

Acupuncture and Related Therapies for Endometriosis: A Network Meta-Analysis of Randomized Controlled Trials

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Background: Acupuncture and related therapies are effective and safe ways to relieve the pain, and improve the health and quality of life in women with endometriosis-related pain. However, it is still unclear which treatment is the most effective. Our study aims to summarize the evidence and determine the most effective and safe method to treat the endometriosis.

Methods: We searched PubMed, EMBASE, Cochrane Library, and Web of science, China Biology Medicine, China National Knowledge Infrastructure, Wan fang Data, Chinese Scientific Journal Database and conducted manual searches of relevant papers, summarized randomized clinical trials of acupuncture-related therapies for endometriosis from database inception to 21 April 2024. After independent literature screening and data extraction that pain VAS was selected as the primary outcome measure. The quality evaluation was conducted by Review Manager 5.4. Perform network meta-analysis (NMA) used Stata 15.0 software.

Results: Forty-two eligible trials involving six acupuncture-related interventions and 3,635 participants were included in this NMA. Pairwise meta-analyses show that combination therapy was more efficacious than western medicine and Chinese herb medicine for pain VAS scores, serum CA125 level and response rate results. The NMA estimates indicated that: for pain VAS scores, acupuncture (SMD: -2.33; 95% CI: -4.37, -0.29) and combination therapy (SMD: 1.79 95% CI: 1.21, 2.41) were superior to western medicine. For serum CA125 level, acupoint application (SMD: -11.33 95% CI: -20.28, -2.97) and combination therapy (SMD: 6.20; 95% CI: 1.60, 10.75) were associated with better efficacy when considered alongside western medicine. For response rate, combination therapy (SMD: 0.20; 95% CI: 0.14, 0.29) and auricular therapy (SMD: 8.01; 95% CI: 2.08, 45.37) were more efficacious than western medicine. The comprehensive ranking results show that acupoint catgut embedding was the best performing at lowering pain VAS scores, acupoint application was identified as the most effective in reducing serum CA125 level, and auricular therapy was ranked first in improving the response rate.

Conclusion: Acupoint catgut embedding, auricular therapy, acupoint application and combination therapy may be the best solutions for the treatment of endometriosis. Additional trials are needed to develop higher-quality evidence and optimal regimens.

Keywords: acupuncture, endometriosis, randomized controlled trials, network meta-analysis

Introduction

Endometriosis (EMs) is characterized by the endometrial tissue appears, grows, infiltrates, and bleeds repeatedly in the lining of the uterus and in areas outside of the uterus, subsequently causing pain, joint pain, infertility, and nodules.^{1,2} Clinical manifestations include dysmenorrhea, pelvic pain, dyspareunia, and infertility.³ It affects approximately 6% to 10% of women of childbearing age.⁴ Epidemiological studies reveal that women with EMs have a higher risk of developing ovarian and breast cancer, melanoma, asthma, rheumatoid arthritis, and cardiovascular disease.⁵ EMs

seriously affects women's physical health, mental health and quality of life.⁶ Therefore, effective interventions remain critical. Currently, the mainstay of drug therapy for EMs is hormone suppressive drugs.⁷ In the context of endometriosis-related pain in patients with no current plans to become pregnant: combined oral contraceptives or progestins are low-cost drugs that should be considered as a first-line medical therapy.⁸

Although medication is helpful, a large proportion of women (10.0–43.5%) discontinue drugs due to the presence of side effects, such as uterine bleeding, vomiting, breast discomfort, depression, weight gain, and moodiness.^{9–12} As such, non-pharmacological approaches are favoured. Acupuncture and its related therapies are characterized by safety and few side effects, and have unique advantages in treating diseases. Acupuncture and related therapies can be roughly divided into invasive and non-invasive methods. Invasive methods include manual acupuncture, electroacupuncture, or ear acupuncture. Non-invasive methods include acupressure, moxibustion, and application of various stimulating patches and pellets.¹³ Studies have shown that acupuncture and related therapies are effective and safe ways to relieve dysmenorrhea, shortening the pain duration, and improve the health and quality of life in women with endometriosis-related pain.^{14,15}

Although acupuncture has been investigated for pain relief and there is still a lack of efficacy comparison between different acupuncture and related therapies. It is still unknown which acupuncture-related therapies is more effective in treating endometriosis. The current studies^{14–18} are limited to traditional meta-analysis and have not compared different acupuncture-related therapies. Therefore, this work aims to determine the efficacy of each acupuncture therapy on endometriosis by using network meta-analysis (NMA) and ranking the different types of acupuncture-related therapies. We hope that this study will provide clinicians with a clear understanding of the efficacy of different acupuncture treatments, assist patients with endometriosis in selecting the optimal treatment plan, and offer researchers insights into potential avenues for future study designs.

Methods

PROSPERO has registered the protocol (CRD42024534622). This research was based on the checklist of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) 2020 and extension statement for network meta-analyses (PRISMA-NMA), as well as the reporting items of systematic reviews and meta-analyses related to acupuncture^{19,20} ([Appendix 1](#)).

Strategy for Literature Search

In order to obtain RCTs of acupuncture-related therapies for EMs, we searched four English databases (PubMed, EMBASE, Cochrane Library, and Web of Science) and four Chinese databases [China Biology Medicine (CBM), China National Knowledge Infrastructure (CNKI), Wan Fang Data, and Chinese Scientific Journal Database (VIP)] for literature on acupuncture-related therapies for endometriosis from inception to 21 April 2024. Use a combination of Medical Subject Headings (MeSH) and free words for retrieval. The MESH keywords included “Acupuncture”, “Acupuncture Points”, “Ear Acupuncture”, “Acupuncture Analgesia”, “Acupuncture Therapy”, “Endometriosis”, “Endometrioma”, “Randomized Controlled Trial”, “RCT”. In addition, manual searches of reference lists in relevant articles. Language is English or Chinese. The complete search strategy is recorded in [Appendix 2](#).

Inclusion Criteria

(1) Population: The definitive diagnostic criteria of EMs have been reported in the literature, such as guideline, expert consensus, or textbook. (2) Intervention: The following interventions of treatment group were available: acupuncture (AC), electro-acupuncture (EA), moxibustion (MOX), and other acupuncture-related therapies (such as auricular therapy (AT), acupoint catgut embedding (ACE), acupoint application (AA) or the comparison of various acupuncture-related therapies). (3) Comparison: The control group was acupuncture-related techniques with other techniques or non-acupuncture treatment. (4) Outcomes: The primary outcome measure was the pain visual analogue scale (VAS), while secondary outcomes included serum cancer antigen 125 (CA125) level and response rate. (5) Study Design: Randomized controlled trials (RCTs) from peer-reviewed articles in Chinese or English were included.

Exclusion Criteria

(1) The same group included three and more interventions. (2) Studies that did not report clear original data of outcome indicators. (3) Similar studies or studies reporting the same results. (4) Conference abstracts and dissertations.

Primary and Secondary Outcomes

Primary outcome: pain visual analogue scale (VAS).

Secondary outcomes: serum cancer antigen 125 (CA125) level and response rate.

Data Extraction

Two reviewers (YW, YG) extracted and collated the following data using a standardized data extraction form include study characteristics (the name of the author and the journal, year of publication), population (age, sample size, disease duration), intervention (name, treatment duration and frequency), outcomes, and adverse effects. They assessed these full-text papers, independently and in duplicate. Another author (GZ) compared the two data extraction forms to evaluated and validated all data extraction.

We aimed to calculate mean and standard deviation change from baseline and postintervention values about pain VAS and serum CA125 level. For literature reporting VAS scores for multiple pains, including pelvic pain, dysmenorrhea, and dyspareunia, means and standard deviations were obtained after combining the subgroups. For articles that only reported 95% CI or IQR, they were converted to mean and standard deviation before proceeding to the next step of analysis.^{21,22} In addition, for the response rate, we classified the clinically cured, effective, apparently effective reported in the literature as response, and the ineffective as non-response. If the trial had been a three-arm trial, it was split and reorganized into all paired two-arm trials. Statistical tables of raw data in [Appendix 3](#).

Risk Assessment of Bias in Inclusion Studies

Review Manager 5.4 and IBM SPSS Statistics 21.0 were used to assess the risk of bias in included literature and calculate the weighted Cohen's kappa coefficient (κ).²³ Each randomized controlled trial was evaluated according to the following seven items: (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); (7) Other bias. Two reviewers (ZX and XL) independently conducted a bias risk assessment. Any disagreements were resolved through consensus.

Statistical Analysis

Paired meta-analysis was conducted using the Stata software program (Version 15.0).²⁴ We analyze each treatment separately to determine the standard mean difference (SMD) in pain VAS scores and serum CA125 level between the different acupuncture-related therapies. For the categorically variable of response rate, risk ratio (RR) was used. The use of fixed or random effects approaches were depended on the presence of heterogeneity, with random effects analysis should be applied when the I-square (I^2) was greater than 50%, otherwise a fixed-effect model should be used.

To facilitate the comparison of acupuncture-related therapies that were not directly compared in RCTs, we performed NMAs. A network diagram was created to visualize the direct and indirect comparison of different acupuncture-related therapy modes. We used the mvmeta and network packages in Stata and GeMTC 0.14.3 for Bayesian statistical calculations. GeMTC is based on the Markov Chain Monte Carlo (MCMC) consensus model within the Bayesian framework. Simulations are performed using four chains, with the number of iterations set to 400,000 (the first 20,000 for annealing), and the steady state of the model is tested by evaluating the Potential Scale Reduction Factor (PSRF). The ranking probability analysis was conducted to generate the cumulative area under the ranking curve (SUCRA) value for acupuncture-related therapies. Using closed-loop evaluation to compare the inconsistency between the size of direct and indirect effects, if the 95% CI of the inconsistency factor (if) includes 0, then the direct and indirect evidence is consistent. Detailed steps of inconsistency testing in [Appendix 4](#). Construct a funnel plot to evaluate the presence of small sample effects in the included studies.

Results

Study Search and Description

A total of 808 relevant experiments were found through literature search. Following the deduplication process, 523 studies have been retained. After reading the title and abstract, there are 169 remaining. Further detailed full-text screening was conducted, with 127 studies excluded because they did not meet the established criteria. Therefore, the final screening included 42 RCTs^{25–66} with 3,656 patients with EMs, of which 2 RCTs were in English,^{25,26} one was a three-arm trial³⁹ and the others were all two-arm trials. Eleven interventions were included: acupuncture (AC), electro-acupuncture (EA), moxibustion (MOX), auricular therapy (AT), acupoint catgut embedding (ACE), acupoint application (AA), Chinese herb medicine (CH), hormone drugs (western medicine, WM), usual care (UC), sham acupuncture (sAC) and combination therapy (any acupuncture-related therapy combination of the other therapies). Figure 1 illustrates the results of the literature screening. Tables 1 and 2 record the baseline data, detailed acupuncture intervention methods, and outcome indicators of the included studies.

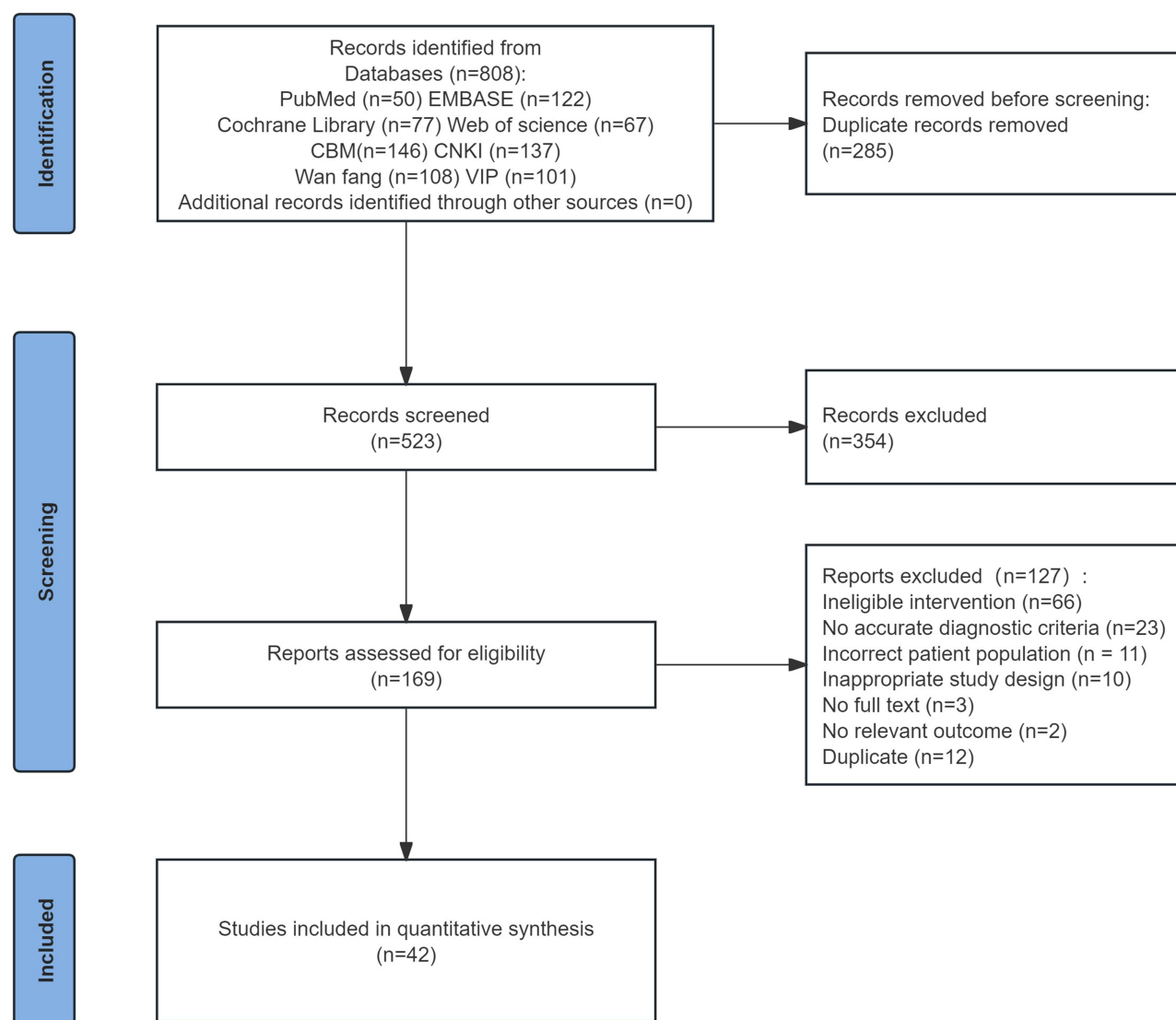


Figure 1 Flow diagram of preferred reporting items identified, included, and excluded for systematic reviews and meta-analyses (PRISMA).

Table I Baseline Characteristics of the Included Studies

References	Country	Diagnostic Criteria	Intervention			Control			Type of Outcomes
			Treatment	n	Years (Mean \pm sd)/Range	Treatment	n	Years (Mean \pm sd)/Range	
Li P S 2023 ²⁵	China	CMA	AC	51	30.3 \pm 4.6	sAC	53	30.1 \pm 4.5	①
Armour M 2021 ²⁶	Australia	PD	Combination therapy	14	33.4 \pm 7.3	UC	15	33.4 \pm 7.3	①
Xiang DF 2001 ²⁷	China	GCTNPCM	AT	37	22–45	CH	30	24–47	③
Jin YB 2009 ²⁸	China	COG	AT	40	33.83 \pm 5.88	EA	40	34.93 \pm 6.15	③
Zhang H 2018 ²⁹	China	CMA	Combination therapy	42	37 \pm 9	CH	41	36 \pm 8	②
Xiang DF 2011 ³⁰	China	CMA	AC	30	34.6 \pm 5.9	CH	28	34.6 \pm 4.9	①②
Chen LN 2010 ³¹	China	GCTNPCM	AC	35	17–41	WM	26	17–41	③
Zhang P 2017 ³²	China	OG and GTCM	MOX	45	35.8 \pm 7.8	WM	45	33.5 \pm 6.8	②③
Jiang BF 2018 ³³	China	GCTNPCM	Combination therapy	48	30.25 \pm 7.58	WM	48	32.60 \pm 10.01	①③
Teng H 2016 ³⁴	China	CAIM	AC	43	39 \pm 4	WM	37	38 \pm 3	②
Ma WJ 2023 ³⁵	China	OG	Combination therapy	64	32.42 \pm 4.16	WM	64	31.18 \pm 4.63	①②③
Yu WT 2022 ³⁶	China	CMA	Combination therapy	36	32.03 \pm 6.64	CH	36	33.89 \pm 4.55	①②③
Lu S 2014 ³⁷	China	PD	MOX	37	30.0 \pm 10.23	CH	32	30.0 \pm 9.23	③
Zhang XH 2017 ³⁸	China	OG	Combination therapy	45	22.80 \pm 7.20	CH	45	21.70 \pm 6.30	①②③
Niu XX 2012 ³⁹	China	CMA	MOX	31	21–45	Combination therapy	33	21–45	②
			CH	29	21–45				
An XY 2016 ⁴⁰	China	CMA	AA	34	28.2 \pm 2.2	WM	33	27.8 \pm 2.3	①②③
Chen YB 2021 ⁴¹	China	GTCM	Combination therapy	35	35 \pm 7	WM	35	34 \pm 8	③
Xu LP 2017 ⁴²	China	CMA and GCTNPCM	Combination therapy	30	31.23 \pm 3.23	WM	30	31.24 \pm 3.22	①②③
Pan HL 2023 ⁴³	China	CMA	Combination therapy	46	30.51 \pm 4.57	WM	45	30.63 \pm 4.59	①②③
Wei W 2015 ⁴⁴	China	CMA	Combination therapy	30	35.6 \pm 8.9	WM	30	36.1 \pm 8.3	②③
Ru HM 2015 ⁴⁵	China	OG	Combination therapy	135	24–35	WM	134	23–33	③
Liu YL 2023 ⁴⁶	China	CMA	Combination therapy	30	33.57 \pm 2.36	WM	30	33.12 \pm 2.81	②
Yu L 2021 ⁴⁷	China	COG	Combination therapy	30	34.28 \pm 5.17	WM	30	35.57 \pm 4.82	①②
Wu JX 2013 ⁴⁸	China	GCTNPCM	Combination therapy	30	23–46	WM	30	26–45	③
Zhao JQ 2023 ⁴⁹	China	CMA	Combination therapy	40	36.98 \pm 5.32	CH	40	36.58 \pm 3.84	①③
Wan YT 2022 ⁵⁰	China	OG	Combination therapy	115	34.97 \pm 6.84	CH	60	35.75 \pm 8.52	③
Fang LX 2018 ⁵¹	China	OG, GCTNPCM, and GTCM	Combination therapy	40	30.5 \pm 2.8	ACE	40	32.5 \pm 1.2	③
Dong Q 2022 ⁵²	China	GTCM	Combination therapy	60	31.72 \pm 4.67	MOX	60	31.68 \pm 4.56	③
Zeng R 2010 ⁵³	China	CAIM	Combination therapy	40	35 \pm 6.5	AC	40	36 \pm 6.8	③
Wang YJ 2018 ⁵⁴	China	GCTNPCM	Combination therapy	40	37.8 \pm 3.5	CH	40	35.2 \pm 3.6	③
Zuo DD 2020 ⁵⁵	China	CMA and GCTNPCM	Combination therapy	43	39.79 \pm 4.55	WM	43	40.98 \pm 5.00	①③

(Continued)

Table I (Continued).

References	Country	Diagnostic Criteria	Intervention			Control			Type of Outcomes
			Treatment	n	Years (Mean ± sd)/Range	Treatment	n	Years (Mean ± sd)/Range	
Cong HF 2018 ⁵⁶	China	CMA	ACE	33	33.94 ± 5.98	AC	32	31.31 ± 5.86	① ③
Men JN 2023 ⁵⁷	China	CMA	Combination therapy	52	32.63±4.69	CH	47	32.05±4.21	① ② ③
Zhang MY 2017 ⁵⁸	China	GCTNPCM	Combination therapy	60	40.25±2.43	WM	60	40.19±2.3	②
Xi LL 2021 ⁵⁹	China	GTCM	Combination therapy	40	32±7	WM	40	32±7	③
Zhang CM 2023 ⁶⁰	China	GCTNPCM	Combination therapy	40	34.25±7.56	AC	40	34.40±7.47	③
Chen M 2010 ⁶¹	China	GCTNPCM	Combination therapy	34	30.7±5.48	CH	36	30.2±8.21	③
Feng Y 2014 ⁶²	China	GCTNPCM	Combination therapy	39	30.6±3.1	WM	39	31.3±3.2	③
Li X 2020 ⁶³	China	CMA	Combination therapy	30	40.2 ± 5.6	WM	30	40.1 ± 5.7	② ③
Hu YG 2019 ⁶⁴	China	PD	Combination therapy	30	23–46	WM	30	23–47	③
Liu ZX 2016 ⁶⁵	China	GCTNPCM	Combination therapy	30	31.64 ± 8.12	WM	30	30.43 ± 7.63	① ③
Du X 2010 ⁶⁶	China	PD	Combination therapy	93	32–46	WM	93	33–45	③

Abbreviations: CMA, Chinese Medical Association; PD, Pathologic Diagnosis; GCTNPCM, Guideline for Clinical Trials of New Patent Chinese Medicines; COG, Chinese Obstetrics & Gynecology; OG, Obstetrics and Gynecology; GTCM, Gynecologic Terms in Chinese Medicine; CAIM, Chinese Association of Integrative Medicine; AC, acupuncture; EA, electro-acupuncture; MOX, moxibustion; AT, auricular therapy; ACE, acupoint catgut embedding; AA, acupoint application; CH, Chinese herb medicine; WM, western medicine; UC, usual care; sAC, sham acupuncture. ① VAS scores; ② CAI25; ③ response rate.

Table 2 Descriptions of the Included Acupuncture and Related Therapies That are Included

References	Intervention	Acupuncture Points Used	Retention Time	Acupuncturist Qualifications	Acupuncture Reaction	Timing of Treatment	Frequency and Course of Acupuncture
Li P S 2023 ²⁵	AC	Guanyuan (CV4), Sanyinjiao (SP6), Taichong (LR3), Zhaohai (KI6), Qichong (ST30)	30 min	Y	Y	N	Three a week for 12 weeks
	sAC	Guanyuan (CV4), Sanyinjiao (SP6), Taichong (LR3), Zhaohai (KI6), Qichong (ST30)	30 min	Y	N	N	Three a week for 12 weeks"
Armour M 2021 ²⁶	Combination therapy	AC+UC:Sanyinjiao (SP6), Diji (SP8), Xuehai (SP10), Guilai (ST25), Zusanli (ST36), Zhongji (CV3), Guanyuan (CV4), Taichong (LR3)	25–30 min	N	Y	N	Two a week for 8 weeks
Xiang DF 2001 ²⁷	AT	Tingzhong(CO _{6.10}), Pizhixia(AT ₄), Neifenmi(CO ₁₈), Jiaogan(AH _{6a}), Neishengzhiqi(TF ₂)	N	N	N	Treatment is started 5 days before menstruation until menstruation occurs	Every other day, 4 times a month for 3 months
Jin YB 2009 ²⁸	AT	Neishengzhiqi(TF ₂), Pizhixia(AT ₄), Shenmen(TF ₄), Neifenmi(CO ₁₈)	30 min	N	N	Stop treatment during menstruation	Every other day for 3 months
	EA	Qihai (CV6), Guanyuan (CV4), Sanyinjiao (SP6), Diji (SP8), Tianshu (ST25), Zigong (EX-CA1)	30 min	N	Y	Stop treatment during menstruation	Every other day for 3 months
Zhang H 2018 ²⁹	Combination therapy	AC+CH:Zhongwan (CV12), Xiawan (CV10), Qihai (CV6), Guanyuan (CV4), Shuidao (ST28), Zigong (EX-CA1), Shangliao (BL31), Ciliao (BL32), Zhongliao (BL33), Xialiao (BL34)	30 min	N	N	N	Five a week for 3 months
Xiang DF 2011 ³⁰	AC	Zhongwan (CV12), Xiawan (CV10), Qihai (CV6), Guanyuan (CV4), Zhongji (CV3), Wailing (ST26), Shuidao (ST28), Qixue (KI13)	20 min	N	N	Treatment is started 1 week before menstruation until menstruation occurs	Three a week for 3 months
Chen LN 2010 ³¹	AC	Zhongwan (CV12), Xiawan (CV10), Qihai (CV6), Guanyuan (CV4), Zhongji (CV3), Wailing (ST26)	30 min	N	N	Treatment is started 1 week before menstruation until menstruation occurs	Once a day for 3 months
Zhang P 2017 ³²	MOX	Dazhui (GV14), Mingmen (GV4)	N	N	N	N	Every other day for 3 months
Jiang BF 2018 ³³	Combination therapy	MOX+CH:Zigong (EX-CA1), Zhongji (CV3), Guanyuan (CV4), Qihai (CV6), Zusanli (ST36), Sanyinjiao (SP6)	15–20 min	N	N	N	Once a day for 12 weeks

(Continued)

Table 2 (Continued).

References	Intervention	Acupuncture Points Used	Retention Time	Acupuncturist Qualifications	Acupuncture Reaction	Timing of Treatment	Frequency and Course of Acupuncture
Teng H 2016 ³⁴	AC	Zhongji (CV3), Guanyuan (CV4), Zigong (EX-CA1), Shangliao (BL31), Ciliao (BL32), Zhongliao (BL33), Xialiao (BL34), Shuidao (ST28), Guilai (ST25), Shenshu (BL23), Pigen (EX-B4), Sanyinjiao (SP6)	N	N	N	N	Two a week for 3 months
Ma WJ 2023 ³⁵	Combination therapy	AC+WM:Geshu (BL17), Taichong (LR3), Xuehai (SP10), Qihai (CV6), Sanyinjiao (SP6)	30 min	N	N	N	Once a day for 3 months
Yu WT 2022 ³⁶	Combination therapy	AA+CH:Shenque (CV8), Guanyuan (CV4), Qihai (CV6), Zigong (EX-CA1)	4h	N	N	Stop treatment during menstruation	Once a day for 3 months
Lu S 2014 ³⁷	MOX	Zhongji (CV3), Guanyuan (CV4), Qihai (CV6)	30 min	N	N	N	Three a week for 3 weeks
Zhang XH 2017 ³⁸	Combination therapy	MOX+CH:Guanyuan (CV4), Shenque (CV8), Zigong (EX-CA1), Sanyinjiao (SP6), Xuehai (SP10), Diji (SP8)	N	N	N	Treatment is started 2 days before menstruation until menstruation occurs	Once a day for 3 months
Niu XX 2012 ³⁹	MOX	Guanyuan (CV4), Zhongji (CV3), Zigong (EX-CA1), Sanyinjiao (SP6)	N	N	N	Treatment is started 1–2 days before menstruation until menstruation occurs	Once a day for 3 months
	Combination therapy	MOX+CH:Guanyuan (CV4), Zhongji (CV3), Zigong (EX-CA1), Sanyinjiao (SP6)	N	N	N	Treatment is started 1–2 days before menstruation until menstruation occurs	Once a day for 3 months
An XY 2016 ⁴⁰	AA	Shenque (CV8), Zhongji (CV3), Zigong (EX-CA1), Ciliao (BL32)	6h	N	N	N	Once a day for 3 months
Chen YB 2021 ⁴¹	Combination therapy	MOX+WM:Guanyuan (CV4), Zigong (EX-CA1), Xuehai (SP10)	30 min	N	N	N	Every other day for 3 months
Xu LP 2017 ⁴²	Combination therapy	MOX+CH:Ashi points, Guanyuan (CV4), Qihai (CV6), Qugu (CV2), Sanyinjiao (SP6), Zusanli (ST36), Shenshu (BL23)	20–30 min	N	N	Treatment is started 1 week before menstruation until menstruation occurs	Once a day for 3 months
Pan HL 2023 ⁴³	Combination therapy	MOX+AA:Shenque (CV8), Qihai (CV6), Guilai (ST25), Shenshu (BL23), Shangliao (BL31), Ciliao (BL32), Zhongliao (BL33), Xialiao (BL34), Ashi points	20 min	N	N	Treatment starts in the second half of the menstrual cycle for 10 consecutive sessions	Once a day for 3 months
Wei W 2015 ⁴⁴	Combination therapy	AC+CH:Zhongji (CV3), Guanyuan (CV4), Daheng (SP15), Tianshu (ST25), Wailing (ST26), Zusanli (ST36), Sanyinjiao (SP6)	20 min	N	N	N	3 months

Ru HM 2015 ⁴⁵	Combination therapy	AC+CH:Sanyinjiao (SP6), Qixue (KI13), Dahe (KI12), Zigong (EX-CA1), Diji (SP8), Taixi (KI3), Qihai (CV6), Guanyuan (CV4)	N	N	N	N	3 months
Liu YL 2023 ⁴⁶	Combination therapy	ACE+WM:Shenque (CV8), Guanyuan (CV4), Qihai (CV6), Zhongji (CV3), Zigong (EX-CA1)	N	N	N	N	Once a day for 12 weeks
Yu L 2021 ⁴⁷	Combination therapy	ACE+CH:Shenshu (BL23)	N	N	N	N	Once a month for 12 months
Wu JX 2013 ⁴⁸	Combination therapy	EA+CH enema:Zhongji (CV3), Guanyuan (CV4), Zigong (EX-CA1), Sanyinjiao (SP6), Diji (SP8), Xuehai (SP10), Taichong (LR3)	40 min	N	Y	N	Once a day for 3 months
Zhao JQ 2023 ⁴⁹	Combination therapy	AC+CH:Sanyinjiao (SP6), Qihai (CV6), Baihui (GV20)	50 min	N	Y	N	Six a week for 3 months
Wan YT 2022 ⁵⁰	Combination therapy	AA+CH:Shenque (CV8), Guilai (ST25), Zigong (EX-CA1), Guanyuan (CV4), Shenshu (BL23), Yaoyangguan (GV3)	2 h	N	N	Treatment for 14 days after the end of menstruation	Once a day for 3 months
Fang LX 2018 ⁵¹	Combination therapy	ACE+CH:Diji (SP8), Sanyinjiao (SP6), Shenshu (BL23), Xuehai (SP10)	N	N	N	N	Two a week for 5 months
	ACE	Diji (SP8), Sanyinjiao (SP6), Shenshu (BL23), Xuehai (SP10)	N	N	N	N	Two a week for 5 months
Dong Q 2022 ⁵²	Combination therapy	MOX+CH:Xuehai (SP10), Sanyinjiao (SP6), Zigong (EX-CA1), Tianshu (ST25), Guanyuan (CV4), Zhongji (CV3)	10 min	N	N	Treatment is started 2 days before menstruation until menstruation occurs	Once a day for 3 months
	MOX	Xuehai (SP10), Sanyinjiao (SP6), Zigong (EX-CA1), Tianshu (ST25), Guanyuan (CV4), Zhongji (CV3)	10 min	N	N	N	Once a day for 3 months
Zeng R 2010 ⁵³	Combination therapy	AC+MOX:Guanyuan (CV4), Zhongji (CV3), Tianshu (ST25), Zusanli (ST36), Sanyinjiao (SP6), Taichong (LR3)	30 min	N	Y	N	Once a day for 2 months
	AC	Guanyuan (CV4), Zhongji (CV3), Tianshu (ST25), Zusanli (ST36), Sanyinjiao (SP6), Taichong (LR3)	30 min	N	Y	N	Once a day for 2 months
Wang YJ 2018 ⁵⁴	Combination therapy	MOX+CH:Guanyuan (CV4), Qihai (CV6), Zhongji (CV3), Sanyinjiao (SP6), Hegu (LI4)	30 min	N	N	Treatment is started 3 days before menstruation until menstruation occurs	Once a day for 3 months
Zuo DD 2020 ⁵⁵	Combination therapy	ACE+WM:Guanyuan (CV4), Tianshu (ST25), Zhongji (CV3), Zigong (EX-CA1), Diji (SP8), Qihai (CV6), Ciliao (BL32), Taichong (LR3), Xuehai (SP10), Zusanli (ST36), Sanyinjiao (SP6)	N	N	N	N	Once a month for 3 months
Cong HF 2018 ⁵⁶	ACE	Sanyinjiao (SP6), Xuehai (SP10), Diji (SP8), Zigong (EX-CA1), Guanyuan (CV4)	N	N	N	N	Once a week for 12 weeks

(Continued)

Table 2 (Continued).

References	Intervention	Acupuncture Points Used	Retention Time	Acupuncturist Qualifications	Acupuncture Reaction	Timing of Treatment	Frequency and Course of Acupuncture
Men JN 2023 ⁵⁷	AC	Sanyinjiao (SP6), Xuehai (SP10), Diji (SP8), Zigong (EX-CA1), Guanyuan (CV4)	30 min	N	Y	N	Three a week for 12 weeks
Zhang MY 2017 ⁵⁸	Combination therapy	ACE+CH:Shenshu (BL23), Ciliao (BL32), Qihai (CV6), Guanyuan (CV4), Tianshu (ST25), Zigong (EX-CA1), Zusanli (ST36), Sanyinjiao (SP6)	N	N	N	N	Once a month for 3 months
Xi LL 2021 ⁵⁹	Combination therapy	ACE+CH:Shenshu (BL23), Sanyinjiao (SP6), Ciliao (BL32), Zigong (EX-CA1), Xuehai (SP10), Guanyuan (CV4)	N	N	N	N	N
Zhang CM 2023 ⁶⁰	Combination therapy	AC+WM:Zigong (EX-CA1), Xuehai (SP10), Sanyinjiao (SP6), Hegu (LI4), Taichong (LR3)	30 min	N	Y	N	Every other day for 3 months
	Combination therapy	AC+CH:Zhongwan (CV12), Qihai (CV6), Guanyuan (CV4), Zhongji (CV3)	30 min	N	Y	Stop treatment during menstruation	Two a week for 12 weeks
	AC	Zhongwan (CV12), Qihai (CV6), Guanyuan (CV4), Zhongji (CV3)	30 min	N	Y	Stop treatment during menstruation	Two a week for 12 weeks
Chen M 2010 ⁶¹	Combination therapy	AC+AA:Zhongji (CV3), Guanyuan (CV4), Zigong (EX-CA1), Sanyinjiao (SP6)	N	N	N	N	Once a day for 3 months
Feng Y 2014 ⁶²	Combination therapy	AC+CH:Qihai (CV6), Guanyuan (CV4), Sanyinjiao (SP6), Qixue (KI13), Dahe (KI12), Zigong (EX-CA1), Diji (SP8), Taixi (KI3)	30 min	N	Y	Treatment starts 3–5 days before menstruation for 7 consecutive days	Once a day for 3 months
Li X 2020 ⁶³	Combination therapy	ACE+CH enema:Shenshu (BL23)	N	N	N	N	Two a month for 3 months
Hu YG 2019 ⁶⁴	Combination therapy	MOX+CH:Shenshu (BL23), Zhongji (CV3), Ciliao (BL32), Zigong (EX-CA1), Qihai (CV6), Guanyuan (CV4), Sanyinjiao (SP6)	15–20 min	N	N	N	Once a day for 12 weeks
Liu ZX 2016 ⁶⁵	Combination therapy	MOX+CH:Zigong (EX-CA1), Zhongji (CV3), Ciliao (BL32), Guanyuan (CV4), Qihai (CV6), Shenshu (BL23), Zusanli (ST36), Fenglong (ST40), Sanyinjiao (SP6)	15–20 min	N	N	Treatment starts 1 days before menstruation for 7 consecutive days	Once a day for 3 months
Du X 2010 ⁶⁶	Combination therapy	AT+CH:Neishengzhiqi (TF ₂), Gan (CO ₁₂), Yidan (CO ₁₁), Shen (CO ₁₀), Fu (AH ₈), Shengshangxian (TG _{2p}), Erbeigou (P ₃), Ermigen (R ₂), Pizhixia (AT ₄), Neifenmi (CO ₁₈)	2–3 min	N	N	N	2–3 times a week for 6 months

Notes: Y, reported; N, No reported.

Abbreviations: AC, acupuncture; EA, electro-acupuncture; MOX, moxibustion; AT, auricular therapy; ACE, acupoint catgut embedding; AA, acupoint application; CH, Chinese herb medicine; WM, western medicine; UC, usual care; sAC, sham acupuncture.

Quality Assessment of Included Studies

The risk of bias for each trial is shown in [Figure 2](#). In 42 trials, 32 studies (76.19%) had a low risk, 9 studies (21.43%) had an unclear risk, and 1 study (2.38%) had a high risk for the random sequence generation ($Kappa=0.675$). Four studies (9.52%) had a low risk, 38 studies (90.48%) had an unclear risk of allocation concealment ($Kappa=1$). One study (2.38%) had a low risk, 41 studies (97.62%) had a high risk of blinding of participants and personnel ($Kappa=0.656$). Three studies (7.14%) had a low risk, 39 studies (92.86%) had an unclear risk of blinding of outcome assessment ($Kappa=1$). Thirty studies (71.43%) had a low risk, 12 studies (28.57%) had an unclear risk of blinding of incomplete outcome data ($Kappa=0.667$). Forty-two studies (100%) had a low risk for the selective reporting ($Kappa=1$) and other bias ($Kappa=1$).

Results of Pairwise Meta-Analyses

Pairwise meta-analyses show that combination therapy was more efficacious than WM and CH for pain VAS, CA125 and response rate results ([Table 3](#)).

Network Meta-Analysis Results

Three network plots were constructed using Stata 15.0. The thicker the line, the more studies there are on the two intervention measures, and circle size is positively correlated with the sample size of patients for the corresponding intervention ([Figure 3](#)).

17 studies reported pain VAS scores, involving eight interventions and 1,305 patients. The findings of the NMA indicated that AC was more effective than WM (SMD: -2.33 ; 95% CI: $-4.37, -0.29$). Furthermore, combination therapy demonstrated superior efficacy compared to CH (SMD: 1.07 ; 95% CI: $0.23, 1.92$), UC (SMD: 2.57 ; 95% CI: $0.12, 5.02$), and WM (SMD: 1.79 ; 95% CI: $1.21, 2.41$) ([Table 4](#)). The results of the ranking exercise indicated that the four most effective interventions in reducing the VAS scores were ACE (76.8%), AA (70.1%), AC (66.6%), and combination therapy (66.6%), while the least effective was WM (10.2%; [Figure 4A](#)).

A total of 18 studies were identified that reported on CA125, involving seven distinct interventions and 1,457 patients. The analysis results of the NMA demonstrated that AA was more effective than AC SMD: $(-10.40, 95\% \text{ CI: } -19.29, -0.88)$, CH (SMD: -9.57 95% CI: $-17.79, -1.96$), MOX (SMD: -11.33 95% CI: $-20.28, -2.97$), and WM (SMD: -11.86 95% CI: $-18.81, -4.86$). The combination therapy demonstrated superior efficacy compared to CH (SMD: 4.41 ; 95% CI: $1.59, 7.24$), WM (SMD: 6.20 ; 95% CI: $1.60, 10.75$) and MOX (SMD: 6.75 ; 95% CI: $3.72, 8.94$) ([Table 4](#)). The ranking results of the ranking indicated that the top four interventions for increasing the response rate were AA (86.3%), combination therapy (79.8%), sAC (48.9%), and AC (46.0%), while the worst was MOX (17.2%) ([Figure 4B](#)).

A total of 33 studies were identified that reported response rates involving nine distinct interventions and 2,969 patients. The findings of the NMA indicated that the combination therapy was more efficacious than CH (SMD: 0.26 ; 95% CI: $0.16, 0.41$) and WM (SMD: 0.20 ; 95% CI: $0.14, 0.29$). The results demonstrated that AT was more effective than WM (SMD: 8.01 ; 95% CI: $2.08, 45.37$) ([Table 4](#)). The results of the ranking indicated that the top four interventions to increase the response rate were AT (93.2%), combination therapy (77.2%), AA (68.3%), and EA (67.5%), while the least effective was WM (11.2%) ([Figure 4C](#)).

The inconsistency test results indicate that the serum CA125 level included four closed loops, with the IF with 95% confidence interval (CI) of these closed loops containing 0, suggesting the absence of any significant inconsistencies ([Figure 5A](#)). The results of the inconsistency test indicate that the response rate included four closed-loop studies, for which the 95% CI contained 0, suggesting the absence of any significant inconsistencies ([Figure 5B](#)). As illustrated in the funnel plot, all included studies are symmetrically distributed on both sides of the vertical line $X = 0$, indicating a very low probability of a small sample effect ([Figure 6](#)).

Adverse Events

Of the 42 included trials, 7 reported adverse events ([Table 5](#)). Three WM-related trials reported adverse consequences such as irregular vaginal bleeding, headache, nausea and more. Five studies with acupuncture and related therapies reported subcutaneous hematoma, skin occurs, dizziness and more. One study with CH reported subcutaneous flashes,

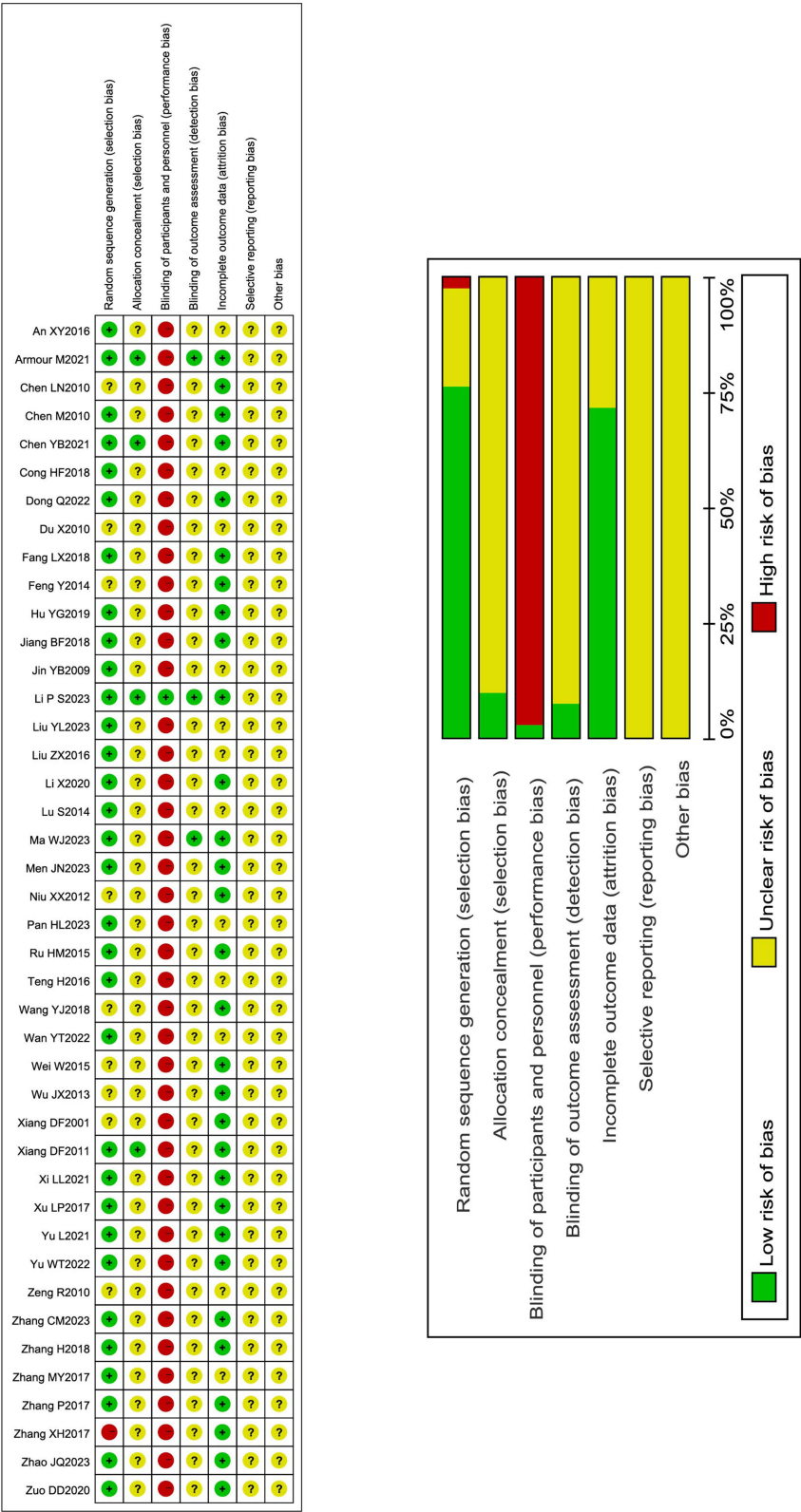


Figure 2 Quality assessment of included studies.

Table 3 Pairwise Meta-Analyses

Comparison	Pairwise RR/MD (95% CI)	Number of Patients	Number of Studies	Heterogeneity Test	
				I ² (%)	p value
Pain VAS scores					
Combination therapy vs WM	−1.801[−2.349 −1.254]	641	8	82.90	0.000*
Combination therapy vs CH	−1.119[−1.327 −0.911]	341	4	0.00	0.000*
Serum CA125 level					
Combination therapy vs WM	−6.720[−9.363 −4.077]	639	8	61.30	0.000*
Combination therapy vs CH	−4.566[−6.036 −3.095]	406	5	0.00	0.000*
Response rate					
Combination therapy vs WM	1.112[1.023 1.208]	1444	15	0.00	0.012*
Combination therapy vs CH	1.178[1.028 1.349]	666	7	0.00	0.019*
Combination therapy vs AC	1.222[0.776 1.926]	160	2	0.00	0.387

Notes: *Significant difference.

Abbreviations: WM, western medicine; CH, Chinese herb medicine; AC, acupuncture.

vaginal bleeding, and vaginal dryness. In general, the lower incidence of adverse events in the treatment of EMs with acupuncture-related therapies compared with western medicine suggests the safety of acupuncture-related therapies.

Discussion

A comprehensive network meta-analysis evaluated and compared the efficacy and safety of a range of acupuncture-therapies for endometriosis, encompassing electro-acupuncture, moxibustion, auricular therapy, and nearly all other related techniques. The effectiveness of pain VAS scores, serum CA125 level, response rate, and adverse events was evaluated through the analysis of 42 eligible RCTs, which included a total of 3,656 participants.

Pairwise meta-analyses show that combination therapy was superior to both WM and CH in reducing pain scores, decreasing serum CA125 levels, and increasing response rate. The NMA analysis results indicate that: for pain VAS scores, all acupuncture-related was more efficacious than WM and the ranking results showed that the top one was ACE. For serum CA125 level, all acupuncture-related was more efficacious than WM and the ranking results showed that the top one was AA. For response rate, all acupuncture-related was more efficacious than WM and the ranking results showed that the top one was AT. Safety analyses indicate that the lower incidence of adverse events in the treatment of EMs with acupuncture-related therapies compared with western medicine.

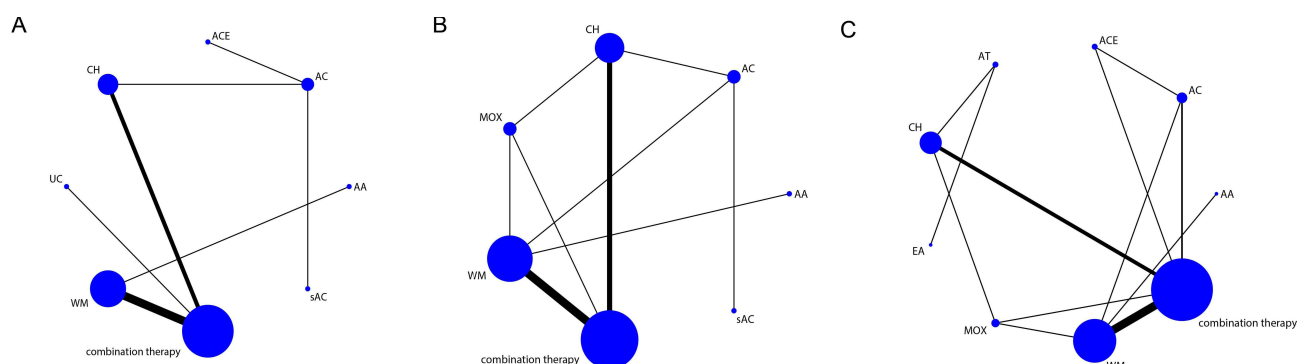


Figure 3 The network structure for treatment comparisons. (A) pain VAS scores; (B) serum CA125 level; (C) response rate. AC, acupuncture; EA, electroacupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; AT, auricular therapy; AA, acupoint application; ACE, acupoint catgut embedding; WM, hormone drugs; UC, usual care; sAC, sham acupuncture.

Table 4 Network Meta-Analysis Results

Pain VAS Scores								
AA								
0.93 (−1.69, 3.56)	AC							
1.24 (−1.88, 4.33)	0.30 (−1.36, 1.94)	ACE						
−0.67 (−2.63, 1.27)	−1.60 (−3.35, 0.16)	−1.91 (−4.32, 0.53)	CH					
−2.18 (−5.17, 0.84)	−3.11 (−6.24, 0.05)	−3.42 (−6.95, 0.19)	−1.51 (−4.10, 1.11)	UC				
−1.40 (−3.05, 0.24)	−2.33 (−4.37, −0.29)*	−2.63 (−5.26, 0.01)	−0.73 (−1.77, 0.31)	0.78 (−1.75, 3.28)	WM			
0.40 (−1.35, 2.15)	−0.54 (−2.48, 1.43)	−0.84 (−3.38, 1.75)	1.07 (0.23, 1.92)*	2.57 (0.12, 5.02)*	1.79 (1.21, 2.41)*	Combination therapy		
0.86 (−2.23, 3.98)	−0.07 (−1.68, 1.55)	−0.37 (−2.67, 1.93)	1.54 (−0.86, 3.93)	3.04 (−0.52, 6.56)	2.26 (−0.35, 4.88)	0.47 (−2.08, 3.00)	sAC	
Serum CA125 Level								
AA								
−10.40 (−19.29, −0.88)*	AC							
−9.57 (−17.79, −1.96)*	0.89 (−6.77, 7.04)	CH						
−11.33 (−20.28, −2.97)*	−0.89 (−9.35, 6.11)	−1.80 (−6.42, 2.96)	MOX					
−11.86 (−18.81, −4.86)*	−1.44 (−7.71, 4.07)	−2.32 (−5.72, 1.89)	−0.57 (−5.21, 4.95)	WM				
−5.14 (−12.93, 1.99)	5.27 (−1.94, 11.07)	4.41 (1.59, 7.24)*	6.20 (1.60, 10.75)*	6.75 (3.72, 8.94)*	Combination therapy			
−8.66 (−25.95, 8.57)	1.66 (−12.90, 15.80)	0.92 (−14.98, 16.78)	2.66 (−13.56, 19.01)	3.13 (−12.56, 18.68)	−3.50 (−19.30, 12.26)	sAC		
Response Rate								
AA								
3.69 (0.66, 27.16)	AC							
2.13 (0.32, 14.73)	0.56 (0.14, 2.22)	ACE						
0.37 (0.03, 3.14)	0.10 (0.01, 0.56)	0.18 (0.02, 1.19)	AT					
3.10 (0.68, 15.62)	0.85 (0.27, 2.30)	1.48 (0.42, 5.24)	8.01 (2.08, 45.37)*	CH				
0.89 (0.06, 18.16)	0.25 (0.02, 2.68)	0.42 (0.03, 5.41)	2.40 (0.52, 14.45)	0.29 (0.03, 3.10)	EA			
1.81 (0.37, 10.57)	0.49 (0.14, 1.67)	0.88 (0.21, 3.75)	4.99 (0.92, 34.10)	0.60 (0.23, 1.49)	2.09 (0.18, 25.26)	MOX		
3.98 (0.99, 17.89)	1.09 (0.39, 2.67)	1.94 (0.55, 6.39)	10.50 (2.40, 64.97)*	1.30 (0.72, 2.29)	4.46 (0.46, 49.01)	2.20 (0.92, 5.18)	WM	
0.80 (0.19, 3.75)	0.22 (0.08, 0.53)*	0.39 (0.12, 1.23)	2.11 (0.50, 12.46)	0.26 (0.16, 0.41)*	0.91 (0.09, 9.31)	0.44 (0.19, 1.04)	0.20 (0.14, 0.29)*	Combination therapy

Notes: *Bold values indicate significant difference.

Abbreviations: AC, acupuncture; EA, electroacupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; AT, auricular therapy; AA, acupoint application; ACE, acupoint catgut embedding; WM, hormone drugs; UC, usual care; sAC, sham acupuncture.

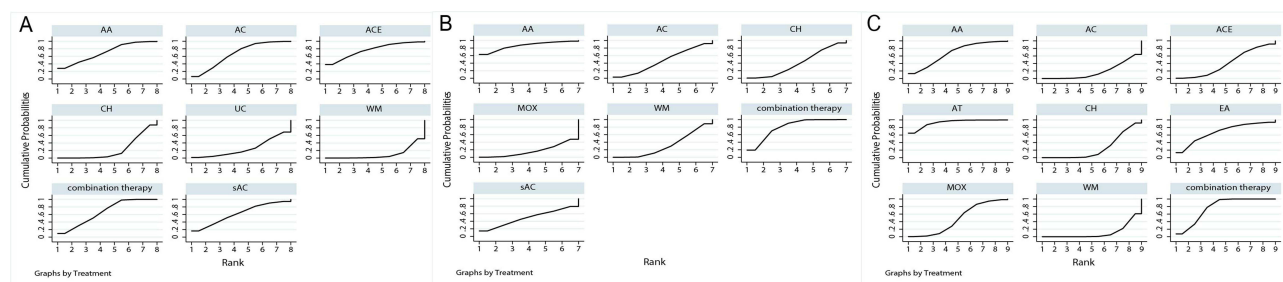


Figure 4 The surface under the cumulative ranking curves (Graphs by Treatment). (A) pain VAS scores; (B) serum CA125 level; (C) response rate. AC, acupuncture; EA, electroacupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; AT, auricular therapy; AA, acupoint application; ACE, acupoint catgut embedding; WM, hormone drugs; UC, usual care; sAC, sham acupuncture.

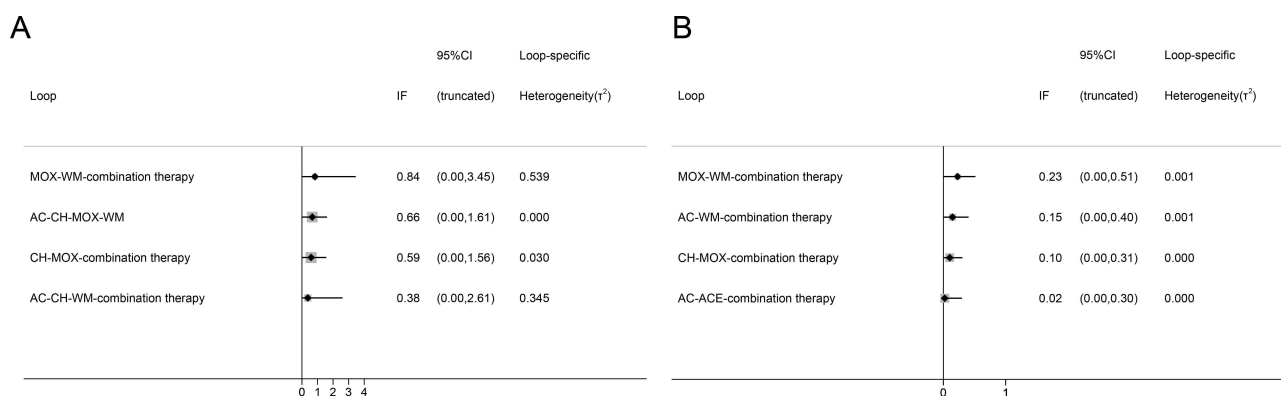


Figure 5 Inconsistency test. (A) serum CA125 level; (B) response rate. AC, acupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; ACE, acupoint catgut embedding; WM, hormone drugs.

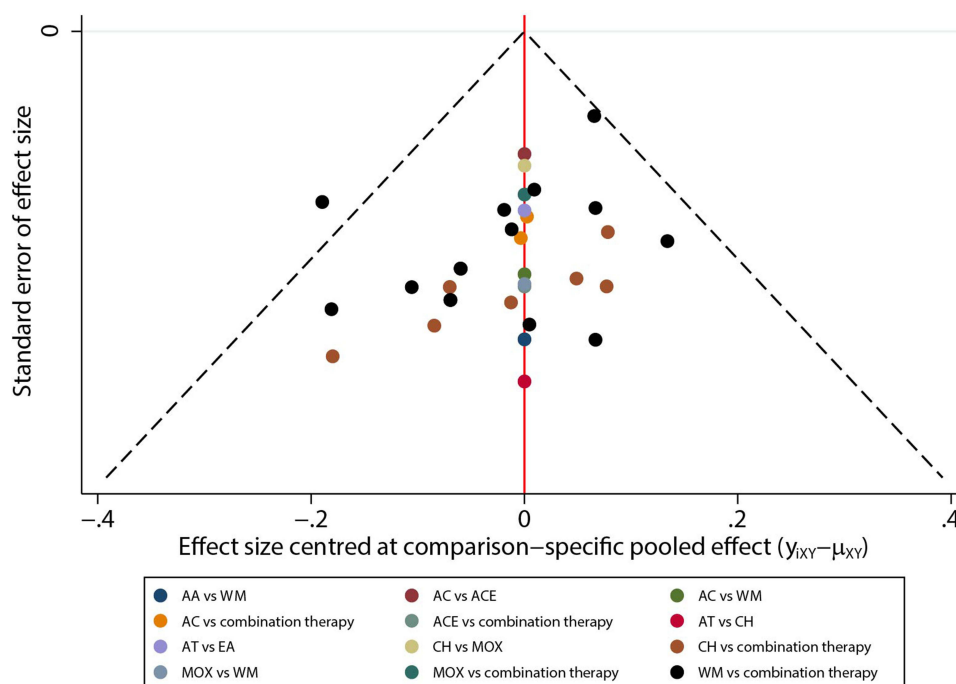


Figure 6 Funnel diagram. AC, acupuncture; EA, electroacupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; AT, auricular therapy; AA, acupoint application; ACE, acupoint catgut embedding; WM, hormone drugs.

Table 5 Adverse Events

References	Adverse Events
Li P S 2023 ²⁵	AC: 3 cases of subcutaneous hematoma (3/51).
Chen LN 2010 ³¹	sAC: 3 cases of subcutaneous hematoma (1/53).
Yu WT 2022 ³⁶	WM: 2 cases of abdominal distension and nausea (2/26).
Yu L 2021 ⁴⁷	AA: itchy skin occurs in a few cases.
Zuo DD 2020 ⁵⁵	WM: 3 cases of irregular vaginal bleeding (3/30), 2 cases of breast tenderness (2/30), 2 cases of nausea (2/30), 1 case of headache (1/30).
Men JN 2023 ⁵⁷	Combination therapy: 1 case of dizzy (1/43), 1 case of stomach discomfort (1/43).
	Combination therapy: 1 case of vaginal dryness (1/52), 2 cases of vaginal bleeding (2/52).
	CH: 1 case of hot flashes (1/47), 1 case of vaginal bleeding (1/47), 1 case of vaginal dryness (1/47).
Zhang MY 2017 ⁵⁸	Combination therapy: 1 case of nausea (1/60).
	WM: 6 cases of nausea (6/60), 2 cases of vertigo (2/60), 1 case of vomiting (1/60), 3 cases of sweating (3/60), 1 case of flushed (1/60).

Abbreviations: AC, acupuncture; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; AA, acupoint application; WM, hormone drugs; sAC, sham acupuncture.

EMs occurrence involves many factors, including distinctive genetic, environmental, and immunological factor.⁶⁷ The theory of retrograde menstruation/ transplantation is further supported by the discovery that women with EMs have more menstrual blood flow and endometrial tissue debris than women without the disorder.⁶⁸ Chronic pain (dysmenorrhea, cyclic and acyclic lower abdominal pain) is a central problem for our patients.⁶⁹ The aim of treatment is also to relief of pain. The pain VAS measurement was originally used in the field of psychology as a means of assessing an individual's overall sense of well-being. Woodforde and Merskey were first reported use of the VAS pain scale in patients presenting with a range of pain conditions.⁷⁰ At present, pain VAS is the most commonly used pain assessment scale in the field of EMs.⁷¹ A study examined the VAS demonstrated excellent test–retest reliability and validity with an intraclass correlation coefficient (ICC) of 0.97⁷². This indicates that the VAS is a reliable tool for assessing pain intensity.

For a long time, acupuncture-related therapies have been used to manage various types of gynaecological pain, and there is a lot of evidence to support its efficacy in gynaecological pain management.^{14,73–76} More and more evidence indicates that acupuncture-related therapies can alleviate pain.⁷⁷ Numerous peripheral chemicals including neurotransmitters, neuropeptides, and cytokines are involved in acupuncture-related therapies inhibition of pain. Acupuncture can by modulating the inflammatory levels of Interleukin-1 beta, tumor necrosis factor- α , prostaglandin E2, and prostaglandin F2 α to relieve pain.^{55,78,79} In addition, acupuncture-related therapies can through spinal and supraspinal mechanisms to inhibition of pain. In the spinal cord, the inactivation of spinal microglia and astrocytes, respectively, mediates the immediate and long-term analgesic effects of acupuncture.⁸⁰ The brain regions related to the descending pain regulation system include the anterior cingulate cortex, the periaqueductal gray matter of the midbrain, and the rostral ventromedial area medulla.⁸¹ Acupuncture-related therapies can achieve analgesic effects by inhibiting the activation of glial cells and regulating the functions of the corresponding brain regions.⁸²

The most frequently used biomarker for endometriosis is CA125. CA125 levels are used to assess the severity of endometriosis and the effectiveness of treatment and are a valuable tool for monitoring treatment progress and response.⁸³ However, some studies have shown that the biomarkers evaluated, including serum CA125 levels, cannot be evaluated in a meaningful manner, and the evidence is insufficient or of poor quality.^{84,85} Dorien et al put forth the argument that CA-125 appears to exhibit diminished sensitivity, particularly in advanced stages of endometriosis, as opposed to all stages collectively, while its specificity can be poor due to its rise in other gynaecological diseases.⁸⁶ A summary of the literatures related to endometriosis reveal that current serum CA125 level still uses as an outcome indicator for evaluating the efficacy of interventions. However, the effects of various interventions on serum CA125 level are not the same. Whether serum CA125 level can be used as an improved outcome indicator for endometriosis remains to be further explored. It is suggested to use the special evaluation scale for endometriosis and more appropriate specific markers to evaluate the clinical efficacy of acupuncture-related therapies in the treatment of endometriosis in the future.

With the continuous development of acupuncture, a variety of acupuncture-related therapies including electroacupuncture, auricular therapy, acupoint catgut embedding, acupoint application and so on have gradually formed. The current research suggests that acupuncture-related therapies have a positive clinical impact on a diverse range of diseases, with a broad spectrum of indications. The efficacy of acupuncture and related therapies in the treatment of various types of pain disorders has been confirmed. And compared with drug therapy, acupuncture and related therapies minimal and mild side effects,⁸⁷ which can effectively relieve nausea, dizziness, gastrointestinal discomfort and other symptoms caused by drugs. The relaxation effect and attention to individual patients during acupuncture treatment can bring psychological comfort and support, and help alleviate the psychological pressure caused by disease and drug treatment.⁸⁸ These studies show that acupuncture-related therapies have great potential for endometriosis.

Compared to previously published researches, this study includes a comprehensive database,¹⁴ a large number of included studies, and encompasses the latest RCT studies on endometriosis.¹⁶ It also assesses almost all acupuncture-related therapies.^{15,17,18} And that the NMA method employed in this study integrates both direct and indirect evidence, compensating for the scarcity of direct evidence through the inclusion of indirect evidence, thereby facilitating a comparative analysis of the efficacy of various acupuncture-related therapies for endometriosis. The results indicate that acupuncture-related treatments such as acupoint application, acupoint catgut embedding, and acupoint catgut embedding show potential therapeutic effects in alleviating the symptoms of endometriosis. It should be noted that our study is not without limitations. (1) The trials included in the study encompassed a broad spectrum of population characteristics and treatment cycles. Although the consistency of the findings across the studies mitigated this concern, it could still lead to imprecise estimates of the effects. (2) Almost all of participants were Chinese, which lacked diversity, and the rigor and scientificity of the content needed to be further verified. (3) The study exhibits a lack of consistency, with the diagnostic criteria for included research being diverse. The point selection of acupuncture-related therapies and the course of treatment were different which may introduce potentially heterogeneity and affect the level of evidence within the research. (4) Acupuncture-related therapies involve variety of methods, and it is difficult to form a closed loop between them. Therefore, this study classified them as combination therapy and could not specifically analyze which combination therapy is the best treatment mode.

Conclusions

Given our meta-analysis results, acupuncture-related therapies could be considered a potential treatment method and warrants further investigation. Among them, acupoint catgut embedding, auricular therapy, acupoint application and combination therapy may be the best solutions for the treatment of endometriosis. In subsequent investigations within this domain, it is imperative that clinical studies adhere rigorously to established guidelines and protocols.

Data Sharing Statement

Data included in article, supplementary material and references in article.

Acknowledgments

We thank all researchers and study participants for their contributions to this project.

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.

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Disclosure

The authors declare no conflict of interest.

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