BMJ Open

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Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-087340
Article Type:	Original research
Date Submitted by the Author:	28-Apr-2024
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Keywords:	Meta-Analysis, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY, Chronic Pain, COMPLEMENTARY MEDICINE

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Effects of Cupping Therapy on Chronic Musculoskeletal Pain and Collateral Problems: A Systematic Review and Meta-Analysis

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All authors declare no conflicts of interest.

Abstract

Introduction: Chronic musculoskeletal pain (CMP) is a prevalent and distressing condition. Cupping therapy, one of the most popular complementary and alternative medicines, has been widely used to reduce CMP. But the evidence remains controversial on the effect of cupping therapy on CMP. The objective of this review and meta-analysis is to assess the effectiveness of cupping therapy in CMP patients.

Methods: The protocol was registered at PROSPERO before starting the data extraction (registration number: CRD42023406219). Studies were identified by a comprehensive search of databases up to December 2023. A total of 10 randomized control trials were included in this meta-analysis.

Results: The results showed that cupping therapy (SMD = -1.23; 95% CI = -2.02 to -0.44; P = 0.002; I2 = 95%) had a significant reduction effect on CMP patients' pain intensity. But cupping therapy had non-significant improvement effects on functional disability (SMD = -0.58; 95% CI = -1.34 to 0.17; P = 0.13; I^2 = 76%) and mental health (SMD = -0.21; 95% CI = -0.81 to 0.38; P = 0.48; I^2 = 63%). Although the difference was not significant, based on the SMD, wet cupping therapy had a better trend on reducing pain intensity (wet cupping therapy: SMD = -1.47, 95% CI = -2.39 to -0.55 VS dry cupping therapy: SMD = -1.20, 95% CI = -2.12 to -0.29; *P* = 0.69).

Conclusions: This study indicates that cupping therapy is efficient in alleviating pain intensity in CMP patients. But it can't improve functional disability and mental health

significantly. Among different cupping therapy types, wet cupping therapy seems to be more helpful for individuals with CMP to decline pain intensity.

Keywords: chronic musculoskeletal pain, cupping therapy, complementary and alternative medicine, meta-analysis

Background

Chronic musculoskeletal pain (CMP) is widely known as a common problem around the world, which has a high prevalence and causes a heavy burden. According to the Global Burden of Diseases, Injuries, and Risk Factors Study 2017 (GBD 2017), almost 1.3 billion people around the world were suffering from musculoskeletal disorders in 2017, of which 89.08% were diagnosed with osteoarthritis, low back pain and neck pain (1). These musculoskeletal disorders may develop into CMP. Furthermore, in the recent 30 years, the burden of non-fatal diseases like musculoskeletal disorders has increased sharply all over the world. A study published in the Lancet has reported that the global years lived with disability (YLDs) of CMP in 2013 was almost 1.2 billion. Among the top ten causes of global YLDs, low back pain and neck pain are ranked first and fourth respectively (2). Moreover, CMP is also responsible for the high financial cost. For example, based on the Chilean health system, the annual expected cost for CMP is USD $1387.2 million and equivalent to 0.417% of the national GDP (3).

In addition to the impact on healthy life expectancy and financial burden, CMP usually brings restricted daily activities and negative mental health to individuals. Original research has found that the pain threshold and pain tolerance value of patients with chronic back pain were significantly lower than healthy participants and these lower pain-related parameters may contribute to the persistence of chronic pain (4). The persistent CMP can interfere with individuals' physical functions. For example, the

reductions in strength and endurance induced by fibromyalgia can lead to the restrictions in participation during leisure-time activities and work-related activities (5) (6). Moreover, CMP can also affect individuals' psychological status. One survey including 122 CMP patients has indicated that the pain interference was negatively correlated with several mental health components (e.g., vitality and calmness) significantly (7). In addition to daily mental states, CMP even causes the mental illness. For example, the patients with long-term low back pain, who experienced the moderate to severe pain dysfunction at the initial assessment, were easier to remain chronical depression (8). Therefore, it is necessary to find effective treatments and rehabilitation measures for patients with CMP to alleviate pain and collateral problems, such as functional disability and unhealthy mental states.

The conventional therapies for CMP include drug treatments and surgical interventions, which inevitably produce some adverse side effects. Some drugs like opioid painkillers, have been opposed by current guidelines for CMP, because of the rising rates of opioid overdose deaths and other serious harms (9). It has been indicated that long-term use of nonopioid drugs for relieving CMP (e.g., non-steroidal anti-inflammatory drugs, and Cyclooxygenase-2) may produce serious gastrointestinal side effects and increase cardiovascular risks (10, 11). Another usual therapy, the surgical interventions have been proven, to some extent, effective in CMP conditions, especially in osteoarthritis. However, operations usually cause a high prevalence (80%) of postoperative pain (12). These adverse impacts of drug treatments and surgical

interventions result in a growing interest in non-pharmacological measures in response to CMP (13, 14).

Cupping therapy, a type of complementary and alternative medicine, has been widely applied to alleviate CMP, such as chronic neck pain (15, 16) and chronic low back pain (17). The normal impacts after cupping therapy are circular erythematous spots with no painful sense and no restriction to daily activities. Some researchers have suggested that cupping therapy can improve blood flow (18, 19), which may contribute to its therapeutic effect. The increasing blood flow has been indicated effective in removing glutamate (20), lactate, and pyruvate (21), which are biochemical biomarkers in CMP regions. In fact, several researchers have demonstrated the obvious alleviation effects of cupping therapy on CMP patients' pain intensity (22, 23). For example, Volpato et al. have indicated that a single-time dry cupping therapy can effectively decrease pain intensity, which is presented by the Brief Pain Inventory (BPI) score, in low back (pre-cupping: 4.22 ± 2.53; post-cupping: 1.66 ± 1.97, $P < 0.05$) (22). Wet cupping therapy, another type of cupping therapy adding blood-letting to dry cupping therapy, has been also demonstrated effective for reducing CMP (23-25). Some comprehensive treatments combining cupping therapy and other physical therapies or techniques (e.g., pulsatile cupping, cupping massage) have been also demonstrated effective for relieving CMP (26, 27). Compared to separate methods, the integrated approaches may produce better therapeutic effects. But more clinical trials are needed to clarify the differences in the effect of alleviating CMP between these two kinds of

approaches.

Although numerous studies have clarified the potential effectiveness of cupping therapy in treating CMP, there still remain the opposite results. For instance, Silva et al. have indicated that dry cupping therapy is not superior to sham cupping for improving the Numerical Pain Rating Scale (NPRS) score (dry cupping therapy: 3.3 ± 2.9 VS sham cupping therapy: 2.7 ± 1.9; Mean $_{\text{between-group differences}}$ = 0.6, 95% confidence intervals = -0.4 to 1.6) in patients with non-specific chronic low back pain (28). Another study has also revealed no statistically significant improvement is found in physical function (e.g. difficulty in walking) of osteoarthritis patients after multiple-times wet cupping treatments (pre-cupping: 1.68 ± 0.63 VS post-cupping: 0.906 ± 0.40, $P > 0.05$) (29). Both high pain intensity and poor physical function are harmful symptoms in CMP patients, while these inconsistent findings cannot identify whether cupping therapy is effective for the improvement of clinical symptoms (e.g., pain and physical function) of CMP or not. Considering that CMP has a lasting harmful effect on patients, there is an urgent need to examine studies related to the effectiveness of cupping therapy on CMP scientifically and comprehensively.

The purpose of this study is to evaluate the effect of cupping therapy on clinical outcomes (i.e., pain intensity, functional disability, and mental health) in CMP patients through a meta-analysis from a more comprehensive and systematic perspective.

Methods

Search Strategy and Study Selection

This meta-analysis was conducted according to the PRISMA guidelines (http://www.prisma-statement.org/). The protocol was registered at PROSPERO (http://www.crd.york.ac.uk/ PROSPERO) before starting the data extraction (registration number: CRD42023406219).

Four electronic databases, including PubMed (2000-2023), Web of Science (1948-2023), EBSCO (2000-2023), and Cochrane Library (1990-2023), were searched respectively for relevant articles until December 20, 2023. The searching criteria was set based on the following keywords and Mesh terms: ((“chronic musculoskeletal pain” [Title/Abstract] OR “chronic musculoskeletal disorder” [Title/Abstract]) OR (“fibromyalgia” [Mesh] OR “fibromyalgia” [Title/Abstract]) OR (“osteoarthritis” [Mesh] OR “osteoarthritis” [Title/Abstract]) OR (“myalgia” [Mesh] OR “myalgia” [Title/Abstract] OR “muscle pain” [Title/Abstract]) OR (“back pain” [Mesh] OR “back pain” [Title/Abstract]) OR (“neck pain” [Mesh] OR “neck pain” [Title/Abstract]) OR (“shoulder pain” [Mesh] OR “shoulder pain” [Title/Abstract]) OR “knee pain” [Title/Abstract] OR “hip pain” [Title/Abstract] OR (“chronic pain” [Mesh] OR “chronic pain” [Title/Abstract])) AND (“cupping therapy” [Mesh] OR “cupping therapy” [Title/Abstract] OR “cupping treatment” [Title/Abstract] OR “dry cupping” [Title/Abstract] OR “ wet cupping” [Title/Abstract] OR “cupping massage” [Title/Abstract] OR “cupping” [Title/Abstract]).

Two independent reviewers (Y.-Y.J. and R.W.) screened the titles and abstracts of all potentially suitable publications and assessed their eligibility through reading in full.

If a disagreement remained after discussion, a third arbitrator (Z.-M.B.) was consulted for a consensus.

Inclusion Criteria

Trails were eligible for inclusion if they met the following criteria with the PICOS principle (population, intervention, comparison/control, outcome and study design): 1) participants were suffering from musculoskeletal pain and/or stiffness for more than three months, which is the diagnostic criteria of CMP (30); 2) participants in the experimental group received interventions related to cupping therapy (e.g., dry cupping, wet cupping, pulsating cupping, and cupping massage); 3) the comparison intervention was limited to no treatment or sham/placebo interventions during experimental treatments; 4) the outcomes were pain intensity, functional disability, or mental health; and 5) only publications designed as randomized control trials (RCTs) were covered.

Exclusion Criteria

The exclusion criteria for the selected trials were as follows: 1) reviews, abstracts, protocols, case reports, observational studies, non-English publications, non-peer-reviewed articles (e.g., academic dissertations and conference posters); 2) no sufficient evidence to judge the duration of disease as chronic condition (i.e. less than three months); 3) pain sites containing visceral or orofacial regions; and 4) participants in control groups received other active treatments, such as traditional Hijamah technique, standard medical care, and ischemic compression.

Quality Assessment

Two authors independently examined the quality of included studies using the Cochrane Collaboration tool. The risk of bias was evaluated as "low," "high," or "unclear" in the seven domains: 1) random sequence generation (selection bias): 2) allocation concealment (selection bias); 3) blinding of participants and personnel (performance bias); 4) blinding of outcome assessment (detection bias); 5) incomplete outcome data (attrition bias); 6) selective reporting (reporting bias); and 7) other bias (31). If there was a disagreement between two authors, a third arbitrator (Z-M.B.) was consulted to reach a consensus.

Data Extraction

From each included article, the following data were extracted by two independent reviewers: author(s), publication year, country, subjects' demographical characteristics (e.g., age and gender), sample size, pain site(s), duration of CMP, experimental intervention (i.e., dosage of cupping therapy), control intervention, and the reported outcomes (e.g., pain intensity, functional disability, or mental health).

Meta-analysis

In this meta-analysis, the outcome indicators were measured on different tools. For example, the pain intensity was assessed by the Numerical Pain Rating Scale (NPRS), the Visual Analog Scale (VAS), or the Brief Pain Inventory (BPI). The functional disability was measured by the Neck Disability Index (NDI), the Oswestry Disability Questionnaire (ODQ), the Oswestry Disability Index (ODI), the Fibromyalgia Impact Questionnaire (FIQ), the Funktionsfragebogen Hannover Rücken (FFbH-R), or the

Roland Morris Disability Questionnaire (RMDQ). Meanwhile, the mental health was evaluated by the Short-Form 36 health survey questionnaire (SF-36) or the BPI. Because of the different measurements of outcomes, the standardized mean differences (SMDs) with 95% confidence intervals (CIs) were chosen to analyze the compositive effects, and $P < 0.05$ was set as the significant level.

According to the Cochran Handbook for Systematic Review, both the post-intervention values (i.e., Mean $_{\text{post-intervention}} \pm$ SD $_{\text{post-intervention}}$) of the outcome and the changes from baseline (i.e., Mean $_{\text{of changes}} \pm$ SD $_{\text{of changes}}$) could be used for the summary statistic value in this study (32). If studies reported CI instead of SD, we would convert CI into SD by the formula "$\sqrt{N} \times (l_{\text{upper}} - l_{\text{lower}})/c$". The upper and lower limits of the CI were denoted by the l_{upper} and the l_{lower}. And c was a constant depending on the CI and the sample size (33).

The heterogeneity among included studies was evaluated by the I^2 index. The low, moderate, high, and very high heterogeneity was identified when $I^2 \leq 25\%$, $I^2 \leq 50\%$ and $>25\%$, $I^2 \leq 75\%$ and $> 50\%$, and $I^2 > 75\%$ respectively (33). For the low or moderate heterogeneity, a fixed-effect model would be chosen. When the heterogeneity was high or very high, a random-effect model would be applied to synthesize the effect size (34). If $I^2 > 50\%$ and with a sufficient number of studies (at least 10 studies), the publication bias was detected by the asymmetry of funnel plots or the Egger's test (35, 36).

The subgroup analyses based on cupping therapy types, pressure types, painful sites, age groups, and the frequency of treatments were performed. Furthermore, the

robust of the meta-analysis was investigated by the sensitive analysis with the one-leave out method. The Review Manager software (Review Manager 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration) was used to perform the meta-analysis.

Results

Search Result

The flowchart in **Supplemental Figure 1** shows the search procedure. From our preliminary search of four databases, a total of 1356 records were returned. Of 1064 non-duplicate records, 29 potentially eligible studies were examined in full-text after screening titles and abstracts. Finally, a total of 34 data points from 10 studies that meet the inclusion criteria were pooled in the quantitative analysis.

The Characteristics of Included Studies

The basic characteristics of the included studies are shown in **Supplemental Table 1.** These articles came from six different countries around the world (i.e., Saudi Arabia, n = 1, 10.0%; Brazil, n = 2, 20.0%; China, n = 2, 20.0%; Germany, n = 5, 50.0%). The subjects in all studies were adults over the age of 18 years. For genders of the recruited subjects, 9 studies recruited both males and females in the experimental groups and control groups. Among these 10 studies, five studies (50.0%) assessed the effect of cupping therapy on chronic back pain, four studies (40.0%) involved chronic neck pain, and only one study (10.0%) involved chronic pain in neck and shoulder. The duration of illness varied from 20.0 to 189.6 months in 9 articles. Only one article didn't report the exact course of the disease.

For experimental interventions, most studies (n = 6, 60.0%) examined the effect of dry cupping therapy, two studies reported pulsation cupping therapy, which was a modern cupping therapy using a pulsatile negative pressure produced by a mechanical device with a pump. Two studies focused on wet cupping therapy. And only one study involved cupping massage therapy, which was a treatment with the cupping glasses being moved over the skin surface with negative pressure (37). For control groups, the interventions consisted of sham/placebo cupping therapy (n = 3, 30.0%), waiting list control methods (n = 4, 50.0%), and resting (n = 1, 12.5%).

The pain intensity, as the primary outcome in this meta-analysis, was involved in all studies. As for the secondary outcomes, seven studies reported mental health conditions and nine studies reported functional disability. For the pain intensity, four measurements were used (the NPS: n = 1; the NPRS: n = 1; the VAS: n = 7; the BPI: n = 1). The functional disability was measured by the ODQ (n =1), the ODI (n = 1), the NDI (n = 4), the FIQ (n=1), the FFbH-R (n = 1), and the RMDQ (n = 1). The subjects in 7 trials accepted mental health tests by the SF-36 (n = 6) and the BPI (n = 1).

In addition, the quality of the included articles was evaluated according to the guidelines provided by Higgins (31). **Supplemental Figure 2** showed the risk of bias across all included studies. The quality bias mainly came from the blinding of outcome assessment (detection bias) and the other bias.

The Effect of Cupping Therapy on Pain Intensity

A total of fourteen data points in ten studies reported the influence of cupping

therapy on pain intensity in participants with CMP. Overall, as shown in **Figure 1**, there is a significant difference between experimental groups and control groups based on a random-effect model (SMD = -1.23; 95% CI = -2.02 to -0.44; P = 0.002; I^2 = 95%). And sensitivity analysis showed that the results were relatively robust.

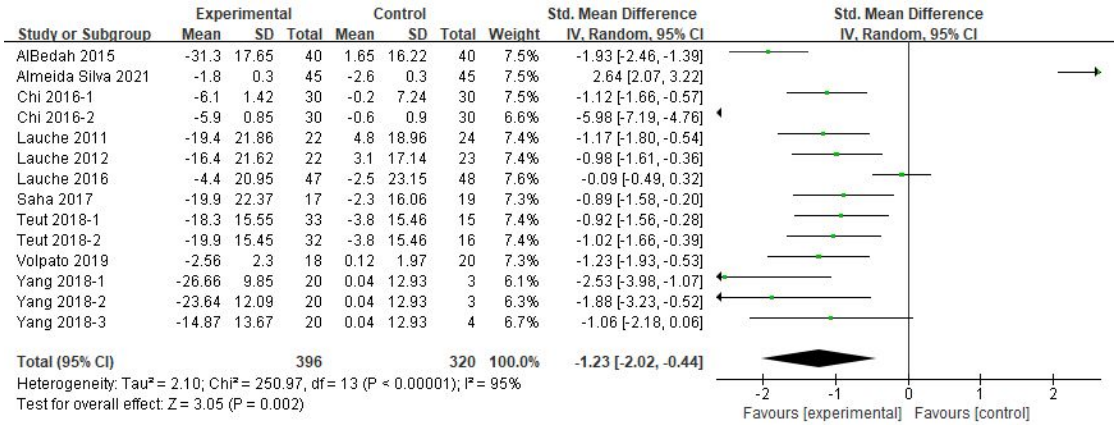

Figure 1 The effect of cupping therapy on pain intensity

Table 1 presents the effectiveness of cupping therapy on pain intensity for different subgroups. No significant difference was found in the effects of dry cupping and wet cupping (P = 0.69). But both of them were useful to reduce pain intensity compared to control groups. Additionally, the effect of wet cupping (SMD = -1.47, 95% CI = -2.39 to -0.55, P = 0.002) appeared to be more obvious than that of dry cupping (SMD = -1.20, 95% CI = -2.12 to -0.29, P = 0.01). For the subgroup analysis based on the different types of negative pressure, both the effects of pulsation pressure and non-pulsation pressure were superior to the effects of control interventions (pulsation VS control: SMD= -1.31, 95% CI = -1.90 to -0.71, P < 0.0001; non-pulsation VS control:

SMD= -1.13, 95% CI = -2.15 to -0.11, P = 0.03). However, there was no significant difference between pulsation pressure and non-pulsation pressure (P = 0.77). A subgroup analysis based on the frequency of treatments was also conducted. The results indicated a larger effect of a single-time cupping treatment compared to comparisons (SMD = -2.04, 95% CI = -3.08 to -0.99, P = 0.0001), while no significant effect for multiple-times cupping treatment (SMD = -0.48; 95% CI = -1.58 to 0.62; P = 0.39). As for the subgroup analysis based on the pain sites and the age of patients, there was a significant improving effect of cupping therapy in patients with neck/shoulder pain (SMD = -1.86, 95% CI = -2.74 to -0.98, P < 0.0001) and aged more than 45 years (SMD = -0.81, 95% CI = -1.20 to -0.41, P < 0.00001).

Table 1 The effect of cupping therapy on pain intensity for different subgroups

Subgroups	**N**	**n**	**SMD**	**95%CI**	***P* value (subtotal effect)**	**I^2**
Type of cupping therapy	10	716	-1.23	-2.02 to -0.44	0.002	95%
Dry cupping	8	589	-1.20	-2.12 to -0.29	0.01	95%
Wet cupping	2	125	-1.47	-2.39 to -0.55	0.002	80%
Difference between subgroups					0.69	
Type of negative pressure	10	716	-1.23	-2.02 to -0.44	0.002	95%
Pulsation	2	142	-1.31	-1.90 to -0.71	< 0.0001	42%
Non-pulsation	9	574	-1.13	-2.15 to -0.11	0.03	96%
Difference between subgroups					0.77	

Frequency of treatments	10	716	-1.23	-2.02 to -0.44	0.002	95%
Single time	4	273	-2.04	-3.08 to -0.99	0.0001	90%
Multiple times	6	443	-0.48	-1.58 to 0.62	0.39	95%
Difference between subgroups					0.04	
Painful site	10	716	-1.23	-2.02 to -0.44	0.002	95%
Neck/Shoulder	5	317	-1.86	-2.74 to -0.98	< 0.0001	89%
Back	5	399	-0.42	-1.69 to 0.85	0.52	97%
Difference between subgroups					0.62	
Age of participants	10	716	-1.23	-2.02 to -0.44	0.002	95%
> 45 years	5	318	-0.81	-1.20 to -0.41	< 0.00001	63%
< 45 years	5	398	-1.59	-3.20 to 0.01	0.05	97%
Difference between subgroups					0.35	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

The Effect of Cupping Therapy on Functional Disability

Twelve data points from 9 studies were synthesized to assess the influence of cupping therapy on functional disability in CMP patients. **Figure 2** presents that the cupping therapy has no significant effect on decreasing the functional disability in CMP patients (SMD = -0.24, 95% CI = -0.93 to 0.46, $P = 0.51$, $I^2 = 93\%$). However, according to the effect size, cupping therapy seemed to have a better improvement effect trend on functional disability than comparisons. And sensitivity analysis showed that the results

were relatively robust.

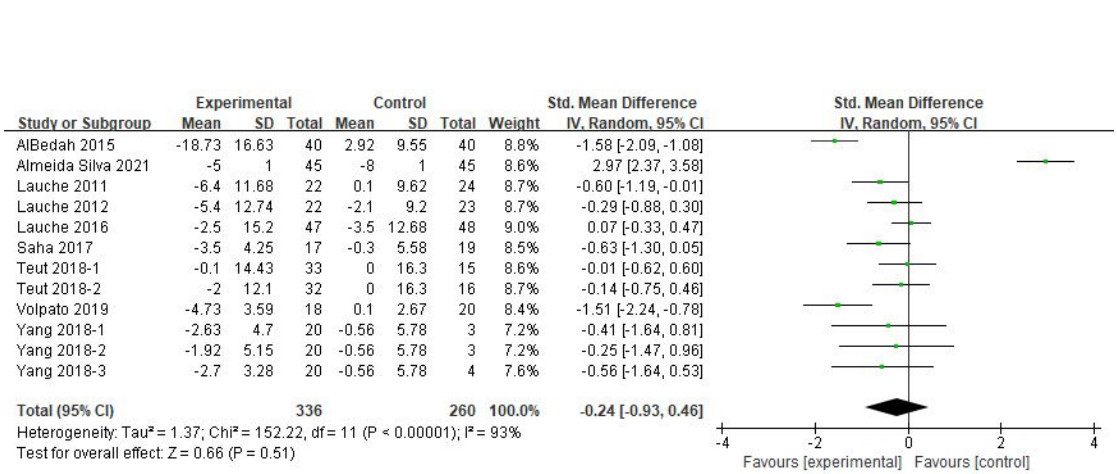

Figure 2 The effect of cupping therapy on functional disability

As depicted in **Table 2,** dry cupping therapy, wet cupping therapy, pulsation pressure cupping therapy, and non-pulsation pressure cupping therapy had effective recovery trends on the functional disability in CMP patients, but not statistically significant (dry cupping therapy: SMD = -0.09, 95% CI = -0.86 to 0.69, *P* =0.83; wet cupping therapy: SMD = -0.95, 95% CI = -2.21 to 0.32, *P* =0.14; pulsation cupping therapy: SMD = -0.13, 95% CI = -0.51 to 0.26, *P* =0.52; non-pulsation cupping therapy: SMD = -0.26, 95% CI = -1.24 to 0.73, *P* =0.61). For the frequency of treatments, a significant difference was found in the effect between the single-time cupping therapy (SMD = -0.65, 95% CI = -1.20 to -0.11, *P* = 0.02) and the control group. However, no significant difference was found in the effect between the multiple-times cupping therapy (SMD = 0.01, 95% CI = -0.99 to 1.01, *P* = 0.98) and the control group. For the

subgroup analysis based on the pain sites and the age of patients, there was a significant improving effect of cupping therapy in patients with neck/shoulder pain (SMD = -0.48, 95% CI = -0.79 to -0.16, $P = 0.003$) and aged more than 45 years (SMD = -0.23, 95% CI = -0.47 to 0.01, $P = 0.06$).

Table 2 Effects of cupping on functional disability for different subgroups

Subgroups	N	n	SMD	95%CI	*P* value (subtotal effect)	I^2
Type of cupping therapy	9	596	-0.24	-0.93 to 0.46	0.51	93%
Dry cupping	7	471	-0.09	-0.86 to 0.69	0.83	92%
Wet cupping	2	125	-0.95	-2.21 to 0.32	0.14	91%
Difference between subgroups					0.26	
Type of negative pressure	9	596	-0.24	-0.93 to 0.46	0.51	93%
Pulsation	2	142	-0.13	-0.51 to 0.26	0.52	0%
Non-pulsation	8	454	-0.26	-1.24 to 0.73	0.61	95%
Difference between subgroups					0.81	
No. of treatments	9	596	-0.24	-0.93 to 0.46	0.51	93%
Single time	3	153	-0.65	-1.20 to -0.11	0.02	45%
Multiple times	6	443	0.01	-0.99 to 1.01	0.98	96%
Difference between subgroups					0.25	
Painful site	9	596	-0.24	-0.93 to 0.46	0.51	93%
Neck/Shoulder	4	197	-0.48	-0.79 to -0.16	0.003	0%
Back	5	399	-0.03	-1.26 to 1.20	0.96	97%

Difference between subgroups					0.49	
Age of participants	9	596	-0.24	-0.93 to 0.46	0.51	93%
> 45 years	5	294	-0.23	-0.47 to 0.01	0.06	0%
< 45 years	4	278	-0.22	-1.97 to 0.48	0.81	97%
Difference between subgroups					0.99	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

The Effect of Cupping Therapy on Mental Health

Eight data points from 7 studies were pooled to evaluate the effectiveness of cupping therapy on mental health in CMP individuals. **Figure 3** shows that there is no significant difference in mental health between the cupping therapy group and the control group using a fixed-effect modal (SMD = 0.12, 95% CI = -0.07 to 0.30, P = 0.23, I^2 = 0%). However, according to the effects size, the cupping therapy seems to have an effective trend in the improvement of mental health. And sensitivity analysis showed that the results were relatively robust.

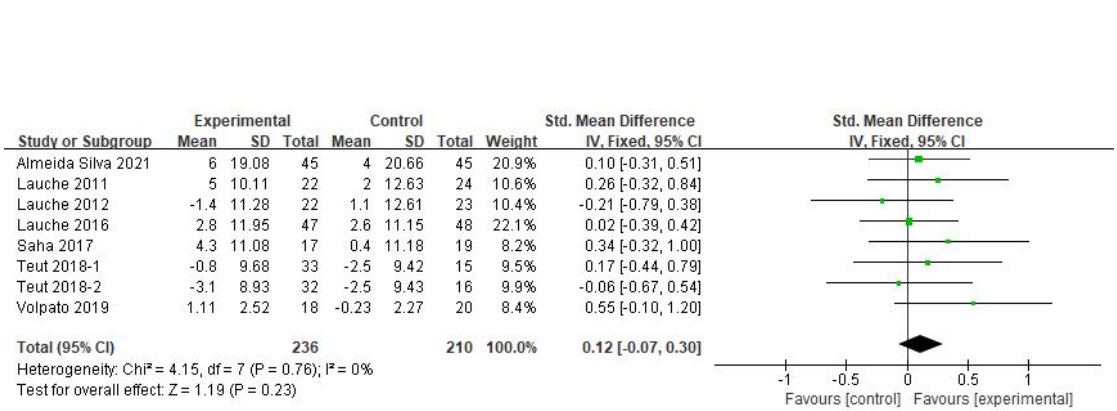

Figure 3 The effect of cupping therapy on mental health

Table 3 showed the effects of cupping therapy on mental health for five subgroups. With regard to different types of cupping therapy, we did not find a significant effect of dry cupping therapy (SMD = 0.15, 95% CI = -0.05 to 0.35, *P* = 0.14) and wet cupping therapy (SMD = -0.21, 95% CI = -0.79 to 0.38, *P* = 0.49) on CMP patients' mental health. In addition, no significant effect was found when conducting the subgroup analyses based on the types of negative pressure (pulsation: SMD = 0.05, 95% CI = -0.38 to 0.48, *P* =0.81; non-pulsation: SMD = 0.13, 95% CI = -0.08 to 0.34, *P* =0.23), the frequency of treatments (single-time: SMD = 0.16, 95% CI = -0.58 to 0.90, *P* =0.67; multiple-time: SMD = 0.11, 95% CI = -0.10 to 0.32, *P* =0.30), pain sites (neck/shoulder: SMD = 0.12, 95% CI = -0.23 to 0.47, *P* =0.99; back: SMD = 0.11, 95% CI = -0.11 to 0.34, *P* =0.32) and the age of participants (more than 45 years: SMD = 0.07, 95% CI = -0.16 to 0.29, *P* =0.55; less than 45 years: SMD = 0.23, 95% CI = -0.12 to 0.58, *P* =0.20).

Table 3 The effect of cupping therapy on mental health for different subgroups

Subgroups	N	n	SMD	95%CI	*P* value (subtotal effect)	I^2
Type of cupping therapy	7	446	0.12	-0.07 to 0.30	0.23	0%
Dry cupping	6	401	0.15	-0.05 to 0.35	0.14	0%
Wet cupping	1	45	-0.21	-0.79 to 0.38	0.49	-

Difference between subgroups					0.26	
Type of negative pressure	7	446	0.12	-0.07 to 0.30	0.23	0%
Pulsation	1	96	0.05	-0.38 to 0.48	0.81	0%
Non-pulsation	6	350	0.13	-0.08 to 0.34	0.23	0%
Difference between subgroups					0.75	
No. of treatments	7	446	0.12	-0.07 to 0.30	0.23	0%
Single time	2	83	0.16	-0.58 to 0.90	0.67	65%
Multiple times	5	363	0.11	-0.10 to 0.32	0.30	0%
Difference between subgroups					0.90	
Painful site	7	446	0.12	-0.07 to 0.30	0.23	0%
Neck/Shoulder	3	127	0.12	-0.23 to 0.47	0.51	0%
Back	4	319	0.11	-0.11 to 0.34	0.32	0%
Difference between subgroups					0.99	
Age of participants	7	446	0.12	-0.07 to 0.30	0.23	0%
> 45 years	5	318	0.07	-0.16 to 0.29	0.55	0%
< 45 years	2	128	0.23	-0.12 to 0.58	0.20	23%
Difference between subgroups					0.45	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

Discussion

This meta-analysis suggested that cupping therapy had a positive effect on

reducing CMP patients' pain intensity and improvement trends on their functional disability and mental health. Based on the subgroup analyses in pain intensity, dry cupping therapy, wet cupping therapy, pulsation pressure, and non-pulsation pressure cupping therapy showed a significant difference when compared to the control group, respectively. Our meta-analysis also indicated that the single-time cupping therapy seemed to reduce pain intensity more significantly than the multiple-times cupping therapy. In addition, there are differences in alleviating the effects of cupping therapy on different painful sites. Cupping therapy was effective for decreasing pain intensity and functional disability in patients with chronic neck/shoulder pain rather than in patients with chronic back pain.

Our results demonstrated that cupping therapy could effectively reduce pain intensity in CMP patients. This might be explained by the neurobiological foundations. It is widely confirmed that both nociceptive afferent fibers (Aδ and C fibers) and mechanosensitive Aβ fibers project in the same way onto interneurons or ascending projection neurons (38). However, the rate of signal transmission from the mechanoreceptor (Aβ) up to the dorsal horn was faster than that from the Aδ and C fibers, so that the Aβ fibers would activate the corresponding multi-receptive dorsal horn interneuron before the Aδ and C fibers (39). Based on the theory mentioned above, we speculated that the faster Aβ afferents (i.e., mechanosensitive afferent fibers) caused by the negative pressure of cupping therapy could block out pain sensation from the slower pain conducting Aδ and C fibers (i.e., nociceptive afferent fibers). This might

partly explain the effects of cupping therapy on the pain intensity in CMP individuals. On the other hand, cupping therapy has been indicated to result in vascular ectasia for increasing blood flow significantly (19), which may be related to the therapeutic effect of cupping therapy on CMP. The increased blood flow under the cup after cupping therapy could play a positive role in the clearance of inflammatory cytokines locally. Several studies have demonstrated that musculoskeletal pain following exercises caused upregulation of transcripts for inflammatory such as interleukin-1 (IL-1)(40, 41) and interleukin-6 (IL-6) (42) in the exercised limbs. These transcripts for inflammation were sensitivity to musculoskeletal sensitization, which was a preclinical model of muscle pain (42). In other words, lowering the inflammatory cytokines (i.e., IL-1 and IL-6) might imply the alleviation of inflammatory response and the reduction of muscle pain. Therefore, the acceleration of blood circulation caused by negative pressure suction of cupping therapy could accelerate the clearance of inflammatory factors, alleviate inflammatory reactions, and thus release muscle pain.

Although our meta-analysis found that cupping therapy could effectively reduce CMP patients' pain intensity, the recovery effect of cupping therapy on their functional disability was not significant. The potential reason might be that the outcomes related to pain intensity in our included studies in this meta-analysis (17, 43, 44) were usually evaluated in resting state rather than moving state. Nevertheless, the pain in moving state usually impeded patients' daily activities and contributed to the functional disability (45). Some musculoskeletal pain usually occurred during the moving process

with muscle contraction or joint friction and compression. For example, the individual with patellar tendinopathy only experienced pain when the keen was flexed and extended (e.g., walking down stairs and jumping) (46). This type of functional dysfunction was attributed to the pain induced by the altered biomechanical relationship between muscles, joints, and bones. According to the neurobiological foundation theory, the single-time cupping therapy might impede the pain conduction in CMP patients at rest state, while it was not sufficient to affect the biomechanical relationships of anatomical structures such as muscles, bones, and joints. Hence, patients with CMP still suffered from the functional disability due to the pain produced in moving state.

For another outcome, our results showed that, compared to the control group, cupping therapy had no effectiveness in promoting CMP patients' mental health. The non-significant group difference between cupping therapy and placebo therapy on mental health has been reported previously (e.g., sham cupping therapy). For example, Lauche et al. applied dry cupping therapy with 50-100 mm-diameter cups and a 10-15 minutes retention time for 141 fibromyalgia syndrome patients and used the SF-36 questionnaire to monitor changes in mental health. The findings demonstrated that cupping therapy and sham cupping therapy played similar roles in improving patients' mental health like anxiety, depression, and loss of behavioral or emotional control (44). Among the 10 included studies in our meta-analysis, the SF-36 was the mostly tool for accessing mental health (n = 6, 60.0%). After viewing the specific questions in SF-36, we supposed that the subjective questionnaire reflected the mental situations during the

past 4 weeks (47). Hence, the survey after the single cupping therapy immediately couldn't indicate the effects of cupping therapy on CMP patients' mental health accurately. This might partly explain the reason that, in our meta-analysis, there is no significant difference in the improvement effect on CMP patients' mental health between cupping therapy and sham cupping therapy.

The findings also demonstrated that the type of cupping therapy (i.e., dry cupping or wet cupping therapy) was an important influential factor for the recovery effect of cupping therapy on CMP. We found that compared to dry cupping therapy, wet cupping therapy (i.e., cupping therapy with the treated regions pricked) was more helpful in reducing pain intensity and functional disability in patients with CMP, but not helpful for increasing mental health. It was known that high levels of oxidant and oxidative stress could cause pain by increasing the free radical damage to cell membranes (48). The pricked skins induced by wet cupping therapy could cause blood and other body fluids escaping, which could accelerate the process of evacuating oxidants and decreasing oxidative stress, thereby reducing muscle pain. For this state, wet cupping therapy was regarded as an antioxidant application to release pain intensity (49). Dry cupping therapy only increased blood circulation inside the skin and accelerated the flow of oxidant in local areas covered by the cups instead of quickly eliminating oxidants from the body. It might be the reason that wet cupping therapy had more pronounced effects on alleviating pain than dry cupping therapy. For mental health, wet cupping therapy-induced incisions might cause more negative emotions (e.g., fear of

invasive wound) rather than positive emotions (e.g., relaxation or soothing power of cupping therapy) caused by suction treatment. One animal experiment about mood status demonstrated that sheep conducted worse aversive behavior patterns in response to the pricking stimulus than the slight pressure and kneading stimulus (50). That might be the potential reason that wet cupping therapy, compared with dry cupping therapy, was more efficacious in pain intensity but not in mental health.

To the best of our knowledge, this is the first study to demonstrate and integrate the effects of cupping therapy on clinical outcomes (i.e., pain intensity, functional disability, and mental health) in CMP patients. However, there are still some limitations. First, we only considered the immediate effect of cupping therapy, because of the limited original researches included in this meta-analysis. Nevertheless, our team has proposed the delayed effect of cupping therapy on muscular performance in one previous study (51). Hence, we inferred that there was the possibility of the delayed effect of cupping therapy on CMP. Further evidence-based studies are needed to assess the time-effect to prove our speculation. Second, the heterogeneity of the included studies was relatively high because of differences in cupping dose. Therefore, the caution should be exercised in interpreting the results of this meta-analysis. Third, considering the readability for international readers, we only included relevant literature from four English databases. While cupping therapy, as a traditional Chinese medical treatment, may have been studied by more Chinese scholars. That may cause the bias of synthesized effect size. Last, the number of studies included in this systematic review is

limited (n = 10). In the future, as more RCT literatures are available, we will reexamine the evidences. The purpose of this systematic review is to evaluate the available evidence and provide the integrated effect size for the effectiveness of the separate cupping therapy on clinical outcomes in CMP patients.

Conclusion

This systematic review and meta-analysis demonstrates that cupping therapy is effective in reducing pain intensity for individuals with CMP. However, CMP patients' functional disability and mental health can't be improved by cupping therapy. Among different cupping therapy types, wet cupping therapy seems to show better effects on reducing pain intensity.

Strengths and limitations of this study

To the best of our knowledge, this is the first study to demonstrate and integrate the effects of cupping therapy on clinical outcomes (i.e., pain intensity, functional disability, and mental health) in CMP patients. However, there are still some limitations: 1) only considering the immediate effect of cupping therapy; 2) the relatively high heterogeneity of the included studies because of differences in cupping dose; and 3) the limited number of studies included in this systematic review.

Declarations

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The data underlying the article are available in the article and in its online supplementary material.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was not supported by fundings.

Authors' contributions

Conceptualization, X.H. and T.-T.S; methodology, Y.-Y.J., R.W and Z.-M.B.; formal analysis, Y.-Y.J and L.-K.Y.; writing—original draft preparation, Y.-Y.J.; writing—review and editing, X.H. and Y.-Y.J.; visualization, Y.-Y.J.; supervision, X.H. and T.-T.S. All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Acknowledgement

Dr. Xiao Hou and Dr. Tingting Sun contributed equally to this work.

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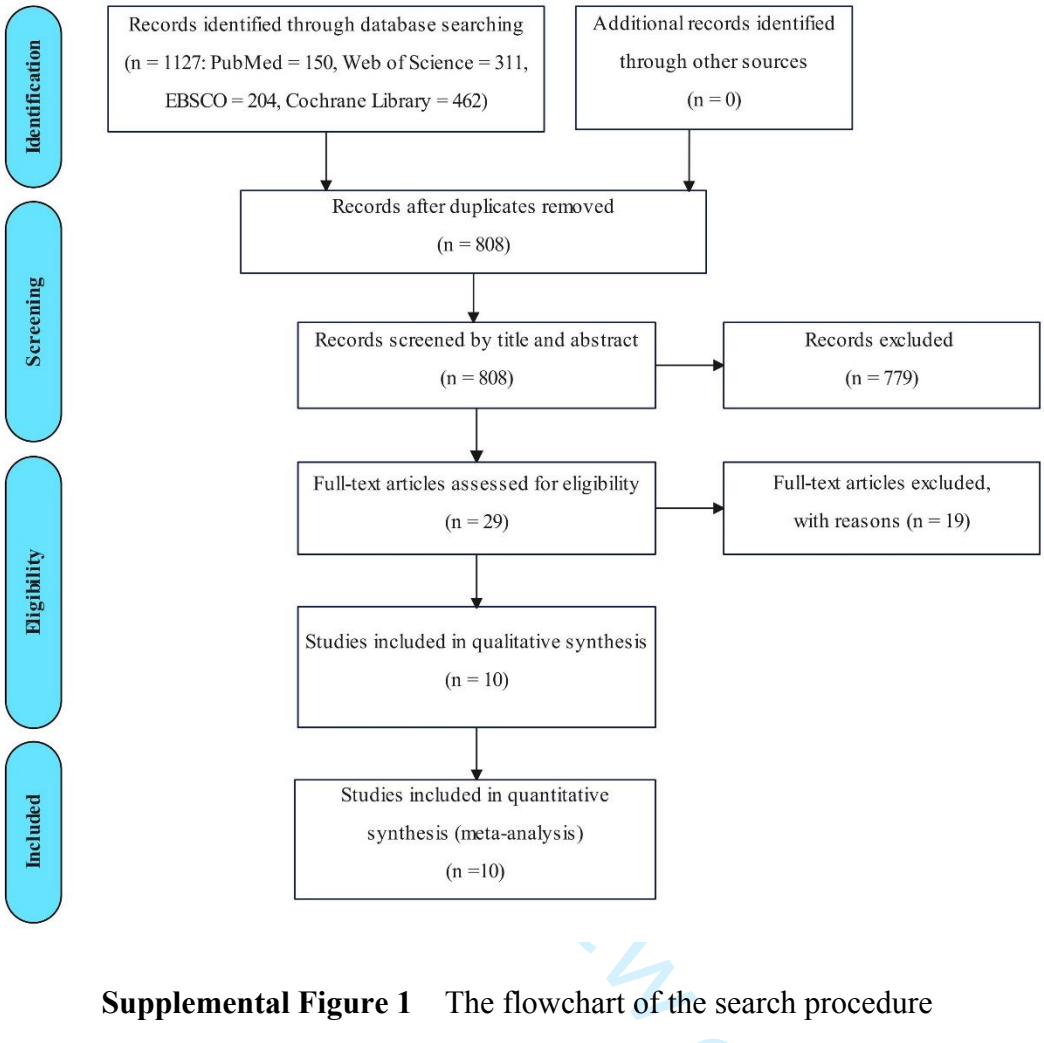
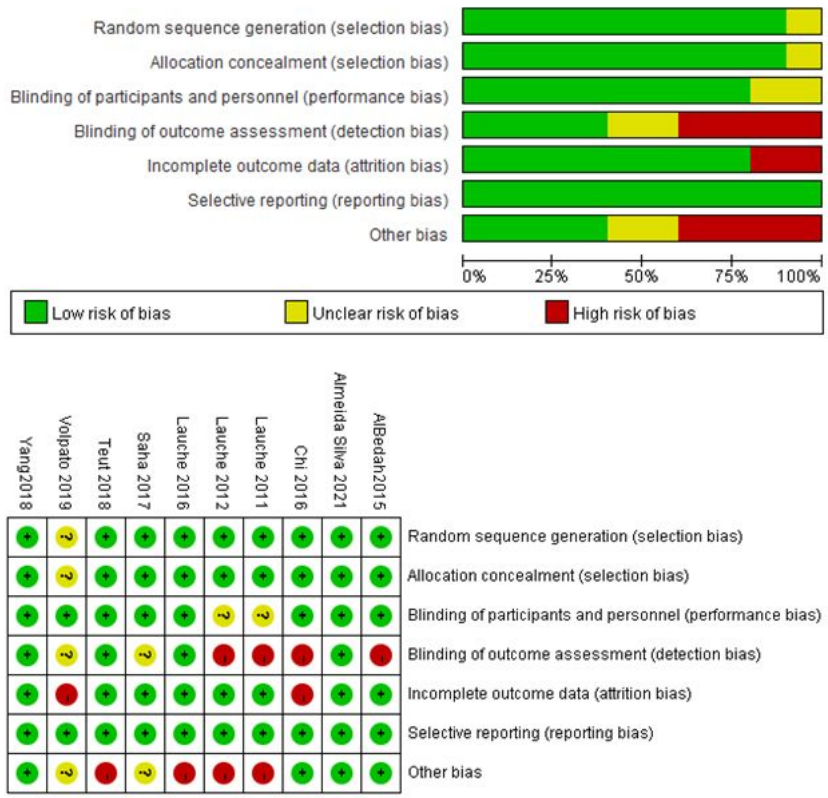


Supplemental Figure 1 The flowchart of the search procedure



Supplemental Figure 2 The bias of the included studies

Supplemental Table 1 The characteristics of included studies

No.	Author(s) Publication year	Country	Age (mean ± SD) Gender (male/female)	Sample size	Painful site(s)	Duration of illness (mean ± SD)	EG intervention (dosages, cupping therapy)	CG intervention	Outcomes 1. Pain intensity 2. Functional disability 3. Mental health
1	Al Bedah et al. 2015	Saudi Arabia	**EG:** 36.48 ± 9.3 y 22/18 **CG:** 36.43 ± 9.4 y 17/23	**EG:** 40 **CG:** 40	Low back	**EG:** 4.45 ± 4.8 y **CG:** 3.85 ± 3.9 y	**Wet cupping therapy** (cup size: 40 cc; duration: 5 min; negative pressure caused by manual pumping; frequency: three times per week for 2 weeks)	**Resting** Rescue treatment: acetaminophen no more than 1500 mg per day	1. NRS 2. ODQ 3. NA

							Rescue treatment: acetaminophen no more than 1500 mg per day		
2	Almeida Silva et al. 2021	Brazil	**EG:** 30 ± 11.0 y 16/29 **CG:** 32 ± 13.0 y 7/38	**EG:** 45 **CG:** 45	Low back	**EG:** 44 ± 32 mo **CG:** 58 ± 51 mo	**Dry cupping therapy** (cup size: 4.5 cm; duration: 10 min; negative pressure: 300 millibars; frequency: once per week for 8 times)	**Sham-cupping therapy** (cup size: 4.5 cm; duration: 10 min; negative pressure: 0; frequency: once per week for 8 times)	1. NPRS 2. ODI 3. SF-36
3	Chi et al. 2016	China	**EG:** 43.6 ± 8.0 y	**EG:** 30 **CG:** 30	Neck, shoulder	**EG:** 20.17 ± 8.53 mo	**Dry cupping therapy** (cup size: 4 cm; duration: 10 min; negative pressure caused by	**Resting**	1. VAS (neck, shoulder) 2. NA

			3/27			**CG:** 20.03 ±	placing the burning swab in-		3. NA
			CG: 42.5 ±			9.21 mo	and-out; frequency: single		
			7.4 y				intervention)		
			2/28						
4	Lauche et	Germany	**EG:** 48.6 ±	**EG:** 22	Neck	**EG:** 6.3 ± 6.1	**Dry cupping therapy** (cup	**Waiting list control**	1. VAS (rest,
	al.		11.2 y	**CG:** 24		y	size: 25 to 50 mm; duration:		movement)
	2011		7/15			**CG:** 8.0 ± 7.6	10 - 20 min; negative pressure		2. NDI
			CG: 53.0 ±			y	caused by heating the air		3. SF-36
			11.4 y				inside; frequency: once per 3 -		
			4/20				4 days for 5 times)		
5	Lauche et	Germany	**EG:** 54.8 ±	**EG:** 25	Neck	**EG:** 12.0 ±	**Wet cupping therapy** (cup	**Waiting list control**	1. VAS (rest,
	al.		9.6 y	**CG:** 25		10.3 y	size: 25 - 50 mm; duration: 10	Fixed dosage of Pa	movement)
	2012						- 15 min; negative pressure	and Me if started for	2. NDI

			7/18			**CG:** 10.4 ±	caused by heating the air	4 weeks before the	3. SF-36
			CG: 57.2 ±			11.5 y	inside; frequency: single	study	
			9.4 y				intervention)		
			9/16				Fixed dosage of Pa and MA		
							started for 4 weeks before the		
							study		
6	Lauche et	Germany	**EG:** 54.35	**EG:** 47	Back	**EG:** 11.6 ±	**Dry cupping therapy** (cup	**CG: Sham-cupping**	1. VAS
	al.		± 10.6 y	**CG:** 48		9.2 y	size: 50 - 100 mm; duration:	**therapy** (cup size:	2. FIQ
	2016		1/46			**CG:** 11.2 ±	10 - 15 min; negative pressure:	50 - 100 mm;	3. SF-36
			CG: 56.3 ±			8.9 y	caused by a mechanical	duration: 10 - 15	
			8.7 y				device; frequency: twice per	min; negative	
			1/47				week for 5 times)	pressure: 0;	

							Fixed dosage of Me if started before the study	frequency: twice per week for 5 times) Fixed dosage of Me if started before the study	
7	Saha et al. 2017	Germany	**EG:** 54.3 ± 8.6 y 4/21 **CG:** 53.3 ± 11.1 y 0/25	**EG:** 25 **CG:** 25	Neck	**EG:** 7.5 ± 6.6 y **CG:** 8.1 ± 7.2 y	**Cupping massage therapy** (cup size: 3.5 - 5 cm; duration: 10 min; frequency: twice per week for 5 times)	**Waiting list control** Fixed treatments if started except invasive treatments before the study	1. VAS (rest, movement) 2. NDI 3. SF-36
8	Teut et al. 2018	Germany	**EG1:** 49.0 ± 13.7 y	**EG1:** 37 **EG2:** 36	Low back	**EG1:** 13.1 ± 9.3 y	**EG1: Pulsatile cupping therapy-high vacuum** (cup	**Waiting list control** Rescue treatment:	1. VAS 2. FFbH-R

16/21 **EG2:** 47.5 ± 13.8 y 13/23 **CG:** 50.7 ± 10.7 y 12/15	**CG:** 37	**EG2:** 15.8 ± 12.9 y **CG:** 13.2 ± 11.2 y	size: 10 cm; duration: 8 min; negative pressure: 150 - 350 mbar; frequency: 8 sessions for 4 weeks) **EG2: Pulsatile cupping therapy-low vacuum** (cupping size: 10 cm; duration: 8 min; negative pressure: 70 mbar; frequency: 8 sessions for 4 weeks) **EG1, 2:** Rescue treatment: paracetamol no more than 2000 mg per day	paracetamol no more than 2000 mg per day	3. SF-36

9	Volpato et al. 2019	Brazil	**EG:** 27.16 ± 8.43 y 3/15 **CG:** 25.42 ± 9.18 y 5/15	**EG:** 18 **CG:** 20	Low back	NA	**Dry cupping therapy** (cup size: 50 mm; duration: 15 min; negative pressure: 300 millibars; frequency: single intervention)	**Placebo cupping therapy** (cup size: 50 mm; duration: 15 min; negative pressure: 0; frequency: single intervention)	1. BPI 2. RMDQ 3. BPI
10	Yang et al. 2018	China	**EG1:** 23.95 ± 2.21 y 6/14 **EG2:** 27.10 ± 5.27 y 4/16	**EG1:** 20 **EG2:** 20 **EG3:** 20 **CG:** 10	Neck	**EG1:** 2.61 ± 2.01 y **EG2:** 2.55 ± 2.73 y **EG3:** 3.68 ± 2.55 y	**EG1: Pulsatile cupping therapy-high frequency** (cup size: 68 mm; duration: 80 times per min for 8 min; negative pressure: 0.02 – 0.04	**Waiting list control**	1. VAS 2. NDI 3. NA

EG3: 26.00 ± 4.15 y	**CG:** 2.65 ± 1.53 y	MPa; frequency: single intervention)
1/19		**EG2: Pulsatile cupping therapy-low frequency** (cup size: 68 mm; duration: 30 times per min for 8 min; negative pressure: 0.02 – 0.04 MPa; frequency: single intervention)
CG: 24.7 ± 2.5 y		**EG3: Static cupping therapy** (cup size: 68 mm; duration: 8 min; negative pressure: 0.02 –
3/7		

											0.04 MPa; frequency: single intervention)

Abbreviations: EG, Experimental Group; CG, Control Group; NA, Not Assessed; y, years; mo, months; Pain; Me, Medicine; NRS, Numeric Rating Scale; ODQ, Oswestry Disability Questionnaire; SF-36, Short Form 36-health survey questionnaire; PRS, Numerical Pain Rating Scale; ODI, Oswestry Disability Index; VAS, Visual Analog Scale; NDI, Neck Disability Index; FIQ, Fibromyalgia Impact Questionnaire; FFbH-R, Funktionsfragebogen Hannover Rücken; BPI, Brief Pain Inventory; RMDQ, Roland Morris Disability Questionnaire.

BMJ Open

Effects of Cupping Therapy on Chronic Musculoskeletal Pain and Collateral Problems: A Systematic Review and Meta-Analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-087340.R1
Article Type:	Original research
Date Submitted by the Author:	02-Feb-2025
Complete List of Authors:	Jia, Yuanyuan; Beijing Sport University, Key Laboratory of Sports and Physical Health Ministry of Education; Beijing Sport University, School of Sport Science Wang, Rong; Beijing Sport University, Yu, Laikang; Beijing Sport University, Department of Sports Performance Bai, Zhenmin ; Beijing Sport University Sun, Tingting; Beijing Sport University Hou, Xiao; Beijing Sport University, ; Beijing Sport University,
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Complementary medicine, Rehabilitation medicine
Keywords:	Meta-Analysis, Chronic Pain, COMPLEMENTARY MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY

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Effects of Cupping Therapy on Chronic Musculoskeletal Pain and Collateral Problems: A Systematic Review and Meta-Analysis

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All authors declare no conflicts of interest.

Abstract

Objectives Chronic musculoskeletal pain (CMP) is a prevalent and distressing condition. Cupping therapy, one of the most popular complementary and alternative medicines, has been widely used to reduce CMP. But the evidence remains controversial on the effect of cupping therapy on CMP. The objective of this review and meta-analysis is to assess the effectiveness of cupping therapy in CMP patients.

Design Systematic review and meta-analysis.

Data sources PubMed, Web of Science, EBSCO, Cochrane Library and China National Knowledge Infrastructure (CNKI) were searched through 20 December 2024.

Eligibility criteria for selecting studies We included randomized control trials (RCTs) that compared cupping therapy for CMP patients on outcomes (i.e., pain intensity, functional disability and mental health).

Data extraction and synthesis Two independent reviewers used standardized methods to search, screen and code included studies. Risk of bias was assessed using the Cochrane Collaboration and Evidence Project tools. Meta-analysis was conducted using random and fixed effects models. Findings were summarized in GRADE evidence profiles.

Results The results showed that cupping therapy (SMD = -1.23; 95% CI = -2.02 to -0.44; P = 0.002; I^2 = 95%) had a significant reduction effect on CMP patients' pain intensity with moderate quality based on a random-effect model. But cupping therapy had no improvement effects on functional disability (SMD = -0.58; 95% CI = -1.34 to 0.17; P = 0.13; I^2 = 76%) and mental health (SMD = -0.21; 95% CI = -0.81 to 0.38; P = 0.48; I^2 = 63%).

Conclusions This study indicates that cupping therapy is efficient in alleviating pain intensity in CMP patients with immediate effects. But it cannot improve functional disability and mental health significantly.

PROSPERO registration number CRD42023406219.

Strengths and limitations of this study

1. Interest in complementary and alternative medicines for CMP such as cupping therapy is growing.
2. Effects of cupping therapy on CMP clinical outcomes (i.e., pain intensity, functional disability, and mental health) are integrated.
3. The immediate effect of cupping therapy was considered, due to the limited number of original studies included in this meta-analysis.

Keywords: chronic musculoskeletal pain, cupping therapy, complementary and alternative medicine, meta-analysis

Background

Chronic musculoskeletal pain (CMP) is a prevalent global issue, associated with a high incidence and significant burden on healthcare systems. In 2019, the estimated global prevalence of chronic musculoskeletal disorders reached 1.52 billion cases (95% uncertainty intervals: 1.43 to 1.60 billion), with an age-standardized prevalence rate (ASPR) of 18,407 per 100,000 people. Furthermore, chronic musculoskeletal disorders accounted for 147 million years lived with disability (YLDs) in 2019 (95% uncertainty intervals: 106 to 195 million) and a high ASYR of 1791 per 100,000 people (95% uncertainty intervals: 1288 to 2367)[1]. In addition to the substantial health burden, the treatment of CMP also occurs high financial cost. For example, based on the Chilean health system, the annual expected cost for CMP is USD $1387.2 million and equivalent to 0.417% of the national GDP [2].

In addition to the impact on healthy, life expectancy and financial burden, CMP usually accompanies restricted daily activities and negative mental health to individuals. Original research has found that the pain threshold and pain tolerance value of patients with chronic back pain were significantly lower than healthy participants and these lower pain-related parameters may contribute to the persistence of chronic pain [3]. The persistent CMP can interfere with individuals' physical functions. For example, the reductions in strength and endurance induced by fibromyalgia can lead to the restrictions in participation during leisure-time activities and work-related activities [4] [5]. Moreover, individuals' psychological states can also influence the condition of CMP. For example, chronic low back pain (CLBP) patients with depression experienced significantly more severe pain (5.86 ± 2.27) compared to their non-depressed counterparts (4.34 ± 2.20; $P < 0.001$)[6]. Another survey including 122 CMP patients has indicated that the pain interference was negatively correlated with several mental health components (e.g., vitality and calmness) significantly [7]. In addition to daily mental states, CMP even causes the mental illness. For example, the patients with long-term low back pain, who experienced the moderate to severe pain dysfunction at the initial assessment, were easier to remain chronical depression [8]. Therefore, it is necessary to find effective treatments and rehabilitation measures for patients with CMP to alleviate pain and collateral problems, such as functional disability and unhealthy mental states.

Treatment options for CMP generally encompass pharmacological therapies and, where appropriate, surgical interventions, both of which may be accompanied by certain adverse side effects. Some drugs like opioid painkillers, have been opposed by current guidelines for CMP, because of the rising rates of opioid overdose deaths and other serious harms [9]. It has been indicated that long-term use of nonopioid drugs for relieving CMP (e.g., non-steroidal anti-inflammatory drugs, and Cyclooxygenase-2) may produce serious gastrointestinal side effects and increase cardiovascular risks [10 11]. Another usual therapy, the surgical interventions have been proven, to some extent, effective in CMP conditions, especially in osteoarthritis. However, operations usually

cause a high prevalence (80%) of postoperative pain [12]. These adverse impacts of drug treatments and surgical interventions result in a growing interest in non-pharmacological measures in response to CMP [13 14].

Cupping therapy, a type of complementary and alternative medicine, has been widely applied to alleviate CMP, such as chronic neck pain [15 16] and chronic low back pain [17]. The normal impacts after cupping therapy are circular erythematous spots with no painful sense and no restriction to daily activities. Some researchers have suggested that cupping therapy can improve blood flow [18 19], which may contribute to its therapeutic effect. The increasing blood flow has been indicated effective in removing glutamate [20], lactate, and pyruvate [21], which are biochemical biomarkers in CMP regions. In fact, several researchers have demonstrated the obvious alleviation effects of cupping therapy on CMP patients' pain intensity [22 23]. For example, Volpato et al. have indicated that a single-time dry cupping therapy can effectively decrease pain intensity, which is presented by the Brief Pain Inventory (BPI, assessing pain level with 0 = no pain/no interference to 10 = most pain/most interference) score, in low back (pre-cupping: 4.22 ± 2.53; post-cupping: 1.66 ± 1.97, $P < 0.05$) [22]. Wet cupping therapy, another type of cupping therapy adding blood-letting to dry cupping therapy, has been also demonstrated effective for reducing CMP [23-25]. Some comprehensive treatments combining cupping therapy and other physical therapies or techniques (e.g., pulsatile cupping, cupping massage) have been also demonstrated effective for relieving CMP [26 27]. Compared to separate methods, the integrated approaches may produce better therapeutic effects. But more clinical trials are needed to clarify the differences in the effect of alleviating CMP between these two kinds of approaches.

Although numerous studies have clarified the potential effectiveness of cupping therapy in treating CMP, there still remain the opposite results. For instance, Silva et al. have indicated that dry cupping therapy is not superior to sham cupping for improving the Numerical Pain Rating Scale (NPRS, assessing pain level with 0 = no pain/no interference to 10 = most pain/most interference) score (dry cupping therapy: 3.3 ± 2.9 VS sham cupping therapy: 2.7 ± 1.9; Mean $_{\text{between-group differences}}$ = 0.6, 95% confidence intervals = -0.4 to 1.6) in patients with non-specific chronic low back pain [28]. Another study has also revealed no statistically significant improvement is found in physical function (e.g. difficulty in walking) of osteoarthritis patients after multiple-times wet cupping treatments (pre-cupping: 1.68 ± 0.63 VS post-cupping: 0.906 ± 0.40, $P > 0.05$) [29]. Both high pain intensity and poor physical function are harmful symptoms in CMP patients, while these inconsistent findings cannot identify whether cupping therapy is effective for the improvement of clinical symptoms (e.g., pain and physical function) of CMP or not. Considering that CMP has a lasting harmful effect on patients, there is an urgent need to examine studies related to the effectiveness of cupping therapy on CMP scientifically and comprehensively.

The purpose of this study is to evaluate the effect of cupping therapy on clinical outcomes (i.e., pain intensity, functional disability, and mental health) in CMP patients

through a meta-analysis from a more comprehensive and systematic perspective.

Methods

Search Strategy and Study Selection

This meta-analysis was reported according to the PRISMA guidelines (http://www.prisma-statement.org/). The protocol was registered at PROSPERO (http://www.crd.york.ac.uk/ PROSPERO) before starting the data extraction (registration number: CRD42023406219).

Four electronic databases, including PubMed, Web of Science, EBSCO, Cochrane Library and China National Knowledge Infrastructure (CNKI), were searched respectively for relevant articles until December 20, 2024. The searching criteria was set based on the following keywords: (“chronic musculoskeletal pain” OR “chronic musculoskeletal disorder” OR “fibromyalgia” OR “osteoarthritis” OR “myalgia” OR “muscle pain” OR “back pain” OR “neck pain” OR “shoulder pain” OR “knee pain” OR “hip pain” OR “chronic pain”) AND (“cupping therapy” OR “cupping treatment” OR “dry cupping” OR “wet cupping” OR “cupping massage”). The full search strategies for all databases were shown in **Supplementary File 1**.

Two independent reviewers (Y.-Y.J. and R.W.) screened the titles and abstracts of all potentially suitable publications and assessed their eligibility through reading in full. If a disagreement remained after discussion, a third arbitrator (Z.-M.B.) was consulted for a consensus.

Inclusion Criteria

Trials were eligible for inclusion if they met the following criteria with the PICOS principle (population, intervention, comparison/control, outcome and study design): 1) participants were suffering from musculoskeletal pain and/or stiffness for more than three months, which is the diagnostic criteria of CMP [30]; 2) participants in the experimental group received interventions related to cupping therapy (e.g., dry cupping, wet cupping, pulsating cupping, and cupping massage); 3) the comparison intervention was limited to no treatment or sham/placebo interventions during experimental treatments; 4) the outcomes were pain intensity, functional disability, or mental health; and 5) only publications designed as randomized control trials (RCTs) were covered.

Exclusion Criteria

The exclusion criteria for the selected trials were as follows: 1) reviews, abstracts, protocols, case reports, observational studies, non-English/Chinese publications, non-peer-reviewed articles (e.g., academic dissertations and conference posters); 2) no sufficient evidence to judge the duration of disease as chronic condition (i.e. less than three months); 3) pain sites containing visceral or orofacial regions; and 4) participants in control groups received other active treatments, such as traditional Hijamah technique, standard medical care, and ischemic compression.

Quality Assessment

Two authors independently examined the quality of included studies using the Cochrane Collaboration tool. The risk of bias was evaluated as "low," "high," or "unclear" in the seven domains: 1) random sequence generation (selection bias): 2) allocation concealment (selection bias); 3) blinding of participants and personnel (performance bias); 4) blinding of outcome assessment (detection bias); 5) incomplete outcome data (attrition bias); 6) selective reporting (reporting bias); and 7) other bias [31]. If there was a disagreement between two authors, a third arbitrator (Z-M.B.) was consulted to reach a consensus.

Data Extraction

From each included article, the following data were extracted by two independent reviewers: author(s), publication year, country, subjects' demographical characteristics (e.g., age and gender), sample size, pain site(s), duration of CMP, experimental intervention (i.e., dosage of cupping therapy), control intervention, and the reported outcomes (e.g., pain intensity, functional disability, or mental health). If there was a disagreement between two authors, a third arbitrator (Z-M.B.) was consulted to reach a consensus.

Meta-analysis

In this meta-analysis, the outcome indicators were measured on different tools. For example, the pain intensity was assessed by the Numerical Pain Rating Scale (NPRS), the Visual Analog Scale (VAS), or the Brief Pain Inventory (BPI). The functional disability was measured by the Neck Disability Index (NDI), the Oswestry Disability Questionnaire (ODQ), the Oswestry Disability Index (ODI), the Fibromyalgia Impact Questionnaire (FIQ), the Funktionsfragebogen Hannover Rücken (FFbH-R), or the Roland Morris Disability Questionnaire (RMDQ). Meanwhile, the mental health was evaluated by the Short-Form 36 health survey questionnaire (SF-36) or the BPI. Because of the different measurements of outcomes, the standardized mean differences (SMDs) with 95% confidence intervals (CIs) were chosen to analyze the compositive effects, and $P < 0.05$ was set as the significant level.

According to the Cochran Handbook for Systematic Review, both the post-intervention values (i.e., Mean $_{\text{post-intervention}} \pm$ SD $_{\text{post-intervention}}$) of the outcome and the changes from baseline (i.e., Mean $_{\text{of changes}} \pm$ SD $_{\text{of changes}}$) could be used for the summary statistic value in this study [32]. Post-measurement data selected in this study refers to the immediate test results following the final cupping intervention. If studies reported CI instead of SD, we would convert CI into SD[33].

The heterogeneity among included studies was evaluated by the I^2 index. The low, moderate, high, and very high heterogeneity was identified when $I^2 \leq 25\%$, $I^2 \leq 50\%$ and >25%, $I^2 \leq 75\%$ and > 50%, and $I^2 > 75\%$ respectively [33]. For the low or moderate heterogeneity, a fixed-effect model would be chosen. When the heterogeneity was high or very high, a random-effect model would be applied to synthesize the effect size [34]. If $I^2 > 50\%$ and with a sufficient number of studies (at least 10 studies), the publication bias was detected by the asymmetry of funnel plots or the Egger's test [35 36].

The subgroup analyses based on cupping therapy types, pressure types, painful

sites, age groups, and the frequency of treatments were performed. Furthermore, the robust of the meta-analysis was investigated by the sensitive analysis with the one-leave out method. The Review Manager software (Review Manager 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration) was used to perform the meta-analysis. Finally, the GRADEpro online tool (gdt.gradepro.org) was used to assess the overall quality of evidence in this systematic review and meta-analysis.

Results

Search Result

The flowchart in **Supplemental File 2** shows the search procedure. From our preliminary search of four databases, a total of 1356 records were returned. Of 1064 non-duplicate records, 29 potentially eligible studies were examined in full-text after screening titles and abstracts. Finally, a total of 34 data points from 10 studies that meet the inclusion criteria were pooled in the quantitative analysis.

The Characteristics of Included Studies

The basic characteristics of the included studies are shown in **Supplemental File 3.** These articles came from six different countries around the world (i.e., Saudi Arabia[37], n = 1, 10%; Brazil[38 39], n = 2, 20%; China[40 41], n = 2, 20%; Germany[27 42-45], n = 5, 50%). The subjects in all studies were adults over the age of 18 years. For genders of the recruited subjects, 9 studies recruited both males and females in the experimental groups and control groups. And one study included only females in the control group[27]. Among these 10 studies, five studies (50%) assessed the effect of cupping therapy on chronic back pain[37-39 44 45], four studies (40%) involved chronic neck pain[27 41-43], and only one study (10%) involved chronic pain in neck and shoulder[40]. The duration of illness varied from 20.0 to 189.6 months in 9 articles. Only one article didn't report the exact course of the disease[39].

For experimental interventions, most studies (n = 5, 50%) examined the effect of dry cupping therapy, two studies reported pulsation cupping therapy, which was a modern cupping therapy using a pulsatile negative pressure produced by a mechanical device with a pump[41 45]. Two studies focused on wet cupping therapy[37 43]. And only one study involved cupping massage therapy, which was a treatment with the cupping glasses being moved over the skin surface with negative pressure[27]. For control groups, the interventions consisted of sham/placebo cupping therapy (n = 3, 30%)[38 39 44], waiting list control methods (n = 5, 50%)[27 41-43 45], and resting (n = 2, 20%)[37 40].

The pain intensity, as the primary outcome in this meta-analysis, was involved in all studies. As for the secondary outcomes, seven studies reported mental health conditions and nine studies reported functional disability. For the pain intensity, four measurements were used (the NPS: n = 1; the NPRS: n = 1; the VAS: n = 7; the BPI: n = 1). The functional disability was measured by the ODQ (n =1), the ODI (n = 1), the NDI (n = 4), the FIQ (n=1), the FFbH-R (n = 1), and the RMDQ (n = 1). The subjects in 7 trials accepted mental health tests by the SF-36 (n = 6) and the BPI (n = 1).

In addition, the quality of the included articles was evaluated according to the

guidelines provided by Higgins [31]. **Supplemental File 2** showed the risk of bias across all included studies. The quality bias mainly came from the blinding of outcome assessment (detection bias) and the other bias.

The Effect of Cupping Therapy on Pain Intensity

A total of fourteen data points in ten studies reported the influence of cupping therapy on pain intensity in participants with CMP. Overall, as shown in **Figure 1**, there is a significant difference between experimental groups and control groups based on a random-effect model (SMD = -1.17; 95% CI = -1.93 to -0.42; P = 0.002; I^2 = 94%). And sensitivity analysis showed that the results were relatively robust (**Supplementary File 3**). The studies are symmetrically distributed on either side of the pooled effect size line, suggesting the absence of publication bias (**Supplementary File 2**). The GRADE assessment indicated moderate confidence in the estimated effect (**Supplementary File 4**).

Table 1 presents the effectiveness of cupping therapy on pain intensity for different subgroups. No significant difference was found in the effects of dry cupping and wet cupping (P = 0.60). But both of them were useful to reduce pain intensity compared to control groups. Additionally, there was no significant difference between the effect of wet cupping (SMD = -1.47, 95% CI = -2.39 to -0.55, P = 0.002) and that of dry cupping (SMD = -1.13, 95% CI = -2.00 to -0.27, P = 0.01). For the subgroup analysis based on the different types of negative pressure, both the effects of pulsation pressure and non-pulsation pressure were superior to the effects of control interventions (pulsation VS control: SMD= -1.31, 95% CI = -1.90 to -0.71, P < 0.0001; non-pulsation VS control: SMD= -1.06, 95% CI = -1.93 to -0.42, P = 0.03). However, there was no significant difference between pulsation pressure and non-pulsation pressure (P = 0.67). A subgroup analysis based on the frequency of treatments was also conducted. The results indicated a larger effect of a single-time cupping treatment compared to comparisons (SMD = -1.87, 95% CI = -2.71 to -1.03, P < 0.0001), with a significant effect (P = 0.05) for multiple-times cupping treatment (SMD = -0.48; 95% CI = -1.58 to 0.62; P = 0.39). As for the subgroup analysis based on the pain sites and the age of patients, there was a significant improving effect of cupping therapy in patients with neck/shoulder pain (SMD = -1.68, 95% CI = -2.38 to -0.98, P < 0.0001) and aged more than 45 years (SMD = -0.81, 95% CI = -1.20 to -0.41, P < 0.00001).

Table 1 The effect of cupping therapy on pain intensity for different subgroups

Subgroups	**N**	**n**	**SMD**	**95%CI**	***P* value (subtotal effect)**	**I^2**
Type of cupping therapy	10	656	-1.17	-1.93 to -0.42	0.002	94%
Dry cupping	8	531	-1.13	-2.00 to -0.27	0.01	94%
Wet cupping	2	125	-1.47	-2.39 to -0.55	0.002	80%
Difference between subgroups					0.60	
Type of negative pressure	10	656	-1.17	-1.93 to -0.42	0.002	94%
Pulsation	2	142	-1.31	-1.90 to -0.71	< 0.0001	42%

Non-pulsation	8	514	-1.06	-2.04 to -0.08	0.03	95%
Difference between subgroups					0.67	
Frequency of treatments	10	656	-1.17	-1.93 to -0.42	0.002	94%
Single time	4	213	-1.87	-2.71 to -1.03	< 0.0001	81%
Multiple times	6	443	-0.48	-1.58 to 0.62	0.39	95%
Difference between subgroups					0.05	
Painful site	10	656	-1.17	-1.93 to -0.42	0.002	94%
Neck/Shoulder	5	257	-1.68	-2.38 to -0.98	< 0.0001	79%
Back	5	399	-0.42	-1.69 to 0.85	0.52	97%
Difference between subgroups					0.09	
Age of participants	10	656	-1.17	-1.93 to -0.42	0.002	94%
> 45 years	5	318	-0.81	-1.20 to -0.41	< 0.00001	63%
< 45 years	5	338	-1.54	-3.14 to 0.05	0.06	96%
Difference between subgroups					0.38	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

The Effect of Cupping Therapy on Functional Disability

Twelve data points from 9 studies were synthesized to assess the influence of cupping therapy on functional disability in CMP patients. **Figure 2** presents that the cupping therapy has no significant effect on decreasing the functional disability in CMP patients (SMD = -0.24, 95% CI = -0.93 to 0.46, P = 0.51, I^2 = 93%). And sensitivity analysis showed that the results were relatively robust (**Supplementary File 3**). The distribution of studies in the funnel plot appears approximately symmetrical, indicating that there is no evidence of publication bias (**Supplementary File 2**). The GRADE assessment indicated moderate confidence in the estimated effect (**Supplementary File 4**).

As depicted in **Table 2,** dry cupping therapy, wet cupping therapy, pulsation pressure cupping therapy, and non-pulsation pressure cupping therapy cannot improve the functional disability in CMP patients (dry cupping therapy: SMD = -0.09, 95% CI = -0.86 to 0.69, P =0.83; wet cupping therapy: SMD = -0.95, 95% CI = -2.21 to 0.32, P =0.14; pulsation cupping therapy: SMD = -0.13, 95% CI = -0.51 to 0.26, P =0.52; non-pulsation cupping therapy: SMD = -0.26, 95% CI = -1.24 to 0.73, P =0.61). For the frequency of treatments, a significant difference was found in the effect between the single-time cupping therapy (SMD = -0.65, 95% CI = -1.20 to -0.11, P = 0.02) and the control group. However, no significant difference was found in the effect between the multiple-times cupping therapy (SMD = 0.01, 95% CI = -0.99 to 1.01, P = 0.98) and the control group. For the subgroup analysis based on the pain sites, there was a significant improving effect of cupping therapy in patients with neck/shoulder pain (SMD = -0.48, 95% CI = -0.79 to -0.16, P = 0.003).

Table 2 Effects of cupping on functional disability for different subgroups

Subgroups	N	n	SMD	95%CI	*P* value (subtotal effect)	I^2
Type of cupping therapy	9	596	-0.24	-0.93 to 0.46	0.51	93%
Dry cupping	7	471	-0.09	-0.86 to 0.69	0.83	92%
Wet cupping	2	125	-0.95	-2.21 to 0.32	0.14	91%
Difference between subgroups					0.26	
Type of negative pressure	9	596	-0.24	-0.93 to 0.46	0.51	93%
Pulsation	2	142	-0.13	-0.51 to 0.26	0.52	0%
Non-pulsation	7	454	-0.26	-1.24 to 0.73	0.61	95%
Difference between subgroups					0.81	
No. of treatments	9	596	-0.24	-0.93 to 0.46	0.51	93%
Single time	3	153	-0.65	-1.20 to -0.11	0.02	45%
Multiple times	6	443	0.01	-0.99 to 1.01	0.98	96%
Difference between subgroups					0.25	
Painful site	9	596	-0.24	-0.93 to 0.46	0.51	93%
Neck/Shoulder	4	197	-0.48	-0.79 to -0.16	0.003	0%
Back	5	399	-0.03	-1.26 to 1.20	0.96	97%
Difference between subgroups					0.49	
Age of participants	9	596	-0.24	-0.93 to 0.46	0.51	93%
> 45 years	5	294	-0.23	-0.47 to 0.01	0.06	0%
< 45 years	4	278	-0.22	-1.97 to 0.48	0.81	97%
Difference between subgroups					0.99	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

The Effect of Cupping Therapy on Mental Health

Eight data points from 7 studies were pooled to evaluate the effectiveness of cupping therapy on mental health in CMP individuals. **Figure 3** shows that there is no significant difference in mental health between the cupping therapy group and the control group using a fixed-effect modal (SMD = 0.12, 95% CI = -0.07 to 0.30, *P* = 0.23, I^2 = 0%). And sensitivity analysis showed that the results were relatively robust (**Supplementary File 3**). The studies are symmetrically distributed on either side of the pooled effect size line, suggesting the absence of publication bias (**Supplementary File 2**). The GRADE assessment showed high quality of evidence, indicating considerable certainty in the effect estimate (**Supplementary File 4**).

Table 3 showed the effects of cupping therapy on mental health for five subgroups. With regard to different types of cupping therapy, we did not find a significant effect of dry cupping therapy (SMD = 0.15, 95% CI = -0.05 to 0.35, *P* = 0.14) and wet cupping therapy (SMD = -0.21, 95% CI = -0.79 to 0.38, *P* = 0.49) on CMP patients' mental health. In addition, no significant effect was found when conducting the subgroup analyses based on the types of negative pressure (pulsation: SMD = 0.05, 95% CI = -

0.38 to 0.48, *P* =0.81; non-pulsation: SMD = 0.13, 95% CI = -0.08 to 0.34, *P* =0.23), the frequency of treatments (single-time: SMD = 0.16, 95% CI = -0.58 to 0.90, *P* =0.67; multiple-time: SMD = 0.11, 95% CI = -0.10 to 0.32, *P* =0.30), pain sites (neck/shoulder: SMD = 0.12, 95% CI = -0.23 to 0.47, *P* =0.99; back: SMD = 0.11, 95% CI = -0.11 to 0.34, *P* =0.32) and the age of participants (more than 45 years: SMD = 0.07, 95% CI = -0.16 to 0.29, *P* =0.55; less than 45 years: SMD = 0.23, 95% CI = -0.12 to 0.58, *P* =0.20).

Table 3 The effect of cupping therapy on mental health for different subgroups

Subgroups	N	n	SMD	95%CI	*P* value (subtotal effect)	I^2
Type of cupping therapy	7	446	0.12	-0.07 to 0.30	0.23	0%
Dry cupping	6	401	0.15	-0.05 to 0.35	0.14	0%
Wet cupping	1	45	-0.21	-0.79 to 0.38	0.49	-
Difference between subgroups					0.26	
Type of negative pressure	7	446	0.12	-0.07 to 0.30	0.23	0%
Pulsation	1	96	0.05	-0.38 to 0.48	0.81	0%
Non-pulsation	6	350	0.13	-0.08 to 0.34	0.23	0%
Difference between subgroups					0.75	
No. of treatments	7	446	0.12	-0.07 to 0.30	0.23	0%
Single time	2	83	0.16	-0.58 to 0.90	0.67	65%
Multiple times	5	363	0.11	-0.10 to 0.32	0.30	0%
Difference between subgroups					0.90	
Painful site	7	446	0.12	-0.07 to 0.30	0.23	0%
Neck/Shoulder	3	127	0.12	-0.23 to 0.47	0.51	0%
Back	4	319	0.11	-0.11 to 0.34	0.32	0%
Difference between subgroups					0.99	
Age of participants	7	446	0.12	-0.07 to 0.30	0.23	0%
> 45 years	5	318	0.07	-0.16 to 0.29	0.55	0%
< 45 years	2	128	0.23	-0.12 to 0.58	0.20	23%
Difference between subgroups					0.45	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

Discussion

This meta-analysis suggested that cupping therapy had a positive immediate effect on reducing CMP patients' pain intensity. But cupping therapy cannot improve their functional disability and mental health. Based on the subgroup analyses in pain intensity, dry cupping therapy, wet cupping therapy, pulsation pressure, and non-pulsation pressure cupping therapy showed a significant difference when compared to the control group, respectively. In addition, cupping therapy was effective for decreasing pain

intensity and functional disability in patients with chronic neck/shoulder pain rather than in patients with chronic back pain.

Our results demonstrated that cupping therapy could effectively reduce pain intensity in CMP patients with immediate effects. This might be explained by the neurobiological foundations. It is widely confirmed that both nociceptive afferent fibers (Aδ and C fibers) and mechanosensitive Aβ fibers project in the same way onto interneurons or ascending projection neurons [46]. However, the rate of signal transmission from the mechanoreceptor (Aβ) up to the dorsal horn was faster than that from the Aδ and C fibers, so that the Aβ fibers would activate the corresponding multi-receptive dorsal horn interneuron before the Aδ and C fibers [47]. Based on the theory mentioned above, we speculated that the faster Aβ afferents (i.e., mechanosensitive afferent fibers) caused by the negative pressure of cupping therapy could block out pain sensation from the slower pain conducting Aδ and C fibers (i.e., nociceptive afferent fibers). This might partly explain the effects of cupping therapy on the pain intensity in CMP individuals. On the other hand, cupping therapy has been indicated to result in vascular ectasia for increasing blood flow significantly [19], which may be related to the therapeutic effect of cupping therapy on CMP. The increased blood flow under the cup after cupping therapy could play a positive role in the clearance of inflammatory cytokines locally. Several studies have demonstrated that musculoskeletal pain following exercises caused upregulation of transcripts for inflammatory such as interleukin-1 (IL-1)[48 49] and interleukin-6 (IL-6) [50] in the exercised limbs. These transcripts for inflammation were sensitivity to musculoskeletal sensitization, which was a preclinical model of muscle pain [50]. In other words, lowering the inflammatory cytokines (i.e., IL-1 and IL-6) might imply the alleviation of inflammatory response and the reduction of muscle pain. Therefore, the acceleration of blood circulation caused by negative pressure suction of cupping therapy could accelerate the clearance of inflammatory factors, alleviate inflammatory reactions, and thus release muscle pain.

Although our meta-analysis found that cupping therapy could effectively reduce CMP patients' pain intensity, the recovery effect of cupping therapy on their functional disability was not significant. The potential reason might be that the outcomes related to pain intensity in our included studies in this meta-analysis [17 51 52] were usually evaluated in resting state rather than moving state. Nevertheless, the pain in moving state usually impeded patients' daily activities and contributed to the functional disability [53]. Some musculoskeletal pain usually occurred during the moving process with muscle contraction or joint friction and compression. For example, the individual with patellar tendinopathy only experienced pain when the knee was flexed and extended (e.g., walking down stairs and jumping) [54]. This type of functional dysfunction was attributed to the pain induced by the altered biomechanical relationship between muscles, joints, and bones. According to the neurobiological foundation theory, the single-time cupping therapy might impede the pain conduction in CMP patients at rest state, while it was not sufficient to affect the biomechanical relationships of anatomical structures such as muscles, bones, and joints. Hence, patients with CMP still suffered from the functional disability due to the pain produced in moving state.

For another outcome, our results showed that, compared to the control group,

cupping therapy had no effectiveness in promoting CMP patients' mental health. Wet cupping therapy-induced incisions might cause more negative emotions (e.g., fear of invasive wound) rather than positive emotions (e.g., relaxation or soothing power of cupping therapy) caused by suction treatment. One animal experiment about mood status demonstrated that sheep conducted worse aversive behavior patterns in response to the pricking stimulus than the slight pressure and kneading stimulus [55]. Moreover, the non-significant group difference between cupping therapy and placebo therapy on mental health has been reported previously (e.g., sham cupping therapy). For example, Lauche et al. applied dry cupping therapy with 50-100 mm-diameter cups and a 10-15 minutes retention time for 141 fibromyalgia syndrome patients and used the SF-36 questionnaire to monitor changes in mental health. The findings demonstrated that cupping therapy and sham cupping therapy played similar roles in improving patients' mental health like anxiety, depression, and loss of behavioral or emotional control [52]. Among the 10 included studies in our meta-analysis, the SF-36 was the mostly used tool for accessing mental health (n = 6, 60%). After viewing the specific questions in SF-36, we supposed that the subjective questionnaire reflected the mental situations during the past 4 weeks [56]. Hence, the survey after the single cupping therapy immediately couldn't indicate the effects of cupping therapy on CMP patients' mental health accurately. This might partly explain the reason that, in our meta-analysis, there is no significant difference in the improvement effect on CMP patients' mental health between cupping therapy and sham cupping therapy.

To the best of our knowledge, this is the first study to demonstrate and integrate the effects of cupping therapy on clinical outcomes (i.e., pain intensity, functional disability, and mental health) in CMP patients. However, there are still some limitations. First, we only considered the immediate effect of cupping therapy, because of the limited original researches included in this meta-analysis. Nevertheless, our team has proposed the delayed effect of cupping therapy on muscular performance in one previous study [57]. Hence, we inferred that there was the possibility of the delayed effect of cupping therapy on CMP. Further evidence-based studies are needed to assess the time-effect to prove our speculation. Second, the heterogeneity of the included studies was relatively high because of differences in cupping dose. Therefore, the caution should be exercised in interpreting the results of this meta-analysis. Last, the results of a meta-analysis are contingent upon the studies included in the analysis. The number of studies included in this systematic review is limited (n = 10). In the future, as more RCT literatures are available, we will reexamine the evidences. The purpose of this systematic review is to evaluate the available evidence and provide the integrated effect size for the effectiveness of the separate cupping therapy on clinical outcomes in CMP patients.

Conclusion

This systematic review and meta-analysis demonstrates that cupping therapy is effective in reducing pain intensity for CMP individuals with immediate effects. However, CMP patients' functional disability and mental health cannot be improved by cupping therapy. Considering the high heterogeneity of the studies, caution is warranted in interpreting the findings of this research.

Figure Legends

Figure 1 The effect of cupping therapy on pain intensity
Figure 2 The effect of cupping therapy on functional disability
Figure 3 The effect of cupping therapy on mental health

Declarations

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The data underlying the article are available in the article and in its online supplementary material.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was funded by the State Natural Sciences Foundation (grant number: 82405615).

Contributorship statement

Conceptualization, X.H. and T.-T.S; methodology, Y.-Y.J., R.W and Z.-M.B.; formal analysis, Y.-Y.J and L.-K.Y.; writing—original draft preparation, Y.-Y.J.; writing—review and editing, X.H. and Y.-Y.J.; visualization, Y.-Y.J.; supervision, X.H. and T.-T.S. All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Y.-Y.J. and R.W have contributed equally to this work and share the first authorship. X.H. and T.-T.S have contributed equally to this work and share the corresponding authorship. Xiao Hou is the guarantor.

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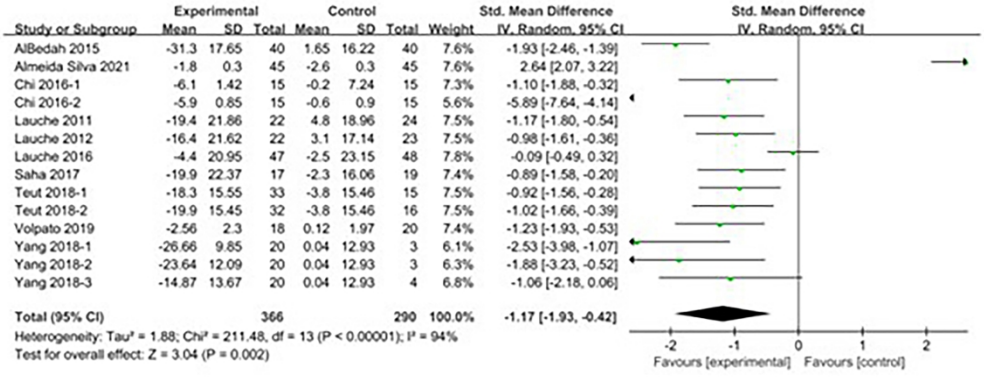


Figure 1 The effect of cupping therapy on pain intensity

226x90mm (600 x 600 DPI)

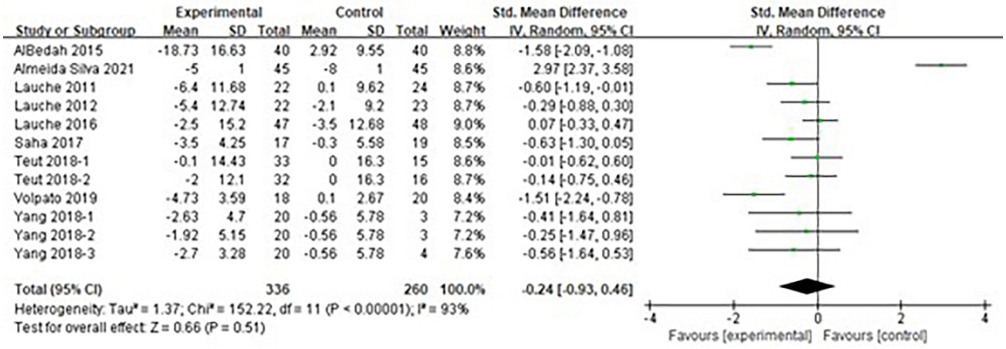


Figure 2 The effect of cupping therapy on functional disability

257x90mm (600 x 600 DPI)

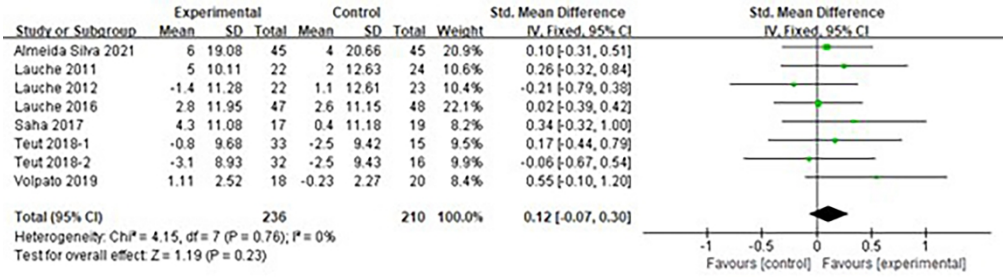
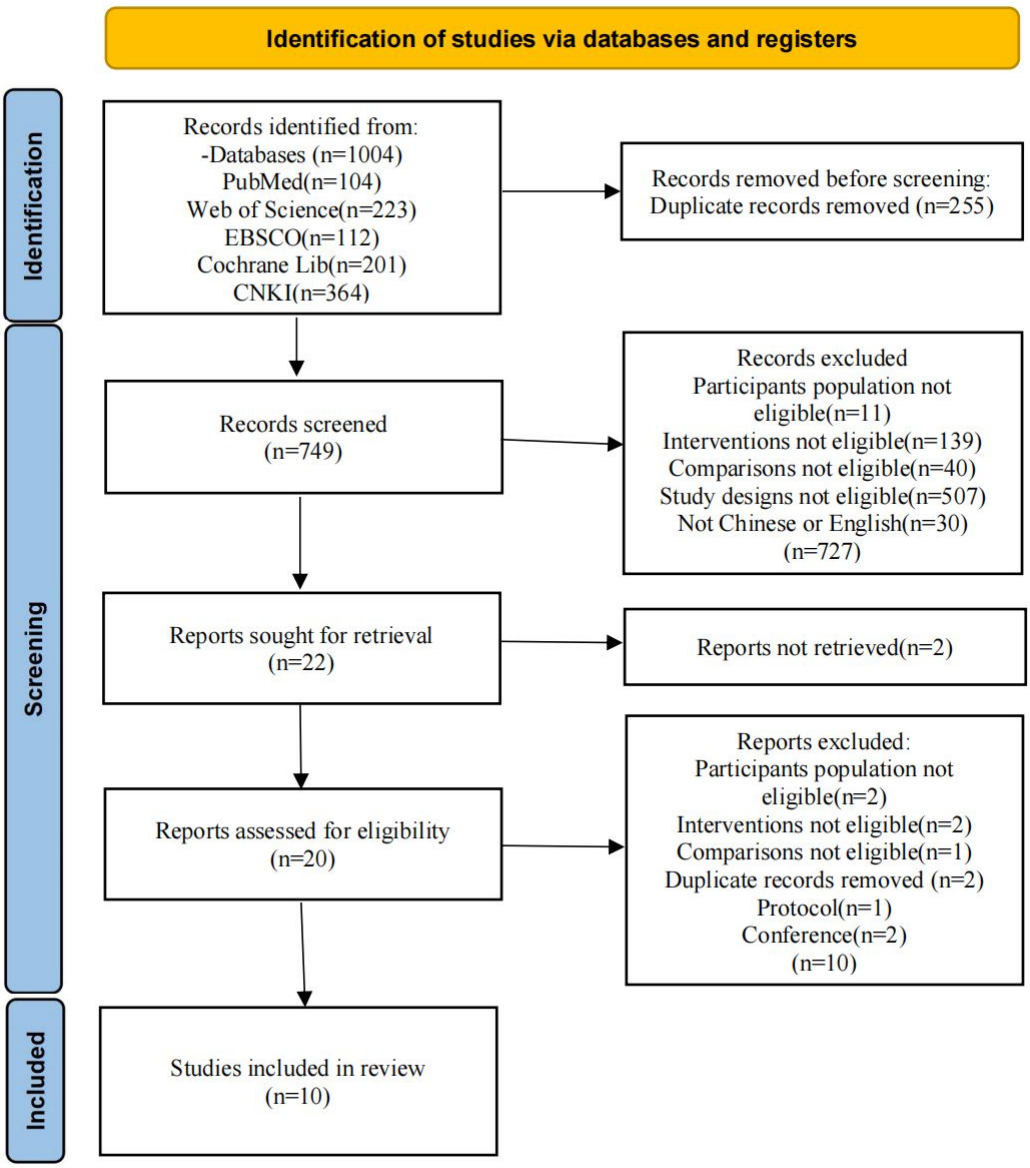
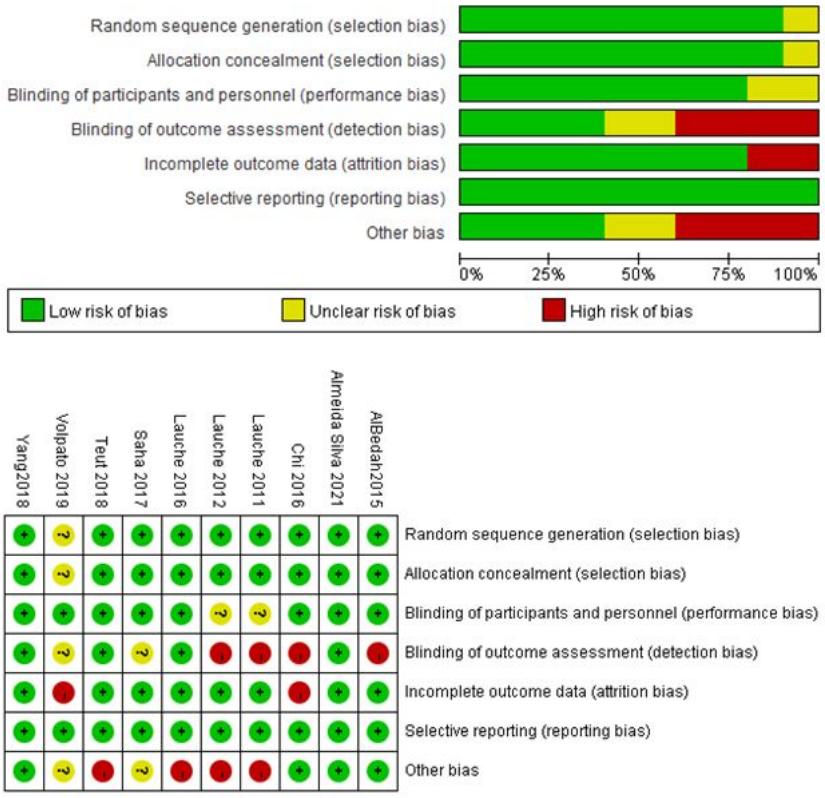


Figure 3 The effect of cupping therapy on mental health

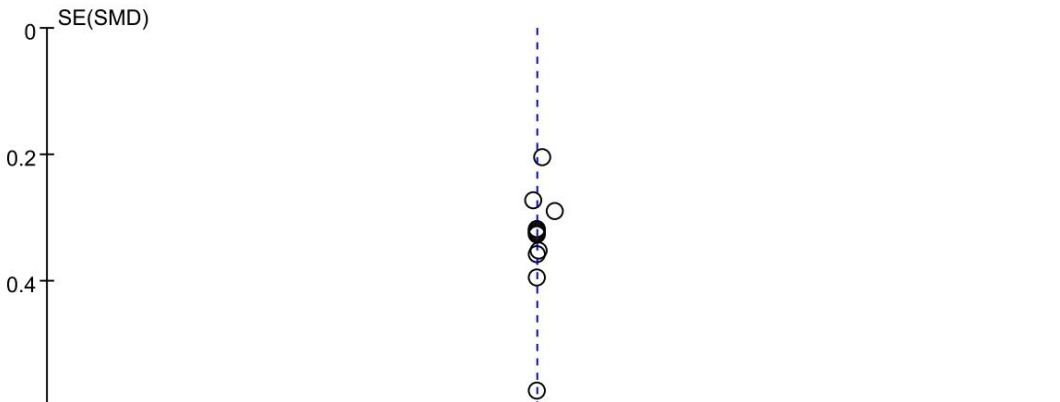
323x90mm (600 x 600 DPI)



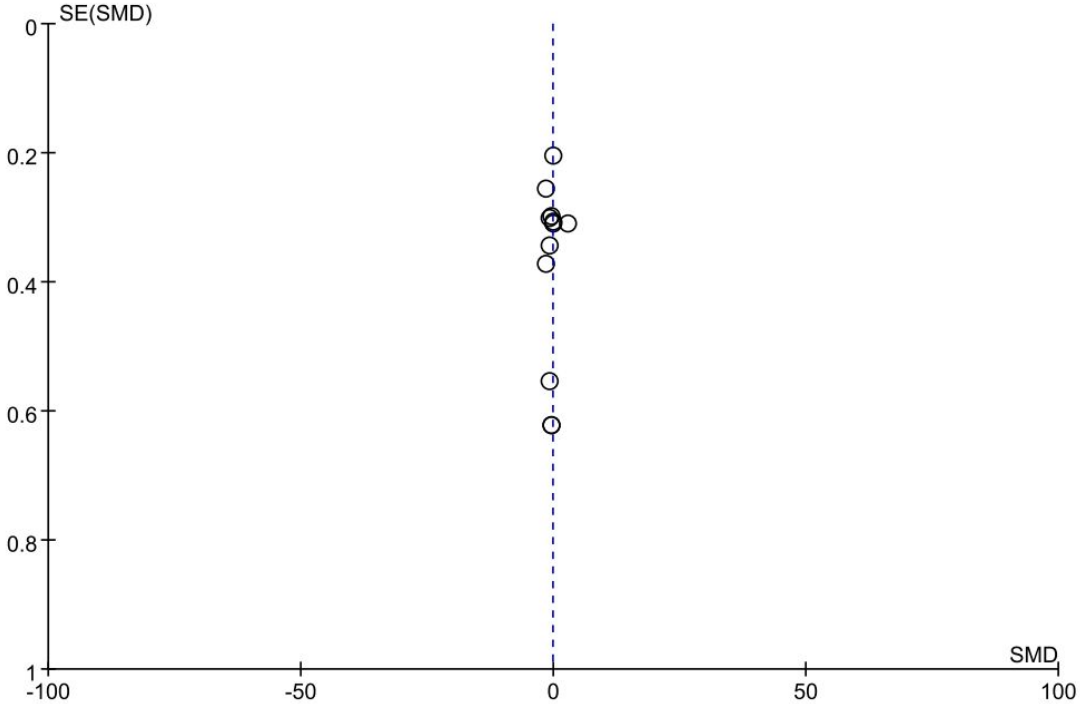
Supplemental Figure 1 The flowchart of the search procedure



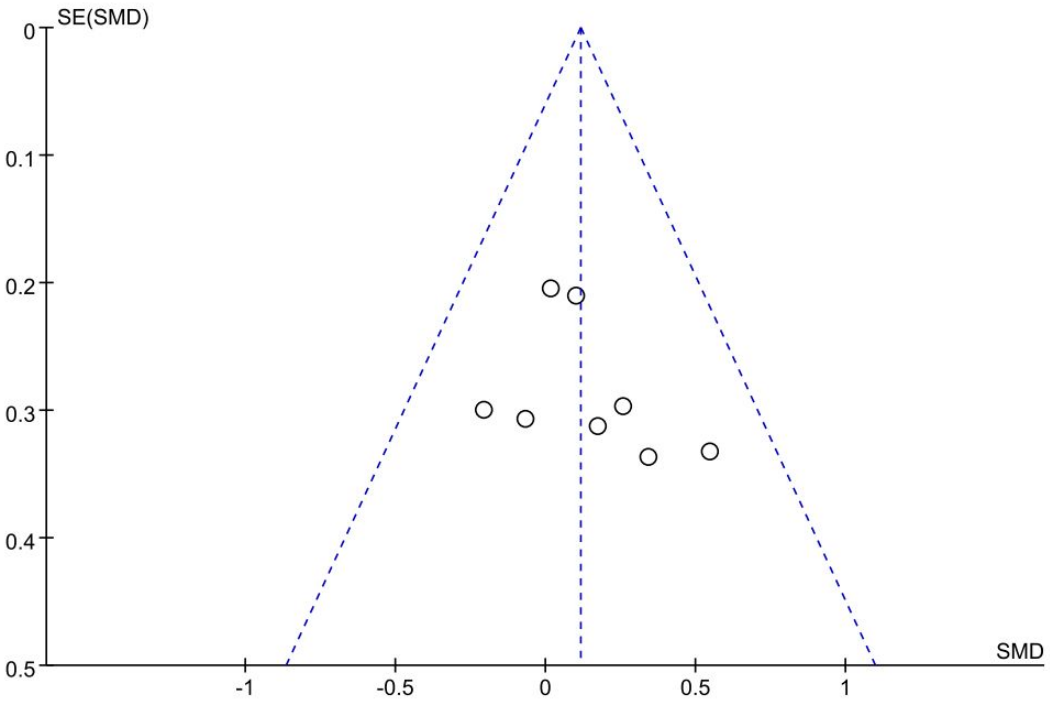
Supplemental Figure 2 The bias of the included studies



Supplemental Figure 3 The funnel plot for pain intensity



Supplemental Figure 4 The funnel plot for functional disability



Supplemental Figure 5 The funnel plot for mental health

Search strategy used in database

PubMed

	Searches
#1	(((((((“chronic musculoskeletal disorder”[Title/Abstract]) OR (“chronic musculoskeletal pain”[Title/Abstract]) OR (“chronic pain”[MeSH Terms] OR “chronic pain”[Title/Abstract])) OR (“hip pain”[Title/Abstract])) OR (“knee pain”[Title/Abstract])) OR (“shoulder pain”[MeSH Terms] OR “shoulder pain”[Title/Abstract])) OR (“neck pain”[MeSH Terms] OR “neck pain”[Title/Abstract])) OR (“back pain”[MeSH Terms] OR “back pain”[Title/Abstract])) OR (“myalgia”[MeSH Terms] OR “myalgia”[Title/Abstract] OR “muscle pain”[Title/Abstract])) OR (“osteoarthritis”[MeSH Terms] OR “osteoarthritis”[Title/Abstract])) OR (“fibromyalgia”[MeSH Terms] OR ‘fibromyalgia”[Title/Abstract]))
#2	(((((“cupping therapy”[Mesh Terms]) OR (“cupping therapy”[Title/Abstract])) OR (“cupping treatment”[Title/Abstract])) OR (“dry cupping”[Title/Abstract])) OR (“wet cupping”[Title/Abstract])) OR (“cupping massage”[Title/Abstract])))))
#3	#1 AND #2

Web of Science

	Searches
#1	((((((((((TS=("chronic musculoskeletal pain")) OR TS=("chronic musculoskeletal disorder")) OR TS=(fibromyalgia))OR TS=(osteoarthritis)) OR TS=(myalgia)) OR TS=("muscle pain")) OR TS=("back pain")) OR TS=("neck pain")) OR TS=("shoulder pain")) OR TS=("knee pain")) OR TS=("hip pain")) OR TS=("chronic pain")
#2	(((((TS=("cupping therapy")) OR TS=("cupping treatment")) OR TS=("dry cupping")) OR TS=("wet cupping")) OR TS=("cupping massage"))
#3	#1 AND #2

EBSCO

	Searches
S1	AB "chronic musculoskeletal pain" OR AB "chronic musculoskeletal disorder" OR AB "fibromyalgia" OR AB "osteoarthritis" OR AB "myalgia" OR AB "muscle pain" OR AB "back pain" OR AB "neck pain" OR AB "shoulder pain" OR AB "knee pain" OR AB "hip pain" OR AB "chronic pain"
S2	AB "cupping therapy" OR AB "cupping treatment" OR AB "dry cupping" OR AB "wet cupping" OR AB "cupping massage"
S3	S1 AND S2

Cochrane Library

	Filters	Searches
#1	Title Abstract Keyword	"chronic musculoskeletal pain" OR "chronic musculoskeletal disorder" OR "fibromyalgia" OR "osteoarthritis" OR "myalgia" OR "muscle pain" OR "back pain" OR "neck pain" OR "shoulder pain" OR "knee pain" OR "hip pain" OR "chronic pain"
#2	Title Abstract Keyword	"cupping therapy" OR "cupping treatment" OR "dry cupping" OR "wet cupping" OR "cupping massage"
#3	#1 AND #2	

China National Knowledge Infrastructure

	Filters	Searches
#1	主题	慢性肌肉骨骼疼痛 + 慢性肌肉骨骼疾病 + 纤维肌痛 + 骨关节炎 + 肌痛 + 肌肉疼痛 + 背痛 + 背部疼痛 + 颈痛 + 颈部疼痛 + 肩痛 + 肩部疼痛 + 膝痛 + 膝关节疼痛 + 髋痛 + 髋关节疼痛 + 慢性疼痛
#2	主题	拔罐 + 拔罐疗法 + 拔罐治疗 + 干罐 + 湿罐 + 走罐
#3	#1 AND #2	

Supplemental Table 1 The characteristics of included studies

No.	Author(s) Publication year	Country	Age (mean ± SD) Gender (male/female)	Sample size	Painful site(s)	Duration of illness (mean ± SD)	EG intervention (dosage of cupping therapy)	CG intervention	Outcomes 1. Pain intensity 2. Functional disability 3. Mental health
1	Al Bedah et al. 2015	Saudi Arabia	**EG:** 36.48 ± 9.3 y 22/18 **CG:** 36.43 ± 9.4 y 17/23	**EG:** 40 **CG:** 40	Low back	**EG:** 4.45 ± 4.8 y **CG:** 3.85 ± 3.9 y	**Wet cupping therapy** (cup size: 40 cc; duration: 5 min; negative pressure caused by manual pumping; frequency: three times per week for 2 weeks) Rescue treatment: acetaminophen no more than 1500 mg per day	**Resting** Rescue treatment: acetaminophen no more than 1500 mg per day	1. NRS 2. ODQ 3. NA
2	Almeida Silva et al.	Brazil	**EG:** 30 ± 11.0 y	**EG:** 45 **CG:** 45	Low back	**EG:** 44 ± 32 mo	**Dry cupping therapy** (cup size: 4.5 cm; duration: 10 min;	**Sham-cupping therapy** (cup size:	1. NPRS 2. ODI

	2021		16/29 **CG:** 32 ± 13.0 y 7/38			**CG:** 58 ± 51 mo	negative pressure: 300 millibars; frequency: once per week for 8 times)	4.5 cm; duration: 10 min; negative pressure: 0; frequency: once per week for 8 times)	3. SF-36
3	Chi et al. 2016	China	**EG:** 43.6 ± 8.0 y 3/27 **CG:** 42.5 ± 7.4 y 2/28	**EG:** 30 **CG:** 30	Neck, shoulder	**EG:** 20.17 ± 8.53 mo **CG:** 20.03 ± 9.21 mo	**Dry cupping therapy** (cup size: 4 cm; duration: 10 min; negative pressure caused by placing the burning swab in-and-out; frequency: single intervention)	**Resting**	1. VAS (neck, shoulder) 2. NA 3. NA
4	Lauche et al. 2011	Germany	**EG:** 48.6 ± 11.2 y 7/15 **CG:** 53.0 ± 11.4 y 4/20	**EG:** 22 **CG:** 24	Neck	**EG:** 6.3 ± 6.1 y **CG:** 8.0 ± 7.6 y	**Dry cupping therapy** (cup size: 25 to 50 mm; duration: 10 - 20 min; negative pressure caused by heating the air inside; frequency: once per 3 - 4 days for 5 times)	**Waiting list control**	1. VAS (rest, movement) 2. NDI 3. SF-36

5	Lauche et al. 2012	Germany	**EG:** 54.8 ± 9.6 y 7/18 **CG:** 57.2 ± 9.4 y 9/16	**EG:** 25 **CG:** 25	Neck	**EG:** 12.0 ± 10.3 y **CG:** 10.4 ± 11.5 y	**Wet cupping therapy** (cup size: 25 - 50 mm; duration: 10 - 15 min; negative pressure caused by heating the air inside; frequency: single intervention) Fixed dosage of Pa and Me started for 4 weeks before the study	**Waiting list control** Fixed dosage of Pa and Me if started for 4 weeks before the study	1. VAS (rest, movement) 2. NDI 3. SF-36
6	Lauche et al. 2016	Germany	**EG:** 54.35 ± 10.6 y 1/46 **CG:** 56.3 ± 8.7 y 1/47	**EG:** 47 **CG:** 48	Back	**EG:** 11.6 ± 9.2 y **CG:** 11.2 ± 8.9 y	**Dry cupping therapy** (cup size: 50 - 100 mm; duration: 10 - 15 min; negative pressure caused by a mechanical device; frequency: twice per week for 5 times) Fixed dosage of Me if started before the study	**CG: Sham-cupping therapy** (cup size: 50 - 100 mm; duration: 10 - 15 min; negative pressure: 0; frequency: twice per week for 5 times)	1. VAS 2. FIQ 3. SF-36

								Fixed dosage of Me if started before the study	
7	Saha et al. 2017	Germany	**EG:** 54.3 ± 8.6 y 4/21 **CG:** 53.3 ± 11.1 y 0/25	**EG:** 25 **CG:** 25	Neck	**EG:** 7.5 ± 6.6 y **CG:** 8.1 ± 7.2 y	**Cupping massage therap** (cup size: 3.5 - 5 cm; dura 10 min; frequency: twice p week for 5 times)	**Waiting list control** Fixed treatments if started except invasive treatments before the study	1. VAS (rest, movement) 2. NDI 3. SF-36
8	Teut et al. 2018	Germany	**EG1:** 49.0 ± 13.7 y 16/21 **EG2:** 47.5 ± 13.8 y 13/23 **CG:** 50.7 ± 10.7 y	**EG1:** 37 **EG2:** 36 **CG:** 37	Low back	**EG1:** 13.1 ± 9.3 y **EG2:** 15.8 ± 12.9 y **CG:** 13.2 ± 11.2 y	**EG1: Pulsatile cupping therapy-high vacuum** (cup size: 10 cm; duration: 8 min; negative pressure: 150 - 350 mbar; frequency: 8 sessions for 4 weeks) **EG2: Pulsatile cupping therapy-low vacuum** (cup	**Waiting list control** Rescue treatment: paracetamol no more than 2000 mg per day	1. VAS 2. FFbH-R 3. SF-36

			12/15				size: 10 cm; duration: 8 min; negative pressure: 70 mbar; frequency: 8 sessions for 4 weeks) **EG1, 2:** Rescue treatment: paracetamol no more than 2000 mg per day		
9	Volpato et al. 2019	Brazil	**EG:** 27.16 ± 8.43 y 3/15 **CG:** 25.42 ± 9.18 y 5/15	**EG:** 18 **CG:** 20	Low back	NA	**Dry cupping therapy** (cup size: 50 mm; duration: 15 min; negative pressure: 300 millibars; frequency: single intervention)	**Placebo cupping therapy** (cup size: 50 mm; duration: 15 min; negative pressure: 0; frequency: single intervention)	1. BPI 2. RMDQ 3. BPI
10	Yang et al. 2018	China	**EG1:** 23.95 ± 2.21 y 6/14	**EG1:** 20 **EG2:** 20 **EG3:** 20	Neck	**EG1:** 2.61 ± 2.01 y	**EG1: Pulsatile cupping therapy-high frequency** (cup size: 68 mm; duration: 80	**Waiting list control**	1. VAS 2. NDI 3. NA

EG2: 27.10 ± 5.27 y 4/16 **EG3:** 26.00 ± 4.15 y 1/19 **CG:** 24.7 ± 2.5 y 3/7	**CG:** 10	**EG2:** 2.55 ± 2.73 y **EG3:** 3.68 ± 2.55 y **CG:** 2.65 ± 1.53 y	times per min for 8 min; negative pressure: 0.02 – 0.04 MPa; frequency: single intervention) **EG2: Pulsatile cupping therapy-low frequency** (cup size: 68 mm; duration: 30 times per min for 8 min; negative pressure: 0.02 – 0.04 MPa; frequency: single intervention) **EG3: Static cupping therapy** (cup size: 68 mm; duration: 8 min; negative pressure: 0.02 – 0.04 MPa; frequency: single intervention)

Abbreviations: EG, Experimental Group; CG, Control Group; NA, Not Assessed; y, years; mo, months; Pa, pain; Me, Medicine; NRS, Numeric Rating Scale; ODQ, Oswestry Disability Questionnaire; SF-36, Short Form 36-health survey questionnaire; NPRS, Numerical Pain Rating Scale; ODI, Oswestry Disability Index; VAS, Visual Analog Scale; NDI, Neck Disability Index; FIQ, Fibromyalgia Impact Questionnaire; FFbH-R, Funktionsfragebogen Hannover Rücken; BPI, Brief Pain Inventory; RMDQ, Roland Morris Disability Questionnaire.

Supplemental Table 2 Sensitivity analysis with the one-leave out method on pain intensity.

Omitted studies	*SMD*	*95%CI*	P value (subtotal effect)	I^2
Al Bedah et al. 2015	-1.11	-1.90 to -0.32	0.006	94%
Almeida Silva et al. 2021	-1.37	-1.85 to -0.89	<0.00001	92%
Chi et al. 2016	-0.87	-1.64 to -0.10	0.03	94%
Lauche et al. 2011	-1.18	-2.00 to -0.36	0.005	94%
Lauche et al. 2012	-1.20	-2.02 to -0.37	0.004	94%
Lauche et al. 2016	-1.28	-2.13 to -0.43	0.003	94%
Saha et al. 2017	-1.20	-2.02 to -0.39	0.004	94%
Teut et al. 2018	-1.23	-2.13 to -0.33	0.007	95%
Volpato et al. 2019	-1.21	-2.10 to -0.32	0.008	95%
Yang et al. 2018	-1.05	-1.99 to -0.10	0.03	96%
NA	-1.17	-1.93 to -0.42	0.002	94%

Notes:

SMD: Standardized mean difference; *CI*: confidence interval.

Supplemental Table 3 Sensitivity analysis with the one-leave out method on functional disability.

Omitted studies	*SMD*	*95%CI*	P value (subtotal effect)	I^2
Al Bedah et al. 2015	-0.10	-0.80 to 0.59	0.77	92%
Almeida Silva et al. 2021	-0.54	-0.93 to -0.15	0.006	93%
Lauche et al. 2011	-0.20	-0.97 to 0.56	0.60	93%
Lauche et al. 2012	-0.23	-1.00 to 0.54	0.56	93%
Lauche et al. 2016	-0.27	-1.07 to 0.54	0.52	93%
Saha et al. 2017	-0.20	-0.96 to 0.56	0.60	93%
Teut et al. 2018	-0.27	-1.13 to 0.58	0.53	94%
Volpato et al. 2019	-0.12	-0.84 to 0.60	0.75	93%
Yang et al. 2018	-0.19	-1.02 to 0.64	0.66	95%
NA	-0.24	-0.93 to 0.46	0.51	93%

Notes:

SMD: Standardized mean difference; *CI*: confidence interval.

Supplemental Table 4 Sensitivity analysis with the one-leave out method on mental health.

Omitted studies	*SMD*	*95%CI*	P value (subtotal effect)	I^2
Almeida Silva et al. 2021	0.12	-0.09 to 0.33	0.27	0%
Lauche et al. 2011	0.10	-0.10 to 0.30	0.33	0%
Lauche et al. 2012	0.15	-0.05 to 0.35	0.14	0%
Lauche et al. 2016	0.14	-0.07 to 0.36	0.19	0%
Saha et al. 2017	0.09	-0.10 to 0.29	0.35	0%
Teut et al. 2018	0.13	-0.08 to 0.34	0.23	0%
Volpato et al. 2019	0.08	-0.12 to 0.27	0.46	0%
NA	0.12	-0.07 to 0.30	0.23	0%

Notes:

SMD: Standardized mean difference; *CI*: confidence interval.

Summary of findings:

Cupping Therapy compared to placebo for chronic musculoskeletal pain

Patient or population: chronic musculoskeletal pain
Setting:
Intervention: Cupping Therapy
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI) Risk with placebo	Risk with Cupping Therapy	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
pain intensity	-	SMD **1.17 lower** (1.93 lower to 0.42 lower)	-	656 (10 RCTs)	⨁⨁⨁◯ Moderate[a]	
mental health	-	SMD **0.12 higher** (0.07 lower to 0.3 higher)	-	446 (7 RCTs)	⨁⨁⨁⨁ High	
functional disability	-	SMD **0.24 lower** (0.93 lower to 0.46 higher)	-	596 (9 RCTs)	⨁⨁⨁◯ Moderate[b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. I^2 = 94%
b. I^2 = 93%

BMJ Open

Effects of Cupping Therapy on Chronic Musculoskeletal Pain and Collateral Problems: A Systematic Review and Meta-Analysis

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2024-087340.R2
Article Type:	Original research
Date Submitted by the Author:	20-Mar-2025
Complete List of Authors:	Jia, Yuanyuan; Beijing Sport University, Key Laboratory of Sports and Physical Health Ministry of Education; Beijing Sport University, School of Sport Science Wang, Rong; Beijing Sport University, Yu, Laikang; Beijing Sport University, Department of Sports Performance Bai, Zhenmin ; Beijing Sport University Sun, Tingting; Beijing Sport University Hou, Xiao; Beijing Sport University, ; Beijing Sport University,
Primary Subject Heading:	Complementary medicine
Secondary Subject Heading:	Complementary medicine, Rehabilitation medicine
Keywords:	Meta-Analysis, Chronic Pain, COMPLEMENTARY MEDICINE, Musculoskeletal disorders < ORTHOPAEDIC & TRAUMA SURGERY

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Effects of Cupping Therapy on Chronic Musculoskeletal Pain and Collateral Problems: A Systematic Review and Meta-Analysis

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All authors declare no conflicts of interest.

Abstract

Objectives Chronic musculoskeletal pain (CMP) is a prevalent and distressing condition. Cupping therapy, one of the most popular complementary and alternative medicines, has been widely used to reduce CMP. But the evidence remains controversial on the effect of cupping therapy on CMP. The objective of this review and meta-analysis is to assess the effectiveness of cupping therapy in CMP patients.

Design Systematic review and meta-analysis.

Data sources PubMed, Web of Science, EBSCO, Cochrane Library and China National Knowledge Infrastructure (CNKI) were searched through 20 December 2024.

Eligibility criteria for selecting studies We included randomized control trials (RCTs) that compared cupping therapy for CMP patients on outcomes (i.e., pain intensity, functional disability and mental health).

Data extraction and synthesis Two independent reviewers used standardized methods to search, screen and code included studies. Risk of bias was assessed using the Cochrane Collaboration and Evidence Project tools. Meta-analysis was conducted using random and fixed effects models. Findings were summarized in GRADE evidence profiles.

Results The results showed that cupping therapy (SMD = -1.23; 95% CI = -2.02 to -0.44; P = 0.002; I^2 = 95%) had a significant reduction effect on CMP patients' pain intensity with moderate quality based on a random-effect model. But cupping therapy had no improvement effects on functional disability (SMD = -0.58; 95% CI = -1.34 to 0.17; P = 0.13; I^2 = 76%) and mental health (SMD = -0.21; 95% CI = -0.81 to 0.38; P = 0.48; I^2 = 63%).

Conclusions This study indicates that cupping therapy may be efficient in alleviating pain intensity in CMP patients with immediate effects. But it cannot improve functional disability and mental health significantly.

PROSPERO registration number CRD42023406219.

Strengths and limitations of this study

1. The effects of cupping therapy on CMP clinical outcomes were comprehensively synthesized, integrating pain intensity, functional disability, and mental health within one study.
2. A comprehensive subgroup analysis was conducted based on cupping therapy types, pressure types, painful sites, age groups, and treatment frequency, reflecting the broad scope of this study's methodological considerations.
3. Only the immediate effects of cupping therapy were analyzed, as constrained by the time points of data collection in the included original studies.

Keywords: chronic musculoskeletal pain, cupping therapy, complementary and alternative medicine, meta-analysis

Background

Chronic musculoskeletal pain (CMP) is a prevalent global issue, associated with a high incidence and significant burden on healthcare systems. In 2019, the estimated global prevalence of chronic musculoskeletal disorders reached 1.52 billion cases (95% uncertainty intervals: 1.43 to 1.60 billion), with an age-standardized prevalence rate (ASPR) of 18,407 per 100,000 people[1]. Furthermore, chronic musculoskeletal disorders accounted for 147 million years lived with disability (YLDs) in 2019 (95% uncertainty intervals: 106 to 195 million) and a high ASYR of 1791 per 100,000 people (95% uncertainty intervals: 1288 to 2367)[1]. In addition to the substantial health burden, the treatment of CMP also occurs high financial cost. For example, based on the Chilean health system, the annual expected cost for CMP is USD $1387.2 million and equivalent to 0.417% of the national GDP [2].

In addition to the impact on healthy, life expectancy and financial burden, CMP usually accompanies restricted daily activities and negative mental health to individuals. Original research has found that the pain threshold and pain tolerance value of patients with chronic back pain were significantly lower than healthy participants and these lower pain-related parameters may contribute to the persistence of chronic pain [3]. The persistent CMP can interfere with individuals' physical functions. For example, the reductions in strength and endurance induced by fibromyalgia can lead to the restrictions in participation during leisure-time activities and work-related activities [4] [5]. Moreover, individuals' psychological states can also influence the condition of CMP. For example, chronic low back pain (CLBP) patients with depression experienced significantly more severe pain (5.86 ± 2.27) compared to their non-depressed counterparts (4.34 ± 2.20; $P < 0.001$)[6]. Another survey including 122 CMP patients has indicated that the pain interference was negatively correlated with several mental health components (e.g., vitality and calmness) significantly [7]. In addition to daily mental states, CMP even causes the mental illness. For example, the patients with long-term low back pain, who experienced the moderate to severe pain dysfunction at the initial assessment, were easier to remain chronical depression [8]. Therefore, it is necessary to find effective treatments and rehabilitation measures for patients with CMP to alleviate pain and collateral problems, such as functional disability and unhealthy mental states.

Treatment options for CMP generally encompass pharmacological therapies and, where appropriate, surgical interventions, both of which may be accompanied by certain adverse side effects. Some drugs like opioid painkillers, have been opposed by current guidelines for CMP, because of the rising rates of opioid overdose deaths and other serious harms [9]. It has been indicated that long-term use of nonopioid drugs for relieving CMP (e.g., non-steroidal anti-inflammatory drugs, and Cyclooxygenase-2) may produce serious gastrointestinal side effects and increase cardiovascular risks [10 11]. Another usual therapy, the surgical interventions have been proven, to some extent, effective in CMP conditions, especially in osteoarthritis. However, operations usually cause a high prevalence (80%) of postoperative pain [12]. These adverse impacts of drug treatments and surgical interventions result in a growing interest in non-

pharmacological measures in response to CMP [13 14].

Cupping therapy, a type of complementary and alternative medicine, has been widely applied to alleviate CMP, such as chronic neck pain [15 16] and chronic low back pain [17]. The normal impacts after cupping therapy are circular erythematous spots with no painful sense and no restriction to daily activities. Some researchers have suggested that cupping therapy can improve blood flow [18 19], which may contribute to its therapeutic effect. The increasing blood flow has been indicated effective in removing glutamate [20], lactate, and pyruvate [21], which are biochemical biomarkers in CMP regions. In fact, several researchers have demonstrated the obvious alleviation effects of cupping therapy on CMP patients' pain intensity [22 23]. For example, Volpato et al. have indicated that a single-time dry cupping therapy can effectively decrease pain intensity, which is presented by the Brief Pain Inventory (BPI, assessing pain level with 0 = no pain/no interference to 10 = most pain/most interference) score, in low back (pre-cupping: 4.22 ± 2.53; post-cupping: 1.66 ± 1.97, $P<0.05$) [22]. Wet cupping therapy, another type of cupping therapy adding blood-letting to dry cupping therapy, has been also demonstrated effective for reducing CMP [23-25]. Some comprehensive treatments combining cupping therapy and other physical therapies or techniques (e.g., pulsatile cupping, cupping massage) have been also demonstrated effective for relieving CMP [26 27]. Compared to separate methods, the integrated approaches may produce better therapeutic effects. But more clinical trials are needed to clarify the differences in the effect of alleviating CMP between these two kinds of approaches.

Although numerous studies have clarified the potential effectiveness of cupping therapy in treating CMP, there still remain the opposite results. For instance, Silva et al. have indicated that dry cupping therapy is not superior to sham cupping for improving the Numerical Pain Rating Scale (NPRS, assessing pain level with 0 = no pain/no interference to 10 = most pain/most interference) score (dry cupping therapy: 3.3 ± 2.9 VS sham cupping therapy: 2.7 ± 1.9; Mean $_{\text{between-group differences}}$ = 0.6, 95% confidence intervals = -0.4 to 1.6) in patients with non-specific chronic low back pain [28]. Another study has also revealed no statistically significant improvement is found in physical function (e.g. difficulty in walking) of osteoarthritis patients after multiple-times wet cupping treatments (pre-cupping: 1.68 ± 0.63 VS post-cupping: 0.906 ± 0.40, $P > 0.05$) [29]. Both high pain intensity and poor physical function are harmful symptoms in CMP patients, while these inconsistent findings cannot identify whether cupping therapy is effective for the improvement of clinical symptoms (e.g., pain and physical function) of CMP or not. Considering that CMP has a lasting harmful effect on patients, there is an urgent need to examine studies related to the effectiveness of cupping therapy on CMP scientifically and comprehensively.

The purpose of this study is to evaluate the effect of cupping therapy on clinical outcomes (i.e., pain intensity, functional disability, and mental health) in CMP patients through a meta-analysis from a more comprehensive and systematic perspective.

Methods

Search Strategy and Study Selection

This meta-analysis was reported according to the PRISMA guidelines (http://www.prisma-statement.org/). And the completed PRISMA checklist was provided in the supplementary materials (**Supplementary PRISMA Checklist**). The protocol was registered at PROSPERO (http://www.crd.york.ac.uk/ PROSPERO) before starting the data extraction (registration number: CRD42023406219).

Four electronic databases, including PubMed, Web of Science, EBSCO, Cochrane Library and China National Knowledge Infrastructure (CNKI), were searched respectively for relevant articles until December 20, 2024. The searching criteria was set based on the following keywords: (“chronic musculoskeletal pain” OR “chronic musculoskeletal disorder” OR “fibromyalgia” OR “osteoarthritis” OR “myalgia” OR “muscle pain” OR “back pain” OR “neck pain” OR “shoulder pain” OR “knee pain” OR “hip pain” OR “chronic pain”) AND (“cupping therapy” OR “cupping treatment” OR “dry cupping” OR “wet cupping” OR “cupping massage”). The full search strategies for all databases were shown in **Supplementary File 1**.

Two independent reviewers (Y.-Y.J. and R.W.) screened the titles and abstracts of all potentially suitable publications and assessed their eligibility through reading in full. If a disagreement remained after discussion, a third arbitrator (Z.-M.B.) was consulted for a consensus.

Inclusion Criteria

Trials were eligible for inclusion if they met the following criteria with the PICOS principle (population, intervention, comparison/control, outcome and study design): 1) participants were suffering from musculoskeletal pain and/or stiffness for more than three months, which is the diagnostic criteria of CMP [30]; 2) participants in the experimental group received interventions related to cupping therapy (e.g., dry cupping, wet cupping, pulsating cupping, and cupping massage); 3) the comparison intervention was limited to no treatment or sham/placebo interventions during experimental treatments; 4) the outcomes were pain intensity, functional disability, or mental health; and 5) only publications designed as randomized control trials (RCTs) were covered.

Exclusion Criteria

The exclusion criteria for the selected trials were as follows: 1) reviews, abstracts, protocols, case reports, observational studies, non-English/Chinese publications, non-peer-reviewed articles (e.g., academic dissertations and conference posters); 2) no sufficient evidence to judge the duration of disease as chronic condition (i.e. less than three months); 3) pain sites containing visceral or orofacial regions; and 4) participants in control groups received other active treatments, such as traditional Hijamah technique, standard medical care, and ischemic compression.

Quality Assessment

Two authors independently examined the quality of included studies using the Cochrane Collaboration tool. The risk of bias was evaluated as “low,” “high,” or “unclear” in the seven domains: 1) random sequence generation (selection bias): 2) allocation concealment (selection bias); 3) blinding of participants and personnel

(performance bias); 4) blinding of outcome assessment (detection bias); 5) incomplete outcome data (attrition bias); 6) selective reporting (reporting bias); and 7) other bias [31]. If there was a disagreement between two authors, a third arbitrator (Z-M.B.) was consulted to reach a consensus.

Data Extraction

From each included article, the following data were extracted by two independent reviewers: author(s), publication year, country, subjects' demographical characteristics (e.g., age and gender), sample size, pain site(s), duration of CMP, experimental intervention (i.e., dosage of cupping therapy), control intervention, and the reported outcomes (e.g., pain intensity, functional disability, or mental health). If there was a disagreement between two authors, a third arbitrator (Z-M.B.) was consulted to reach a consensus.

Meta-analysis

In this meta-analysis, the outcome indicators were measured on different tools. For example, the pain intensity was assessed by the Numerical Pain Rating Scale (NPRS), the Visual Analog Scale (VAS), or the Brief Pain Inventory (BPI). The functional disability was measured by the Neck Disability Index (NDI), the Oswestry Disability Questionnaire (ODQ), the Oswestry Disability Index (ODI), the Fibromyalgia Impact Questionnaire (FIQ), the Funktionsfragebogen Hannover Rücken (FFbH-R), or the Roland Morris Disability Questionnaire (RMDQ). Meanwhile, the mental health was evaluated by the Short-Form 36 health survey questionnaire (SF-36 mental health). Because of the different measurements of outcomes, the standardized mean differences (SMDs) with 95% confidence intervals (CIs) were chosen to analyze the compositive effects, and $P < 0.05$ was set as the significant level.

According to the Cochran Handbook for Systematic Review, both the post-intervention values (i.e., Mean $_{\text{post-intervention}} \pm$ SD $_{\text{post-intervention}}$) of the outcome and the changes from baseline (i.e., Mean $_{\text{of changes}} \pm$ SD $_{\text{of changes}}$) could be used for the summary statistic value in this study [32]. Post-measurement data selected in this study refers to the immediate test results following the final cupping intervention. If studies reported CI instead of SD, we would convert CI into SD[33].

The heterogeneity among included studies was evaluated by the I^2 index. The low, moderate, high, and very high heterogeneity was identified when $I^2 \leq 25\%$, $I^2 \leq 50\%$ and >25%, $I^2 \leq 75\%$ and > 50%, and $I^2 > 75\%$ respectively [33]. For the low or moderate heterogeneity, a fixed-effect model would be chosen. When the heterogeneity was high or very high, a random-effect model would be applied to synthesize the effect size [34]. If $I^2 > 50\%$ and with a sufficient number of studies (at least 10 studies), the publication bias was detected by the asymmetry of funnel plots or the Egger's test [35 36].

The subgroup analyses based on cupping therapy types, pressure types, painful sites, age groups, and the frequency of treatments were performed. Furthermore, the robust of the meta-analysis was investigated by the sensitive analysis with the one-leave out method. The Review Manager software (Review Manager 5.3; The Nordic Cochrane Centre, The Cochrane Collaboration) was used to perform the meta-analysis.

Finally, the GRADEpro online tool (gdt.gradepro.org) was used to assess the overall quality of evidence in this systematic review and meta-analysis.

Results

Search Result

The flowchart in **Supplemental File 2** shows the search procedure. From our preliminary search of four databases, a total of 1356 records were returned. Of 1064 non-duplicate records, 29 potentially eligible studies were examined in full-text after screening titles and abstracts. Finally, a total of 34 data points from 10 studies that meet the inclusion criteria were pooled in the quantitative analysis.

The Characteristics of Included Studies

The basic characteristics of the included studies are shown in **Supplemental File 3.** These articles came from six different countries around the world (i.e., Saudi Arabia[37], n = 1, 10%; Brazil[38 39], n = 2, 20%; China[40 41], n = 2, 20%; Germany[27 42-45], n = 5, 50%). The subjects in all studies were adults over the age of 18 years. For genders of the recruited subjects, 9 studies recruited both males and females in the experimental groups and control groups. And one study included only females in the control group[27]. Among these 10 studies, five studies (50%) assessed the effect of cupping therapy on chronic back pain[37-39 44 45], four studies (40%) involved chronic neck pain[27 41-43], and only one study (10%) involved chronic pain in neck and shoulder[40]. The duration of illness varied from 20.0 to 189.6 months in 9 articles. Only one article did not report the exact course of the disease[39].

For experimental interventions, most studies (n = 5, 50%) examined the effect of dry cupping therapy, two studies reported pulsation cupping therapy, which was a modern cupping therapy using a pulsatile negative pressure produced by a mechanical device with a pump[41 45]. Two studies focused on wet cupping therapy[37 43]. And only one study involved cupping massage therapy, which was a treatment with the cupping glasses being moved over the skin surface with negative pressure[27]. For control groups, the interventions consisted of sham/placebo cupping therapy (n = 3, 30%)[38 39 44], waiting list control methods (n = 5, 50%)[27 41-43 45], and resting (n = 2, 20%)[37 40].

The pain intensity, as the primary outcome in this meta-analysis, was involved in all studies. As for the secondary outcomes, seven studies reported mental health conditions and nine studies reported functional disability. For the pain intensity, four measurements were used (the NPS: n = 1; the NPRS: n = 1; the VAS: n = 7; the BPI: n = 1). The functional disability was measured by the ODQ (n =1), the ODI (n = 1), the NDI (n = 4), the FIQ (n=1), the FFbH-R (n = 1), and the RMDQ (n = 1). The subjects in 6 trials accepted mental health tests by the SF-36 (n = 6).

In addition, the quality of the included articles was evaluated according to the guidelines provided by Higgins [31]. **Supplemental File 2** showed the risk of bias across all included studies. The quality bias mainly came from the blinding of outcome assessment (detection bias) and the other bias.

The Effect of Cupping Therapy on Pain Intensity

A total of fourteen data points in ten studies reported the influence of cupping therapy on pain intensity in participants with CMP. Overall, as shown in **Figure 1**, there is a significant difference between experimental groups and control groups based on a random-effect model (SMD = -1.17; 95% CI = -1.93 to -0.42; P = 0.002; I^2 = 94%). And sensitivity analysis showed that the results were relatively robust (**Supplementary File 3**). The studies are symmetrically distributed on either side of the pooled effect size line, suggesting the absence of publication bias (**Supplementary File 2**). The GRADE assessment indicated moderate confidence in the estimated effect (**Supplementary File 4**).

Table 1 presents the effectiveness of cupping therapy on pain intensity for different subgroups. No significant difference was found in the effects of dry cupping and wet cupping (P = 0.60). But both of them were useful to reduce pain intensity compared to control groups. Additionally, there was no significant difference between the effect of wet cupping (SMD = -1.47, 95% CI = -2.39 to -0.55, P = 0.002) and that of dry cupping (SMD = -1.13, 95% CI = -2.00 to -0.27, P = 0.01). For the subgroup analysis based on the different types of negative pressure, both the effects of pulsation pressure and non-pulsation pressure were superior to the effects of control interventions (pulsation VS control: SMD= -1.31, 95% CI = -1.90 to -0.71, P < 0.0001; non-pulsation VS control: SMD= -1.06, 95% CI = -1.93 to -0.42, P = 0.03). However, there was no significant difference between pulsation pressure and non-pulsation pressure (P = 0.67). A subgroup analysis based on the frequency of treatments was also conducted. The results indicated a larger effect of a single-time cupping treatment compared to comparisons (SMD = -1.87, 95% CI = -2.71 to -1.03, P < 0.0001), with a significant effect (P = 0.05) for multiple-times cupping treatment (SMD = -0.48; 95% CI = -1.58 to 0.62; P = 0.39). As for the subgroup analysis based on the pain sites and the age of patients, there was a significant improving effect of cupping therapy in patients with neck/shoulder pain (SMD = -1.68, 95% CI = -2.38 to -0.98, P < 0.0001) and aged more than 45 years (SMD = -0.81, 95% CI = -1.20 to -0.41, P < 0.00001).

Table 1 The effect of cupping therapy on pain intensity for different subgroups

Subgroups	N	n	SMD	95%CI	*P* value (subtotal effect)	I^2
Type of cupping therapy	10	656	-1.17	-1.93 to -0.42	0.002	94%
Dry cupping	8	531	-1.13	-2.00 to -0.27	0.01	94%
Wet cupping	2	125	-1.47	-2.39 to -0.55	0.002	80%
Difference between subgroups					0.60	
Type of negative pressure	10	656	-1.17	-1.93 to -0.42	0.002	94%
Pulsation	2	142	-1.31	-1.90 to -0.71	< 0.0001	42%
Non-pulsation	8	514	-1.06	-2.04 to -0.08	0.03	95%
Difference between subgroups					0.67	
Frequency of treatments	10	656	-1.17	-1.93 to -0.42	0.002	94%

Single time	4	213	-1.87	-2.71 to -1.03	< 0.0001	81%
Multiple times	6	443	-0.48	-1.58 to 0.62	0.39	95%
Difference between subgroups					0.05	
Painful site	10	656	-1.17	-1.93 to -0.42	0.002	94%
Neck/Shoulder	5	257	-1.68	-2.38 to -0.98	< 0.0001	79%
Back	5	399	-0.42	-1.69 to 0.85	0.52	97%
Difference between subgroups					0.09	
Age of participants	10	656	-1.17	-1.93 to -0.42	0.002	94%
> 45 years	5	318	-0.81	-1.20 to -0.41	< 0.00001	63%
< 45 years	5	338	-1.54	-3.14 to 0.05	0.06	96%
Difference between subgroups					0.38	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

The Effect of Cupping Therapy on Functional Disability

Twelve data points from 9 studies were synthesized to assess the influence of cupping therapy on functional disability in CMP patients. **Figure 2** presents that the cupping therapy has no significant effect on decreasing the functional disability in CMP patients (SMD = -0.24, 95% CI = -0.93 to 0.46, P = 0.51, I^2 = 93%). And sensitivity analysis showed that the results were relatively robust (**Supplementary File 3**). The distribution of studies in the funnel plot appears approximately symmetrical, indicating that there is no evidence of publication bias (**Supplementary File 2**). The GRADE assessment indicated moderate confidence in the estimated effect (**Supplementary File 4**).

As depicted in **Table 2,** dry cupping therapy, wet cupping therapy, pulsation pressure cupping therapy, and non-pulsation pressure cupping therapy cannot improve the functional disability in CMP patients (dry cupping therapy: SMD = -0.09, 95% CI = -0.86 to 0.69, P =0.83; wet cupping therapy: SMD = -0.95, 95% CI = -2.21 to 0.32, P =0.14; pulsation cupping therapy: SMD = -0.13, 95% CI = -0.51 to 0.26, P =0.52; non-pulsation cupping therapy: SMD = -0.26, 95% CI = -1.24 to 0.73, P =0.61). For the frequency of treatments, a significant difference was found in the effect between the single-time cupping therapy (SMD = -0.65, 95% CI = -1.20 to -0.11, P = 0.02) and the control group. However, no significant difference was found in the effect between the multiple-times cupping therapy (SMD = 0.01, 95% CI = -0.99 to 1.01, P = 0.98) and the control group. For the subgroup analysis based on the pain sites, there was a significant improving effect of cupping therapy in patients with neck/shoulder pain (SMD = -0.48, 95% CI = -0.79 to -0.16, P = 0.003).

Table 2 Effects of cupping on functional disability for different subgroups

Subgroups	**N**	**n**	**SMD**	**95%CI**	***P* value (subtotal effect)**	**I^2**

Type of cupping therapy	9	596	-0.24	-0.93 to 0.46	0.51	93%
Dry cupping	7	471	-0.09	-0.86 to 0.69	0.83	92%
Wet cupping	2	125	-0.95	-2.21 to 0.32	0.14	91%
Difference between subgroups					0.26	
Type of negative pressure	9	596	-0.24	-0.93 to 0.46	0.51	93%
Pulsation	2	142	-0.13	-0.51 to 0.26	0.52	0%
Non-pulsation	7	454	-0.26	-1.24 to 0.73	0.61	95%
Difference between subgroups					0.81	
No. of treatments	9	596	-0.24	-0.93 to 0.46	0.51	93%
Single time	3	153	-0.65	-1.20 to -0.11	0.02	45%
Multiple times	6	443	0.01	-0.99 to 1.01	0.98	96%
Difference between subgroups					0.25	
Painful site	9	596	-0.24	-0.93 to 0.46	0.51	93%
Neck/Shoulder	4	197	-0.48	-0.79 to -0.16	0.003	0%
Back	5	399	-0.03	-1.26 to 1.20	0.96	97%
Difference between subgroups					0.49	
Age of participants	9	596	-0.24	-0.93 to 0.46	0.51	93%
> 45 years	5	294	-0.23	-0.47 to 0.01	0.06	0%
< 45 years	4	278	-0.22	-1.97 to 0.48	0.81	97%
Difference between subgroups					0.99	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

The Effect of Cupping Therapy on Mental Health

Eight data points from 6 studies were pooled to evaluate the effectiveness of cupping therapy on mental health in CMP individuals. **Figure 3** shows that there is no significant difference in mental health between the cupping therapy group and the control group using a fixed-effect modal (SMD = 0.08, 95% CI = -0.12 to 0.27, P = 0.46, I^2 = 0%). And sensitivity analysis showed that the results were relatively robust (**Supplementary File 3**). The studies are symmetrically distributed on either side of the pooled effect size line, suggesting the absence of publication bias (**Supplementary File 2**). The GRADE assessment showed high quality of evidence, indicating considerable certainty in the effect estimate (**Supplementary File 4**).

Table 3 showed the effects of cupping therapy on mental health for five subgroups. With regard to different types of cupping therapy, we did not find a significant effect of dry cupping therapy (SMD = 0.11, 95% CI = -0.10 to 0.32, P = 0.30) and wet cupping therapy (SMD = -0.21, 95% CI = -0.79 to 0.38, P = 0.49) on CMP patients' mental health. In addition, no significant effect was found when conducting the subgroup analyses based on the types of negative pressure (pulsation: SMD = 0.05, 95% CI = -0.38 to 0.48, P =0.81; non-pulsation: SMD = 0.08, 95% CI = -0.14 to 0.30, P =0.47), the frequency of treatments (single-time: SMD = -0.21, 95% CI = -0.79 to 0.38, P =0.49; multiple-time: SMD = 0.11, 95% CI = -0.10 to 0.32, P =0.30), pain sites

(neck/shoulder: SMD = 0.12, 95% CI = -0.23 to 0.47, *P* =0.51; back: SMD = 0.06, 95% CI = -0.18 to 0.29, *P* =0.65) and the age of participants (more than 45 years: SMD = 0.07, 95% CI = -0.16 to 0.29, *P* =0.55; less than 45 years: SMD = 0.10, 95% CI = -0.31 to 0.51, *P* =0.64).

Table 3 The effect of cupping therapy on mental health for different subgroups

Subgroups	N	n	SMD	95%CI	*P* value (subtotal effect)	I^2
Type of cupping therapy	6	408	0.08	-0.12 to 0.27	0.46	0%
Dry cupping	5	363	0.11	-0.10 to 0.32	0.30	0%
Wet cupping	1	45	-0.21	-0.79 to 0.38	0.49	-
Difference between subgroups					0.32	
Type of negative pressure	6	408	0.08	-0.12 to 0.27	0.46	0%
Pulsation	1	96	0.05	-0.38 to 0.48	0.81	-
Non-pulsation	5	312	0.08	-0.14 to 0.30	0.47	0%
Difference between subgroups					0.91	
No. of treatments	6	408	0.08	-0.12 to 0.27	0.46	0%
Single time	1	45	-0.21	-0.79 to 0.38	0.49	-
Multiple times	5	363	0.11	-0.10 to 0.32	0.30	0%
Difference between subgroups					0.32	
Painful site	6	408	0.08	-0.12 to 0.27	0.46	0%
Neck/Shoulder	3	127	0.12	-0.23 to 0.47	0.51	0%
Back	3	281	0.06	-0.18 to 0.29	0.65	0%
Difference between subgroups					0.78	
Age of participants	6	408	0.08	-0.12 to 0.27	0.46	0%
> 45 years	5	318	0.07	-0.16 to 0.29	0.55	0%
< 45 years	1	90	0.10	-0.31 to 0.51	0.64	-
Difference between subgroups					0.89	

Notes:

N: the number of included studies; n: sample size; SMD: standardized mean difference; CI: confidence interval.

Discussion

This meta-analysis suggested that cupping therapy might have a positive immediate effect on reducing CMP patients' pain intensity. But cupping therapy cannot improve their functional disability and mental health. Based on the subgroup analyses in pain intensity, dry cupping therapy, wet cupping therapy, pulsation pressure, and non-pulsation pressure cupping therapy showed a significant difference when compared to the control group, respectively. In addition, cupping therapy might be effective for decreasing pain intensity and functional disability in patients with chronic neck/shoulder pain rather than in patients with chronic back pain.

Our results demonstrated that cupping therapy might effectively reduce pain

intensity in CMP patients with immediate effects. This might be explained by the neurobiological foundations. It is widely confirmed that both nociceptive afferent fibers (Aδ and C fibers) and mechanosensitive Aβ fibers project in the same way onto interneurons or ascending projection neurons [46]. However, the rate of signal transmission from the mechanoreceptor (Aβ) up to the dorsal horn was faster than that from the Aδ and C fibers, so that the Aβ fibers would activate the corresponding multi-receptive dorsal horn interneuron before the Aδ and C fibers [47]. Based on the theory mentioned above, we speculated that the faster Aβ afferents (i.e., mechanosensitive afferent fibers) caused by the negative pressure of cupping therapy could block out pain sensation from the slower pain conducting Aδ and C fibers (i.e., nociceptive afferent fibers). This might partly explain the effects of cupping therapy on the pain intensity in CMP individuals. On the other hand, cupping therapy has been indicated to result in vascular ectasia for increasing blood flow significantly [19], which may be related to the therapeutic effect of cupping therapy on CMP. The increased blood flow under the cup after cupping therapy could play a positive role in the clearance of inflammatory cytokines locally. Several studies have demonstrated that musculoskeletal pain following exercises caused upregulation of transcripts for inflammatory such as interleukin-1 (IL-1)[48 49] and interleukin-6 (IL-6) [50] in the exercised limbs. These transcripts for inflammation were sensitivity to musculoskeletal sensitization, which was a preclinical model of muscle pain [50]. In other words, lowering the inflammatory cytokines (i.e., IL-1 and IL-6) might imply the alleviation of inflammatory response and the reduction of muscle pain. Therefore, the acceleration of blood circulation caused by negative pressure suction of cupping therapy could accelerate the clearance of inflammatory factors, alleviate inflammatory reactions, and thus release muscle pain.

On the other hand, the recovery effect of cupping therapy on their functional disability was not significant. The potential reason might be that the outcomes related to pain intensity in our included studies in this meta-analysis [17 51 52] were usually evaluated in resting state rather than moving state. Nevertheless, the pain in moving state usually impeded patients' daily activities and contributed to the functional disability [53]. Some musculoskeletal pain usually occurred during the moving process with muscle contraction or joint friction and compression. For example, the individual with patellar tendinopathy only experienced pain when the knee was flexed and extended (e.g., walking down stairs and jumping) [54]. This type of functional dysfunction was attributed to the pain induced by the altered biomechanical relationship between muscles, joints, and bones. According to the neurobiological foundation theory, the single-time cupping therapy might impede the pain conduction in CMP patients at rest state, while it was not sufficient to affect the biomechanical relationships of anatomical structures such as muscles, bones, and joints. Hence, patients with CMP still suffered from the functional disability due to the pain produced in moving state.

For another outcome, our results showed that, compared to the control group, cupping therapy had no effectiveness in promoting CMP patients' mental health. Wet cupping therapy-induced incisions might cause more negative emotions (e.g., fear of invasive wound) rather than positive emotions (e.g., relaxation or soothing power of cupping therapy) caused by suction treatment. One animal experiment about mood

status demonstrated that sheep conducted worse aversive behavior patterns in response to the pricking stimulus than the slight pressure and kneading stimulus [55]. Moreover, the non-significant group difference between cupping therapy and placebo therapy on mental health has been reported previously (e.g., sham cupping therapy). For example, Lauche et al. applied dry cupping therapy with 50-100 mm-diameter cups and a 10-15 minutes retention time for 141 fibromyalgia syndrome patients and used the SF-36 questionnaire to monitor changes in mental health. The findings demonstrated that cupping therapy and sham cupping therapy played similar roles in improving patients' mental health like anxiety, depression, and loss of behavioral or emotional control [52]. Among the 10 included studies in our meta-analysis, the SF-36 wasused tool for accessing mental health (n = 6, 60%). After viewing the specific questions in SF-36, we supposed that the subjective questionnaire reflected the mental situations during the past 4 weeks [56]. Hence, the survey after the single cupping therapy immediately could not indicate the effects of cupping therapy on CMP patients' mental health accurately. This might partly explain the reason that, in our meta-analysis, there is no significant difference in the improvement effect on CMP patients' mental health between cupping therapy and sham cupping therapy.

To the best of our knowledge, this is the first study to demonstrate and integrate the effects of cupping therapy on clinical outcomes (i.e., pain intensity, functional disability, and mental health) in CMP patients. However, there are still some limitations. First, we only considered the immediate effect of cupping therapy, because of the limited original researches included in this meta-analysis. Nevertheless, our team has proposed the delayed effect of cupping therapy on muscular performance in one previous study [57]. Hence, we inferred that there was the possibility of the delayed effect of cupping therapy on CMP. Further evidence-based studies are needed to assess the time-effect to prove our speculation. Second, the heterogeneity of the included studies was relatively high because of differences in cupping dose. Therefore, the caution should be exercised in interpreting the results of this meta-analysis. Last, the results of a meta-analysis are contingent upon the studies included in the analysis. The number of studies included in this systematic review is limited (n = 10). In the future, as more RCT literatures are available, we will reexamine the evidences. The purpose of this systematic review is to evaluate the available evidence and provide the integrated effect size for the effectiveness of the separate cupping therapy on clinical outcomes in CMP patients.

Conclusion

This systematic review and meta-analysis demonstrates that cupping therapy may be effective in reducing pain intensity for CMP individuals with immediate effects. However, CMP patients' functional disability and mental health cannot be improved by cupping therapy. Considering the high heterogeneity of the studies, caution is warranted in interpreting the findings of this research.

Figure Legends

Figure 1 The effect of cupping therapy on pain intensity

Figure 2 The effect of cupping therapy on functional disability

Figure 3 The effect of cupping therapy on mental health

Declarations

Patient and Public Involvement

It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The data used in this meta-analysis were extracted from the original studies included in the review.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was funded by the National Natural Sciences Foundation of China (grant number: 82405615).

Contributorship statement

Conceptualization, X.H. and T.-T.S; methodology, Y.-Y.J., R.W and Z.-M.B.; formal analysis, Y.-Y.J and L.-K.Y.; writing—original draft preparation, Y.-Y.J.; writing—review and editing, X.H. and Y.-Y.J.; visualization, Y.-Y.J.; supervision, X.H. and T.-T.S. All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

Y.-Y.J. and R.W have contributed equally to this work and share the first authorship. X.H. and T.-T.S have contributed equally to this work and share the corresponding authorship.

Guarantor: Xiao Hou is the guarantor for this study and assumes responsibility for the accuracy and integrity of the research.

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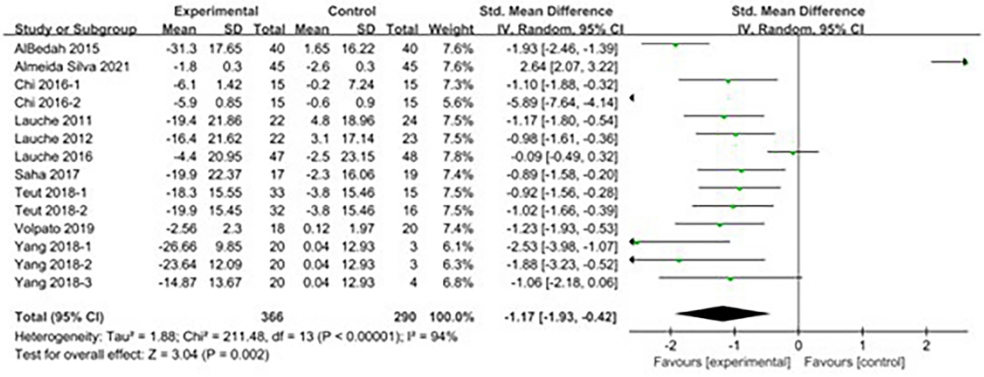

Figure 1 The effect of cupping therapy on pain intensity

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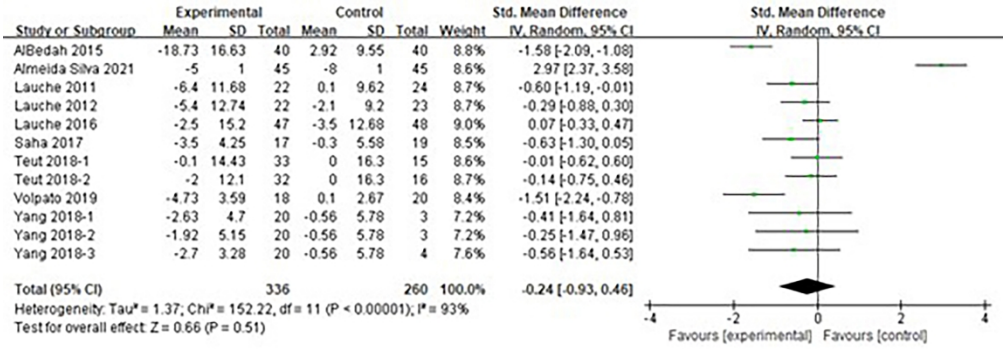

Figure 2 The effect of cupping therapy on functional disability

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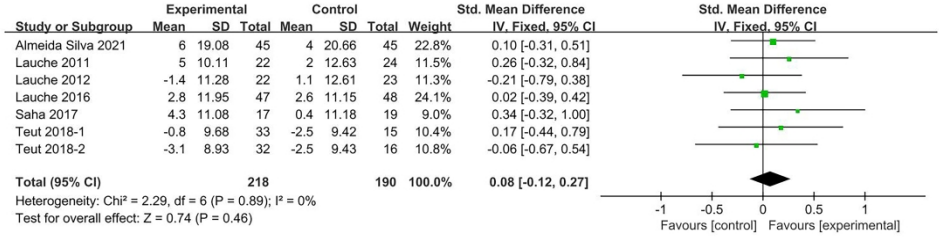


Figure 3 The effect of cupping therapy on mental health

344x90mm (600 x 600 DPI)

Search strategy used in database

PubMed

	Searches
#1	(((((((“chronic musculoskeletal disorder”[Title/Abstract]) OR (“chronic musculoskeletal pain”[Title/Abstract]) OR (“chronic pain”[MeSH Terms] OR “chronic pain”[Title/Abstract])) OR (“hip pain”[Title/Abstract])) OR (“knee pain”[Title/Abstract])) OR (“shoulder pain”[MeSH Terms] OR “shoulder pain”[Title/Abstract])) OR (“neck pain”[MeSH Terms] OR “neck pain”[Title/Abstract])) OR (“back pain”[MeSH Terms] OR “back pain”[Title/Abstract])) OR (“myalgia”[MeSH Terms] OR “myalgia”[Title/Abstract] OR “muscle pain”[Title/Abstract])) OR (“osteoarthritis”[MeSH Terms] OR “osteoarthritis”[Title/Abstract])) OR (“fibromyalgia”[MeSH Terms] OR ‘fibromyalgia”[Title/Abstract]))
#2	(((((“cupping therapy”[Mesh Terms]) OR (“cupping therapy”[Title/Abstract])) OR (“cupping treatment”[Title/Abstract])) OR (“dry cupping”[Title/Abstract])) OR (“wet cupping”[Title/Abstract])) OR (“cupping massage”[Title/Abstract])))))
#3	#1 AND #2

Web of Science

	Searches
#1	((((((((((TS=("chronic musculoskeletal pain")) OR TS=("chronic musculoskeletal disorder")) OR TS=(fibromyalgia))OR TS=(osteoarthritis)) OR TS=(myalgia)) OR TS=("muscle pain")) OR TS=("back pain")) OR TS=("neck pain")) OR TS=("shoulder pain")) OR TS=("knee pain")) OR TS=("hip pain")) OR TS=("chronic pain")
#2	(((((TS=("cupping therapy")) OR TS=("cupping treatment")) OR TS=("dry cupping")) OR TS=("wet cupping")) OR TS=("cupping massage"))
#3	#1 AND #2

EBSCO

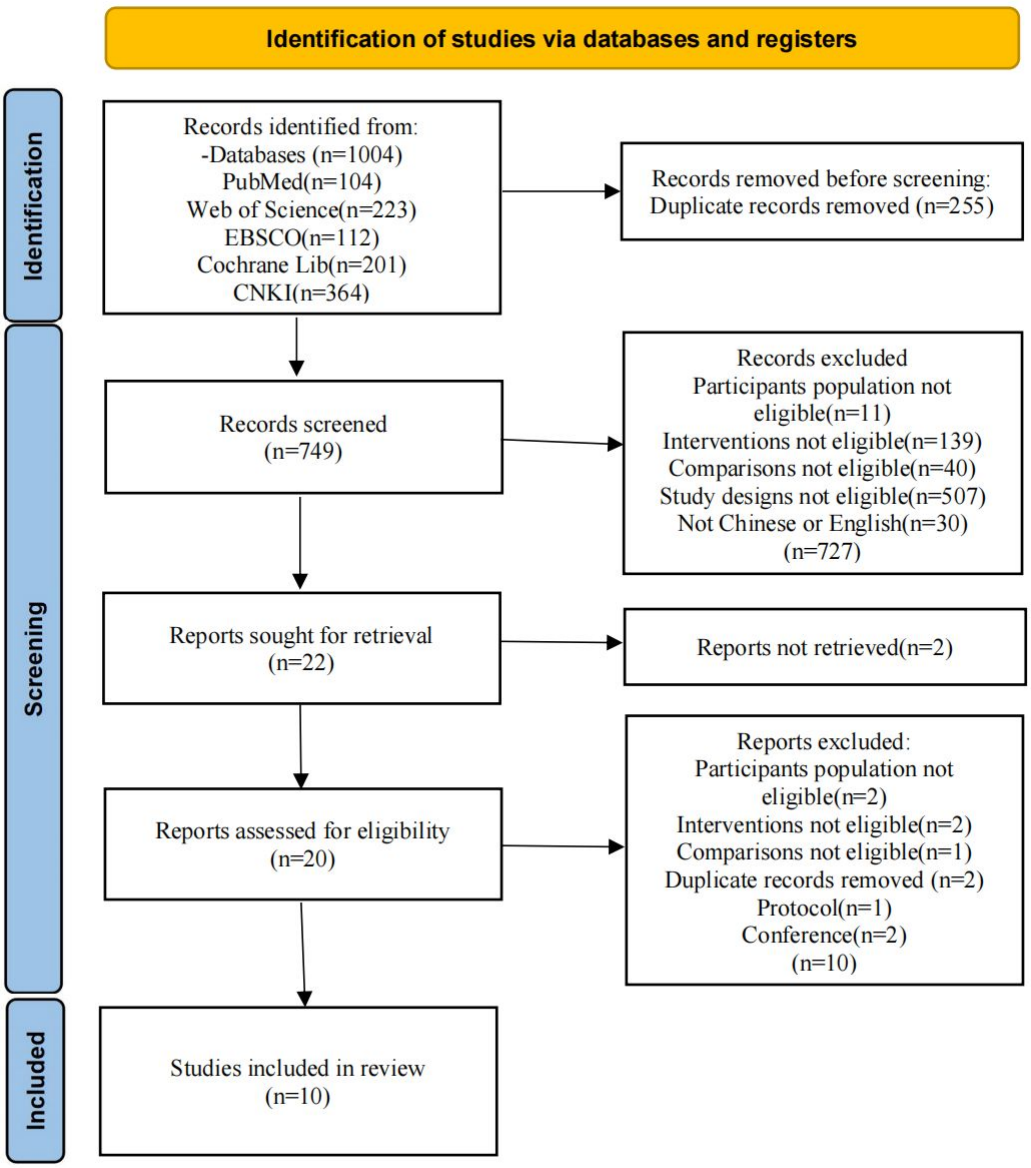
	Searches
S1	AB "chronic musculoskeletal pain" OR AB "chronic musculoskeletal disorder" OR AB "fibromyalgia" OR AB "osteoarthritis" OR AB "myalgia" OR AB "muscle pain" OR AB "back pain" OR AB "neck pain" OR AB "shoulder pain" OR AB "knee pain" OR AB "hip pain" OR AB "chronic pain"
S2	AB "cupping therapy" OR AB "cupping treatment" OR AB "dry cupping" OR AB "wet cupping" OR AB "cupping massage"
S3	S1 AND S2

Cochrane Library

	Filters	Searches
#1	Title Abstract Keyword	"chronic musculoskeletal pain" OR "chronic musculoskeletal disorder" OR "fibromyalgia" OR "osteoarthritis" OR "myalgia" OR "muscle pain" OR "back pain" OR "neck pain" OR "shoulder pain" OR "knee pain" OR "hip pain" OR "chronic pain"
#2	Title Abstract Keyword	"cupping therapy" OR "cupping treatment" OR "dry cupping" OR "wet cupping" OR "cupping massage"
#3	#1 AND #2	

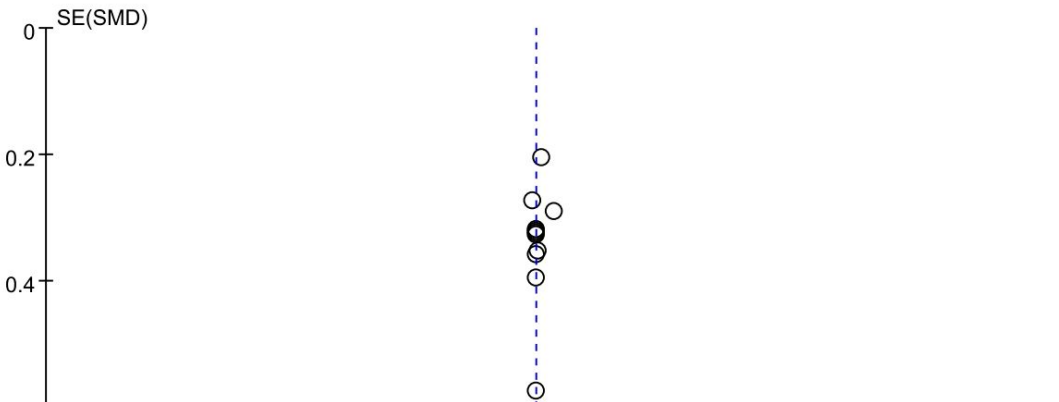
China National Knowledge Infrastructure

	Filters	Searches
#1	主题	慢性肌肉骨骼疼痛 + 慢性肌肉骨骼疾病 + 纤维肌痛 + 骨关节炎 + 肌痛 + 肌肉疼痛 + 背痛 + 背部疼痛 + 颈痛 + 颈部疼痛 + 肩痛 + 肩部疼痛 + 膝痛 + 膝关节疼痛 + 髋痛 + 髋关节疼痛 + 慢性疼痛
#2	主题	拔罐 + 拔罐疗法 + 拔罐治疗 + 干罐 + 湿罐 + 走罐
#3	#1 AND #2	

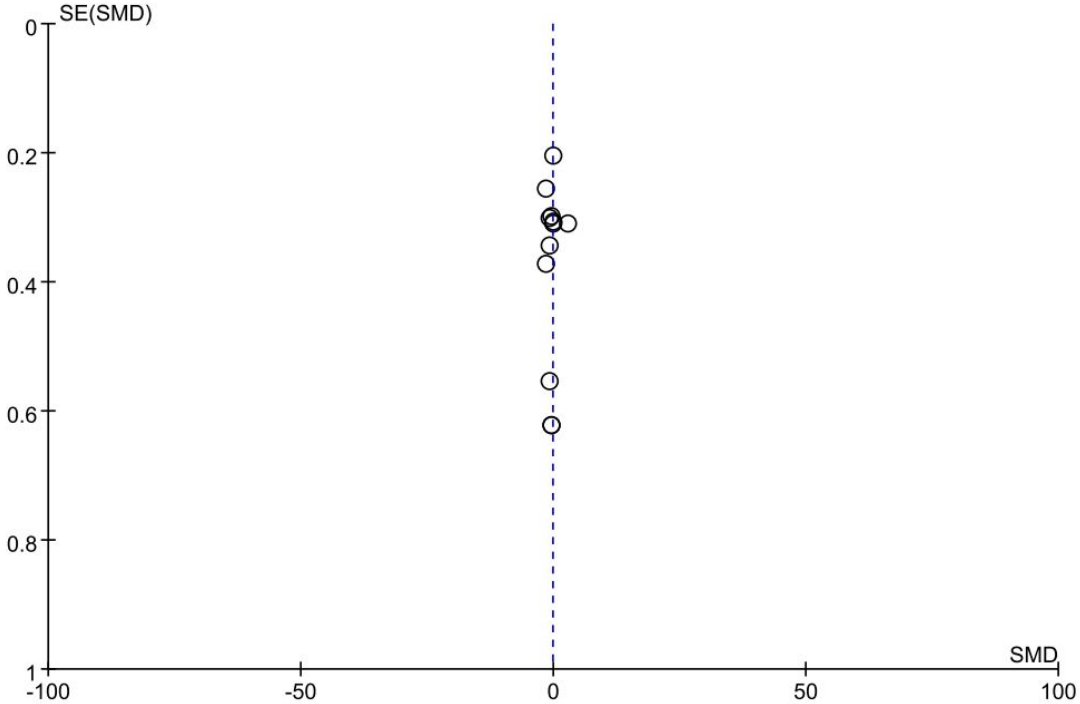


Supplemental Figure 1 The flowchart of the search procedure

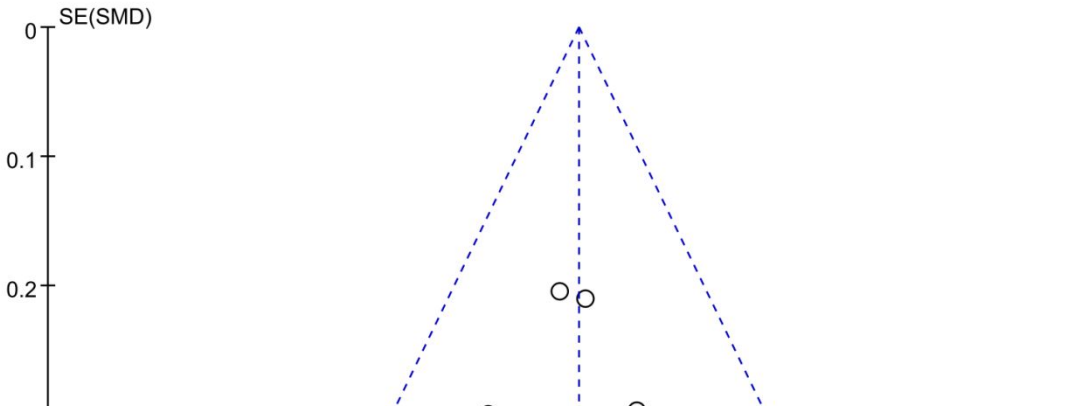
Supplemental Figure 2 The bias of the included studies



Supplemental Figure 3 The funnel plot for pain intensity



Supplemental Figure 4 The funnel plot for functional disability



Supplemental Figure 5 The funnel plot for mental health

Supplemental Table 1 The characteristics of included studies

No.	Author(s) Publication year	Country	Age (mean ± SD) Gender (male/female)	Sample size	Painful site(s)	Duration of illness (mean ± SD)	EG intervention (dosage of cupping therapy)	CG intervention	Outcomes 1. Pain intensity 2. Functional disability 3. Mental health
1	Al Bedah et al. 2015	Saudi Arabia	**EG:** 36.48 ± 9.3 y 22/18 **CG:** 36.43 ± 9.4 y 17/23	**EG:** 40 **CG:** 40	Low back	**EG:** 4.45 ± 4.8 y **CG:** 3.85 ± 3.9 y	**Wet cupping therapy** (cup size: 40 cc; duration: 5 min; negative pressure caused by manual pumping; frequency: three times per week for 2 weeks) Rescue treatment: acetaminophen no more than 1500 mg per day	**Resting** Rescue treatment: acetaminophen no more than 1500 mg per day	1. NRS 2. ODQ 3. NA
2	Almeida Silva et al.	Brazil	**EG:** 30 ± 11.0 y	**EG:** 45 **CG:** 45	Low back	**EG:** 44 ± 32 mo	**Dry cupping therapy** (cup size: 4.5 cm; duration: 10 min;	**Sham-cupping therapy** (cup size:	1. NPRS 2. ODI

	2021		16/29 **CG:** 32 ± 13.0 y 7/38			**CG:** 58 ± 51 mo	negative pressure: 300 millibars; frequency: once per week for 8 times)	4.5 cm; duration: 10 min; negative pressure: 0; frequency: once per week for 8 times)	3. SF-36
3	Chi et al. 2016	China	**EG:** 43.6 ± 8.0 y 3/27 **CG:** 42.5 ± 7.4 y 2/28	**EG:** 30 **CG:** 30	Neck, shoulder	**EG:** 20.17 ± 8.53 mo **CG:** 20.03 ± 9.21 mo	**Dry cupping therapy** (cup size: 4 cm; duration: 10 min; negative pressure caused by placing the burning swab in-and-out; frequency: single intervention)	**Resting**	1. VAS (neck, shoulder) 2. NA 3. NA
4	Lauche et al. 2011	Germany	**EG:** 48.6 ± 11.2 y 7/15 **CG:** 53.0 ± 11.4 y 4/20	**EG:** 22 **CG:** 24	Neck	**EG:** 6.3 ± 6.1 y **CG:** 8.0 ± 7.6 y	**Dry cupping therapy** (cup size: 25 to 50 mm; duration: 10 - 20 min; negative pressure caused by heating the air inside; frequency: once per 3 - 4 days for 5 times)	**Waiting list control**	1. VAS (rest, movement) 2. NDI 3. SF-36

5	Lauche et al. 2012	Germany	**EG:** 54.8 ± 9.6 y 7/18 **CG:** 57.2 ± 9.4 y 9/16	**EG:** 25 **CG:** 25	Neck	**EG:** 12.0 ± 10.3 y **CG:** 10.4 ± 11.5 y	**Wet cupping therapy** (cup size: 25 - 50 mm; duration: 10 - 15 min; negative pressure caused by heating the air inside; frequency: single intervention) Fixed dosage of Pa and Me started for 4 weeks before the study	**Waiting list control** Fixed dosage of Pa and Me if started for 4 weeks before the study	1. VAS (rest, movement) 2. NDI 3. SF-36
6	Lauche et al. 2016	Germany	**EG:** 54.35 ± 10.6 y 1/46 **CG:** 56.3 ± 8.7 y 1/47	**EG:** 47 **CG:** 48	Back	**EG:** 11.6 ± 9.2 y **CG:** 11.2 ± 8.9 y	**Dry cupping therapy** (cup size: 50 - 100 mm; duration: 10 - 15 min; negative pressure caused by a mechanical device; frequency: twice per week for 5 times) Fixed dosage of Me if started before the study	**CG: Sham-cupping therapy** (cup size: 50 - 100 mm; duration: 10 - 15 min; negative pressure: 0; frequency: twice per week for 5 times)	1. VAS 2. FIQ 3. SF-36

								Fixed dosage of Me if started before the study	
7	Saha et al. 2017	Germany	**EG:** 54.3 ± 8.6 y 4/21 **CG:** 53.3 ± 11.1 y 0/25	**EG:** 25 **CG:** 25	Neck	**EG:** 7.5 ± 6.6 y **CG:** 8.1 ± 7.2 y	**Cupping massage therap** (cup size: 3.5 - 5 cm; dura 10 min; frequency: twice p week for 5 times)	**Waiting list control** Fixed treatments if started except invasive treatments before the study	1. VAS (rest, movement) 2. NDI 3. SF-36
8	Teut et al. 2018	Germany	**EG1:** 49.0 ± 13.7 y 16/21 **EG2:** 47.5 ± 13.8 y 13/23 **CG:** 50.7 ± 10.7 y	**EG1:** 37 **EG2:** 36 **CG:** 37	Low back	**EG1:** 13.1 ± 9.3 y **EG2:** 15.8 ± 12.9 y **CG:** 13.2 ± 11.2 y	**EG1: Pulsatile cupping therapy-high vacuum** (cup size: 10 cm; duration: 8 min; negative pressure: 150 - 350 mbar; frequency: 8 sessions for 4 weeks) **EG2: Pulsatile cupping therapy-low vacuum** (cup	**Waiting list control** Rescue treatment: paracetamol no more than 2000 mg per day	1. VAS 2. FFbH-R 3. SF-36

			12/15				size: 10 cm; duration: 8 min; negative pressure: 70 mbar; frequency: 8 sessions for 4 weeks) **EG1, 2:** Rescue treatment: paracetamol no more than 2000 mg per day		
9	Volpato et al. 2019	Brazil	**EG:** 27.16 ± 8.43 y 3/15 **CG:** 25.42 ± 9.18 y 5/15	**EG:** 18 **CG:** 20	Low back	NA	**Dry cupping therapy** (cup size: 50 mm; duration: 15 min; negative pressure: 300 millibars; frequency: single intervention)	**Placebo cupping therapy** (cup size: 50 mm; duration: 15 min; negative pressure: 0; frequency: single intervention)	1. BPI 2. RMDQ 3. NA
10	Yang et al. 2018	China	**EG1:** 23.95 ± 2.21 y 6/14	**EG1:** 20 **EG2:** 20 **EG3:** 20	Neck	**EG1:** 2.61 ± 2.01 y	**EG1: Pulsatile cupping therapy-high frequency** (cup size: 68 mm; duration: 80	**Waiting list control**	1. VAS 2. NDI 3. NA

EG2: 27.10 ± 5.27 y 4/16 **EG3:** 26.00 ± 4.15 y 1/19 **CG:** 24.7 ± 2.5 y 3/7	**CG:** 10	**EG2:** 2.55 ± 2.73 y **EG3:** 3.68 ± 2.55 y **CG:** 2.65 ± 1.53 y	times per min for 8 min; negative pressure: 0.02 – 0.04 MPa; frequency: single intervention) **EG2: Pulsatile cupping therapy-low frequency** (cup size: 68 mm; duration: 30 times per min for 8 min; negative pressure: 0.02 – 0.04 MPa; frequency: single intervention) **EG3: Static cupping therapy** (cup size: 68 mm; duration: 8 min; negative pressure: 0.02 – 0.04 MPa; frequency: single intervention)

Abbreviations: EG, Experimental Group; CG, Control Group; NA, Not Assessed; y, years; mo, months; Pa, pain; Me, Medicine; NRS, Numeric Rating Scale; ODQ, Oswestry Disability Questionnaire; SF-36, Short Form 36-health survey questionnaire; NPRS, Numerical Pain Rating Scale; ODI, Oswestry Disability Index; VAS, Visual Analog Scale; NDI, Neck Disability Index; FIQ, Fibromyalgia Impact Questionnaire; FFbH-R, Funktionsfragebogen Hannover Rücken; BPI, Brief Pain Inventory; RMDQ, Roland Morris Disability Questionnaire.

Supplemental Table 2 Sensitivity analysis with the one-leave out method on pain intensity.

Omitted studies	*SMD*	*95%CI*	P value (subtotal effect)	I^2
Al Bedah et al. 2015	-1.11	-1.90 to -0.32	0.006	94%
Almeida Silva et al. 2021	-1.37	-1.85 to -0.89	<0.00001	92%
Chi et al. 2016	-0.87	-1.64 to -0.10	0.03	94%
Lauche et al. 2011	-1.18	-2.00 to -0.36	0.005	94%
Lauche et al. 2012	-1.20	-2.02 to -0.37	0.004	94%
Lauche et al. 2016	-1.28	-2.13 to -0.43	0.003	94%
Saha et al. 2017	-1.20	-2.02 to -0.39	0.004	94%
Teut et al. 2018	-1.23	-2.13 to -0.33	0.007	95%
Volpato et al. 2019	-1.21	-2.10 to -0.32	0.008	95%
Yang et al. 2018	-1.05	-1.99 to -0.10	0.03	96%
NA	-1.17	-1.93 to -0.42	0.002	94%

Notes:

SMD: Standardized mean difference; *CI*: confidence interval.

Supplemental Table 3 Sensitivity analysis with the one-leave out method on functional disability.

Omitted studies	*SMD*	*95%CI*	P value (subtotal effect)	I^2
Al Bedah et al. 2015	-0.10	-0.80 to 0.59	0.77	92%
Almeida Silva et al. 2021	-0.54	-0.93 to -0.15	0.006	93%
Lauche et al. 2011	-0.20	-0.97 to 0.56	0.60	93%
Lauche et al. 2012	-0.23	-1.00 to 0.54	0.56	93%
Lauche et al. 2016	-0.27	-1.07 to 0.54	0.52	93%
Saha et al. 2017	-0.20	-0.96 to 0.56	0.60	93%
Teut et al. 2018	-0.27	-1.13 to 0.58	0.53	94%
Volpato et al. 2019	-0.12	-0.84 to 0.60	0.75	93%
Yang et al. 2018	-0.19	-1.02 to 0.64	0.66	95%
NA	-0.24	-0.93 to 0.46	0.51	93%

Notes:

SMD: Standardized mean difference; *CI*: confidence interval.

Supplemental Table 4 Sensitivity analysis with the one-leave out method on mental health.

Omitted studies	*SMD*	*95%CI*	P value (subtotal effect)	
Almeida Silva et al. 2021	0.12	-0.09 to 0.33	0.27	2%
Lauche et al. 2011	0.10	-0.10 to 0.30	0.33	2%
Lauche et al. 2012	0.15	-0.05 to 0.35	0.14	2%
Lauche et al. 2016	0.14	-0.07 to 0.36	0.19	2%
Saha et al. 2017	0.09	-0.10 to 0.29	0.35	2%
Teut et al. 2018	0.13	-0.08 to 0.34	0.23	2%
NA	0.12	-0.07 to 0.30	0.23	0%

Notes:

SMD: Standardized mean difference; *CI*: confidence interval.

Summary of findings:

Cupping Therapy compared to placebo for chronic musculoskeletal pain

Patient or population: chronic musculoskeletal pain
Setting:
Intervention: Cupping Therapy
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI) Risk with placebo	Risk with Cupping Therapy	Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
pain intensity	-	SMD **1.17 lower** (1.93 lower to 0.42 lower)	-	656 (10 RCTs)	⨁⨁⨁◯ Moderate[a]	
mental health	-	SMD **0.12 higher** (0.07 lower to 0.3 higher)	-	446 (7 RCTs)	⨁⨁⨁⨁ High	
functional disability	-	SMD **0.24 lower** (0.93 lower to 0.46 higher)	-	596 (9 RCTs)	⨁⨁⨁◯ Moderate[b]	

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: confidence interval; **SMD:** standardised mean difference

GRADE Working Group grades of evidence
High certainty: we are very confident that the true effect lies close to that of the estimate of the effect.
Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.
Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.
Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.

Explanations

a. I^2 = 94%
b. I^2 = 93%

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3-5
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 5
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5-6
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 6
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 6
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6-7
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6-7
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 7
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 7
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 7
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 7
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 7

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	NA
Study characteristics	17	Cite each included study and present its characteristics.	Page 7-8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Page 8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Page 8-12
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 8-12
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	Page 8-12
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	Page 8-12
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	Page 8,10,11
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	NA
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Page 8-12
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 12-14
	23b	Discuss any limitations of the evidence included in the review.	Page 14
	23c	Discuss any limitations of the review processes used.	Page 14
	23d	Discuss implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 2,5
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 5
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	Page 5
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 15
Competing interests	26	Declare any competing interests of review authors.	Page 15
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 15

Note: NA = not applicable

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

PRISMA 2020 Checklist

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