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REVIEW

Effectiveness of Complementary and Alternative Medicine in Fibromyalgia Syndrome: A Network Meta-Analysis

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Objective: Fibromyalgia (FM) is a prevalent chronic disorder characterized by widespread skeletal muscle pain. In recent years, complementary and alternative medicine (CAM) has increasingly been recognized for its potential in treating FM symptoms. This study aims to assess the efficacy of CAM therapies in mitigating the symptoms of FM.

Methods: This systematic review was registered with INPLASY. A thorough search of both English and Chinese databases was undertaken from their inception until April 15, 2023. The search criteria focused on prospective controlled trials examining CAM therapies in FM patients. The statistical analysis employed mean values and standard deviations. Additionally, an evaluation of the literature's quality and potential biases was conducted.

Results: The search yielded 41 articles, encompassing 2877 FM patients and involving 20 different interventions. All studies were randomized controlled trials (RCTs). The results of the network meta-analysis (NMA) indicated that a combination of Acupuncture and Massage therapy, as well as Navel Needling therapy, effectively alleviated pain symptoms in FM patients. Furthermore, Abdominal Acupuncture and Electroacupuncture were found to be beneficial in improving patients' mood and sleep quality.

Conclusion: Acupuncture + Massage and Umbilical Acupuncture emerged as the most efficacious therapies in relieving pain symptoms in FM patients. Abdominal Acupuncture and Electroacupuncture demonstrated their effectiveness in enhancing mood and sleep quality. Overall, CAM therapies exhibited a high safety profile for patients with fibromyalgia.

Keywords: complementary and alternative medicine, CAM, fibromyalgia, FM, effectiveness, network meta-analysis, NMA

Introduction

Fibromyalgia (FM) is a chronic condition characterized by pain, stiffness, and tenderness in the muscles, tendons, and joints. It represents a prevalent form of chronic rheumatic disease. The symptoms of FM encompass skeletal muscle pain, restless sleep, fatigue, anxiety, depression, and cognitive impairment, with skeletal muscle pain being the most frequently reported symptom.[1] In the general population, FM's prevalence is approximately 2% to 4%, with a higher incidence in females and an increase in prevalence with age. In the realm of musculoskeletal disorders, FM is only surpassed by lower back pain and osteoarthritis in terms of prevalence.[2] The complexity and diversity of FM not only diminish the quality of life (QOL) of those affected but also impose a significant financial burden. Studies have indicated that within five years of diagnosis, 24.5% of FM patients are compelled to leave their employment, making FM the second most common condition encountered in rheumatology departments.[3] Research has demonstrated that many FM patients suffer from decreased sleep quality and emotional depression due to pain. Electroencephalogram (EEG) analysis reveals that FM

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patients often require a longer duration to fall asleep and frequently experience awakenings. Hence, treatment strategies should not only address the pain symptoms but also intervene in the psychological well-being of the patients.[4–6] Although global recommended guidelines vary, current guidelines commonly endorse the use of Duloxetine Hydrochloride and Pregabalin. These two medications are not only the most frequently used in clinical settings[7] but also the only ones approved by the Food and Drug Administration (FDA) for treating FM. In recent years, certain physical therapies have gained increasing attention. A review study has found that physical therapy, particularly exercises, can ameliorate pain, fatigue, and negative emotions in FM patients.[8] Additionally, the European League Against Rheumatism (EULAR) recommends exercise as a therapeutic approach for FM.[9]

Complementary and alternative medicine (CAM) encompasses a variety of medical practices outside the mainstream healthcare system. This diverse set includes modalities such as herbal medicine, acupuncture, massage, moxibustion, and electroacupuncture.[10] CAM has demonstrated significant potential as an effective treatment for FM.[11] In 2017, the EULAR recommended in its guidelines that CAM be used as a first-line treatment for FM.[9] Within these EULAR guidelines, acupuncture is specifically recommended as a treatment method. The main goal of this treatment is to alleviate pain symptoms and improve the QOL of patients with FM.[9] Numerous randomized controlled trials (RCTs) focusing on acupuncture have provided evidence that this technique can effectively mitigate pain, insomnia, and other FM symptoms, thereby improving the QOL of patients with FM.[12–14] CAM therapies, including electroacupuncture, acupuncture, and moxibustion, have been shown to positively regulate the quality of life and psychological state of FM patients.[15]

At present, a wide array of CAM treatments are available. Previous studies indicate that over a 12-month period, more than 90% of FM patients have engaged with some form of CAM therapy, which includes, but is not limited to, acupuncture and massage.[16,17] However, a notable disconnect exists in the integration of these treatments, and many studies often involve a combination of various therapies. Furthermore, traditional meta-analyses from regions such as China, South Korea, and the United States exhibit several limitations, including small sample sizes, suboptimal methodological quality, and inconsistent findings, thus hindering the ability to ascertain the specific impact of each CAM treatment on overall therapeutic efficacy.[18–20] This scenario complicates the systematic and comprehensive evaluation of the benefits of each treatment. Network meta-analysis (NMA) represents an innovative approach to meta-analysis, enabling a more intuitive and detailed comparison of the effectiveness of multiple interventions, unlike traditional meta-analyses which are limited to pairwise comparisons. Currently, there is an absence of NMA specifically addressing CAM for FM. This NMA is formulated based on previous studies on CAM and aims to assess the efficacy of various external CAM treatments in FM patients, with the goal of identifying the most effective treatment plan. Accordingly, we utilized NMA to compare the efficacy of different CAM therapies in FM patients, thereby providing a foundation for selecting optimal CAM therapies in the clinical management of FM. This study was conducted to systematically review the effectiveness and safety of CAM therapies in treating FM, particularly focusing on pain, sleep quality, functional ability, and mood. The findings are anticipated to bolster conclusions that can guide and support the clinical application of CAM treatments in FM patients.

Materials and Methods

Protocol and Registration

This meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol for this study has been registered on INPLASY (International Platform of Registered Systematic Review and Meta-analysis Protocols) with the code INPLASY202370002 (doi:10.37766/inplasy2023.7.0002).

Search Strategy

The search strategy was collaboratively developed by two authors, Ye and Miao. It primarily involved a combination of Medical Subject Headings (MeSH) and free-text terms. A comprehensive computerized search was conducted across several databases from their inception until April 15, 2023. The objective was to gather all prospective controlled studies focusing on the external treatment of CAM for Fibromyalgia Syndrome (FMS). The databases searched included the Cochrane Library, PubMed, EMbase, Web of Science, China Journal Full Text Database, Wanfang Academic Journal

Full Text Database, VIP Chinese Scientific and Technological Journal Database, and China Biomedical Literature Database. Additionally, manual searches were carried out to supplement the electronic database findings. The specific search strategy employed in the PubMed database is detailed in Table 1.

Inclusion and Exclusion Criteria

(i) Study type: This meta-analysis includes only RCTs that are published in either Chinese or English. During data analysis, studies with multiple arms are consolidated into two-arm experiments. Instances where the same study is reported in multiple articles are amalgamated into a single entry for analysis.

(ii) Study participants: Eligible participants are those whose clinical diagnosis aligns with the FM diagnostic standards[21–23] as outlined by the American College of Rheumatology (ACR), encompassing criteria from the years 1990, 2010, and 2016. Alternatively, diagnoses based on the FM diagnostic guidelines[24] proposed by the rheumatology department of the Chinese Medical Association (CMA) are also acceptable.

(iii) Interventions: This included any CAM treatments administered to FM patients. The intervention group must use at least one CAM therapy, which can be used alone or in combination. There were no restrictions concerning the materials used, area of treatment, duration of treatment, or frequency of sessions. The control group received oral medication or conventional treatment methods, which included either Chinese or Western medicine, used independently or in combination.

(iv) Exclusion criteria: The following criteria were used to exclude studies: a. Studies that are not RCTs; b. Instances of repeated publication of the same study; c. Non-periodical literature, including conference papers, abstracts, and dissertations; d. Studies lacking clear outcome measures or baseline data; e. Studies without a clear FM diagnosis or those involving the integration of other diseases; f. Pre-post studies within the same patient group; g. Studies where data are not presented in terms of mean and standard deviations.

(v) Type of outcome measure: All studies need to include any of the following outcome measures. The primary objective was to assess the improvement in pain, sleep quality, and mood among FM patients following CAM therapy treatment. The outcome measures employed were as follows: a. Visual Analogue Scale (VAS) with a 10-point scoring system for pain intensity; b. The Number of Tenderness Points to assess physical sensitivity; c. The Fibromyalgia Impact Questionnaire (FIQ-R) score for evaluating the overall impact of FM; d. The Pittsburgh Sleep Quality Index (PSQI) for gauging sleep quality; e. The Hamilton Depression Scale (HAMD) to measure the alleviation of depressive symptoms. The reduction in VAS scores, number of tenderness points, and FIQ-R scores served as indicators for evaluating the intensity of pain and functional status in FM patients. The PSQI score was used to assess sleep quality, while the HAMD score evaluated the extent of improvement in negative emotional states. All included studies were analyzed using the HAMD score, without restricting the application of either the FIQ or FIQ-R scores.

Table 1 PubMed Search Strategy

ID	Search Terms	Results
#1	Fibromyalgia [MeSH Terms]	9784
#2	Fibromyalgia [Title/Abstract] OR Fibromyalgia syndrome [Title/Abstract]	12,382
#3	#1 OR #2	13,816
#4	Electroacupuncture [Title/Abstract] OR Abdominal Acupuncture [Title/Abstract] OR Navel needling [Title/Abstract] OR Auricular needling [Title/Abstract] OR Filiform needle [Title/Abstract] OR Acupuncture [Title/Abstract] OR Needling [Title/Abstract] OR Acupoint [Title/Abstract] OR Massage [Title/Abstract] OR Tuina [Title/Abstract] OR Moxibustion [Title/Abstract] OR Cupping [Title/Abstract] OR Cupping jar [Title/Abstract] OR Needle knife [Title/Abstract]	225,822
#5	#3 AND #4	360

Selection of Studies and Data Extraction

Two independent researchers meticulously screened the literature and extracted pertinent data. Following the initial extraction, they cross-examined each other's findings to ensure accuracy and consistency. In cases of disagreement, the researchers either engaged in a discussion to resolve the issue or, if necessary, sought the opinion of an independent third party for resolution. The extracted data encompassed: a. General information about each study; b. Baseline characteristics of the research subjects and the treatment methods employed; c. Key elements for assessing the risk of bias; d. Outcome measures and related data.

Risk of Bias of the Included Studies

The risk of bias in the included studies was independently assessed by two researchers, Ye and Miao. They also cross-examined their assessments to confirm consistency. In instances where differing opinions arose regarding the quality of a study, a third author, Huang, was consulted for a re-evaluation. The assessment of the risk of bias in RCTs was guided by the tool recommended in the Cochrane Handbook for Systematic Reviews of Interventions, version 5.1.0.[25]

Statistical Analysis

For the NMA, we employed Stata 16.0 software (Stata Corp., College Station, Texas, USA), specifically utilizing the mvmeta package. The mean and standard deviation of the collected data were used for statistical analyses. Literature quality and risk of bias were assessed using RevMan 5.3 software (Cochrane Collaboration, Copenhagen, Denmark). Given that all data in this study are measurement data, we used the mean difference (MD) and the 95% confidence interval (CI) as the effective statistics. Heterogeneity between studies was determined by comparing the prediction interval chart, and anomalies were evaluated using the node splitting method.[26,27] We assessed the similarity between studies by comparing their clinical and methodological characteristics. The league table was utilized to display the comparative results of the outcome indicators for any two treatment techniques. The significance level for the NMA was set at $\alpha = 0.05$. A 95% CI containing 0 was considered statistically insignificant. In cases where a closed loop formed among different treatments, an inconsistency test was required to evaluate the consistency of results through both direct and indirect comparisons. $P \geq 0.05$ and $I^2 \leq 50\%$ indicated no statistical heterogeneity, prompting the selection of a fixed-effects model. Conversely, $P < 0.05$ and $I^2 > 50\%$ indicated significant heterogeneity. To explore the sources of heterogeneity, we employed subgroup analysis, sensitivity analysis, and other methods. If the sources of heterogeneity could not be excluded, a random-effects model was used. The surface under the cumulative ranking curve (SUCRA) was applied to probabilistically rank the efficacy of different treatments and ultimately determine the optimal treatment plan. Stata 16.0 software was also used to draw the publication bias funnel (comparison correction chart). The assessment of literature quality and risk of bias was conducted using RevMan 5.3

Results

Literature Search

The initial search yielded a total of 2163 relevant articles across various databases, including PubMed (n=360), Embase (n=622), Web of Science (n=296), Cochrane Library (n=288), CNKI (n=148), WanFang Data (n=165), VIP (n=89), and the China Biomedical Literature Database (n=195). After successive rounds of meticulous screening, 41 studies were ultimately selected for inclusion in this meta-analysis. Among these, 10 were published in English and 31 in Chinese. The publication years of these studies span from 2002 to 2023. The detailed document retrieval and screening process are illustrated in Figure 1.

Study Characteristics

The meta-analysis encompassed a total of 41 studies, all of which were RCTs.[28–68] These studies involved 20 distinct treatment modalities: Conventional Therapy (CT), Acupuncture (Acu), Dry Needle (DN), Electroacupuncture (EA), Massage Therapy (MT), Acupoint Application (AA), Needle Knife (NK), Moxibustion, Acupoint Injection (AI), Abdominal Acupuncture Therapy (AAT), Umbilical Acupuncture (UA), Catgut Implantation at Acupoint (CIAA)

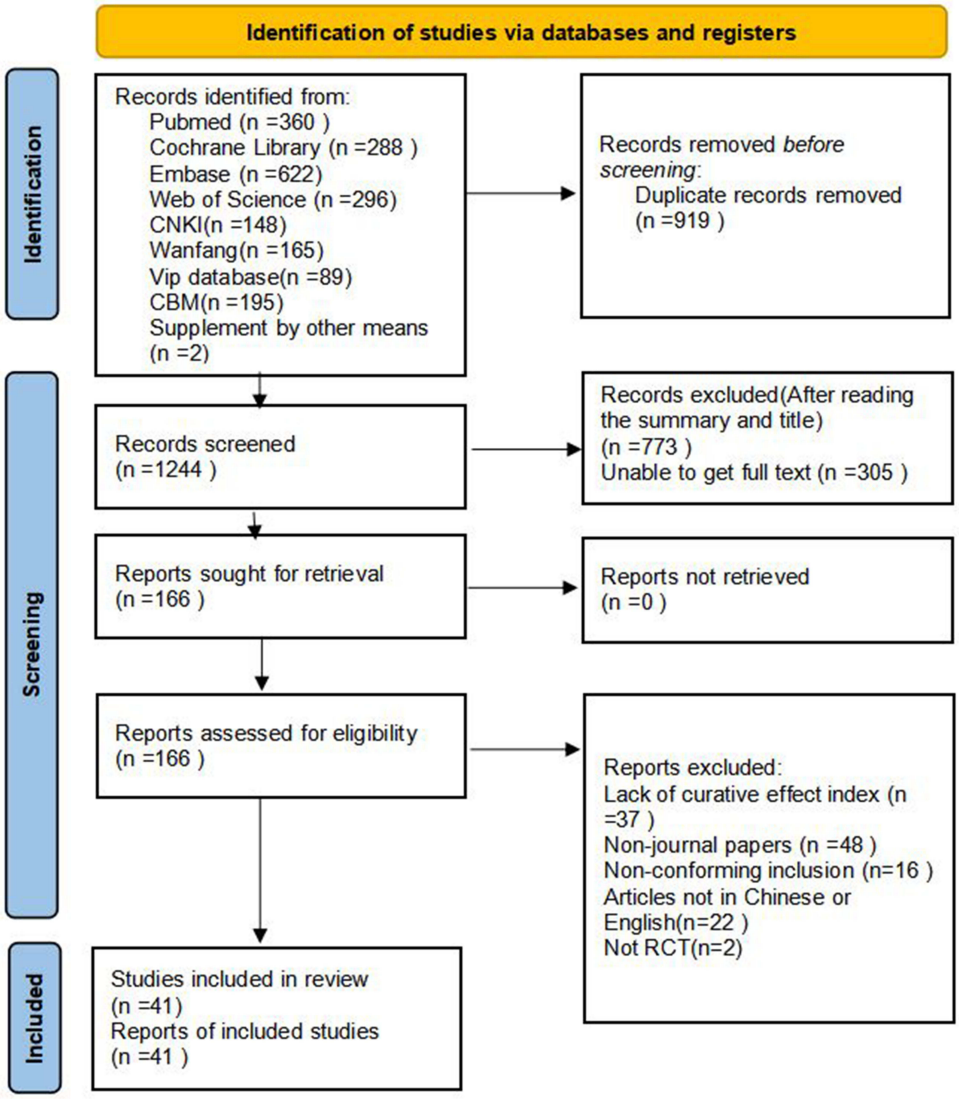

Figure 1 Document screening process and results.

Acupuncture+Massage (Acu+MT), Needle Knife+Moxibustion (NK+Moxibustion), Electroacupuncture+Cupping (EA +Cupping), Acupuncture+Cupping (Acu+Cupping), Acupuncture+Moxibustion (Acu+Moxibustion), Guasha, Electroacupuncture+Plum Blossom Needle (EA+PBN) and Cupping. During the data processing phase, subgroup mergers were implemented for studies that employed a three-arm experimental design. The data were then analyzed based on a two-arm experimental framework. Detailed characteristics of the included studies are provided in Supplementary Table S1. Figure 2 presents the comprehensive network plots of different comparisons for all outcomes.

Literature Quality Evaluation

The quality of the 41 RCTs included in this analysis was thoroughly evaluated. Among these studies, 5 that employed random allocation methods based on registration order, visiting order, outpatient or inpatient number, were identified as high risk due to potential selection bias.[40,41,52,57,66] Conversely, 20 studies were deemed low risk as they utilized a random number table or computerized random generators for subject assignment.[28–32,35–38,42,45,46,53–56,58,60,67,68] However, 16 studies, while mentioning randomization, lacked detailed information about the randomization process and were thus categorized as having unclear risk.[6,33,34,39,43,44,47–51,59,62–65] Regarding allocation concealment, 10 studies provided detailed descriptions of their subject allocation methods and were rated as low risk.[29,30,32,35,38,45,54,58–60] A total

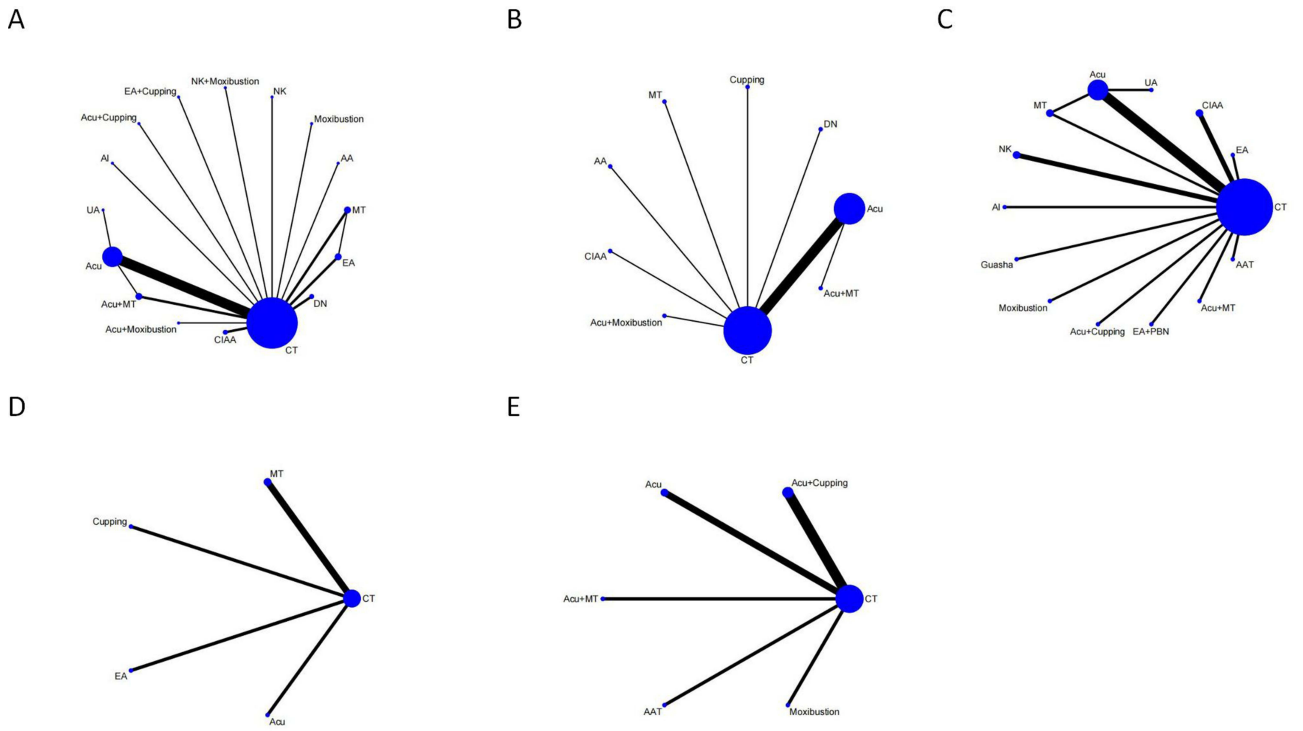

Figure 2 The evidence network of all papers on different treatments. (**A**) VAS score; (**B**) FIQ score; (**C**) Number of tenderness points; (**D**) PSQI score; (**E**) HAMD score. The thickness of the lines represents the number of studies, and the sizes of the nodes indicate the total sample sizes for each treatment.

of 27 studies did not specify their allocation methods, leading to an unclear risk rating.[31,33,34,36,37,39–44,46–53,56,57,61,62,64–66,68] One study reported using a blinding method only for the subjects,[28] while three studies reported using blinding methods solely for data evaluation.[55,63,67] All 41 studies had complete data sets. The criteria for judging selective reporting bias involved cross-examining whether the methodologies described in the literature were consistent with the reported results. All studies were considered low risk in this aspect and reported their findings fully. Other sources of bias remained unclear. The use of RevMan 5.3 software in the risk of bias assessment is depicted in Figure 3.

Meta-Analysis

VAS Score

In the evaluation of the VAS score, 29 studies involving 1864 patients were included. The NMA revealed significant findings in VAS score improvements among the 15 CAM treatments studied. Compared to conventional drug therapy or placebo, the following treatments showed notable benefits: DN therapy (MD=2.07, 95% CI [0.61, 3.53], P=0.005), Acu therapy (MD=1.1, 95% CI [0.37, 1.83], P=0.003), EA therapy (MD=1.88, 95% CI [0.65, 3.12], P=0.003), MT (MD=2.31, 95% CI [0.91, 3.7], P=0.001), AA therapy (MD=2.36, 95% CI [0.32, 4.4], P=0.023), CIAA therapy (MD=1.92, 95% CI [0.47, 3.37], P=0.009), Acu+MT therapy (MD=2.57, 95% CI [1.24, 3.9], P=0), EA+Cupping therapy (MD=2.6, 95% CI [0.61, 4.59], P=0.011). In pairwise comparisons, Acu+MT was significantly more effective than Acu +Moxibustion therapy (MD=2.69, 95% CI [0.29, 5.08], P<0.05). No statistically significant differences were found in other external treatment comparisons (P>0.05). Refer to Supplementary Table S2 for the results of pairwise comparison. Acu+MT exhibited the highest likelihood of reducing the VAS score (77.6%), followed by EA+Cupping (75.3%). As single therapies, MT (71.7%) and AA (70.7%) were also effective, comparable to DN (63.9%) and CIAA (59.4%) in pain relief. These results are detailed in Table 2 and Figure 4A.

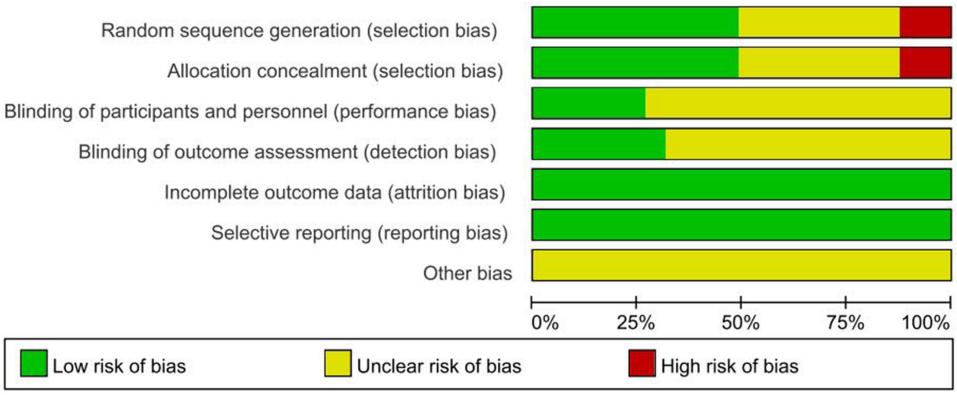

Figure 3 Risk of bias assessment included in the study.

FIQ Score

In the evaluation of the FIQ score, 14 studies with a total of 939 patients were included. The NMA examined 8 types of CAM treatments and their effectiveness in comparison to conventional drug therapy or placebo. The treatments demonstrating significant improvements in FIQ scores were: Acu+MT therapy (MD=28.24, 95% CI [20.43, 36.05], P=0), AA therapy (MD=19.27, 95% CI [10.69, 27.85], P=0), CIAA therapy (MD=10.6, 95% CI [4.56, 16.64], P=0.001), DN therapy (MD=9.7, 95% CI [1.2, 18.2], P=0.025), Acu therapy (MD=6.15, 95% CI [2.64, 9.66], P=0.001). Pairwise comparisons revealed that Acu+MT and AA therapies were superior to Acu+Moxibustion therapy, MT, Acu therapy, and Cupping therapy, with significant statistical differences (P<0.05). Additionally, Acu+MT was found to be more effective than both DN and CIAA (P<0.05). No significant differences were observed in other pairwise comparisons (P>0.05). Refer to Supplementary Table S3 for the results of pairwise comparison. Acu+MT had the highest probability of reducing FIQ scores (99.2%), followed by AA (86.6%), CIAA (64.3%), and DN (57.9%). Other combination therapies did not demonstrate marked advantages in improving FIQ scores. The detailed results are presented in Table 2 and Figure 4B.

Number of Tenderness Points

In the evaluation of the number of tenderness points, 18 studies with a total of 1507 patients were included. The NMA reviewed 13 types of CAM treatments for their effectiveness compared to conventional drug therapy or placebo. Significant reductions in the number of tenderness points were observed with the following treatments: UA therapy (MD=6.9, 95% CI [2.2, 11.6], P=0.004), EA therapy (MD=5.2, 95% CI [0.82, 9.58], P=0.02), MT (MD=4.63, 95% CI [1.33, 7.93], P=0.006), Guasha therapy (MD=4.6, 95% CI [0.32, 8.88], P=0.035), Acu therapy (MD=4.22, 95% CI [2.18, 6.26], P=0), CIAA therapy (MD=3.97, 95% CI [0.91, 7.02], P=0.011), NK therapy (MD=3.15, 95% CI [0.18, 6.12], P=0.038). No significant differences were found in other pairwise comparisons (P>0.05). Refer to Supplementary Table S4 for the results of pairwise comparison. UA therapy had the highest probability (85.7%) of reducing the number of tenderness points, followed by EA (70.3%) and MT (63.6%). Combination therapies also showed unique benefits, such as Acu+MT (63.6%). These results are detailed in Table 2 and Figure 4C.

PSQI Score

In assessing the PSQI score, 5 studies involving a total of 386 patients were included. The NMA focused on 4 types of CAM treatments and their effectiveness relative to conventional drug therapy or placebo. The treatments demonstrating notable improvements in PSQI scores were: MT (MD=2.33, 95% CI [1.55, 3.11], P=0), Acu therapy (MD=1.92, 95% CI [0.78, 3.06], P=0.001), EA therapy (MD=3.5, 95% CI [2.49, 4.51], P=0). Pairwise comparisons indicated that EA therapy was significantly more effective than both Acu therapy and Cupping therapy (P<0.05). No significant differences were observed in other pairwise comparisons (P>0.05). Refer to Supplementary Table S5 for the results of pairwise

Table 2 The SUCRA Values of Each Treatment Modality

Treatment	VAS	Rank	FIQ	Rank	Number of Tenderness Points	Rank	PSQI	Rank	HAMD	Rank
DN	63.9%	5	57.9%	4	—	—	—	—	—	—
Acu	33.3%	12	40.3%	6	58.9%	6	51.6%	3	47.2%	4
EA	58.5%	7	—	—	70.3%	2	98.5%	1	—	—
MT	71.7%	3	34%	7	63.6%	3	66.5%	2	—	—
AA	70.7%	4	86.6%	2	—	—	—	—	—	—
NK	52.2%	10	—	—	43.5%	9	—	—	—	—
Moxibustion	55.7%	8	—	—	25.5%	13	—	—	70.5%	2
AI	28.4%	14	—	—	46.9%	8	—	—	—	—
UA	45.8%	11	—	—	85.7%	1	—	—	—	—
CIAA	59.4%	6	64.3%	3	55.3%	7	—	—	—	—
Acu+MT	77.6%	1	99.2%	1	63.6%	4	—	—	50.9%	3
NK+Moxibustion	32.1%	13	—	—	—	—	—	—	—	—
EA+Cupping	75.3%	2	—	—	—	—	—	—	—	—
Acu+Cupping	54.8%	9	—	—	38%	12	—	—	46.7%	5
Acu+Moxibustion	12.3%	15	19.3%	8	—	—	—	—	—	—
Cupping	—	—	43.2%	5	—	—	32.3%	4	—	—
AAT	—	—	—	—	41.8%	10	—	—	82.2%	1
Guasha	—	—	—	—	61.9%	5	—	—	—	—
EA+PBN	—	—	—	—	40.1%	11	—	—	—	—

Abbreviations: VAS, Visual Analogue Scale; FIQ, Fibromyalgia Impact Questionnaire; PSQI, Pittsburgh Sleep Quality Index; HAMD, Hamilton Depression Scale; DN, Dry Needle; Acu, Acupuncture; MT, Massage therapy; AA, Acupoint Application; NK, Needle Knife; AI, Acupoint Injection; UA, Umbilical Acupuncture; CIAA, Catgut Implantation at Acupoint; AAT, Abdominal Acupuncture therapy; PBN, Plum Blossom Needle; EA, Electroacupuncture.

comparison. The SUCRA of the PSQI scores for FM treated with these four external treatments is detailed in Table 2 and Figure 4D. According to the NMA, EA had the highest likelihood of reducing PSQI scores (98.5%), followed by MT (66.5%) and Acu (51.6%).

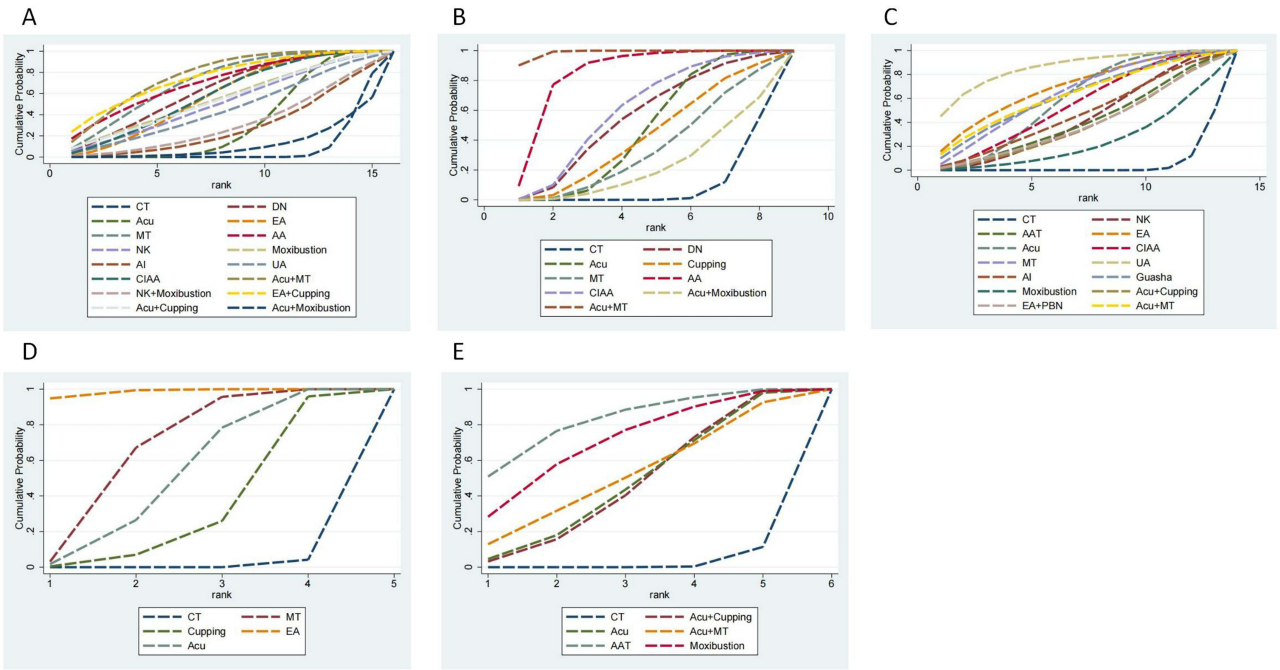

Figure 4 Ranking of the cumulative probabilities for core parameters. (**A**) VAS score; (**B**) FIQ score; (**C**) Number of tenderness points; (**D**) PSQI score; (**E**) HAMD score.

HAMD Score

In assessing the HAMD score, 8 studies involving 541 patients were included. The NMA, examining 5 types of CAM treatments, revealed the following significant improvements in HAMD scores compared to conventional drug therapy or placebo: AAT therapy (MD=6.19, 95% CI [1.81, 10.57], P=0.006), Moxibustion therapy (MD=5.14, 95% CI [0.55, 9.73], P=0.028), Acu therapy (MD=3.3, 95% CI [0.04, 6.55], P=0.047), Acu+Cupping therapy (MD=3.31, 95% CI [0.62, 6], P=0.016). No significant differences were noted in other pairwise comparisons (P>0.05). Refer to Supplementary Table S6 for the results of pairwise comparison. AAT therapy was the most effective in reducing the HAMD score (82.2%), followed by Moxibustion (70.5%) and Acu+MT (50.9%). These results are detailed in Table 2 and Figure 4E.

Small Sample Evaluation

The funnel plots for the VAS score, FIQ score, and the number of tenderness points indicate a roughly symmetrical distribution of research points on both sides of the central axis. This symmetry suggests a low likelihood of publication bias in this study. Conversely, the funnel plots for the PSQI score and HAMD score exhibit less symmetry, indicating potential bias or the influence of small sample events. These observations are illustrated in Figure 5.

Adverse Reactions

Among the 41 studies included, 19 different types of CAM treatments were analyzed. Excluding CT, 6 types of CAM treatments reported adverse reactions. Notably, all reported adverse reactions were mild, including skin hematoma and faintness. These reactions did not necessitate additional treatments for recovery. Refer to Table 3 for more details.

Discussion

Summary of Main Results

This study represents the first NMA to encompass all external treatments of CAM in the management of FM. Involving a total of 41 studies with 2877 participants, this NMA compares the efficacy of various commonly utilized external CAM treatments for FM. The results indicate a comparative advantage of these external treatments over CT, particularly in alleviating pain and improving mental health in patients with FM.

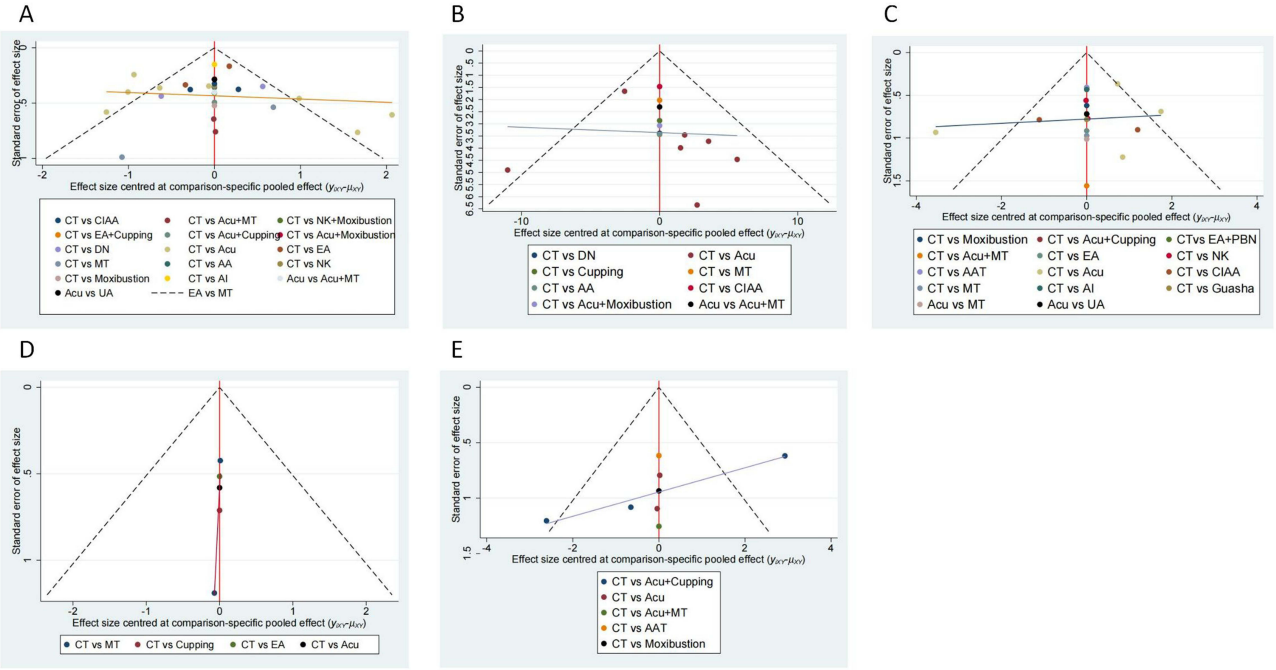

Figure 5 Funnel plot. (**A**) VAS score; (**B**) FIQ score; (**C**) Number of tenderness points; (**D**) PSQI score; (**E**) HAMD score.

Table 3 Adverse Events Associated with Different Treatments

Treatment	Pain (n)	Hematoma (n)	Nausea (n)	Abdominal Pain (n)	Insomnia (n)	Skin Blister (n)	Dizziness and Nausea (n)	Acupuncture Fainting (n)	Stagnant Needle (n)
Acu	1	6	—	—	—	—	—	1	—
AI	—	—	2	1	3	—	—	—	—
Acu +Moxibustion	—	—	—	—	—	1	—	—	—
Cupping	2	—	—	—	—	—	—	—	—
AAT	—	—	—	—	—	—	2	—	—
Acu+Cupping	—	1	—	—	—	—	—	1	1

Abbreviations: Acu, Acupuncture; Moxibustion; AI, Acupoint Injection; AAT, Abdominal Acupuncture therapy.

Utilizing SUCRA, the NMA ranked the effectiveness of different external treatments to identify the most optimal treatment plan for FM. The outcomes suggest that Acu+MT may be the most effective in improving pain-related scores, such as the VAS and FIQ. UA emerged as particularly beneficial in reducing the number of tenderness points in FM patients. EA was found to be more effective in alleviating insomnia symptoms, while AAT excelled in improving depression symptoms and mental state in patients, potentially due to its significant impact on increasing the neurotransmitter 5-hydroxytryptamine (5-HT).[69] Moreover, the study noted that external CAM treatments generally do not cause severe adverse reactions. These treatments are considered safe and reliable, with patients demonstrating good tolerance towards them.

Explanation of the Research Results

The etiology of FM has been previously attributed to central sensitization. Central sensitization refers to the heightened responsiveness of nociceptors in the central nervous system to normal or sub-threshold afferent inputs, leading to increased pain sensitivity.[70] FM is characterized as a form of central sensitization of the nervous system, where neural circuits are disrupted, resulting in hyperalgesia – an amplified sensitivity to pain and an exaggerated response to painful stimuli. This hypersensitivity contributes to other associated symptoms such as fatigue, insomnia, anxiety, and cognitive dysfunction.[71] Acupuncture, a form of external treatment, involves the insertion of thin, solid needles into specific points on the skin. It is believed to function by modulating various physiological processes in the human body.[72]

Our research indicates that combination therapies are more effective than monotherapies in treating FM. Specifically, Acu+MT appears to be the most effective, efficiently alleviating pain symptoms in FM patients. Pain in FM is frequently accompanied by emotional and psychological symptoms. Consequently, newer forms of acupuncture, such as EA, are gaining prominence for their ability to address these additional symptoms, including anxiety and depression in FM patients.[73] Prior research has demonstrated that EA can improve insomnia symptoms in patients with moderate to severe insomnia, with a notable decrease in PSQI scores.[74,75] UA represents an innovative form of acupuncture, performed at the navel. It integrates the comprehensive principles of Traditional Chinese Medicine (TCM) and the holographic medical concept, earning recognition within the global acupuncture community.[76] Studies have shown that navel needles, particularly when combined with localized movements, can relax diseased muscles and alleviate local muscle pain through holographic therapy. Thus, UA is widely employed in various painful conditions.[77] AAT involves acupuncture and moxibustion at specific abdominal points.[78] Its efficacy is rooted in the shared embryological origin of the abdominal enteric nervous system and the brain's central nervous system, both of which originate from the neural crest and utilize the same neurotransmitters. Abdominal neurons can regulate neural activity similarly to brain neurons, leading to the abdomen being referred to as "the second brain"[79] A preliminary meta-analysis supports the efficacy of AAT in treating depression, showing that the HAMD scores in the AAT treatment group were significantly lower than those in the control group, aligning with our findings.[80]

In previous meta-analyses, acupuncture and massage have emerged as significant topics in the treatment of FM, demonstrating their effectiveness.[81,82] Recent studies indicate that acupuncture can enhance the regulation of opioid peptides, including β-endorphins and opioid receptors (MOR receptors), as well as γ-aminobutyric acid (GABA), GABA

receptors, 5-HT, and 5-HT receptors. This process involves the upregulation of 5-HT1A and the downregulation of 5-HT7R, which activates the downstream analgesic pathway. This activation promotes phosphorylated signal transduction through protein kinase A (PKA) and extracellular signal-regulated kinase 1/2 (ERK 1/2), culminating in an analgesic effect.[83–85] Furthermore, studies have validated that massage therapy can inhibit the transmission of pain signals to the central brain via the nervous system, thereby reducing the intensity of pain signals received by the brain.[86] Inflammation is also a crucial factor in pain etiology, particularly the inflammatory response mediated by T cells. Research has shown that massage therapy facilitates the transformation of macrophages from the M1 to M2 type, leading to the production of anti-inflammatory cytokines such as IL-4, IL-10, and TGF-β.[87]

Comparison with Other Studies

The current landscape of meta-analyses on FM is somewhat limited, and existing studies typically focus on comparing a specific external treatment with a placebo or conventional drug therapy. For instance, a 2022 meta-analysis on acupuncture, involving 12 studies and 715 subjects, revealed that acupuncture offers both short-term and long-term benefits. In the short term, it effectively alleviates FM pain, while in the long term, it enhances patients' overall health. However, compared to control treatments, acupuncture's impact on fatigue, sleep, and physical function is not entirely conclusive.[82] A 2015 meta-analysis on massage therapy, which incorporated 10 studies, indicated that various types of massage can improve patients' QOL and reduce pain levels to some extent. Subgroup analysis of different massage techniques identified myofascial release therapy as particularly beneficial in improving a range of FM symptoms, notably pain, anxiety, and depression. This study, however, was limited to English and Portuguese literature, implying a focus on Western-style massage rather than TCM approaches.[88] Unlike conventional meta-analyses, NMA allows for the direct and indirect comparison and analysis of multiple treatments, facilitating the identification of the most optimal treatment plan. This research included 41 articles, encompassing nearly all existing CAM treatments for FM. It systematically evaluated the efficacy of various external treatments on pain, fatigue, sleep, and patient safety. Our findings align with those of previous meta-analyses, suggesting that external treatments, particularly acupuncture and massage, are not only safe but also effective in producing analgesic effects in FM patients and substantially improving their QOL.

Limitations and Clinical Significance

This research has certain limitations. Firstly, the inclusion criteria were restricted to Chinese and English literature, leaving out studies published in other languages. This limitation may have resulted in a lack of comprehensive global insights. Secondly, for some types of external treatments, the available research was limited to only one or two studies. This scarcity of data can introduce a certain level of bias and affects the generalizability of the findings. Thirdly, the nature of the treatments makes complete blinding of the subjects challenging. External treatments often require interaction and communication between the physician and the patient, which can influence the patient's perception and response to the treatment. Finally, in the context of FM, there is no established gold standard evaluation index. Measures such as the VAS score and FIQ score are heavily reliant on the subjective experiences of the patients, leading to potential issues with objectivity.

Future research should consider more extensive RCTs with stricter guidelines to enhance data quality. For newer external treatment modalities, there is a need for extensive, multi-center RCT research, and the results should be reported with precision. Given the broad spectrum of FM symptoms, future studies should not only focus on pain evaluation but also incorporate assessments of patients' psychological states for more comprehensive results. Additionally, the safety profiles of these external treatments warrant systematic and scientific evaluation to ensure patient well-being and treatment efficacy.

Conclusion

The findings from this research indicate that external treatments within the realm of CAM are more effective than control treatments in alleviating pain, reducing anxiety, and enhancing sleep quality in FM patients. Furthermore, combining two CAM therapies often yields more favorable outcomes. Collectively, CAM treatments can be regarded as safe and effective for managing FM and may be considered as a viable alternative treatment option.

Data Sharing Statement

The data used to support the findings of this study are available from the published literature.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

References

1. Giorgi V, Sirotti S, Romano ME, et al. Fibromyalgia: one year in review 2022. *Clin Exp Rheumatol*. 2022;40(6):1065–1072. doi:10.55563/clinexprheumatol/if9gk2
2. Marques AP, Santo A, Berssaneti AA, et al. Prevalence of fibromyalgia: literature review update. *Rev Bras Reumatol Engl Ed*. 2017;57(4):356–363. doi:10.1016/j.rbre.2017.01.005
3. Sarzi-Puttini P, Giorgi V, Marotto D, et al. Fibromyalgia: an update on clinical characteristics, aeti-pathogenesis and treatment. *Nat Rev Rheumatol*. 2020;16(11):645–660. doi:10.1038/s41584-020-00506-w
4. Overman CL, Kool MB, Silva JAPD, et al. The prevalence of severe fatigue in rheumatic diseases: an international study. *Clin Rheumatol*. 2016;35(2):409–415. doi:10.1007/s10067-015-3035-6
5. Bigatti SM, Hernandez AM, Cronan TA, et al. Sleep disturbances in fibromyalgia syndrome: relationship to pain and depression. *Arthritis Rheum*. 2008;59(7):961–967. doi:10.1002/art.23828
6. Harding SM. Sleep in fibromyalgia patients: subjective and objective findings.Am. *J Med Sci*. 1998;315(6):367–376. doi:10.1097/00000441-199806000-00005
7. Chinn S, Caldwell W, Gritsenko K. Fibromyalgia pathogenesis and treatment options update. *Curr Pain Headache Rep*. 2016;20(4):25. doi:10.1007/s11916-016-0556-x
8. Antunes MD, Marques AP. The role of physiotherapy in fibromyalgia: current and future perspectives. *Front Physiol*. 2022;13:968292. doi:10.3389/fphys.2022.968292
9. Macfarlane GJ, Kronisch C, Dean LE, et al. EULAR revised recommendations for the management of fibromyalgia. *Ann Rheum Dis*. 2017;76:318–328. doi:10.1136/annrheumdis-2016-209724
10. James PB, Wardle J, Steel A, et al. Traditional, complementary and alternative medicine use in Sub-Saharan Africa: a systematic review. *BMJ Glob Health*. 2018;3(5):e000895. doi:10.1136/bmjgh-2018-000895
11. Kocyigit BF, Sagtaganov Z, Yessirkepov M, et al. Assessment of complementary and alternative medicine methods in the management of ankylosing spondylitis, rheumatoid arthritis, and fibromyalgia syndrome. *Rheumatol Int*. 2023;43(4):617–625. doi:10.1007/s00296-022-05267-1
12. Minakawa Y, Saito S, Matsumoto Y, et al. Effects of acupuncture therapy on drug-resistant fibromyalgia: an exploratory single-arm nonrandomized trial. *Med Acupunct*. 2022;34(3):193–200. doi:10.1089/acu.2022.0005
13. Celenay ST, Kulunkoglu BA, Yasa ME, et al. A comparison of the effects of exercises plus connective tissue massage to exercises alone in women with fibromyalgia syndrome: a randomized controlled trial. *Rheumatol Int*. 2017;37(11):1799–1806. doi:10.1007/s00296-017-3805-3
14. Mist SD, Jones KD. Randomized controlled trial of acupuncture for women with fibromyalgia: group acupuncture with traditional chinese medicine diagnosis-based point selection. *Pain Med*. 2018;19(9):1862–1871. doi:10.1093/pm/pnx322
15. Dias PA, Guimarães ABB, Albuquerque Ade O, et al. Short-term complementary and alternative medicine on quality of life in women with fibromyalgia. *J Integr Med*. 2016;14(1):29–35. doi:10.1016/S2095-4964(16)60235-2
16. Prabhakar A, Kaiser JM, Novitch MB, et al. The role of complementary and alternative medicine treatments in fibromyalgia: a comprehensive review. *Curr Rheumatol Rep*. 2019;21(5):14. doi:10.1007/s11926-019-0814-0
17. Crofford LJ, Appleton BE. Complementary and alternative therapies for fibromyalgia. *Curr Rheumatol Rep*. 2001;3(2):147–156. doi:10.1007/s11926-001-0010-9
18. Kim J, Kim SR, Lee H, et al. Comparing verum and sham acupuncture in fibromyalgia syndrome: a systematic review and meta-analysis. *Evid Based Complement Alternat Med*. 2019;2019:8757685. doi:10.1155/2019/8757685
19. Yang B, Yi G, Hong W, et al. Efficacy of acupuncture on fibromyalgia syndrome: a meta-analysis. *J Tradit Chin Med*. 2014;34(4):381–391. doi:10.1016/s0254-6272(15)30037-6
20. Langhorst J, Klose P, Musial F, et al. Efficacy of acupuncture in fibromyalgia syndrome--A systematic review with a meta-analysis of controlled clinical trials. *Rheumatology*. 2010;49(4):778–788. doi:10.1093/rheumatology/kep439

21. Wolfe F, Smythe HA, Yunus MB, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Report of the Multicenter Criteria Committee. *Arthritis Rheum*. 1990;33(2):160–172. doi:10.1002/art.1780330203
22. Wolfe F, Clauw DJ, Fitzcharles MA, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteriaSemin. *Arthritis Rheum*. 2016;46 (3):319–329. doi:10.1016/j.semarthrit.2016.08.012
23. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res*. 2010;62(5):600–610. doi:10.1002/acr.20140
24. Chinese Rheumatology Association. Guidelines for the diagnosis and treatment of fibromyalgia syndrome, *Chin J Rheumatol*. 2011;15(8):559–561. Chinese. doi:10.3760/cma.j.issn.1007-7480.2011.08.012
25. Higgins JPT, Green S, editors. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration; 2011. Available from http://handbook-5-1.cochrane.org/. Accessed September 15, 2023.
26. Riley RD, Higgins JP, Deeks JJ. Interpretation of random effects meta-analyses. *BMJ*. 2011;342:d549. doi:10.1136/bmj.d549
27. Dias S, Welton NJ, Caldwell DM, et al. Checking consistency in mixed treatment comparison meta-analysis. *Stat Med*. 2010;29(7–8):932–944. doi:10.1002/sim.3767
28. Casanueva B, Rivas P, Rodero B, et al. Short-term improvement following dry needle stimulation of tender points in fibromyalgia. *Rheumatol Int*. 2014;34(6):861–866. doi:10.1007/s00296-013-2759-3
29. Garrido-Ardila EM, González-López-Arza MV, Jiménez-Palomares M, et al. Effects of physiotherapy vs acupuncture in quality of life, pain, stiffness, diffificulty to work and depression of women with fibromyalgia: a randomized controlled trial. *J Clin Med*. 2021;10(17):3765. doi:10.3390/jcm10173765
30. Castro-Sánchez AM, Garcia-López H, Fernández-Sánchez M, et al. Benefits of dry needling of myofascial trigger points on autonomic function and photoelectric plethysmography in patients with fibromyalgia syndrome. *Acupunct Med*. 2020;38(3):140–149. doi:10.1136/acupmed-2017-011504
31. Vittorio S, Erica S, Cinzia C, et al. Comparison between acupuncture and nutraceutical treatment with Migratens® in patients with fibromyalgia syndrome: a prospective randomized clinical trial. *Nutrients*. 2020;12(3):821. doi:10.3390/nu12030821
32. Karatay S, Okur SC, Uzkeser H, et al. Effects of acupuncture treatment on fibromyalgia symptoms, serotonin, and substance P levels: a randomized sham and placebo-controlled clinical trial. *Pain Med*. 2018;19(3):615–628. doi:10.1093/pm/pnx263
33. Guo AS, Li AH. Observation on therapeutic effect of electroacupuncture combined with TDP irradiation on 36 cases of fibromyalgia syndrome. *Med J Communicat*. 2010;24(4):410–411. Chinese.
34. Yang XM, Liu CX. The clinical research into primary fibromyalgia syndrome treated with fibromyalgia mixture in combination with massage. *Henan Tradit Chin Med*. 2017;37(4):689–691. Chinese. doi:10.16367/j.issn.1003-5028.2017.04.0245
35. Nadal-Nicolás Y, Rubio-Arias JA, Martínez-Olcina M, et al. Effffects of manual therapy on fatigue, pain, and psychological aspects in women with fibromyalgia. *Int J Environ Res Public Health*. 2020;17(12):4611. doi:10.3390/ijerph17124611
36. Jiang CJ, Zhang J, Zhang R, et al. Clinical study of treading and balancing manipulation on fibromyalgia syndrome and insomnia. *J Tianjin Univ Tradit Chin Med*. 2022;41(5):579–583. Chinese. doi:10.11656/j.issn.1673-9043.2022.05.08
37. Jiang CJ, Zhang J. Clinical observation of trampling-balancing manipulation for the treatment of patients with fibromyalgia syndrome. *J Guangzhou Univ Tradit Chin Med*. 2023;40(1):136–141. Chinese. doi:10.13359/j.cnki.gzxbtcm.2023.01.022
38. Ozen S, Cosar SNS, Cabioglu MT, et al. A comparison of physical therapy modalities versus acupuncture in the treatment of fibromyalgia syndrome: a pilot study. *J Altern Complement Med*. 2019;25(3):296–304. doi:10.1089/acm.2018.0330
39. Wang LM. Clinical observation on the treatment of fibromyalgia syndrome with immune application therapy at spring and autumn equinox. *Chin J Mod Drug Appl*. 2016;10(17):276–277. Chinese. doi:10.14164/j.cnki.cn11-5581/r.2016.17.181
40. Chen QH, Yao XM. Small needle knife combined with amitriptyline and psychobehavioral therapy Clinical observation on 60 cases of fibromyalgia syndrome. *Chin J Tradit Med Sci Tec*. 2014;21(5):556–557. Chinese.
41. Zhao RH, Zhu YB. Observation on therapeutic effect of herb-partitioned moxibustion on fibromyalgia syndrome. *Zhongguo Zhen Jiu*. 2009;29 (3):200–202. Chinese.
42. Wu X. Clinical observation on local combined with acupoint ozone water injection in the treatment of fibromyalgia syndrome. *Pract Clin J Integr Tradit Chin West Med*. 2021;21(2):80–82. Chinese. doi:10.13638/j.issn.1671-4040.2021.02.038
43. Zhang QQ, Bi N, Zhang ZB, et al. Observation on therapeutic effect of umbilical acupuncture on 35 cases of fibromyalgia syndrome. *Zhejiang J Tradit Chin Med*. 2021;56(7):523. Chinese. doi:10.13633/j.cnki.zjtcm.2021.07.040
44. Wu D, Xiong AS, Ling N, et al. Effect of Acupoint Catgut Embedding on the SOD and MDA in the Fibromyalgia Syndrome Patients. *Clin J Tradit Chin Med*. 2016;28(7):983–986. Chinese. doi:10.16448/j.cjtcm.2016.0348
45. Guo AS, Li AH, Chen X, et al. Clinical effect of observation of acupoint catgut embedding on fibromyalgia syndrome. *Chin J Bas Med Tradit Chin Med*. 2014;20(3):380–381+422. Chinese. doi:10.19945/j.cnki.issn.1006-3250.2014.03.044
46. Wang CM. Treatment of 28 cases of fibromyalgia by semiconductor laser irradiation. *J Pract Tradit Chin Intern Med*. 2008;22(1):58. Chinese. doi:10.13729/j.issn.1671-7813.2008.01.052
47. Wu H, Liu Y. Observation on therapeutic effect of acupuncture at Huatuo Jiaji acupoints combined with electroacupuncture on fibromyalgia syndrome. *Mod J Integr Tradit Chin West Med*. 2022;31(11):1487–1491. Chinese. doi:10.3969/j.issn.1008-8849.2022.11.006
48. Gong WZ, Wang YQ. Observations on the therapeutic effect of acupuncture on fibromyalgia syndrome. *Shanghai J Acu Mox*. 2010;29 (11):725–727. Chinese.
49. Liu Q, Li F. Acupuncture treatment of 30 cases of fibromyalgia. *J Min Inv Med*. 2002;2:183–184. Chinese.
50. Yu JF, Long L, Qin HQ, et al. Clinical observation on the treatment of fibromyalgia syndrome with zhengqingfengtongning combined with acupuncture and moxibustion. *Hubei J Tradit Chin Med*. 2016;38(6):37–38. Chinese.
51. Chen YD. Clinical research of acupuncture, chiropractic therapy combined with amitriptyline in the treatment of fibromyalgia syndrome. *China Prac Med*. 2015;10(23):24–25. Chinese. doi:10.14163/j.cnki.11-5547/r.2015.23.012
52. Fan DH, Su MY. Clinical study on the treatment of back fibromyalgia syndrome with needle knife oblique needling combined with heat-sensitive moxibustion. *J Changchun Univ Tradit Chin Med*. 2012;28(6):983–985. Chinese. doi:10.13463/j.cnki.cczyy.2012.06.056
53. Jia SJ. Treatment of fibromyalgia syndrome with acupuncture medication combined. *J Changchun Univ Tradit Chin Med*. 2013;29(5):802–804. Chinese. doi:10.13463/j.cnki.cczyy.2013.05.017

54. Li CD, Fu XY, Jiang ZY, et al. Clinical study on combination of acupuncture,cupping and medicine for treatment of fibromyalgia syndrome. *Zhongguo Zhen Jiu*. 2006;26(1):8–10. Chinese. doi:10.13703/j.0255-2930.2006.01.003
55. Li DH, Yang L, Li J. Fibromyalgia syndrome treated with acupuncture at the acupoints of the affected meridians and heavy moxibustion at painful points: a randomized controlled trial. *Zhongguo Zhen Jiu*. 2016;36(2):147–151. Chinese. doi:10.13703/j.0255-2930.2016.02.011
56. Yang XM, Liu CX. Clinical effect of massage combined with internal heated needle therapy in treatment of fibromyalgia syndrom. *J Anhui Univ Chin Med*. 2017;36(1):39–42. Chinese. doi:10.3969/j.issn.2095-7246.2017.01.013
57. Xiong XQ, Peng QS, Qian JH. Primary fibromyalgia treated by acupuncture combined with Chinese Massage Therapy. *J Sichuan Tradit Chin Med*. 2015;33(6):159–163. Chinese.
58. Hadianfard MJ, Parizi MH. A randomized clinical trial of fibromyalgia treatment with acupuncture compared with fluoxetine. *Iran Red Crescent Med J*. 2012;14(10):631–640.
59. Martin DP, Sletten CD, Williams BA, et al. Improvement in fibromyalgia symptoms with acupuncture: results of a randomized controlled trial. *Mayo Clin Proc*. 2006;81(6):749–757. doi:10.4065/81.6.749
60. Lauche R, Spitzer J, Schwahn B, et al. Efficacy of cupping therapy in patients with the fibromyalgia syndrome-A randomised placebo controlled trial. *Sci Rep*. 2016;6:37316. doi:10.1038/srep37316
61. Ye YR, Wang J. Effect of Acupuncture on the Sleep and Life Quality in the Fibromyalgia Syndrome Patients. *World J Sle Med*. 2019;6 (8):1054–1056. Chinese. doi:10.3969/j.issn.20957130.2019.01.019
62. Gong ZM, Hayinula G. Therapeutic effect of small needle knife therapy on patients with fibromyalgia syndrome. *Med Equ*. 2016;29(12):87–88. Chinese.
63. Yang CM, Zhang J, Wang Z, et al. Observations on the therapeutic effect of abdominal acupuncture combining with anti-depressant on fibromyalgia syndrome. *J Yunnan Univ Tradit Chin Med*. 2015;38(5):53–55+69. Chinese. doi:10.19288/j.cnki.issn.1000-2723.2015.05.012
64. Cao JQ, Li Y. Treatment of 56 cases of fibromyalgia syndrome with acupuncture and antidepressants. *Chin Arch Tradit Chin Med*. 2003; (5):813–814. Chinese. doi:10.13193/j.archtcm.2003.05.175.caojq.109
65. Wang J, Gao MZ, Gao LQ, et al. Treatment of Fibromyalgia by Tongdu Massage Clinical observation on 31 cases of syndrome. *Chin J Tradit Med Sci Tec*. 2010;17(1):72–73. Chinese.
66. Tang SM, Liu EL, Wang ZW. Clinical study on scraping treatment of fibromyalgia syndrome. *J Sichuan Tradit Chin Med*. 2008;7:108–109. Chinese.
67. Jiang ZY, Li CD, Qiu L, et al. Combination of acupuncture,cupping and medicine for treatment of fibromyalgia syndrome: a multi-central randomized controlled trial. *Zhongguo Zhen Jiu*. 2010;30(4):265–269. Chinese. doi:10.13703/j.0255-2930.2010.04.001
68. Wu XQ. Therapeutic effect of electro-acupuncture and plum-blossom needle combined with chinese herbs in the treatment of fibromyalgia syndrome. *Chin Gen Pract*. 2013;16(36):3621–3623. Chinese. doi:10.3969/j.issn.1007-9572.2013.10.104
69. Sun YZ, Liu YL, Zhao XT, et al. SUN's abdominal acupuncture for depression after methamphetamine withdrawal: a randomized controlled trial. *Zhongguo Zhen Jiu*. 2022;42(1):18–22. doi:10.13703/j.0255-2930.20210515-k0002
70. Harvey RJ, Yee BK. Glycine transporters as novel therapeutic targets in schizophrenia, alcohol dependence and pain. *Nat Rev Drug Discov*. 2013;12(11):866–885. doi:10.1038/nrd3893
71. Siracusa R, Paola RD, Cuzzocrea S, et al. Fibromyalgia: pathogenesis, mechanisms, diagnosis and treatment options update. *Int J Mol Sci*. 2021;22 (8):3891. doi:10.3390/ijms22083891
72. Chon TY, Lee MC. Acupuncture. *Mayo Clin Proc*. 2013;88(10):1141–1146. doi:10.1016/j.mayocp.2013.06.009
73. Moreira RM, Rosário RC, Boggiss EA, et al. Effect of systemic and auricular acupuncture with a 2/100 hz frequency and nogier frequency in fibromyalgia: a randomized clinical trial, pilot study. *J Acupunct Meridian Stud*. 2023;16(4):139–151. doi:10.51507/j.jams.2023.16.4.139
74. Lee B, Kim BK, Kim HJ, et al. Efficacy and safety of electroacupuncture for insomnia disorder: a multicenter, randomized, assessor-blinded, controlled trial. *Nat Sci Sleep*. 2020;12:1145–1159. doi:10.2147/NSS.S281231
75. Yin X, Li W, Wu H, et al. Efficacy of electroacupuncture on treating depression-related insomnia: a randomized controlled trial. *Nat Sci Sleep*. 2020;12:497–508. doi:10.2147/NSS.S253320
76. Qi Y. Umbilicus needling therapy,umbilicus holographic theory and umbilicus diagnosis. *Zhongguo Zhen Jiu*. 2004;24(10):70–75. Chinese. doi:10.13703/j.0255-2930.2004.10.035
77. Wang T, Gong XW, Bao YH, et al. Umbilical acupuncture in the treatment of cervicogenic headache: a randomized controlled. *Study J Zhejiang Chin Med Univ*. 2022;46(11):1283–1287+1291. Chinese. doi:10.16466/j.issn1005-5509.2022.11.018
78. Wang YZ. Internationalization and innovation of abdominal acupuncture. *Zhongguo Zhen Jiu*. 2013;33(9):833–835. Chinese. doi:10.13703/j.0255-2930.2013.09.021
79. Li JH, Duan R, Li L, et al. Unique characteristics of "the second brain"-The enteric nervous system. *Sheng Li Xue Bao*. 2020;72(3):382–390. Chinese. doi:10.13294/j.aps.2020.0032
80. Su IJ, Liao L, Huang FA. Meta-analysis of the effect of abdominal acupuncture on post-stroke depression. *Med Acupunct*. 2021;33(4):269–277. doi:10.1089/acu.2021.0001
81. Li YH, Wang FY, Feng CQ, et al. Massage therapy for fibromyalgia: a systematic review and meta-analysis of randomized controlled trials. *PLoS One*. 2014;9(2):e89304. doi:10.1371/journal.pone.0089304
82. Zheng CQ, Zhou TX. Effect of acupuncture on pain, fatigue, sleep, physical function, stiffness, well-being, and safety in fibromyalgia: a systematic review and meta-analysis. *Pain Res*. 2022;15:315–329. doi:10.2147/JPR.S351320
83. Pei P, Liu L, Zhao LP, et al. Electroacupuncture exerts an anti-migraine effect via modulation of the 5-HT7 receptor in the conscious rat. *Acupunct Med*. 2019;37(1):47–54. doi:10.1136/acupmed-2017-011410
84. Liu L, Xu XB, Qu ZY, et al. Determining 5HT7R's involvement in modifying the antihyperalgesic effects of electroacupuncture on rats with recurrent migraine. *Front Neurosci*. 2021;15:668616. doi:10.3389/fnins.2021.668616
85. Chen Y, Li D, Li N, et al. Role of nerve signal transduction and neuroimmune crosstalk in mediating the analgesic effects of acupuncture for neuropathic pain. *Front Neurol*. 2023;14:1093849. doi:10.3389/fneur.2023.1093849
86. Miake-Lye IM, Mak S, Lee J, et al. Massage for pain: an evidence map. *J Altern Complement Med*. 2019;25(5):475–502. doi:10.1089/acm.2018.0282

87. Waters-Banker C, DuPont-Versteegden EE, Kitzman PH, et al. Investigating the mechanisms of massage efficacy: the role of mechanical immunomodulation. *J Athl Train*. 2014;49(2):266–273. doi:10.4085/1062-6050-49.2.25
88. Yuan SLK, Matsutani LA, Marques AP. Effectiveness of different styles of massage therapy in fibromyalgia: a systematic review and meta-analysis. *Man Ther*. 2015;20(2):257–264. doi:10.1016/j.math.2014.09.003