Contents lists available at ScienceDirect

Integrative Medicine Research

Review Article

Acupuncture for endometriosis: A systematic review and meta-analysis

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A B S T R A C T

Background: Current endometriosis treatments do not always provide symptom relief, with many using complementary approaches. This study examined the effectiveness of acupuncture on pain and quality of life in people with endometriosis.
Methods: Searches were conducted on Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Allied and Complementary Medicine Database (AMED) and Embase (Ovid), Epistemonikos, and Cumulative Index to Nursing and Allied Health Literature (CINAHL; EBSCOhost) on 20 March 2023. Trials were included if they used penetrating acupuncture. Risk of bias was assessed with Cochrane RoB2 and GRADE for overall evidence certainty. Random-effects meta-analyses were undertaken, using Hedges' g or mean difference (MD) both with 95 % confidence intervals (CI).
Results: Six studies involving a total of 331 participants were included. Evidence for benefit was found for acupuncture compared to non-specific acupuncture on overall pelvic pain ($g = 1.54$, 95 % CI 0.92 to 2.16, 3 RCTs, $n = 231$, low certainty evidence, $p < 0.001$), menstrual pain ($g = 1.67$, 95 % CI 1.23 to 2.12, 1 RCT, $n = 106$, moderate certainty evidence, $p < 0.001$), and non-specified pelvic pain (MD -2.77, 95 % CI 2.15 to 3.38, 2 RCTs, $n = 125$, low certainty evidence, $p < 0.001$), and compared to usual care on menstrual pain ($g = 0.9$, 95 % CI 0.15 to 1.64, 1 RCT, $n = 19$, very low certainty evidence, $p = 0.02$). Most studies reported low rates of adverse events.
Conclusion: Acupuncture treatment for endometriosis demonstrated clinically relevant improvements in pelvic pain and should be considered as a potential treatment intervention.
Study registration: PROSPERO ID: CRD42023408700.

1. Introduction

Endometriosis is characterized by the presence of endometrial-like tissue outside the uterus.[1] The prevalence of endometriosis in women and those assigned female at birth is estimated to be around 10 % by laparoscopy[2,3] and up to 18 % when other methods are added, such as ultrasound, magnetic resonance imaging (MRI), or histopathology.[4] Primary symptoms of endometriosis are non-cyclical pelvic pain, dysmenorrhea and fatigue.[5] Endometriosis has deleterious effects on emotional and mental health, fertility, sexual and romantic relationships, work and study all of which may negatively impact quality of life.[5–11]

Current treatments for endometriosis include surgical and medical management. Medical management has low satisfaction with symptom relief,[12] resulting in high rates of non-adherence or discontinuation of medication.[13–15] Due to these limitations, many people with endometriosis use complementary therapies to manage their symptoms.[16,17] Previous research indicates that non-hormonal or complementary treatment options are important research priorities for people with endometriosis,[18,19] with a strong interest in holistic treatment options such as acupuncture.[20]

Acupuncture is the practice of inserting fine needles at specific points on the body, with the aim of inducing health-related benefits.[21] Potential mechanisms of acupuncture for treating endometriosis related symptoms include: a decrease in prostaglandin levels,[22] decreases in nerve growth factor,[23] increases in endogenous opioid release,[24] and a decrease in mechanical allodynia.[23] Given the substantial financial burden of endometriosis[7,25] and the substantial out of pocket costs incurred when using complementary therapies such as acupuncture,[16] it is vital to ensure that there is accurate information on how effective it is to allow informed decision making by consumers. In addition, with development of national and international guidelines for the treatment of endometriosis there is an urgent need for an up-to-date meta-analysis on this topic.[14,26]

This systematic review and meta-analysis aimed to determine the effect of acupuncture on endometriosis-related pelvic pain and health related quality of life (HRQoL) with the aim of contributing to evidence-based guidelines for endometriosis.[27]

2. Methods

Systematic review and meta-analysis were performed following the recommendations of the centre for Reviews and Dissemination and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklists.[28,29] This review was registered at the International Prospective Register of Systematic Reviews PROSPERO (Prospero ID: CRD42023408700) on 22 March 2023. The study was conducted without publication of study protocol. No post-registration modification was required.

2.1. Criteria for inclusion and exclusion

The Population Intervention Comparison Outcome Study-design (PICOS) was used to establish inclusion/exclusion criteria.[30]

2.1.1. Study types

Only randomized controlled trials (RCTs) were included. Cross-over randomized control trials were eligible to be included, but only phase 1 data was used in the meta-analysis due to concerns about carry over effects.

2.1.2. Participant types

People of reproductive age with pelvic pain or dysmenorrhea with a confirmed diagnosis of endometriosis via one or more of laparoscopy, ultrasound scan, MRI, or histopathology were included.

2.1.3. Intervention types and controls

Acupuncture can be delivered under different theoretical frameworks.[31] These frameworks dictate many facets of the treatment, including diagnosis, point location, point selection, co-interventions such as moxibustion, needling style, retention time for needles, and stimulation style. The following being most common frameworks used: Traditional Chinese, Five Element, Japanese or Biomedical (sometimes called "Western").[32,33] All types of penetrating acupuncture including microsystem acupuncture such as ear-acupuncture were eligible for inclusion. Studies were excluded if acupuncture was not used as a primary intervention in at least one treatment arm or if non-invasive acupuncture was used. All comparator interventions, including no treatment, were eligible for inclusion.

2.1.4. Outcomes measures

Primary outcome was pain severity measured by Visual Analogue Scale (VAS), Numeric Rating Scale (NRS), or other validated tools. Secondary outcomes included treatment-related adverse events, HRQoL measured by the Endometriosis Health Profile (EHP-30), Short Form-36 Health Survey (SF-36), or other HRQoL measures, the most bothersome symptom, and changes in analgesic medication as per the core outcome set for endometriosis.[34]

2.1.5. Others

Studies in English and German were considered for inclusion.

2.2. Literature searches

Search terms Endometri* AND (Acupunctur* OR Acumox* OR Acupuntura OR Electroacupunctur* OR Needle Mox* OR Acustimulation OR Acupoint* OR Acu-Mox*) and MeSH terms were used to search title/abstract. The search was conducted on 20 March 2023 on the Cochrane Central Register of Controlled Trials (CENTRAL), PubMed, Allied and Complementary Medicine Database (AMED; Ovid), Epistemonikos, CINAHL (EBSCOhost) and Embase (Ovid) without any time limits, restrictions, or published search filters. Duplicates were removed using Zoteros duplicate finder. See Supplementary Material for the detailed search strategy (Supplement 1). Two researchers (NG and KK) independently screened the identified papers manually based on the predefined eligibility criteria without using automated tools. Discrepancies were resolved through discussion. If necessary, a third party (KC) was consulted.

2.3. Data extraction

Data were extracted manually from the included studies[35–40] and their associated study protocols (when available)[41–43] by two researchers (NG and KK) independently. Where discrepancies occurred, they were solved by discussion and, if necessary, a third party (KC) was consulted.

Treatment details were extracted based on the Revised Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA),[31] (Supplement 2). The STRICTA checklist contains six main items (1. Acupuncture rationale, 2. Details of needling, 3. Treatment regimen, 4. Other components of treatment, 5. Practitioner background, 6. Control or comparator interventions) and was designed to ensure complete and transparent reporting of acupuncture interventions for accurate interpretation and replication. STRICTA has become a recognized standard for reporting acupuncture treatments in research and is an official extension of the CONsolidated Standards Of Reporting Trials (CONSORT) statement.[31]

Characteristic data including country, sample size, type of diagnosis, mean age, and outcome measures were extracted.

2.4. Quality of included studies

2.4.1. Acupuncture quality

Methodological reporting of acupuncture intervention was assessed using the National Institute for Complementary Medicine Acupuncture Network (NICMAN) scale.[44] NICMAN scale is recommended for use in conjunction with the STRICTA checklist to assess the reporting of acupuncture interventions in research. It contains 11 items covering four main domains (reporting according to PICOS; acupuncture point selection, location, depth of insertion, and manipulation; needle brand and dimensions; and adequate administration based on total numbers of treatments and qualification of practitioners). A higher score (total of 23) indicates a higher quality of reporting. Scores were assessed independently by two researchers (NG and KK), with discrepancies resolved by discussion. If consensus could not be reached, then the third author (MA) made the final assessment.

2.4.2. Risk of bias

Risk of bias was assessed using the revised Cochrane Risk-of-bias (RoB2) tool for individually randomized, parallel-group trials (current version dated 22 August 2019) and for cross-over trials (revised on 18 March 2021).[45] The RoB2 tool is a structured, validated tool for appraising the risk of bias in randomized trials. It contains a fixed domains of randomization process, deviations from intended interventions, missing outcome, measurement of the outcome, and selection of reported results. For cross-over designs, an additional domain addresses the risk of bias in relation to carryover effects. The risk of bias assessment was independently performed by NG and KK without the use of automated tools. Discrepancies were discussed until consensus was reached, and a third party was consulted (KC, AB) or the third author (MA) when necessary. One of the authors (MA) was an author in one of the studies included for analysis[35] and was therefore not involved in any form of data extraction or review for that paper.

2.4.3. Certainty of evidence

Certainty of evidence was assessed using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE).[46] Certainty was downgraded from 'high certainty' by one level for serious concerns and two for very serious concerns. Domains include risk of bias, indirectness, inconsistency, imprecision, and potential publication bias. GRADE was assessed independently by two researchers (NG and KK). Discrepancies were resolved by discussion and with the assistance of the third author (MA).

2.5. Data analysis

Random-effects meta-analyses were conducted using the Comprehensive Meta-Analysis software (Version 3.0) for pain severity and HRQoL. Differences between intervention and control group at the end of treatment and follow-up were calculated using Hedges' g (g) for effect size or mean difference (MD), both with 95 % confidence intervals (CI).[47] Effect sizes were categorized as small (0.2), moderate (0.5), or large (0.8) as per Cohen.[48] A random effects model was used due to the underlying clinical heterogeneity of the trials. Statistical heterogeneity between studies was quantified using Cochran's Q, with a P-value of <0.05 indicating significant heterogeneity.[49]

2.5.1. Subgroup analysis

Subgroup analysis was planned for the different theoretical frameworks (e.g., TCM-style vs. Japanese-style acupuncture), total number of treatments, and mode of stimulation (manual vs. electro).

2.5.2. Data imputation and sensitivity analysis

For studies that did not report a mean and standard deviation (SD), the median, interquartile ranges (IQR), and sample size were converted using McGrath's method for unknown non-normal distributions,[50] and using the Hozo's method where the range was provided instead of the IQR.[51,52] Results from a box plot were estimated using a web plot digitizer.[53] To determine the effect of these imputation methods, where the primary outcome of pain severity had at least two studies contributing data, if one or more of these were using imputed data a sensitivity analysis was undertaken to determine if removing the imputed data changed the outcome.

3. Results

3.1. Study characteristics

The database search yielded 1074 hits, with 263 were removed as duplicates, and 787 papers were excluded based on title and abstract. Twenty-four full text publications were assessed for eligibility, of which six studies could not be retrieved through local collections, interlibrary loan, or direct correspondence with authors. Further twelve studies were excluded due to absence of randomization ($N = 5$), Chinese language ($N = 5$), or acupuncture was not provided as a primary intervention in at least one intervention arm ($N = 2$). Six studies were included in the final analysis, with a total of 371 participants (Fig. 1). An overview of the characteristics of included studies are reported in Table 1.

3.1.1. Study design

Four studies used a parallel group design with an acupuncture group and a control group. One study used a cross-over design in which both groups acted as intervention group and control group.[37] Due to a sustained effect in group 1 after acupuncture treatment, the results of the second treatment unit were excluded from the meta-analysis. One study was a three-arm study with two control groups, but only one control group was randomized.[40]

3.1.2. Country

Two studies were conducted in China,[36,40] two in English speaking countries (Australia and USA),[35,39] one in Austria[37] and one in Brazil.[38]

3.1.3. Sample sizes

Sample sizes ranged from 18 to 106 with a median of 58.5 participants. Two studies were feasibility studies with small sample sizes.[35,39] The median sample sizes of the feasibility studies was 23.5,[35,39] while the median of the other studies was 88.[36–38,40]

3.1.4. Mean age

One study looked at adolescent girls (13–22 years) with a mean age of 17.4 years.[39] One study did not report the participants' ages.[40] The mean age of the remaining studies ranged from 30.1 to 33.64 years.[35–38] The overall mean age was 29.9 years.

3.1.5. Type of diagnosis

All studies used surgery (laparoscopy or laparotomy) to diagnose endometriosis, but surgery was not mandatory in two studies: one study allowed participation if the diagnosis was made by visual detection methods (ovarian endometrioma detected by ultrasound or magnetic resonance imaging),[36] and one study included women on the waiting list for laparoscopy.[37]

3.2. Intervention detail

3.2.1. Acupuncture rationale

Style of acupuncture: all studies used manual acupuncture, including TCM-style ($N = 2$),[35,37] Japanese-style ($N = 1$),[39] and ear acupuncture ($N = 1$).[40] Two studies did not specify the style of acupuncture used.

Rationale for treatment: rationale for treatment protocol was based on previous study protocols ($N = 1$),[35] based on TCM theory ($N = 1$),[38] or based on a treatment manual developed in a focus group format.[39] Remaining three studies did not provide a rationale for the treatment protocol.

Extent of treatment variation: fixed treatment protocols were used in three studies,[35,36,38] semi-individualized treatment was used in one study using a fixed set of points plus three variable points according to individual presentations,[37] and one study used individualized points based on individual participants' symptoms following an *a priori*-determined decision algorithm.[39] One study did not report the extent of treatment variation.

3.2.2. Details of needling

Number of needles: an average of 12.8 needles were used (range: 8–19) per session. The number of needles was either fixed ($N = 3$),[35,36,38] or varied depending on the individual situation ($N = 2$).[37,39] In one study, the number of needle insertions remained unclear.[40]

Acupuncture points: either body acupuncture points ($N = 5$)[35–39] or ear points ($N = 1$)[40] were used. Four studies reported the name of body points used ($N = 4$).[35–38] Frequently used points were local points in the lower abdomen ($N = 4$), Spleen 6 ($N = 4$), Liver 3 ($N = 4$), Stomach 36 ($N = 3$), Spleen 10 ($N = 3$), Spleen 9 ($N = 2$), Liver 8 ($N = 2$), Kidney 10 ($N = 2$).

Depth: the depth of needle insertion either followed TCM literature ($N = 3$),[35–37] superficial at skin level ($N = 1$),[39] or not reported ($N = 2$).[38,40]

Response: *De Qi* response was sought in three studies[35–37] (awareness of needle described as a heavy, aching, dull, tingling, or distending sensation).[35,54] One study sought slight echo in contrast to strong *De Qi* ($N = 1$),[39] and two studies did not report on any needling response ($N = 2$).[38,40]

Needle stimulation: needles were stimulated manually ($N = 1$),[36] or electrically ($N = 1$).[39] One study applied no stimulation,[35] while three studies did not report on needle stimulation.[37,38,40]

Needle retention time: needles were left in place for 20–30 min ($N = 2$),[35,36] ≤ 20 min ($N = 2$),[38,39] or the time was not reported ($N = 2$).[37,40]

Table 1
Study characteristics of included studies.

Study	Armor 2021	Li 2023	Rubi-Klein 2010	Sousa 2016	Wayne 2008	Xiang 2002
Country	Australia	China	Austria	Brazil	USA	China
Diagnosed by	Laparoscopy	Laparoscopy/endometrioma by ultrasound or MRI	Laparoscopy	Laparoscopy /waiting list for laparoscopy	Laparoscopy	Laparoscopy
Outcome measure	NRS, EHP, analgesic	VAS, EHP, analgesic	VAS, SF 36, analgesic	VAS, EHP	NRS, EHP	Unclear
Total # of participants/after dropouts	29/19	106/106	101/83	46/42	18/14	67/67 (+8)*
# of participants in acupuncture group/after dropouts	14/12	53/53	47/42	23/20	10/9	37/37
# of participants in control group/after dropouts	15/7	53/53	54/41	23/22	8/5	30/30 (8/8)[a]
# of arms	2	2	2	2	2	3
Mean age	33.4	30.2	33.64	30.81	17.4	NR
Style of acupuncture	TCM-style	Not specified	TCM-style	Not specified	Japanese-style	Ear acupuncture
Reasoning for treatment	Yes	No	No	Yes	Yes	No
Treatment variations	Fixed protocol	Fixed protocol	Semi-individualized (fixed + 3 variable points)	Fixed protocol	Manualized according to TCM-diagnosis following a predefined algorithm	Unclear
# of needle insertions used each session	14	9	9–15	19	8–12	Unclear
Names of points used	SP 6, SP 8, SP 10, ST 29, ST 36, CV 3, CV 4, LR 3	CV 4, SP 6, LR 3, KI 6, ST 30	Bl 32, ST 29, ST 36, CV 3, SP 6 + three out of LR 3, LR 8, SP 9, SP 10, KI 10,	Bl 17, GB 29, ST 36, CV 3, SP 6, LR 3, LR 8, SP 9, SP 10, KI 10	Not predefined	Ting Zhong, Pi Zhi Xia, Nei Fen Mi, Jiao Gan, Nei Sheng, Zhi Qi
Depth of insertion	Consistent with literature	15–35 mm	Varying according to TCM-diagnosis	NR	1–2 mm superficial	NR
Response sought	*De Qi*	*De Qi*	*De Qi*	NR	Slight echo	NR
Needle stimulation	No stimulation	Manually every 10 min	NR	NR	Electrically	NR
Needle retention time	> 20–30 min	> 20–30 min	NR	≤ 20 min	≤ 20 min	NR
Needle type: Disposable sterile stainless-steel needles, 0.18–0–3 × 25–40 mm or other	Yes	Yes	Yes	Yes	0.18–16 mm sterile single use gold and silver needles	NR
Total # of treatments	16	9 + x	10	5	16	12
Frequency of treatments	Twice/week	Starting one week before menstruation, during menstruation daily, when pain occurred	Twice/week	Once/week	Twice/week	Starting 5 days before menstruation every other day, four times each cycle
Total duration of treatment	8 weeks	12 weeks	5 weeks	5 weeks	8 weeks	12 weeks
Other treatment components	Contraceptives, analgesics	Analgesics	Moxibustion, analgesics	Contraceptives	Ear acupuncture, Moxibustion	NR
Setting and context	Private clinics and university	Hospitals	Hospital	NR	Private clinics or at home of participants	Hospital
Practitioner background	Registered acupuncturists	Doctors of TCM + protocol training	Registered acupuncturists	Physiotherapist (competency on acupuncture unclear)	Licensed acupuncturists + protocol training	NR
Rationale for comparator	No	No	No	No	Yes	Yes
Description of comparator	As per medical advice but no TCM	Non-specific acupuncture: superficial at non-acupuncture points without stimulation	Non-specific acupuncture: acupuncture at points with no correlation to endometriosis	Non-specific acupuncture: simulated therapy with needle insertion 3 cm apart from original point	Non-penetrating sham acupuncture, sham ear acupuncture, sham moxibustion	Chinese herbal medicine (No intervention)[a]

* Data of third treatment arm in parentheses, since not randomized and excluded from this meta-analysis (for the outcomes in this meta-analysis only second treatment group as comparator group with Chinese herbal medicine as control intervention). EHP-30, endometriosis health profile; MRI, magnetic resonance imaging; NR, not reported; NRS, numeric rating scale; SF 36, short form (endometriosis questionnaire on quality of life); TCM, Traditional Chinese medicine; VAS, visual analogue scale.
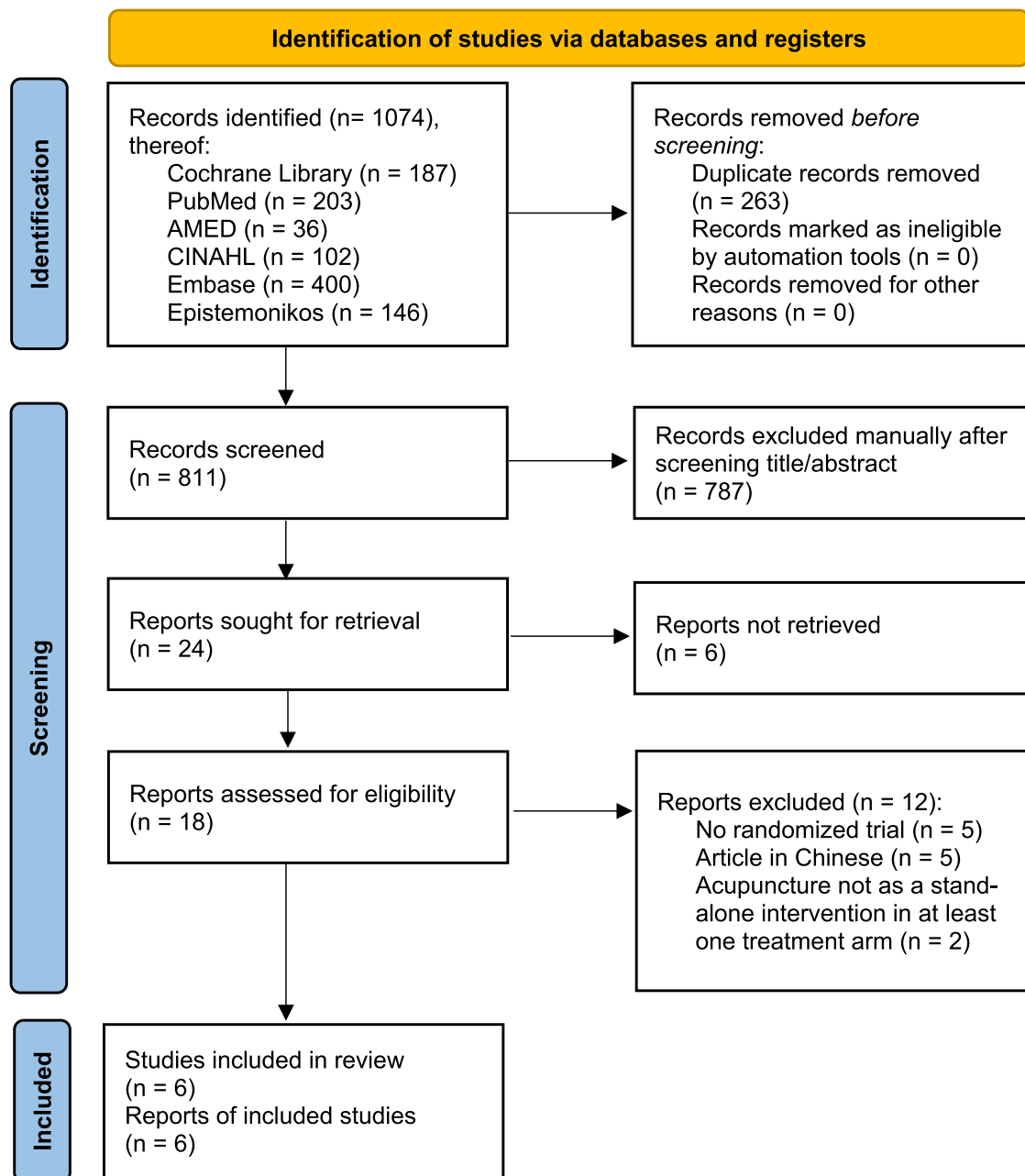
Fig. 1. PRISMA flowchart of study selection and results.

Needle type: sterile, disposable stainless-steel needles 0.18–0.3 × 25–40 mm ($N = 4$)[35–38] or sterile, disposable gold and silver needles 0.18–16 mm ($N = 1$)[39] were used. One study did not report the needle type used.[40]

3.2.3. Treatment regimen

Number of sessions: total number of treatment sessions ranged from five to 16. One study reported varying numbers according to participants' pain symptoms during menstruation with a maximum of 16 sessions.[36]

Frequency and duration: treatment frequency ranged from once weekly to daily and was administered either throughout the whole menstrual cycle ($N = 4$)[35,37–39] or only before and during menstruation ($N = 2$).[36,40] Treatment duration ranged from 5 to 12 weeks with a mean of 8.33 weeks.

3.2.4. Other components of treatment

Other treatment components included usual care: hormonal treatment ($N = 2$)[35,38] and/or analgesics ($N = 3$),[35–37] moxibustion (part of TCM treatment along with acupuncture, involving igniting dried herbs and using its warmth to stimulate acupuncture points)[55] ($N = 2$),[37,39] ear acupuncture ($N = 1$),[39] or no additional treatment component ($N = 1$).[40]

Treatment settings could be multicenter ($N = 3$)[35,36,39] or single-center ($N = 2$)[37,40,] and included hospitals ($N = 3$),[36,37,40] private clinics ($N = 2$),[35,39] university ($N = 1$),[35] or participants' homes ($N = 1$).[39] One study did not clearly report the study setting.[38]

3.2.5. Practitioner background

Practitioners were either licensed/registered acupuncturists ($N = 3$)[35,37,39] or doctors of TCM ($N = 1$)[36] One study included physiotherapists, and the competency regarding acupuncture was un-

clear.[38] Practitioners in two studies received training in the treatment protocol prior to commencement.[36,39] One study did not provide information on practitioners' backgrounds.[40]

3.2.6. Comparator

Three of six studies used variations of non-specific acupuncture (where penetrating acupuncture was used either at non-acupuncture points or points which were chosen as having no influence on pelvic pain) as a comparator. These include superficial at non-acupuncture points without stimulation,[36] non-specific acupuncture at well-defined points with no association to endometriosis (short intestine 9, gallbladder 31, lungs 1, stomach 8),[37] and simulated therapy with needle insertion 3 cm apart from acupuncture points.[38] In contrast to the penetrating non-specific acupuncture, one study used a sham acupuncture protocol (non-invasive devices).[39] One study compared acupuncture with usual care[35] and one study used Chinese herbal treatment.[40] Two of six studies provided a rationale for the control intervention.[39,40]

3.3. Quality/risk of bias of included studies

3.3.1. Acupuncture quality

NICMAN scores ranged from 13[40] to 22[35,39] out of 23, with a mean of 19. The quality of acupuncture delivered in trials has been improving over time. Studies from 2016 and earlier had a mean NICMAN score of 17.75 while those undertaken in the last three years had a mean NICMAN score of 21.5. The primary factors that caused a reduction in the NICMAN score were that most studies did not provide information on the acupuncture point selection,[36–38,40] needling depth and manipulation,[37,38,40] and point location.[38,40]

3.3.2. Risk of bias

Risk of bias for pain severity was low risk for one study, some concerns for two studies, and three studies had a high risk of bias (Fig. 2). Detailed risk of bias information is reported in Supplement 3.

- Randomization

Three studies were at low risk of randomization bias, and three studies did not provide details on the randomization process and were assessed as unclear.

- Carryover effect

The carryover effect was assessed only for the cross-over trial.[37] There was a sustained treatment effect in the acupuncture group after phase 1, suggesting a high risk of bias for phase 2 data. Therefore, only phase 1 data were included in the meta-analysis.

- Deviations from intended intervention

Three studies provided a study protocol, two of which were rated as having a low risk of deviation from the intended intervention. The third study did not provide enough information. The three studies without a study protocol did not report deviation from treatment and the risk of bias was unclear.

- Missing outcome data

Outcome data were adequately reported in five studies and at low risk of bias. Dropout rates in one study might depend on the true value, leading to a high risk of bias.

- Measurement of the outcome

Participants were not blinded in two studies, and at high risk of bias. Four studies had a low risk of bias.

- Selection of the reported results

One study did not provide details of an analysis plan and was assessed as unclear. Five studies were at a low risk of bias.

3.3.3. Certainty of evidence (GRADE)

The certainty of evidence ranged from moderate to very low as outlined in the summary of findings table (Table 2).

3.3.4. Publication bias

Due to the small number of studies, publication bias was not assessed.

3.4. Intervention effects

Three studies did not report mean and SD in the text of the manuscript[35–37]. For these three studies mean and SD were estimated from the median, IQR, and sample size,[35] from the median, range, and sample size,[36] and from a box and whisker plot.[37]

3.4.1. Pain severity

Reporting of pain severity varied between studies. Studies reported menstrual pain,[35,36,40] non-menstrual pelvic pain, chronic pelvic pain,[38,39] or simply as pain.[37] The studies that did not specify menstrual pain or non-menstrual/non-cyclical pain were grouped as 'non-specified pelvic pain' in this meta-analysis. This meta-analysis included analysis on menstrual pain, non-menstrual pain, non-specified pelvic pain, and overall pelvic pain.

Two studies reported both menstrual and non-menstrual pain.[35,36] In one of these studies, the baseline for non-menstrual pain was zero.[36] Since the eligibility criteria for this meta-analysis was pain symptoms, the data on non-menstrual pain for this study were excluded, with only the data on menstrual pain being included in the meta-analysis.

- Acupuncture versus non-specific acupuncture

There was evidence of a large effect for acupuncture compared to non-specific acupuncture on overall pelvic pain at the end of treatment ($g = 1.54$, 95 % CI 0.92 to 2.16; 3 RCTs, $n = 231$, low certainty evidence, $p<0.001$) (Fig. 3A). There was evidence of a large effect on menstrual pain at the end of treatment ($g = 1.67$, 95 % CI 1.23 to 2.12, 1 RCT, $n = 106$, moderate certainty evidence, $p<0.001$) and for non-specified pelvic pain at the end of treatment (Fig. 3B) (MD −2.77, 95 % CI 2.15 to 3.38, 2 RCTs, $n = 125$, low certainty evidence, $p<0.001$). There was evidence of a large effect for non-specified pelvic pain ($g = 2.44$, 95 % CI 1.68 to 3.19, 1 RCT, $n = 42$, very low certainty evidence, $p<0.001$) at follow-up. There was no evidence of a difference in menstrual pain at follow-up ($g = 0.19$, 95 % CI −0.19 to 0.57, 1 RCT, $n = 106$, moderate certainty evidence, $p = 0.33$).

A sensitivity analysis removing studies where imputation was used did not change the direction of effect for overall pelvic pain at the end of treatment ($g = 2.11$, 95 % CI 1.39 to 2.82, 1 RCT, $n = 46$, $p<0.001$) or for non-specified pelvic pain at the end of treatment ($g = 2.65$, 95 % CI 1.94 to 3.36, 1 RCT, $n = 46$, $p<0.001$).

- Acupuncture versus usual care

There was evidence of a large effect on menstrual pain at the end of treatment for acupuncture compared to usual care and ($g = 0.9$, 95 % CI 0.15 to 1.64, 1 RCT, $n = 19$, very low certainty evidence, $p = 0.02$). There was no evidence of a difference in non-menstrual pain at the end of treatment ($g = 0.68$, 95 % CI −0.05 to 1.41, 1 RCT, $n = 19$, very low certainty evidence, $p = 0.07$).

- Acupuncture versus sham acupuncture

There was no evidence of a difference for non-specified pelvic pain for a Japanese acupuncture protocol compared to a sham acupuncture protocol at the end of treatment ($g = 0.13$, 95 % CI −0.76 to 1.02, 1 RCT, $n = 14$, very low certainty evidence, $p = 0.77$), or at follow-up ($g = 0.2$, 95 % CI −0.69 to 1.09, 1 RCT, $n = 14$, very low certainty evidence, $p = 0.66$).

- Acupuncture versus Chinese herbal medicine

Table 2

Summary of findings for acupuncture for endometriosis.

Outcomes	Anticipated absolute effects* (95 % CI)		Number of participants (studies)	Certainty of evidence (GRADE)	Comments
	Risk with comparator	Risk with Acupuncture			
Acupuncture compared to non-specific acupuncture for endometriosis					
Pain (overall) at end of treatment		Hedges' g 1.54 higher (0.917 higher to 2.16 higher)	231 (3 RCTs)	⊕⊕◯◯ Low[a,b]	There was a large beneficial effect on overall pain at the end of treatment for acupuncture when compared to non-specific acupuncture
Pain (non-specified) assessed with 10 cm VAS at end of treatment	The mean pain (non-specified) was **5.75 cm**	MD 2.77 cm lower (2.149 lower to 3.384 lower)	125 (2 RCTs)	⊕⊕◯◯ Low[a,c]	There was a clinically significant reduction (>2 cm on 10 cm VAS or >20 %) in non-specified pelvic pain at the end of treatment for acupuncture when compared to non-specific acupuncture
Pain (menstrual) at end of treatment		Hedges' g 1.67 higher (1.23 higher to 2.12 higher)	106 (1 RCT)	⊕⊕⊕◯ Moderate[c]	There was a large beneficial effect on menstrual pain at the end of treatment for acupuncture when compared to non-specific acupuncture
Pain (non-specified) at follow-up		Hedges' g 2.44 higher (1.68 higher to 3.19 higher)	42 (1 RCT)	⊕◯◯◯ Very low[d,e]	There was a large beneficial effect on non-specified pelvic pain at the end of the follow-up period for acupuncture when compared to non-specific acupuncture
Pain (menstrual) at follow-up		Hedges' g 0.19 higher (0.19 lower to 0.57 higher)	106 (1 RCT)	⊕⊕⊕◯ Moderate[c]	There was no evidence of benefit on menstrual pain at the end of the follow-up period for acupuncture when compared to non-specific acupuncture
Health Related Quality of Life (HRQoL) at end of treatment		Hedges' g 1.24 higher (0.73 lower to 3.21 higher)	148 (2 RCTs)	⊕◯◯◯ Very low[b,c,d]	There was no evidence of benefit on health-related quality of life at the end of treatment for acupuncture when compared to non-specific acupuncture
Health Related Quality of Life (HRQoL) at follow-up		Hedges' g 0.6 higher (0.32 lower to 0.44 higher)	106 (1 RCT)	⊕⊕⊕◯ Moderate[c]	There was no evidence of benefit on health-related quality of life at the end of the follow-up period for acupuncture when compared to non-specific acupuncture
Acupuncture compared to usual care for endometriosis					
Pain (menstrual) at end of treatment		Hedges' g 0.9 higher (0.15 higher to 1.64 higher)	19 (1 RCT)	⊕◯◯◯ Very low[e,f]	There was a large beneficial effect on menstrual pain at the end of treatment for acupuncture when compared to usual care

(*continued on next page*)

Table 2 (*continued*)

Outcomes	Anticipated absolute effects* (95 % CI)		Number of participants (studies)	Certainty of evidence (GRADE)	Comments
	Risk with comparator	Risk with Acupuncture			
Pain (non-menstrual) at end of treatment		Hedges' g 0.68 higher (0.05 lower to 1.41 higher)	19 (1 RCT)	⊕◯◯◯ Very low[e,f]	There was no evidence of benefit on non-menstrual pain at the end of treatment for acupuncture when compared to usual care
Health Related Quality of Life (HRQoL) assessed with: EHP-30 at 4-week follow-up		Hedges' g 0.76 higher (0.02 higher to 1.49 higher)	19 (1 RCT)	⊕◯◯◯ Very low[e,f]	There was a moderately beneficial effect on health-related quality of life at 4-week follow-up for acupuncture when compared to usual care
Acupuncture compared to sham acupuncture for endometriosis					
Pain (non-specified) at end of treatment		Hedges' g 0.13 higher (0.76 lower to 1.02 higher)	14 (1 RCT)	⊕◯◯◯ Very low[e,g]	There is no evidence of benefit on non-specified pelvic pain at the end of treatment for Japanese style acupuncture compared to sham acupuncture
Pain (non-specified) at follow-up		Hedges' g 0.2 higher (0.69 lower to 1.09 higher)	14 (1 RCT)	⊕◯◯◯ Very low[e,g]	There is no evidence of benefit on non-specified pelvic pain at follow-up for Japanese style acupuncture compared to sham acupuncture
Health Related Quality of Life (HRQoL) at end of treatment		Hedges' g 1.3 higher (0.32 higher to 2.28 higher)	14 (1 RCT)	⊕◯◯◯ Very low[e,g]	There is evidence of a large beneficial effect on health-related quality of life at end of treatment for Japanese style acupuncture compared to sham acupuncture
Health Related Quality of Life (HRQoL) at follow-up		Hedges' g 1.56 higher (0.54 higher to 2.58 higher)	14 (1 RCT)	⊕◯◯◯ Very low[e,g]	There is evidence of a large beneficial effect on health-related quality of life at follow-up for Japanese style acupuncture compared to sham acupuncture
Acupuncture compared to Chinese Herbal Medicine for endometriosis					
Pain (menstrual) at end of treatment		Hedges' g 1.67 higher (1.12 higher to 2.22 higher)	67 (1 RCT)	⊕◯◯◯ Very low[c,h]	There is evidence of a large beneficial effect on menstrual pain at the end of the treatment for acupuncture when compared to Chinese herbal medicine.

* The risk in the intervention group (and its 95 % confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95 % CI).CI, confidence interval; RCT, randomized controlled trial; VAS, visual analogue scale MD, mean difference; EHP-30, endometriosis health profile.GRADE Working Group grades of evidenceHigh certainty: we are very confident that the true effect lies close to that of the estimate of the effect.Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect.Explanations.

[a] . Downgraded 1 level for serious risk of bias: most studies are at unclear or high risk of bias in a minimum of one domain due to lack of blinding and lack of study protocol leading to uncertainty of deviation from intended intervention; No information on randomization process, no ITT analysis with a potential impact on the results; missing outcome data.

[b] . Downgraded 1 level for serious inconsistency: Despite random effects model significant (*P*<0.05) heterogeneity present.

[c] . Downgraded 1 level for serious imprecision: Small sample size.

[d] . Downgraded 1 level for serious risk of bias: unclear risk of bias due to lack of blinding and lack of study protocol leading to uncertainty of deviation from intended intervention.

[e] . Downgraded 2 levels for very serious imprecision: Very small sample size.

[f] . Downgraded 2 levels for very serious risk of bias: Lack of participants' blinding leading to high risk of bias for high risk of influence on patient-reported outcomes.

[g] . Downgraded 1 level for serious risk of bias: no information on randomization process, no ITT analysis with a potential impact on the results.

[h] . Downgraded 2 level for very serious risk of bias: no information on randomization process; lack of blinding, lack of study protocol leading to uncertainty of deviation from intended intervention and lack of pre-specified analysis plan, no ITT analysis with a potential impact on the results; lack of information on measurement of outcome and outcome assessment.

	Randomisation process	Carryover effect*	Deviations from the intended interventions	Missing outcome data	Measurement of the outcome	Selection of the reported result	Overall
Armour 2021	+	NA	+	+	-	+	-
Li 2023	+	NA	+	+	+	+	+
Rubi-Klein 2010	!	-	!	-	+	+	-
Sousa 2016	+	NA	!	+	+	+	!
Wayne 2008	!	NA	!	+	+	+	!
Xiang 2002	!	NA	!	+	-	!	-

NA: not applicable

* only relevant for the crossover trial by Rubi-Klein

+ Low risk   ! Some concerns   - High risk

There was evidence of a large benefit on menstrual pain for acupuncture compared to Chinese herbal medicine at the end of treatment ($g = 1.67$, 95 % CI 1.12 to 2.22, 1 RCT, $n = 67$, very low certainty evidence, $p < 0.001$).

3.4.2. Adverse events

Four studies reported mild adverse events after acupuncture treatment ($n = 222$).[35–37,39] Adverse events included bruising, soreness at the needle site, lightheadedness or hypotonic reaction, that occurred after 0.5 % to 6.7 % of acupuncture treatments, without need for medical intervention. One event of hypotension was reported that required medical attention, which stabilized after 30 min. Two studies did not report adverse events.[38,40]

3.4.3. Health-related quality of life

- Acupuncture versus non-specific acupuncture

There was no evidence of a difference for acupuncture compared to non-specific acupuncture on HRQoL at the end of treatment (Fig. 3C) ($g = 1.24$, 95 % CI −0.73 to 3.21; 2 RCTs, $n = 148$, very low certainty evidence, $p = 0.22$) or at follow-up ($g = 0.6$, 95 % CI −0.32 to 0.44, 1 RCT, $n = 106$, moderate certainty evidence, $p = 0.76$).

- Acupuncture versus usual care

There were moderate improvements in HRQoL at four weeks follow-up for acupuncture compared to usual care ($g = 0.76$, 95 % CI 0.02 to 1.49, 1 RCT, $n = 19$, very low certainty evidence, $p = 0.04$).

- Acupuncture versus sham acupuncture

There was evidence of a large benefit for acupuncture compared to sham acupuncture on HRQoL at the end of treatment ($g = 1.3$, 95 % CI 0.32 to 2.28, 1 RCT, $n = 14$, very low certainty evidence, $p = 0.01$), and at eight weeks follow up ($g = 1.56$, 95 % CI 0.54 to 2.58,1 RCT, $n = 14$, very low certainty evidence, $p = 0.003$).
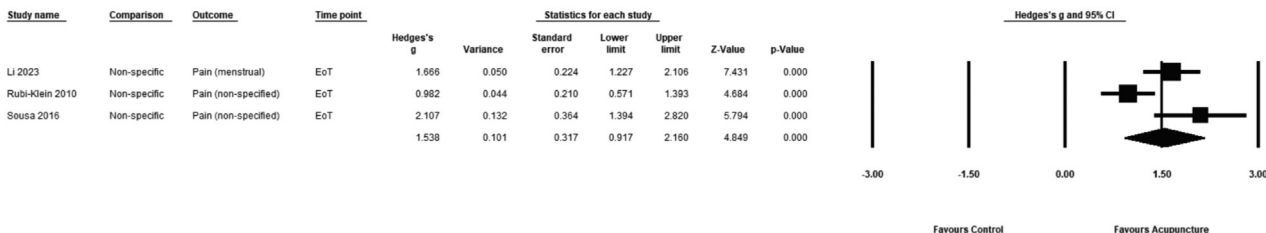
3.4.4. Most bothersome symptom

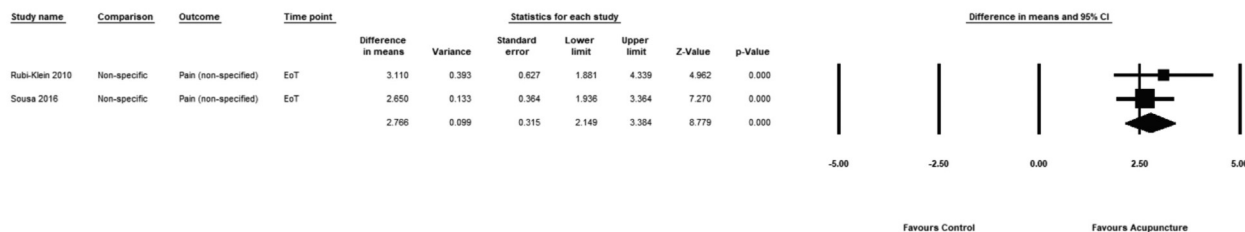No study reported on the most bothersome symptom.

3.4.5. Changes in analgesic medication

Three studies reported on the use of analgesic medication. Due to the heterogenous nature of data collection this could not be included in the meta-analysis. One study ($n = 19$) reported a mean reduction in days where analgesia was used per month from 11.0 (9.6) to 7.5 (8.3) in the acupuncture group compared to 8.8 (9.7) to 7.3 (7.5) in the usual care group.[35] Another study ($n = 83$) reported a significant decrease ($p = 0.03$) in the acupuncture group compared to non-specific acupuncture, with 54 % of participants did not use analgesics after treatment compared to 21 % at baseline.[37]

(A) Overall pelvic pain

Study name	Comparison	Outcome	Time point	Hedges's g	Variance	Standard error	Lower limit	Upper limit	Z-Value	p-Value
Li 2023	Non-specific	Pain (menstrual)	EoT	1.666	0.050	0.224	1.227	2.106	7.431	0.000
Rubi-Klein 2010	Non-specific	Pain (non-specified)	EoT	0.982	0.044	0.210	0.571	1.393	4.684	0.000
Sousa 2016	Non-specific	Pain (non-specified)	EoT	2.107	0.132	0.364	1.394	2.820	5.794	0.000
				1.538	0.101	0.317	0.917	2.160	4.849	0.000

Hedges's g and 95% CI

Favours Control — Favours Acupuncture

(B) Non-specified pelvic pain

Study name	Comparison	Outcome	Time point	Difference in means	Variance	Standard error	Lower limit	Upper limit	Z-Value	p-Value
Rubi-Klein 2010	Non-specific	Pain (non-specified)	EoT	3.110	0.393	0.627	1.881	4.339	4.962	0.000
Sousa 2016	Non-specific	Pain (non-specified)	EoT	2.650	0.133	0.364	1.936	3.364	7.270	0.000
				2.766	0.099	0.315	2.149	3.384	8.779	0.000

Difference in means and 95% CI

Favours Control — Favours Acupuncture

(C) Health related quality of life (HRQoL)

Study name	Comparison	Outcome	Time point	Hedges's g	Variance	Standard error	Lower limit	Upper limit	Z-Value	p-Value
Li 2023	Non-specific	HRQoL	EoT	0.260	0.038	0.194	-0.120	0.640	1.342	0.179
Sousa 2016	Non-specific	HRQoL	EoT	2.270	0.140	0.374	1.536	3.003	6.066	0.000
				1.239	1.009	1.004	-0.729	3.208	1.234	0.217

Hedges's g and 95% CI

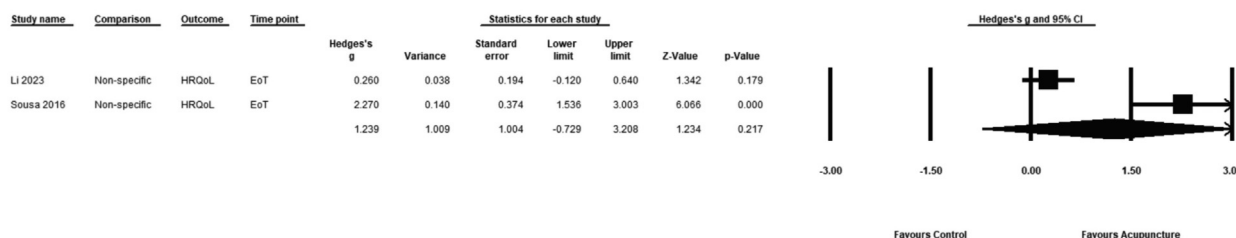Favours Control — Favours Acupuncture

Fig. 3. Acupuncture vs non-specific acupuncture on (A) overall pelvic pain; (B) non-specified pelvic pain; (C) HRQoL.

3.4.6. Subgroup analysis

Subgroup analysis could not be performed as each subgroup was too small (<3) to provide reliable conclusions.

4. Discussion

Acupuncture for endometriosis demonstrated benefit in reducing the severity of menstrual pain and overall pelvic pain when compared to non-specific acupuncture, usual care, and Chinese herbal medicine. Reductions in pelvic pain severity were clinically relevant, with reductions in VAS scores for pelvic pain >20 %, well in excess of the minimum clinically important difference.[56] Similar benefits were observed for HRQoL when compared to sham acupuncture and to usual care. Although a meta-analysis could not be performed, studies generally reported greater reductions in analgesic usage in the acupuncture versus the comparison groups.

None of the included studies fulfilled all the criteria on reporting the core outcomes set for endometriosis research.[34] This is unsurprising given that all the included studies started recruitment prior to this publication. However, it is important for future research to include these outcomes as *a priori* outcomes.

The findings of this study demonstrating the effect of acupuncture for endometriosis-related symptoms is consistent with previous reviews.[57,58] Our review provides an important update with the addition of two recently published studies, the use of GRADE for certainty of evidence and the NICMAN scale to evaluate the quality of the acupuncture delivered. There was an improvement in reporting quality of acupuncture interventions on the NICMAN scale and STRICTA in more recent studies. More high-quality studies reporting in line with the STRICTA

guidelines would allow future analysis on the details of treatment methods.

Very few studies investigated medium to long term effects of acupuncture[59] with studies providing conflicting information on the duration of any potential benefits. A longer follow-up may provide more insight into potential long term benefits of acupuncture, similar to the sustained benefits observed for dysmenorrhea for up to one-year follow-up.[60] Another consideration is the financial burden associated with endometriosis, and that potential ongoing acupuncture treatments may add to this burden.[16,61] Future studies investigating different frequencies and doses of acupuncture may provide information on the ideal or a cost-effective dose for the management of endometriosis-related symptoms, at different stages of the disease.[62,63]

There is a clear need for more high-quality randomized controlled trials to draw more accurate conclusions on how effective acupuncture is for managing endometriosis-related symptoms. Future studies should give attention to recruiting sufficient sample size, as this was the main limiting factor for most trials (GRADE). Reporting should include clear reporting on the randomization process, deviation from intervention (RoB2 domain 1,2), adverse events, and needling details (STRICTA, NICMAN scale).

Sham and non-specific acupuncture are associated with larger effects than other pharmacological or physical placebos[64] and are sometimes as powerful as verum acupuncture due to both psychological and physiological effects of needle insertion.[65] Future acupuncture trials may consider that sham acupuncture with skin penetration has only been recommended for trials investigating point specificity, but not for investigating the efficacy of acupuncture treatment.[66] In clinical practice, acupuncture is usually applied as a whole-systems-intervention,[67] with expert consensus suggesting cumulative benefits of combined treatment

of acupuncture and Chinese herbal medicine in the management of endometriosis.[27] Future research using a pragmatic study design may provide a better insight into how acupuncture is delivered in the community clinical setting.[68]

In conclusion, acupuncture may cause a large reduction in pelvic pain compared to non-specific acupuncture at the end of treatment. This reduction probably does not continue after cessation of treatment, however due to the nature of how this was reported in different studies no firm conclusions can be drawn. It is currently uncertain what effect acupuncture has on pain compared to usual care. Acupuncture may improve health related quality of life, but we are very uncertain about the results Acupuncture should be considered in the clinical management of endometriosis for those who have not responded to other interventions and where pelvic pain is a primary concern. Future trials would benefit from investigating acupuncture as part of a whole systems intervention, comparing different 'doses' of acupuncture, having larger sample sizes, undertaking longer post treatment follow-up, and improving reporting in line with STRICTA guidelines.

Acknowledgments

CRediT authorship contribution statement

Nora Giese: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Project administration. **Ki Kyung Kwon:** Formal analysis, Investigation, Writing – review & editing. **Mike Armour:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing – review & editing, Visualization, Supervision, Project administration.

Conflict of interests

As a medical research institute, NICM Health Research Institute (at Western Sydney University) receives research grants and donations from foundations, universities, government agencies, and industry. Sponsors and donors provide united and tied funding for work to advance the vision and mission of the Institute. MA, NG and KK are all trained acupuncturists. MA is editorial board member of the Journal Integrative Medicine Research.

Funding

Ethical statement

Not applicable.

Data availability

The datasets supporting the findings of this study are available within the article and its supplementary files.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2023.101003.

Supplement 1. Search strategies
Supplement 2. STRICTA checklist
Supplement 3. Risk of bias details
Supplement 4. PRISMA checklist

References

1. Tomassetti C, Johnson NP, Petrozza J, Abrao MS, Einarsson JI, Horne AW, et al. An international terminology for endometriosis. *Facts Views Vis ObGyn.* 2021;13(4):295–304.
2. Rowlands IJ, Abbott JA, Montgomery GW, Hockey R, Rogers P, Mishra GD. Prevalence and incidence of endometriosis in Australian women: a data linkage cohort study. *BJOG Int J Obstet Gynaecol.* 2021;128(4):657–665.
3. Viganò P, Parazzini F, Somigliana E, Vercellini P. Endometriosis: epidemiology and aetiological factors. *Best Pract Res Clin Obstet Gynaecol.* 2004;18:177–200.
4. Moradi Y, Shams-Beyranvand M, Khateri S, Gharahjeh S, Tehrani S, Varse F, et al. A systematic review on the prevalence of endometriosis in women. *Indian J Med Res.* 2021;154(3):446–454.
5. Armour M, Sinclair J, Ng CHM, Hyman MS, Lawson K, Smith CA, et al. Endometriosis and chronic pelvic pain have similar impact on women, but time to diagnosis is decreasing: an Australian survey. *Sci Rep.* 2020;10(1):16253.
6. Armour M, Ciccia D, Stoikos C, Wardle J. Endometriosis and the workplace: lessons from Australia's response to COVID-19. *Aust N Z J Obstet Gynaecol.* 2022;62(1):164–167.
7. Armour M, Lawson K, Wood A, Smith CA, Abbott J. The cost of illness and economic burden of endometriosis and chronic pelvic pain in Australia: a national online survey. *PLoS ONE.* 2019;14(10):e0223316.
8. De Graaff AA, D'Hooghe TM, Dunselman GAJ, Dirksen CD, Hummelshoj L, EndoCost Consortium WERF, et al. The significant effect of endometriosis on physical, mental and social wellbeing: results from an international cross-sectional survey. *Hum Reprod.* 2013;28(10):2677–2685.
9. Melis I, Litta P, Nappi L, Agus M, Melis GB, Angioni S. Sexual function in women with deep endometriosis: correlation with quality of life, intensity of pain, depression, anxiety, and body image. *Int J Sex Health.* 2015;27(2):175–185.
10. Van Niekerk LM, Schubert E, Matthewson M. Emotional intimacy, empathic concern, and relationship satisfaction in women with endometriosis and their partners. *J Psychosom Obstet Gynecol.* 2021;42(1):81–87.
11. Della Corte L, Di Filippo C, Gabrielli O, Reppuccia S, La Rosa VL, Ragusa R, et al. The burden of endometriosis on women's lifespan: a narrative overview on quality of life and psychosocial wellbeing. *Int J Environ Res Public Health.* 2020;17(13):4683.
12. Evans S, Villegas V, Dowding C, Druitt M, O'Hara R, Mikocka-Walus A. Treatment use and satisfaction in Australian women with endometriosis: a mixed-methods study. *Intern Med J.* 2022;52(12):2096–2106.
13. The Practice Committee of the American Society for Reproductive MedicineTreatment of pelvic pain associated with endometriosis: a committee opinion. *Fertil Steril.* 2014;101(4):927–935.
14. Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, Kiesel L, et al. ESHRE guideline: endometriosis. *Hum Reprod Open.* 2022;2022(2):hoac009.
15. Burla L, Kalaitzopoulos DR, Metzler JM, Scheiner D, Imesch P. Popularity of endocrine endometriosis drugs and limited alternatives in the present and foreseeable future: a survey among 1420 affected women. *Eur J Obstet Gynecol Reprod Biol.* 2021;262:232–238.
16. Malik A, Sinclair J, Ng CHM, Smith CA, Abbott J, Armour M. Allied health and complementary therapy usage in Australian women with chronic pelvic pain: a cross-sectional study. *BMC Womens Health.* 2022;22(1):1–9.
17. O'Hara R, Rowe H, Fisher J. Managing endometriosis: a cross-sectional survey of women in Australia. *J Psychosom Obstet Gynecol.* 2022;43(3):265–272.
18. Horne AW, Saunders PTK, Abokhrais IM, Hogg L. Top ten endometriosis research priorities in the UK and Ireland. *Lancet.* 2017;389(10085):2191–2192.
19. Greene AD, Lang SA, Kendziorski JA, Sroga-Rios JM, Herzog TJ, Burns KA. Endometriosis: where are we and where are we going? *Reproduction.* 2016:R63–R78.
20. Giese N, Gilbert E, Hawkey A, Armour M. Unmet needs of australians in endometriosis research: a qualitative study of research priorities, drivers, and barriers to participation in people with endometriosis. *Medicina (B Aires).* 2023;59(9):1655.
21. Lao L. Acupuncture techniques and devices. *J Altern Complement Med.* 1996;2(1):23–25.
22. McDonald JL, Cripps AW, Smith PK. Mediators, receptors, and signalling pathways in the anti-inflammatory and antihyperalgesic effects of acupuncture. *Evid-Based Complement Altern Med ECAM.* 2015;2015:975632.
23. McDonald JL, Cripps AW, Smith PK, Smith CA, Xue CC, Golianu B. The anti-inflammatory effects of acupuncture and their relevance to allergic rhinitis: a narrative review and proposed model. *Evid-Based Complement Altern Med ECAM.* 2013;2013:591796.
24. Mayor D. An exploratory review of the electroacupuncture literature: clinical applications and endorphin mechanisms. *Acupunct Med J Br Med Acupunct Soc.* 2013;31(4):409–415.
25. Simoens S, Dunselman G, Dirksen C, Hummelshoj L, Bokor A, Brandes I, et al. The burden of endometriosis: costs and quality of life of women with endometriosis and treated in referral centres. *Hum Reprod.* 2012;27(5):1292–1299.
26. RANZCOG. Australian clinical practice guideline for the diagnosis and management of endometriosis 2021. Available from: https://ranzcog.edu.au/wp-content/uploads/2022/02/Endometriosis-clinical-practice-guideline.pdf. Accessed 1st August 2021.
27. Giese N, Heirs MK. Development of provisional acupuncture guidelines for pelvic pain in endometriosis using an e-Delphi consensus process. *J Integr Complement Med.* 2023;29(3):169–180.
28. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71.
29. Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, et al. PRISMA-S: an extension to the PRISMA statement for reporting literature searches in systematic reviews. *Syst Rev.* 2021;10(1):39.

30. Straus SE, Glasziou P, Richardson WS, Haynes RB. *Evidence-based medicine: how to practice and teach EBM* Elsevier; 2018:336.

31. MacPherson H, Altman DG, Hammerschlag R, Youping L, Taixiang W, White A, et al. Revised STandards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA): extending the CONSORT statement. *PLoS Med.* 2010;7(6):e1000261.

32. Hopton AK, Curnoe S, Kanaan M, Macpherson H. Acupuncture in practice: mapping the providers, the patients and the settings in a national cross-sectional survey. *BMJ Open.* 2012;2(1):e000456.

33. Robinson N, Lorenc A, Ding W, Jia J, Bovey M, Wang XM. Exploring practice characteristics and research priorities of practitioners of traditional acupuncture in China and the EU – A survey. *J Ethnopharmacol.* 2012;140(3):604–613 2012.

34. Duffy J, Hirsch M, Vercoe M, Abbott J, Barker C, Collura B, et al. A core outcome set for future endometriosis research: an international consensus development study. *BJOG Int J Obstet Gynaecol.* 2020;127(8):967–974.

35. Armour M, Cave AE, Schabrun SM, Steiner GZ, Zhu X, Song J, 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.

36. Li PS, Peng XM, Niu XX, Xu L, Hung-Yu Ng E, Wang CC, et al. Efficacy of acupuncture for endometriosis-associated pain: a multicenter randomized single-blind placebo-controlled trial. *Fertil Steril.* 2023. [Internet]Available from:. https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02522262/full. Accessed March 28, 2023.

37. Rubi-Klein K, Kucera-Sliutz E, Nissel H, Bijak M, Stockenhuber D, Fink M, et al. Is acupuncture in addition to conventional medicine effective as pain treatment for endometriosis? A randomised controlled cross-over trial. *Eur J Obstet Gynecol Reprod Biol.* 2010;153(1):90–93.

38. de Sousa TR, de Souza BC, Zomkowisk K, da Rosa PC, Sperandio FF. The effect of acupuncture on pain, dyspareunia, and quality of life in Brazilian women with endometriosis: a randomized clinical trial. *Complement Ther Clin Pract.* 2016;25:114–121.

39. Wayne P, Kerr C, Schnyer R, Legedza A, Savetsky-German J, Shields M, et al. Japanese-style acupuncture for endometriosis-related pelvic pain in adolescents and young women: results of a randomized sham-controlled trial. *J Pediatr Adolesc Gynecol.* 2008;21(5):247–257.

40. Xiang D, Situ Y, Liang X, Cheng L, Zhang G. Ear acupuncture therapy for 37 cases of dysmenorrhea due to endometriosis. *J Tradit Chin Med.* 2002;22(4):282–285.

41. Armour M, Smith C, Schabrun S, Steiner G, Zhu X, Lawson K, et al. Manual acupuncture plus usual care versus usual care alone in the treatment of endometriosis-related chronic pelvic pain: study protocol for a randomised controlled feasibility study. *Pilot Feasibility Stud.* 2018;4(1):10.

42. Liang R, Li P, Peng X, Xu L, Fan P, Peng J, et al. Efficacy of acupuncture on pelvic pain in patients with endometriosis: study protocol for a randomized, single-blind, multi-center, placebo-controlled trial. *Trials.* 2018;19(1):314.

43. Schnyer RN, Iuliano D, Kay J, Shields M, Wayne P. Development of protocols for randomized sham-controlled trials of complex treatment interventions: japanese acupuncture for endometriosis-related pelvic pain. *J Altern Complement Med.* 2008;14(5):515–522.

44. Smith CA, Zaslawski CJ, Cochrane S, Zhu X, Zheng Z, Loyeung B, et al. Reliability of the NICMAN scale: an instrument to assess the quality of acupuncture administered in clinical trials. *Evid Based Complement Alternat Med.* 2017;2017:1–8.

45. Higgins J.P.T., Savović J., Page M.J., Elbers R.G., Sterne J.A.C. Assessing risk of bias in a randomized trial. In: Cochrane Handbook for Systematic Reviews of Interventions [Internet] 2022. Available from: https://training.cochrane.org/handbook/current. Accessed Apr 18, 2023.

46. Schünemann H, Brożek J, Guyatt G, Oxman A, eds. GRADE Handbook For Grading Quality of Evidence and Strength of Recommendations. [Internet]. The GRADE Working Group 2013. Available from: https://gdt.gradepro.org/app/handbook/handbook.html. Accessed Apr 18, 2023.

47. Hedges LV, Olkin I. *Statistical methods for meta-analysis.* San Diego, US: Academic Press; 1985.

48. Cohen J. *Statistical power analysis for the behavioral sciences* Academic Press; 2013:459.

49. Cochran WG. The comparison of percentages in matched samples. *Biometrika.* 1950;37(3/4):256–266.

50. McGrath S, Zhao X, Steele R, Thombs BD, Benedetti A. the DEPRESsion Screening Data (DEPRESSD) Collaboration, et al. Estimating the sample mean and standard deviation from commonly reported quantiles in meta-analysis. *Stat Methods Med Res.* 2020;29(9):2520–2537.

51. Median/Range [Internet]. Available from: http://vassarstats.net/median_range.html. Accessed May 5, 2023.

52. Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. *BMC Med Res Methodol.* 2005;5(1):13.

53. WebPlotDigitizer - Copyright 2010-2022 Ankit Rohatgi [Internet]. Available from: https://apps.automeris.io/wpd/ . Accessed May 15, 2023.

54. Zhu SP, Luo L, Zhang L, Shen SX, Ren XX, Guo MW, et al. Acupuncture De-qi: from characterization to underlying mechanism. *Evid Based Complement Alternat Med.* 2013;2013:1–7.

55. Wang Z, Xu M, Shi Z, Bao C, Liu H, Zhou C, et al. Mild moxibustion for Irritable Bowel Syndrome with Diarrhea (IBS-D): a randomized controlled trial. *J Ethnopharmacol.* 2022;289:115064.

56. Gerlinger C, Schumacher U, Faustmann T, Colligs A, Schmitz H, Seitz C. Defining a minimal clinically important difference for endometriosis-associated pelvic pain measured on a visual analog scale: analyses of two placebo-controlled, randomized trials. *Health Qual Life Outcomes.* 2010;8:138.

57. Xu Y, Zhao W, Li T, Zhao Y, Bu H, Song S. Effects of acupuncture for the treatment of endometriosis-related pain: a systematic review and meta-analysis. *PLoS ONE.* 2017;12(10):e0186616.

58. Mira TAA, Buen MM, Borges MG, Yela DA, Benetti-Pinto CL, Benetti-Pinto CL. Systematic review and meta-analysis of complementary treatments for women with symptomatic endometriosis. *Int J Gynecol Obstet.* 2018;143(1):2–9.

59. Armour M, Smith CA. Treating primary dysmenorrhoea with acupuncture: a narrative review of the relationship between acupuncture 'dose' and menstrual pain outcomes. *Acupunct Med J Br Med Acupunct Soc.* 2016;34(6):416–424.

60. Armour M, Dahlen HG, Zhu X, Farquhar C, Smith CA. The role of treatment timing and mode of stimulation in the treatment of primary dysmenorrhea with acupuncture: an exploratory randomised controlled trial. *PLoS ONE.* 2017;12(7):e0180177.

61. Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, Nardone F de C, Nardone C de C, et al. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril.* 2011;96(2):366–373 e8.

62. Smith CA, Armour M, Shewamene Z, Tan HY, Norman RJ, Johnson NP. Acupuncture performed around the time of embryo transfer: a systematic review and meta-analysis. *Reprod Biomed Online.* 2019;38(3):364–379.

63. Armour M, Smith C, Wang LQ, Naidoo D, Yang GY, MacPherson H, et al. Acupuncture for depression: a systematic review and meta-analysis. *J Clin Med.* 2019;31(8):1140 8.

64. Linde K, Niemann K, Meissner K. Are sham acupuncture interventions more effective than (other) placebos? A re-analysis of data from the cochrane review on placebo effects. *Forsch Komplementärmedizin Res Complement Med.* 2010;17(5) 1–1.

65. Lundeberg T, Lund I, Sing A, Näslund J. Is placebo acupuncture what it is intended to be? *Evid-Based Complement Altern Med ECAM.* 2011;2011:932407.

66. Zia FZ, Olaku O, Bao T, Berger A, Deng Gary, Yin Fan A, et al. The national cancer institute's conference on acupuncture for symptom management in oncology: state of the science, evidence, and research gaps. *J Natl Cancer Inst Monogr.* 2017;2017(52):lgx005.

67. Hullender Rubin LE, Anderson BJ, Craig LB. Acupuncture and in vitro fertilisation research: current and future directions. *Acupunct Med J Br Med Acupunct Soc.* 2018;36(2):117–122.

68. Armour M, Dahlen HG, Smith CA. More than needles: the importance of explanations and self-care advice in treating primary dysmenorrhea with acupuncture. *Evid-Based Complement Altern Med ECAM.* 2016;2016:3467067.