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REVIEW

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

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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 it 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 limit 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 trial[39] 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.

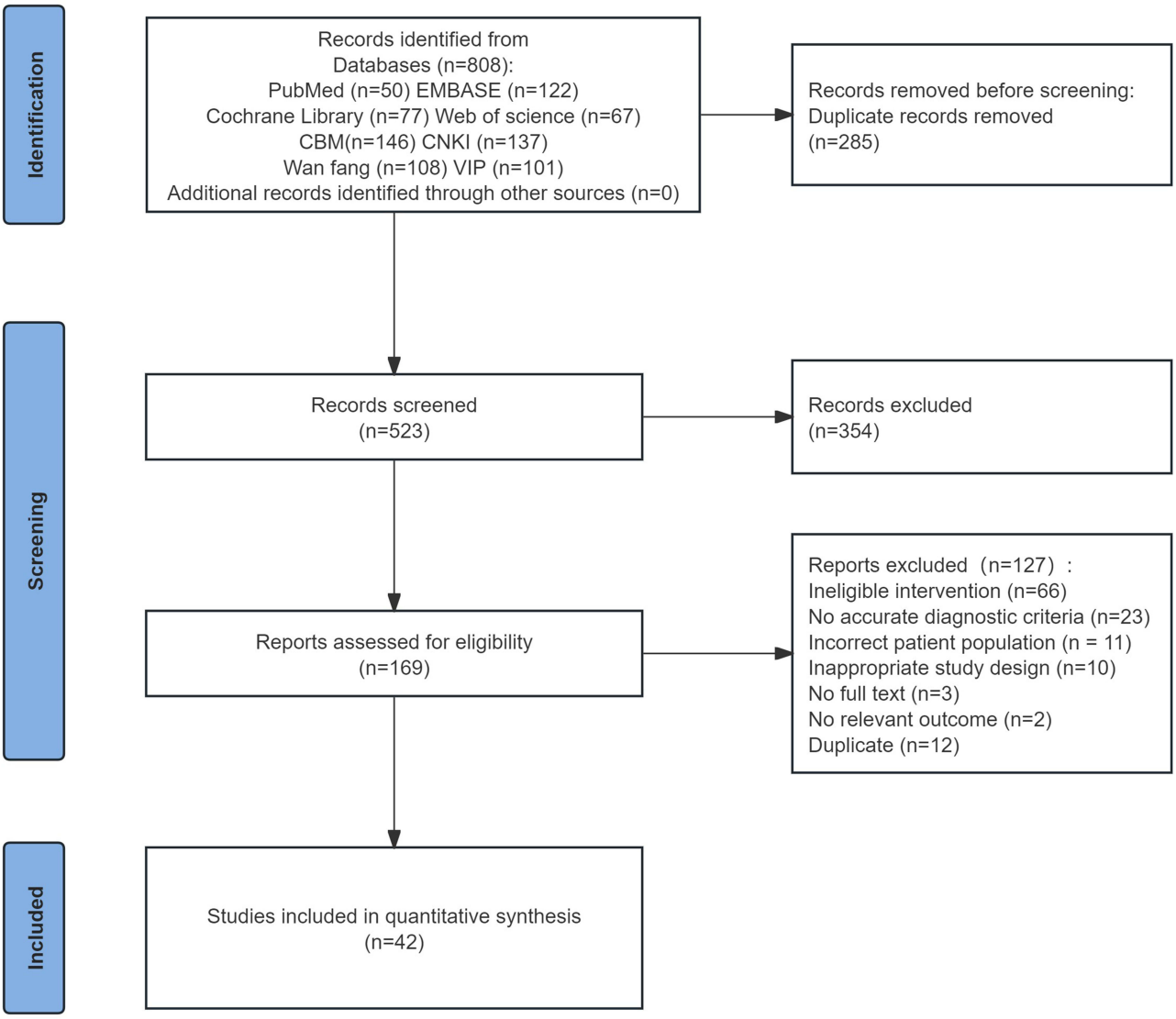

Figure 1 Flow diagram of preferred reporting items identified, included, and excluded for systematic reviews and meta-analyses (PRISMA).

Table 1 Baseline Characteristics of the Included Studies

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

(*Continued*)

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Table 1 (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	①③
Men JN 2023[57]	China	CMA	Combination therapy	52	32.63±4.69	CH	47	32.05±4.21	①②③
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	②③
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	①③
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 CA125; 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($CO_{6.10i}$), 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*)

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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*)

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Table 2 (Continued).

References	Intervention	Acupuncture Points Used	Retention Time	Acupuncturist Qualifications	Acupuncture Reaction	Timing of Treatment	Frequency and Course of Acupuncture
	AC	*Sanyinjiao (SP6), Xuehai (SP10), Diji (SP8), Zigong (EX-CA1), Guanyuan (CV4)*	30 min	N	Y	N	Three a week for 12 weeks
Men JN 2023[57]	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
Zhang MY 2017[58]	Combination therapy	ACE+CH:*Shenshu (BL23), Sanyinjiao (SP6), Ciliao (BL32), Zigong (EX-CA1), Xuehai (SP10), Guanyuan (CV4)*	N	N	N	N	N
Xi LL 2021[59]	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
Zhang CM 2023[60]	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_S), 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: (−10.4095% 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,

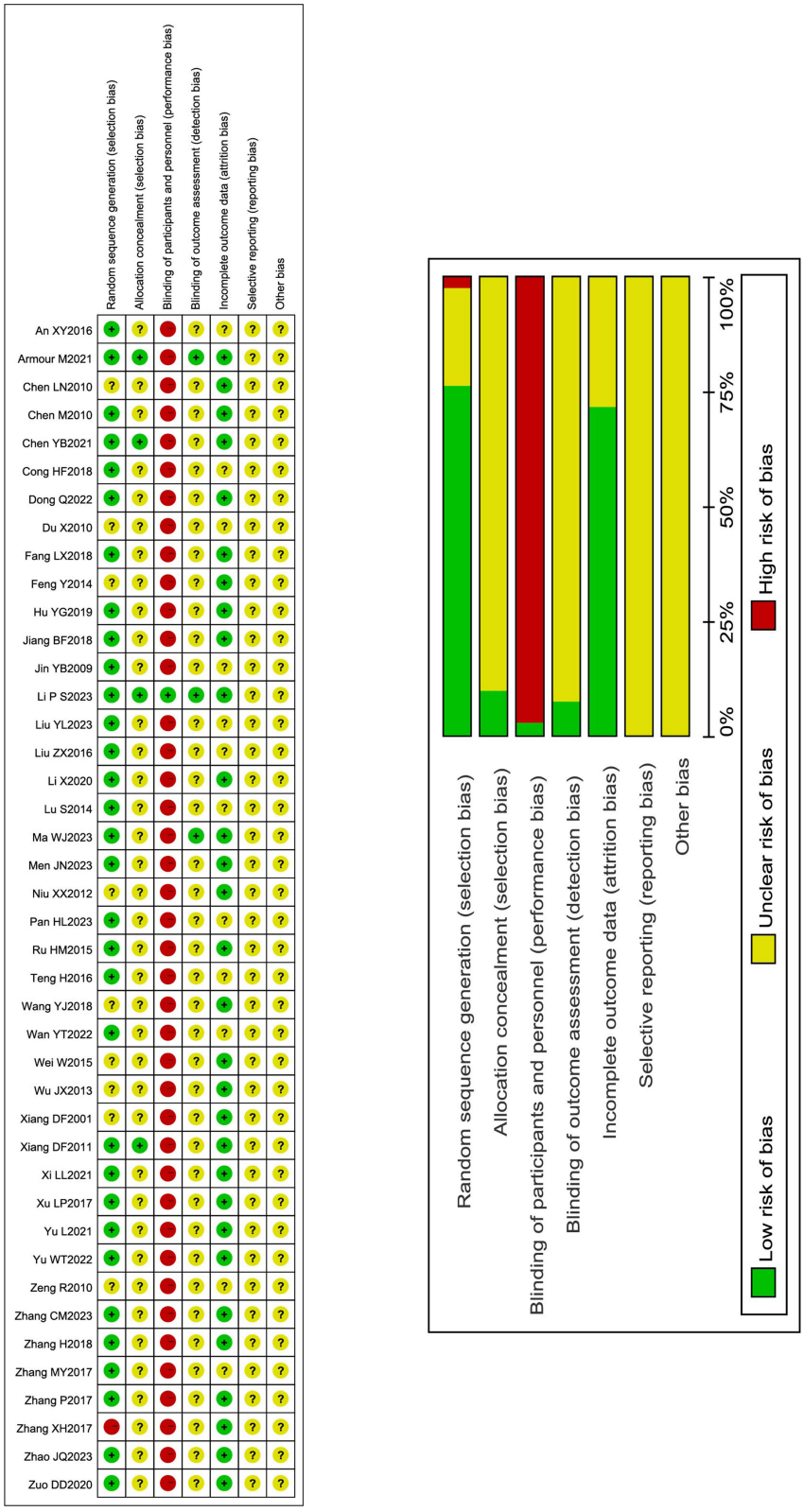

Figure 2 Quality assessment of included studies.

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.

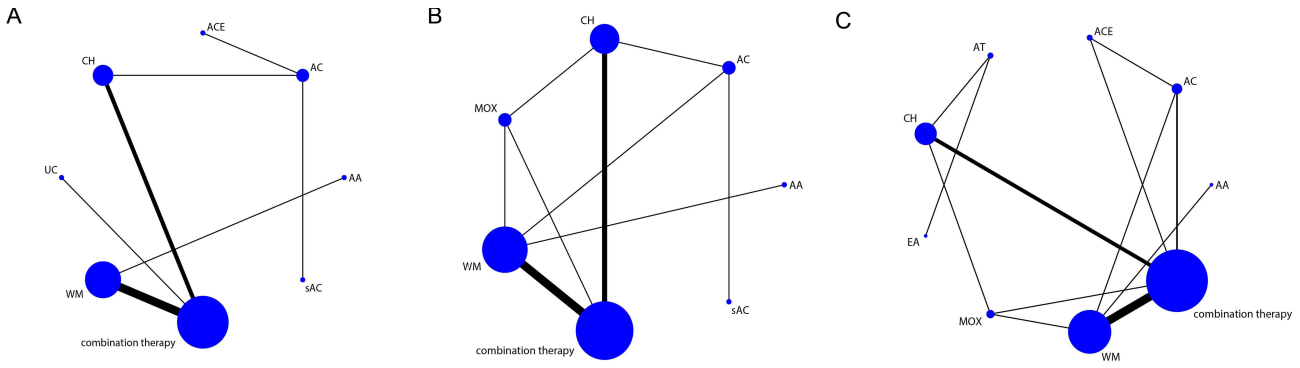

Figure 3 The network structure for treatment comparisons. (**A**) pain VAS scores; (**B**) serum CA125 level; (**C**) response rate. AC, acupuncture; EA, electroacupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; 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.

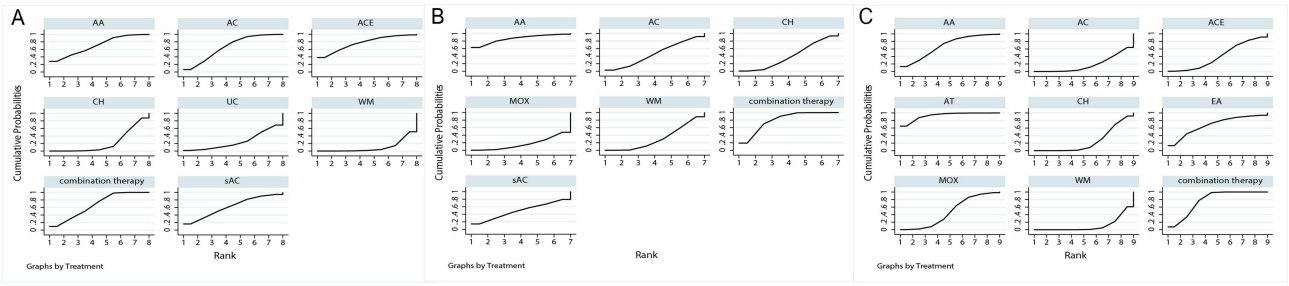

Figure 4 The surface under the cumulative ranking curves (Graphs by Treatment). (**A**) pain VAS scores; (**B**) serum CA125 level; (**C**) response rate. AC, acupuncture; EA, electroacupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies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

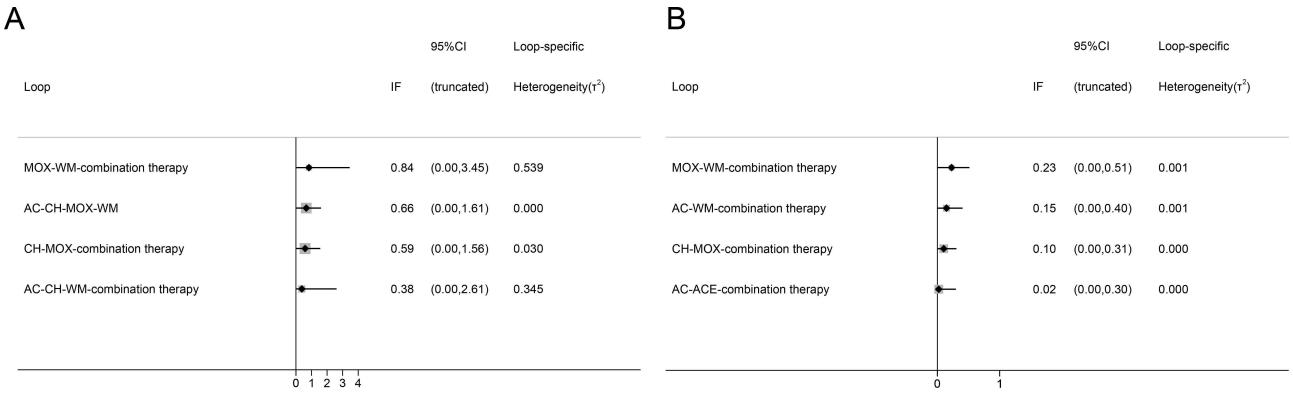

Figure 5 Inconsistency test. (**A**) serum CA125 level; (**B**) response rate. AC, acupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; ACE, acupoint catgut embedding; WM, hormone drugs.

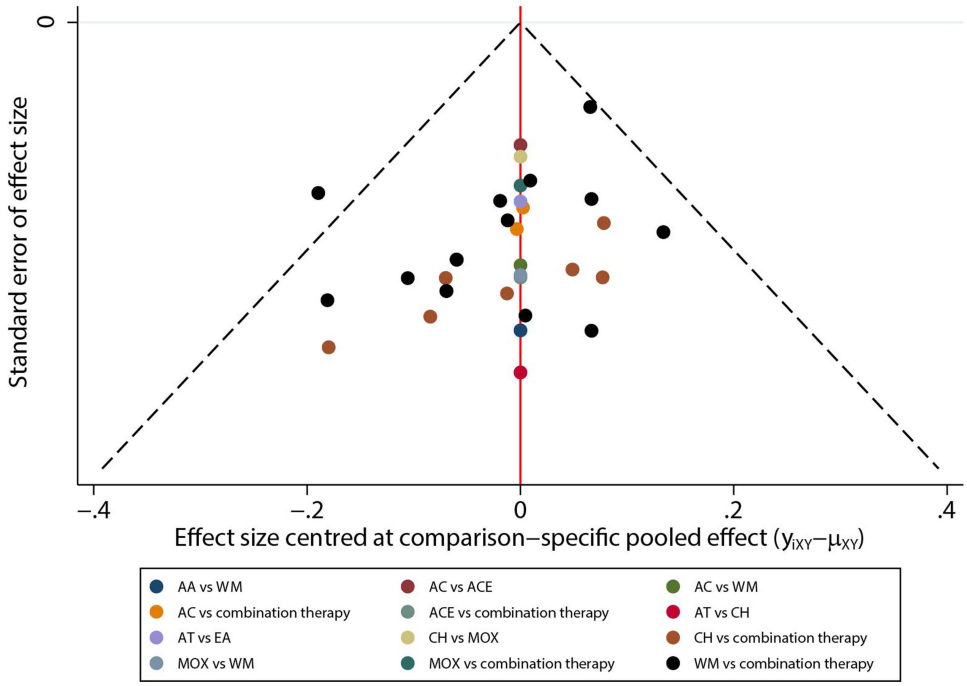

Figure 6 Funnel diagram. AC, acupuncture; EA, electroacupuncture; MOX, moxibustion; CH, Chinese herb medicine; combined therapies, the combination of acupuncture-related therapies and other therapies; AT, auricular therapy; AA, acupoint application; ACE, acupoint catgut embedding; WM, hormone drugs.

Table 5 Adverse Events

References	Adverse Events
Li P S 2023[25]	AC: 3 cases of subcutaneous hematoma (3/51). sAC: 3 cases of subcutaneous hematoma (1/53).
Chen LN 2010[31]	WM: 2 cases of abdominal distension and nausea (2/26).
Yu WT 2022[36]	AA: itchy skin occurs in a few cases.
Yu L 2021[47]	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).
Zuo DD 2020[55]	Combination therapy: 1 case of dizzy (1/43), 1 case of stomach discomfort (1/43).
Men JN 2023[57]	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 flustered (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 0.97[72]. 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 F2α 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.

References

1. Allaire C, Bedaiwy MA, Yong PJ. Diagnosis and management of endometriosis. *Cmaj*. 2023;195(10):E363–e371. doi:10.1503/cmaj.220637
2. Wójcik M, Goździewicz T, Hudáková Z, et al. Endometriosis and the temporomandibular joint-preliminary observations. *J Clin Med*. 2023;12(8):2862. doi:10.3390/jcm12082862
3. Sachedina A, Todd N. Dysmenorrhea, endometriosis and chronic pelvic pain in adolescents. *J Clin Res Pediatr Endocrinol*. 2020;12(Suppl 1):7–17. doi:10.4274/jcrpe.galenos.2019.2019.S0217
4. Zondervan KT, Becker CM, Missmer SA. Endometriosis. *N Engl J Med*. 2020;382(13):1244–1256. doi:10.1056/NEJMra1810764
5. Kvaskoff M, Mu F, Terry KL, et al. Endometriosis: a high-risk population for major chronic diseases? *Hum Reprod Update*. 2015;21(4):500–516. doi:10.1093/humupd/dmv013
6. Márki G, Bokor A, Rigó J, et al. Physical pain and emotion regulation as the main predictive factors of health-related quality of life in women living with endometriosis. *Hum Reprod*. 2017;32(7):1432–1438. doi:10.1093/humrep/dex091
7. Guo SW. Various types of adenomyosis and endometriosis: in search of optimal management. *Fertil Steril*. 2023;119(5):711–726. doi:10.1016/j.fertnstert.2023.03.021
8. Vercellini P, Buggio L, Frattaruolo MP, et al. Medical treatment of endometriosis-related pain. *Best Pract Res Clin Obstet Gynaecol*. 2018;51:68–91. doi:10.1016/j.bpobgyn.2018.01.015
9. Sinaii N, Cleary SD, Younes N, et al. Treatment utilization for endometriosis symptoms: a cross-sectional survey study of lifetime experience. *Fertil Steril*. 2007;87(6):1277–1286. doi:10.1016/j.fertnstert.2006.11.051
10. Kurshan N, Neill Epperson C. Oral contraceptives and mood in women with and without premenstrual dysphoria: a theoretical model. *Arch Womens Ment Health*. 2006;9(1):1–14. doi:10.1007/s00737-005-0102-z
11. Pelkman C. Hormones and weight change. *J Reprod Med*. 2002;47(9 Suppl):791–794.
12. Berlanda N, Somigliana E, Viganò P, et al. Safety of medical treatments for endometriosis. *Expert Opin Drug Saf*. 2016;15(1):21–30. doi:10.1517/14740338.2016.1121991
13. Acar HV. Acupuncture and related techniques during perioperative period: a literature review. *Complement Ther Med*. 2016;29:48–55. doi:10.1016/j.ctim.2016.09.013
14. Xu Y, Zhao W, Li T, et al. Effects of acupuncture for the treatment of endometriosis-related pain: a systematic review and meta-analysis. *PLoS One*. 2017;12(10):e0186616. doi:10.1371/journal.pone.0186616
15. Wang Y, Coyle ME, Hong M, et al. Acupuncture and moxibustion for endometriosis: a systematic review and analysis. *Complement Ther Med*. 2023;76:102963. doi:10.1016/j.ctim.2023.102963
16. Chen C, Li X, Lu S, et al. Acupuncture for clinical improvement of endometriosis-related pain: a systematic review and meta-analysis. *Arch Gynecol Obstet*. 2024;310(4):2101–2114. doi:10.1007/s00404-024-07675-z
17. Giese N, Kwon KK, Armour M. Acupuncture for endometriosis: a systematic review and meta-analysis. *Integr Med Res*. 2023;12(4):101003. doi:10.1016/j.imr.2023.101003
18. Zhu X, Hamilton KD, McNicol ED. Acupuncture for pain in endometriosis. *Cochrane Database Syst Rev*. 2011;2011(9):Cd007864. doi:10.1002/14651858.CD007864.pub2
19. Hutton B, Salanti G, Caldwell DM, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. *Ann Intern Med*. 2015;162(11):777–784. doi:10.7326/M14-2385
20. Wang X, Chen Y, Liu Y, et al. Reporting items for systematic reviews and meta-analyses of acupuncture: the PRISMA for acupuncture checklist. *BMC Complement Altern Med*. 2019;19(1):208. doi:10.1186/s12906-019-2624-3
21. Luo D, Wan X, Liu J, et al. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. *Stat Methods Med Res*. 2018;27(6):1785–1805. doi:10.1177/0962280216669183
22. Wan X, Wang W, Liu J, et al. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol*. 2014;14:135. doi:10.1186/1471-2288-14-135
23. Higgins JP, Altman DG, Gotzsche PC, et al. The Cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928. doi:10.1136/bmj.d5928
24. StataCorp. Stata statistical software:Release 15; 2017.
25. Li PS, Peng XM, Niu XX, et al. Efficacy of acupuncture for endometriosis-associated pain: a multicenter randomized single-blind placebo-controlled trial. *Fertil Steril*. 2023;119(5):815–823. doi:10.1016/j.fertnstert.2023.01.034
26. Armour M, Cave AE, Schabrun SM, et al. Manual acupuncture plus usual care versus usual care alone in the treatment of endometriosis-related chronic pelvic pain: a randomized controlled feasibility study. *J Altern Complement Med*. 2021;27(10):841–849. doi:10.1089/acm.2021.0004
27. Xiang D. Clinical study on the treatment of endometriosis dysmenorrhoea with auricular submerged acupuncture in 37 cases. *J Traditional Chin Med*. 2001;42(10):596–597.
28. Jin Y, Sun Z, Jin H. Randomized controlled study on ear-electroacupuncture treatment of endometriosis-induced dysmenorrhea in patients. *Acupuncture Res*. 2009;34(3):188–192.
29. Zhang H, Zhang Y, Chen M. Clinical observation of abdominal acupuncture plus ginger-partitioned moxibustion at baliao points for pelvic pain in endometriosis. *Shanghai J Acu-mox*. 2018;37(12):1349–1353.
30. Xiang D, Sun Q, Liang X. Effect of abdominal acupuncture on pain of pelvic cavity in patients with endometriosis. *Chin Acu Mox*. 2011;31(2):113–116.
31. Chen l. Abdominal acupuncture treatment for 35 cases of dysmenorrhea caused by endometriosis. *Hunan J Tradit Chin Med*. 2010;26(6):75–76.
32. Zhang P, Liang X, Fan Y. Clinical observation of endometriosis treated with isolated—herbal moxibustion based on the effect of Tonifying Yang on du meridian. *Asian J Tradit Med*. 2017;13(5):121–123.

33. Jiang B. Clinical effects of Guizhi Erchen Decoction combined with moxibustion on patients with dysmenorrhea due to endometriosis. *Med J Chinese People's Health*. 2018;30(23):59–60.
34. Teng H, Wang J, Liu Y, et al. Effect of fire needling on CA-125 levels and EMAb in endometriosis patients. *Shanghai J Acu-mox*. 2016;35(7):844–846.
35. Ma W, Su Q, Chen J, et al. To investigate effect of "Zhi bian through Shui dao" acupuncture therapy on endometriosis patients based on microRNA expression profile change. *J Xinjiang Med Univ*. 2023;46(9):1240–1245+1257.
36. Yu W, Jiang G, Wang P, et al. Clinical observation of cold pain and endometriosis dysmenorrhea (syndrome of cold coagulation and blood stasis). *Clin J Tradit Chin Med*. 2022;34(10):1954–1958.
37. Lu S, Liu X, Zhuang Z. Clinical study on moxibustion treatment of abdominal ren meridian endometriosis disease of pain. *Tradit Chin Med*. 2014;9(4):216–217.
38. Zhang X, Kuang J. Moxibustion combined with medicine therapy to treat cold coagulation and blood stasis type Clinical observation of 45 cases of endometriosis dysmenorrhea. *J Traditional Chinese Med Pharm*. 2017;23(10):106–107.
39. Niu X, Niu Q, Luo X. Clinical observation on effect of moxibustion combined with herbs to treat dysmenorrhoea(Endometriosis). *Liaoning J Tradit Chin Med*. 2012;39(6):1090–1092.
40. An X, Sun S, Chen S, et al. Observation of the clinical efficacy of Orange core pill acupoint application in the treatment of endometriosis (qi stagnation and blood stasis pattern). *Chinese J Clin Ration Drug Use*. 2016;9(30):117–119.
41. Chen Y, Leng J, Lin B-J, et al. Thunder-fire moxibustion combined with mifepristone for ovarian chocolate cyst dysmenorrhea with kidney deficiency and blood stasis: a randomized controlled trial. *Chin Acu Mox*. 2021;41(2):161–164. doi:10.13703/j.0255-2930.20191011-0002
42. Xu L. Lei Huo moxibustion combined with Nei Pain Ling decoction was used to treat 30 cases of endometriosis. *Guangxi J Tradit Chin Med*. 2017;40(3):28–30.
43. Pan H, Zhou Y, Wang F. Observation of Lei Huo moxibustion combined with traditional Chinese medicine acupoint application in the treatment of endometriosis pain. *Med Hygiene*. 2023;5:1.
44. Wei W, Chen L, Li W. Observation of the efficacy of Li Chong decoction plus and minus combined with acupuncture in the treatment of pelvic endometriosis. *J Sichuan Traditl Chin Med*. 2015;33(9):151–152.
45. Ru H. Observation of the clinical efficacy of 135 cases of Guizhi Poria pills combined with acupuncture in the treatment of endometriosis in 135 cases of Lingshou County Hospital. *Med Inf*. 2015;11:169.
46. Liu Y, Fang J, Chen J, et al. The curative effect of endometriosis and its effect on serum indexes of patients. *J Jiangxi Univ Chin Med*. 2023;35(5):39–41+45.
47. Yu L, Zhang P, Quan X. Shaofu Zhuyu decoction enema combined with Shenshu acupoint catgut embedding in treating 30 cases of recurrent endometriosis. *Clin J Chinese Med*. 2021;13(15):119–122.
48. Wu J, Qian X, Long Y, et al. Clinical observation of Shugan Xiaoyu decoction enema combined with acupuncture in the treatment of endometriosis dysmenorrhea. *J Emergency Traditional Chin Med*. 2013;22(11):1947–1948.
49. Zhao J, Zhang T, Cong H. Clinical observation of Sun's acupoint selection acupuncture combined with Guixiang Wenjing Zhitong Capsule on endometriosis dysmenorrhea with cold coagulation and blood stasis type. *Hebei J Trad Chin Med*. 2023;45(2):263–266.
50. Wan Y, Song Y, Chen J, et al. Clinical observation of Tongjingning Decoction combined with acupoint sticking on endometriosis – associated chronic pelvic pain of wet-hot-ecchymosis stases type. *Hebei J Trad Chin Med*. 2022;44(6):927–930+992.
51. Fang L, Zhang X, Liu S. Clinical observation of 30 cases of endometriosis dysmenorrhea, kidney deficiency and blood stasis syndrome in the treatment of endometriosis. *J Gansu Univ Chin Med*. 2018;35(1):84–87.
52. Dong Q, Chen K, Li H, et al. Prospective randomized trial of wenjing yangxue decoction and moxibustion in dysmenorrhea patients with endometriosis. *Med Innovation of China*. 2022;19(31):109–113.
53. Zeng R, Hong W. Warm acupuncture treatment of endometriosis in 40 cases. *China J Chin Med*. 2010;25(2):342–343.
54. Wang Y. Study on the efficacy of Xingui Pain Relief Formula plus or minus combined with moxibustion on endometriosis dysmenorrhea. *J Pract Gynecol Endocrinol*. 2018;5(23):35–36.
55. Zuo D, Han F, Peng Y, et al. Effect of acupoint catgut embedding on the levels of IL-1β, TNF-α, VEGF and MMP-2 in patients with endometriosis of kidney deficiency and blood stasis. *J Chin Acu Mox*. 2020;36(4):44–49.
56. Cong H, Gu Y, Zhang T, et al. Clinical study on acupoint catgut embedding treating dysmenorrhea due to endometriosis. *J Chin Acu Mox*. 2018;34(3):43–46.
57. Men J, Wang D, Li L, et al. Clinical effect of acupoint catgut embedding combined with GuixiangWenjing Zhitong Capsules for the treatment of endometriosis. *Guangxi Med J*. 2023;45(20):2468–2474.
58. Zhang M, Gao J. Observe the clinical curative effect of acupoint catgut embedding with Lichong decoction in treatment of endometriosis. *Shanxi J Tradit Chin Med*. 2017;38(9):1210–1211.
59. Xi L, Liu Y, Guo D, et al. Clinical study of acupuncture plus mifepristone for dysmenorrhea of qi stagnation and blood stasis type in chocolate cyst of ovary. *Shanghai J Acupuncture Moxibustion*. 2021;40(12):1470–1474.
60. Zhang C, Wu T, Wang Y, et al. Clinical observation on the acupuncture combined with yiqi huayu prescription in patients with endometriosis. *J Guangzhou Univ Tradit Chin Med*. 2023;40(12):3091–3096.
61. Chen M, Zhang H, Li J, et al. Clinical observation on acupuncture combined with acupoint sticking therapy for treatment of dysmenorrhea caused by endometriosis. *Chin Acu Mox*. 2010;30(9):725–728.
62. Feng Y, Feng G. The combination of acupuncture and medicine was used to treat endometriosis in 39 cases. *Chin Med Modern Distance Edu China*. 2014;12(3):27–29.
63. Li X, Lai H, Yu L, et al. Clinical efficacy and safety of traditional Chinese medicine enema combined with acupoint embedding in the treatment of recurrent endometriosis. *Chinese J Clin Ration Drug Use*. 2020;13(11):144–145.
64. Hu Y. Clinical efficacy of traditional Chinese medicine combined with moxibustion in the treatment of endometriosis. *Nei Mongol J Tradit Chin Med*. 2019;38(10):102–103.
65. Liu Z, Liu Z. Observation of the efficacy of traditional Chinese medicine combined with moxibustion in the treatment of endometriosis. *J Longdong Univ*. 2016;27(3):78–82.

66. Du X, Gao H, Wei L. A clinical study on the treatment of endomenorrhea with homemade reduction decoction combined with auricular acupressure. *China Health Care Nutr*. 2010;10:196–197.
67. Giudice LC, Kao LC. Endometriosis. *Lancet*. 2004;364(9447):1789–1799. doi:10.1016/S0140-6736(04)17403-5
68. Halme J, Hammond MG, Hulka JF, et al. Retrograde menstruation in healthy women and in patients with endometriosis. *Obstet Gynecol*. 1984;64 (2):151–154.
69. Gruber TM, Mechsner S. Pathogenesis of Endometriosis: the Origin of Pain and Subfertility. *Cells*. 2021;10(6):1381. doi:10.3390/cells10061381
70. Woodforde JM, Merskey H. Some relationships between subjective measures of pain. *J Psychosom Res*. 1972;16(3):173–178. doi:10.1016/0022-3999(72)90041-4
71. Bourdel N, Alves J, Pickering G, et al. Systematic review of endometriosis pain assessment: how to choose a scale? *Hum Reprod Update*. 2015;21 (1):136–152. doi:10.1093/humupd/dmu046
72. Alghadir AH, Anwer S, Iqbal A, et al. Test–retest reliability, validity, and minimum detectable change of visual analog, numerical rating, and verbal rating scales for measurement of osteoarthritic knee pain. *J Pain Res*. 2018;11:851–856. doi:10.2147/JPR.S158847
73. Chen B, Liu S, Jin F, et al. Efficacy of acupuncture-related therapy in the treatment of primary dysmenorrhea: a network meta-analysis of randomized controlled trials. *Heliyon*. 2024;10(10):e30912. doi:10.1016/j.heliyon.2024.e30912
74. Sun Y, Liu Y, Liu B, et al. Efficacy of acupuncture for chronic prostatitis/chronic pelvic pain syndrome: a randomized trial. *Ann Intern Med*. 2021;174(10):1357–1366. doi:10.7326/M21-1814
75. Wang X, Wang N, Liang J, et al. The effectiveness and safety of acupoint catgut embedding for the treatment of primary dysmenorrhea: a protocol for systematic review and meta-analysis. *Medicine*. 2020;99(47):e23222. doi:10.1097/MD.0000000000023222
76. Cao M, Ye F, Xie W, et al. Effectiveness of auricular acupoint therapy targeting menstrual pain for primary dysmenorrhea: a systematic review and meta-analysis of randomized controlled trials. *Worldviews Evid Based Nurs*. 2023;20(6):621–633. doi:10.1111/wvn.12636
77. Zhang R, Lao L, Ren K, et al. Mechanisms of acupuncture-electroacupuncture on persistent pain. *Anesthesiology*. 2014;120(2):482–503. doi:10.1097/ALN.0000000000000101
78. Wang SX, Lu DJ, Li YH. [Observation on therapeutic effect of acupoint application on dysmenorrhea of excess syndrome and effect on prostaglandins]. *Zhongguo Zhen Jiu*. 2009;29(4):265–268. Dutch
79. Chen PB, Chen J, Cui J, et al. [Effects of the Acupoint Catgut Embedding on Nerve-Endocrine-Immune Network in Dysmenorrhea Rats]. *Zhen Ci Yan Jiu*. 2018;43(1):30–34. doi:10.13702/j.1000-0607.170282 Hausa
80. Liang Y, Qiu Y, Du J, et al. Inhibition of spinal microglia and astrocytes contributes to the anti-allodynic effect of electroacupuncture in neuropathic pain induced by spinal nerve ligation. *Acupunct Med*. 2016;34(1):40–47. doi:10.1136/acupmed-2015-010773
81. Chen T, Zhang WW, Chu Y-X, et al. Acupuncture for pain management: molecular mechanisms of action. *Am J Chin Med*. 2020;48(4):793–811. doi:10.1142/S0192415X20500408
82. Gim GT, Lee J-H, Park E, et al. Electroacupuncture attenuates mechanical and warm allodynia through suppression of spinal glial activation in a rat model of neuropathic pain. *Brain Res Bull*. 2011;86(5–6):403–411. doi:10.1016/j.brainresbull.2011.09.010
83. Yonghua chen MP, Zuo Y, Yang B, Wang S, Wang S. Research progress of CA125 in endometriosis:Teaching an old dog new tricks. *Obstet Gynecol Clin Med*. 2022;2(4):191–198. doi:10.1016/j.gocm.2022.10.006
84. Nisenblat V, Prentice L, Bossuyt PMM, et al. Combination of the non-invasive tests for the diagnosis of endometriosis. *Cochrane Database Syst Rev*. 2016;7(7):Cd012281. doi:10.1002/14651858.CD012281
85. Nisenblat V, Bossuyt PMM, Shaikh R, et al. Blood biomarkers for the non-invasive diagnosis of endometriosis. *Cochrane Database Syst Rev*. 2016;2016(5):Cd012179. doi:10.1002/14651858.CD012179
86. Dorien FO, Flores I, Waelkens E, et al. Noninvasive diagnosis of endometriosis: review of current peripheral blood and endometrial biomarkers. *Best Pract Res Clin Obstet Gynaecol*. 2018;50:72–83. doi:10.1016/j.bpobgyn.2018.04.001
87. White A, Hayhoe S, Hart A, et al. Survey of adverse events following acupuncture (SAFA): a prospective study of 32,000 consultations. *Acupunct Med*. 2001;19(2):84–92. doi:10.1136/aim.19.2.84
88. Xu MM, Guo P, Ma Q-Y, et al. Can acupuncture enhance therapeutic effectiveness of antidepressants and reduce adverse drug reactions in patients with depression? A systematic review and meta-analysis. *J Integr Med*. 2022;20(4):305–320. doi:10.1016/j.joim.2022.05.002