrae).mp.	21124
83	(thoracic adj3 spine).mp.	7024
84	cervical spine.mp.	21326
85	or/78-84	302173
86	Intervertebral Disk/	13804
87	(disc or discs).mp.	99973
88	(disk or disks).mp.	53273

89	or/86-88	139200
90	85 and 89	9454
91	herniat*.mp.	21849
92	slipped.mp.	4540
93	prolapse*.mp.	32528
94	displace*.mp.	149806
95	degenerat*.mp.	237832
96	(bulge or bulged or bulging).mp.	9191
97	or/91-96	437364
98	90 and 97	6049
99	intervertebral disk degeneration/ or intervertebral disk displacement/	21747
100	intervertebral disk displacement.mp.	1741
101	intervertebral disc displacement.mp.	18641
102	intervertebral disk degeneration.mp.	152
103	intervertebral disc degeneration.mp.	4850
104	intervertebral disk hernia.mp.	222
105	or/99-104	22513
106	85 and 105	4166
107	20 or 54 or 77 or 98 or 106	156956
108	cupping.mp.	1754
109	ventouse.tw.	237
110	exp phlebotomy/	5704
111	bloodletting.mp.	2994
112	blood letting.mp.	349
113	bloodletting.mp.	2994
114	spilled blood.mp.	13
115	venesection.mp.	686
116	or/108-115	8424
117	107 and 116	86

Ovid-EMBASE 1980 to 2018 Jan **DATE: 2018.01.08**

	Searches	Results
1	Neck Pain/	18952
2	brachial plexus neuropathy/	1779
3	cervical pain.mp.	1285
4	neckache.mp.	23
5	cervicodynia.mp.	17
6	cervicalgia.mp.	176
7	brachialgia/	262
8	brachialgia.mp.	368
9	brachial neuritis.mp.	204
10	brachial neuralgia.mp.	67
11	neck pain.mp.	21299
12	neck injur*.mp.	7234
13	brachial plexus neuropath*.mp.	1944
14	brachial plexus neuritis.mp.	85
15	thoracic outlet syndrome/	2075
16	Torticollis/	4014
17	exp brachial plexus neuropathies/ or exp brachial plexus neuritis/	1779
18	cervico brachial neuralgia.ti,ab.	36
19	cervicobrachial neuralgia.ti,ab.	75
20	(monoradicul* or monoradicl*).tw.	150
21	or/1-20	37046
22	neck/	50115
23	neck muscles/	5295
24	cervical plexus/	1090
25	cervical spine/	31073
26	atlantoaxial joint/	1743
27	atlantooccipital joint/	2016
28	atlas/	1765
29	spinal root/	4655
30	brachial plexus/	7832
31	(odontoid* or cervical or occip* or atlant*).tw.	313982

32	odontoid process/	2481
33	cervical vertebra.mp.	3529
34	cervical vertebrae.mp.	3134
35	cervical plexus.mp.	1403
36	cervical spine.mp.	48597
37	(neck adj3 muscles).mp.	2581
38	(brachial adj3 plexus).mp.	17831
39	(thoracic adj3 vertebrae).mp.	2227
40	neck.mp.	300025
41	(thoracic adj3 spine).mp.	13953
42	(thoracic adj3 outlet).mp.	2435
43	trapezius.mp.	5264
44	or/22-43	622696
45	exp pain/	1091658
46	exp injuries/	66466
47	pain.mp.	1032154
48	ache.mp.	16783
49	sore.mp.	18614
50	stiff.mp.	11265
51	discomfort.mp.	64832
52	injur*.mp.	1377870
53	neuropath*.mp.	267008
54	or/45-53	2799546
55	44 and 54	151698
56	Radiculopathy/	8801
57	temporomandibular joint disorder/	11910
58	myofascial pain/	7225
59	spondylosis/ or cervical spondylosis/	6895
60	Neuritis/	5803
61	exp Arthritis/	395884
62	Fibromyalgia/	17215
63	exp spondylitis/	34738

64	diskitis/	2171
65	spondylolisthesis/	7164
66	radiculopathy.mp.	11998
67	radiculitis.mp.	1260
68	temporomandibular.mp.	25840
69	myofascial pain syndrome*.mp.	1158
70	spinal osteophytosis.mp.	36
71	neuritis.mp.	19219
72	spondylosis.mp.	8026
73	spondylitis.mp.	35047
74	spondylolisthesis.mp.	7954
75	or/56-74	476180
76	44 and 75	27829
77	neck/	50115
78	cervical spine/	31073
79	neck.mp.	300025
80	(thoracic adj3 vertebrae).mp.	2227
81	(thoracic adj3 spine).mp.	13953
82	cervical spine.mp.	48597
83	or/77-82	348878
84	Intervertebral Disk/	11331
85	(disc or discs).mp.	85296
86	(disk or disks).mp.	97488
87	or/84-86	146518
88	83 and 87	9652
89	herniat*.mp.	25041
90	slipped.mp.	3710
91	prolapse*.mp.	41853
92	displace*.mp.	127797
93	degenerat*.mp.	321664
94	(bulge or bulged or bulging).mp.	10599
95	or/89-94	520028

96	88 and 95	5203
97	intervertebral disk hernia/	15253
98	intervertebral disk degeneration/	8780
99	intervertebral disk displacement.mp.	533
100	intervertebral disc displacement.mp.	131
101	intervertebral disk degeneration.mp.	8836
102	intervertebral disc degeneration.mp.	1880
103	or/97-102	23812
104	83 and 103	4121
105	21 or 55 or 76 or 96 or 104	169900
106	cupping.mp.	1908
107	ventouse.tw.	411
108	exp phlebotomy/	9427
109	bloodletting.mp.	672
110	blood letting.mp.	315
111	blood-letting.mp.	315
112	spilled blood.mp.	14
113	venesection.mp.	743
114	106 or 107 or 108 or 109 or 110 or 111 or 112 or 113	12343
115	105 and 114	137

Ovid-AMED 1985 to December 2017		**Date: 2018.01.08.**
	Searches	**Results**
1	Neck Pain/	1031
2	exp Brachial plexus/	282
3	cervical pain.mp.	75
4	neckache.mp.	0
5	cervicodynia.mp.	2
6	cervicalgia.mp.	13
7	brachialgia.mp.	6
8	brachial neuritis.mp.	1

9	brachial neuralgia.mp.	5
10	neck pain.mp.	1380
11	neck injur*.mp.	139
12	brachial plexus neuropath*.mp.	8
13	brachial plexus neuritis.mp.	1
14	thoracic outlet syndrome/ or cervical rib syndrome/	43
15	Torticollis/	70
16	cervico brachial neuralgia.ti,ab.	0
17	cervicobrachial neuralgia.ti,ab.	2
18	(monoradicul* or monoradicl*).tw.	0
19	or/1-18	1941
20	neck/	663
21	neck muscles/	150
22	exp cervical plexus/	30
23	exp cervical vertebrae/	1647
24	Atlanto axial joint/	32
25	Atlanto occipital joint/	17
26	spinal nerve roots/	92
27	(odontoid* or cervical or occip* or atlant*).tw.	3929
28	Axis/	9
29	Odontoid process/	8
30	Thoracic Vertebrae/	302
31	cervical vertebrae.mp.	1678
32	cervical plexus.mp.	11
33	cervical spine.mp.	1163
34	(neck adj3 muscles).mp.	311
35	(brachial adj3 plexus).mp.	203
36	(thoracic adj3 vertebrae).mp.	331
37	neck.mp.	3781
38	(thoracic adj3 spine).mp.	355
39	(thoracic adj3 outlet).mp.	83
40	trapezius.mp.	502
41	or/20-40	7636

42	exp pain/	20488
43	exp injuries/	3007
44	pain.mp.	29672
45	ache.mp.	124
46	sore.mp.	167
47	stiff.mp.	228
48	discomfort.mp.	991
49	injur*.mp.	28051
50	neuropath*.mp.	1781
51	or/42-50	57325
52	41 and 51	4097
53	myofascial pain syndromes/	352
54	exp "Sprains and Strains"/	949
55	exp Spinal Osteophytosis/	35
56	exp Neuritis/	62
57	exp Arthritis/	5513
58	Fibromyalgia/	1647
59	spondylitis/ or discitis/	77
60	spondylosis/ or spondylolysis/ or spondylolisthesis/	140
61	radiculopathy.mp.	285
62	radiculitis.mp.	10
63	temporomandibular.mp.	582
64	myofascial pain syndrome*.mp.	424
65	thoracic outlet syndrome*.mp.	80
66	spinal osteophytosis.mp.	41
67	neuritis.mp.	78
68	spondylosis.mp.	130
69	spondylitis.mp.	358
70	spondylolisthesis.mp.	154
71	or/53-70	9763
72	41 and 71	794
73	exp neck/	710

74	exp cervical vertebrae/	1647
75	Thoracic Vertebrae/	302
76	neck.mp.	3781
77	(thoracic adj3 vertebrae).mp.	331
78	(thoracic adj3 spine).mp.	355
79	cervical spine.mp.	1163
80	or/73-79	5755
81	Intervertebral Disk/	327
82	(disc or discs).mp.	1209
83	(disk or disks).mp.	985
84	or/81-83	1693
85	80 and 84	225
86	herniat*.mp.	390
87	slipped.mp.	27
88	prolapse*.mp.	122
89	displace*.mp.	2548
90	degenerat*.mp.	1676
91	(bulge or bulged or bulging).mp.	63
92	or/86-91	4467
93	85 and 92	141
94	intervertebral disk degeneration/ or intervertebral disk displacement/	342
95	intervertebral disk displacement.mp.	376
96	intervertebral disc displacement.mp.	1
97	intervertebral disk degeneration.mp.	29
98	intervertebral disc degeneration.mp.	22
99	intervertebral disk hernia/	0
100	or/94-99	414
101	80 and 100	54
102	19 or 52 or 72 or 93 or 101	4732
103	cupping.mp.	173
104	ventouse.tw.	2
105	exp Bloodletting/	43

106	exp Cupping/	101
107	bloodletting.mp.	69
108	blood letting.mp.	30
109	bloodletting.mp.	69
110	spilled blood.mp.	0
111	venesection.mp.	0
112	or/103-111	235
113	102 and 112	19

Cochrane Library		**Date: 2018.01.09**
	Searches	**Results**
1	[mh ^"Neck pain"]	845
2	[mh "Brachial Plexus Neuropathies"]	53
3	cervical pain:ti,ab,kw	3071
4	neckache:ti,ab,kw	1
5	cervicodynia:ti,ab,kw	1
6	cervicalgia:ti,ab,kw	11
7	brachialgia:ti,ab,kw	12
8	brachial neuritis:ti,ab,kw	28
9	brachial neuralgia:ti,ab,kw	17
10	neck pain:ti,ab,kw	4667
11	neck injur*:ti,ab,kw	1417
12	brachial plexus neuropath*:ti,ab,kw	75
13	brachial plexus neuritis:ti,ab,kw	28
14	[mh ^"thoracic outlet syndrome"]	18
15	[mh ^"cervical rib syndrome"]	1
16	[mh ^Torticollis]	98
17	[mh "brachial plexus neuropathies"]	53
18	[mh "brachial plexus neuritis"]	25
19	cervico brachial neuralgia:ti,ab,kw	5
20	cervicobrachial neuralgia:ti,ab,kw	115

21	monoradicul* or monoradicl*;ti,ab,kw	26
22	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15 or #16 or #17 or #18 or #19 or #20 or #21	7525
23	[mh ^neck]	486
24	[mh ^"neck muscles"]	216
25	[mh "cervical plexus"]	111
26	[mh "cervical vertebrae"]	994
27	[mh ^"atlanto-axial joint"]	23
28	[mh ^"atlanto-occipital joint"]	8
29	[mh ^"Cervical Atlas"]	4
30	[mh ^"spinal nerve roots"]	150
31	[mh "brachial plexus"]	949
32	odontoid* or cervical or occip* or atlant*:ti,ab,kw	16822
33	[mh ^"odontoid process"]	11
34	[mh ^"Thoracic Vertebrae"]	469
35	cervical vertebrae:ti,ab,kw	1086
36	cervical plexus:ti,ab,kw	217
37	cervical spine:ti,ab,kw	1609
38	neck muscles:ti,ab,kw	704
39	brachial plexus:ti,ab,kw	1237
40	thoracic vertebrae:ti,ab,kw	584
41	neck:ti,ab,kw	15234
42	thoracic spine:ti,ab,kw	741
43	thoracic outlet:ti,ab,kw	41
44	trapezius:ti,ab,kw	530
45	#23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44	33047
46	[mh pain]	39333
47	[mh injuries]	19901
48	pain:ti,ab,kw	107702
49	ache:ti,ab,kw	298
50	sore:ti,ab,kw	2106
51	stiff:ti,ab,kw	296

52	discomfort:ti,ab,kw	9125
53	injur*:ti,ab,kw	39318
54	neuropath*:ti,ab,kw	8396
55	#46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54	161760
56	#45 and #55	10128
57	[mh ^Radiculopathy]	293
58	[mh "temporomandibular joint disorders"]	614
59	[mh "temporomandibular joint dysfunction syndrome"]	179
60	[mh "myofascial pain syndromes"]	451
61	[mh "Sprains and Strains"]	999
62	[mh "Spinal Osteophytosis"]	91
63	[mh Neuritis]	70
64	[mh ^polyradiculopathy]	13
65	[mh arthritis]	10946
66	[mh ^Fibromyalgia]	842
67	[mh ^spondylitis]	20
68	[mh ^discitis]	9
69	[mh ^spondylosis]	126
70	[mh ^spondylolysis]	11
71	[mh ^spondylolisthesis]	155
72	radiculopathy:ti,ab,kw	725
73	radiculitis:ti,ab,kw	38
74	temporomandibular:ti,ab,kw	1111
75	myofascial pain syndrome*:ti,ab,kw	569
76	thoracic outlet syndrome*:ti,ab,kw	35
77	spinal osteophytosis:ti,ab,kw	95
78	neuritis:ti,ab,kw	550
79	spondylosis:ti,ab,kw	411
80	spondylitis:ti,ab,kw	1395
81	spondylolisthesis:ti,ab,kw	460
82	#57 or #58 or #59 or #60 or #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75 or #76 or #77 or #78 or #79 or #80 or #81	17164

83	#45 and #82	1519
84	[mh neck]	486
85	[mh "cervical vertebrae"]	994
86	[mh ^"thoracic vertebrae"]	469
87	neck:ti,ab,kw	15234
88	thoracic vertebrae:ti,ab,kw	584
89	thoracic spine:ti,ab,kw	741
90	cervical spine:ti,ab,kw	1609
91	#84 or #85 or #86 or #87 or #88 or #89 or #90	14188
92	[mh ^"Intervertebral Disk"]	271
93	disc$:ti,ab,kw	3867
94	#92 or #93	3867
95	#91 and #94	541
96	herniat*:ti,ab,kw	1225
97	slipped:ti,ab,kw	49
98	prolapse*:ti,ab,kw	1996
99	displace*:ti,ab,kw	4124
100	degenerat*:ti,ab,kw	5989
101	bulge or bulged or bulging:ti,ab,kw	279
102	#96 or #97 or #98 or #99 or #100 or #101	12784
103	#95 and #102	372
104	[mh ^"intervertebral disk degeneration"]	205
105	[mh ^"intervertebral disk displacement"]	746
106	intervertebral disk displacement:ti,ab,kw	247
107	intervertebral disc displacement:ti,ab,kw	812
108	intervertebral disk degeneration:ti,ab,kw	238
109	intervertebral disc degeneration:ti,ab,kw	416
110	intervertebral disk hernia	419
111	#104 or #105 or #106 or #107 or #108 or #109 or #110	1529
112	#91 and #111	277
113	#112 or #103 or #83 or #56 or #22	11540
114	cupping:ti,ab,kw	340
115	ventouse:ti,ab,kw	56

116	MeSH descriptor: [Bloodletting] explode all trees	100
117	bloodletting:ti,ab,kw	159
118	blood letting:ti,ab,kw	77
119	blood-letting:ti,ab,kw	72
120	spilled blood:ti,ab,kw	6
121	venesection:ti,ab,kw	60
122	#114 or #115 or #116 or #117 or #118 or #119 or #120 or #121	596
123	#113 and #122	43

CHINA Academic Journals Full-text Database

(SU='颈痛' OR SU='颈肩痛' OR SU='颈椎病' OR SU='颈肩部' OR SU='颈椎间盘突出症' OR SU='颈部' OR SU='神经根型颈椎病') AND (SU='罐' OR SU='cupping') AND (SU='随机' or SU='对照') 193

颈痛 : neck pain in Chinese / 颈肩痛 : neck pain in Chinese / 颈椎病 : cervical spondylosis in Chinese / 颈肩部' : neck in Chinese / 颈椎间盘突出症 : cervical disc herniation in Chinese / 颈部 : neck in Chinese / 神经根型颈椎病 : cervical radiculopathy in Chinese / 罐 : cupping in Chinese / 随机 : random in Chinese / 对照 : controlled in Chinese

Korean databases

KoreaMed (Date : 2018.01.11)		
1	경항통 and 부항	0
2	neck pain and cupping	0
3	頸項痛 and 罐	0

KMBASE (Date : 2018.01.11)		
1	경항통 and 부항	0
2	neck pain and cupping	0
3	頸項痛 and 罐	0

OASIS (Date : 2018.01.11)		
1	경항통 and 부항	0
2	neck pain and cupping	0
3	頸項痛 and 罐	0

NDSL (Date : 2018.1.11)		
1	경항통 and 부항	0
2	neck pain and cupping	37
3	頸項痛 and 罐	0

KISS (Date : 2018. 01. 11)		
1	경항통 and 부항	0
2	neck pain and cupping	5
3	頸項痛 and 罐	5

경항통 : neck pain in Korean / 부항 : cupping in Korean / 頸項痛 : neck pain in Chinese / 罐 :

cupping in Chinese

Japan database

J-stage (Date：2018. 01. 11)		
1	neck pain cupping	15

医学中央雑誌刊行会(Ichushi)(Date : 2018. 01. 11)		
#1	(頸椎症性脊髄症/TH or 頸椎症/AL)	10,553
#2	頸椎椎間板ヘルニア/AL	1077
#3	((@頸椎/TH and @脊椎損傷/TH and @捻挫/TH) or 頸椎捻挫/AL)	327
#4	(頸部痛/TH or 頸部疼痛/AL)	2188
#6	頸肩部痛/AL	64
#7	#1 or #2 or #3 or #4 or #5 or #6	13698
#8	cupping/AL	38
#9	吸角/AL	30
#10	#8 or #9	66
#11	#7 AND #10	1

頸椎症 : cervical spondylosis in Japanese / **頸椎椎間板ヘルニア**: cervical disc herniation in Japanese / **頸椎** : cervical vertebrae in Japanese / **脊椎損傷** : vertebral injury in Japanese / **捻挫** : sprain in Japanese / **頸椎捻挫** : sprain of cervical spine in Japanese / **頸部痛** : neck pain in Japanese / **頸部疼痛** : neck pain in Japanese / **頸肩部痛** : neck pain in Japanese / **吸角** : cupping in Japanese

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4-5
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5-6
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5-6, 11
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	6
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	6
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	7, Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	7, Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	11 Figure 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	11-13
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	11-13
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11 Figure 2
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11-13
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	15
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	16
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	16-17
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	17

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

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