

Clinical Evidence of Acupoint Stimulation for Primary Dysmenorrhea: A Systematic Review and Updated Meta-Analysis

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Purpose: Meridian-based acupoint stimulation is increasingly used for primary dysmenorrhea (PD), yet its evidence remains inconsistent. This systematic review aims to evaluate efficacy and safety of both invasive and noninvasive acupoint stimulation for PD through analysis of randomized controlled trials (RCTs).

Methods: The PROSPERO registration number is CRD42024586857. PubMed, Excerpta Medica Database (Embase), Allied and Complementary Medicine Database (AMED), Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, Scopus, VIP Database, China National Knowledge Infrastructure (CNKI), and Wanfang Database were searched up to May 20, 2024. Methodological quality was assessed using the revised Cochrane risk of bias, version 2 tool. Data were synthesized using random-effects models and presented with forest plots. The primary outcomes were assessed based on pain intensity measured using the Visual Analog Scale (VAS) or effective rates, and safety measured by adverse reaction rates. The secondary outcomes included self-reported symptoms and quality of life, uterine hemodynamics, and serum prostaglandin contents.

Results: A total of 22 eligible RCTs with 1955 participants (range 44 to 216) were included. Compared with no treatment or sham treatment, acupoint stimulation demonstrated moderate pain reduction (standardized mean difference [SMD] -2.96 , 95% confidence interval [CI] -4.39 to -1.53). Compared with non-steroidal anti-inflammatory drugs (NSAIDs), acupoint stimulation showed both immediate effects (post-first-treatment SMD -2.85 , 95% CI -4.06 to -1.64) and sustained benefits (3 cycles SMD -1.58 , 95% CI -2.43 to -0.73 ; following 3 cycles SMD -3.74 , 95% CI -5.57 to -1.90), particularly with invasive techniques. The incidence of adverse events did not differ significantly between groups (relative risk [RR] 0.94 , 95% CI 0.26 to 3.33). The GRADE certainty of the evidence ranged from low to moderate, owing to considerable risk of bias and high heterogeneity.

Conclusion: Current evidence suggests that acupoint stimulation may reduce pain intensity in primary dysmenorrhea without increasing adverse reactions, particularly long-term.

Keywords: acupoint stimulation therapy, primary dysmenorrhea, acupuncture, acupressure, sham acupuncture, NSAIDs

Introduction

Primary dysmenorrhea (PD) is a widespread condition distinguished by the recurrent occurrence of menstrual pain in the absence of any detectable pelvic pathology, according to established guidelines.¹ This condition affects a substantial portion of young women, ranging from approximately 71% to 94%, with a notable proportion exceeding 30%, enduring moderate-to-severe menstrual pain.²⁻⁵ Furthermore, approximately 4.6% of PD cases result in functional disability during the critical period of young adulthood.³ The repercussions of menstrual pain transcend mere personal discomfort, which significantly

impedes the daily routines of approximately 15.5% of working women and disrupts the educational endeavors of over 10–40% of students. Consequently, this translates into an average productivity loss of 33% and an annual cumulative total of 8.9 lost productive days.^{3,4,6,7} Moreover, PD-induced central sensitization heightens individuals' susceptibility to functional pain disorders such as irritable bowel syndrome and low back pain.⁸ Even more concerning, dysmenorrhea can exacerbate the prevalence of sleep disorders and elevate the risk of mental health issues including anxiety, depression, and attention deficit hyperactivity disorder (ADHD),^{9–11} with extreme cases leading to suicidal behavior.¹²

Currently, Medical treatment remains the mainstream approach for PD, encompassing both non-hormonal pharmacotherapy and hormonal interventions. Nonsteroidal anti-inflammatory drugs (NSAIDs) serve as the primary non-hormonal pharmacotherapy for PD. However, despite some authors advocating the use of NSAIDs before the onset of menstrual pain, irregular adherence to medication can result in the development of NSAID-resistant dysmenorrhea, with 18% of women with dysmenorrhea reporting ineffectiveness of these drugs.¹³ Furthermore, the gastrointestinal adverse reaction rate associated with NSAIDs can be as high as 32%, significantly hindering their widespread use.¹⁴ Hormone therapy is another medical treatment option; however, due to adverse reaction and cultural factors, fewer patients have reported the use of combined oral contraceptives (COC) for non-contraceptive purposes.¹⁵ COCs act by suppressing ovulation and lessening the endometrial lining of the uterus, which may lead to irregular uterine bleeding. They are also unsuitable for patients with fertility needs.¹⁶ In addition to pharmacological treatments, evidence-based guidelines recommend complementary management including exercise, Transcutaneous Electrical Nerve Stimulation (TENS), acupoint stimulation, behavioral interventions, topical heat, and dietary supplements, with surgery considered for refractory cases.¹

As an effective alternative therapy for PD patients seeking non-pharmacological options,¹⁷ acupoint stimulation may exert its effects through: (1) Regulating the release of prostaglandins to relieve excessive uterine contraction;¹⁸ (2) Improving uterine microcirculation;¹⁹ (3) Regulating uterine oxidative stress response;²⁰ (4) Promoting the release of central analgesic substances.²¹ This therapeutic effect is also rooted in the meridian theory of Traditional Chinese Medicine. Acupoint stimulation can restore the balance of yin and yang in the body, thereby optimizing the functions of the internal organs.²²

Research on acupuncture and acupoint stimulation for PD has been growing; however, the findings have been inconsistent and contradictory. A Cochrane review published in 2011 tentatively concluded that acupuncture was more effective than placebo or Chinese herbs in alleviating menstrual pain.²³

However, subsequent meta-analyses have expressed reservations, noting that current low-quality randomized controlled trials (RCTs) and single well-designed studies are insufficient to conclusively demonstrate the efficacy of acupuncture.²⁴ Furthermore, recently published RCTs on acupoint stimulation were not included in previous systematic reviews. For instance, a systematic review of RCTs on acupoint stimulation for PD conducted in 2012 had several methodological shortcomings, including a lack of registration, unclear inclusion criteria for participants, and no assessment of quality of life.²⁵

In light of the growing number of RCTs on acupoint stimulation for PD and the subsequent demand for nonpharmacological interventions, we conducted a comprehensive systematic review and meta-analysis of the existing evidence to guide clinical practice. Our specific research questions were as follows: (1) Is acupoint stimulation therapy effective in the management of PD? (2) Subgroup analysis was conducted to assess the efficacy of invasive and non-invasive acupoint stimulation compared with sham acupuncture or NSAIDs in the treatment of PD.

Methods

The PROSPERO registration number of this study is CRD42024586857 and complies with the PRISMA declaration requirements.

Search Strategy

We searched PubMed, Excerpta Medica Database (Embase), Allied and Complementary Medicine Database (AMED), Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, Scopus, VIP Database, China National Knowledge Infrastructure (CNKI), and Wanfang Database spanning up to May 2024. The search strategy was developed by building on the methodologies employed in previous similar reviews. Keywords were searched from both the medical subject headings (MeSH) and Chinese Biomedical Literature Service System (Sinomed) databases. The search strategy

included the MeSH terms in combination with free words. The searched MeSH terms were as follows: Acupuncture; Acupuncture Therapy; Acupuncture Analgesia; Acupuncture Points; Acupuncture, Ear; Moxibustion; Acupressure; Electroacupuncture; Dysmenorrhea. Examples of the search formulas are provided in [Appendix 1](#). To avoid overlooking any relevant studies, we did not apply any filter. For incomplete data, we contacted the authors to either exclude these studies or obtain missing information.

Study Selection

Published and unpublished studies were included if they met the following PICOS (participants, intervention, comparison, outcome, study type) criteria:

Participants

Inclusion criteria included:

1. Female participants were of fertile age, had no history of childbirth, and were below 40 years of age.
2. Regular menstrual cycles ranging from 21 to 35 days (28 ± 7 days).
3. A history of primary dysmenorrhea lasting for at least one year.
4. Exclusion of secondary dysmenorrhea confirmed by imaging such as B-ultrasound.¹

Exclusion criteria included:

1. Participants with compromised medical conditions or diagnosed with mental illnesses.
2. Participants suffering from other gynecological disorders.

Interventions

Inclusion criteria included all kinds of commonly used acupoint stimulation methods (including manual acupuncture, electroacupuncture, ear acupuncture, acupressure, and transcutaneous electrical acupoint stimulation (TEAS)), or a combination of the above.

The exclusion criteria were rare treatment methods or interventions that incorporated other therapies in addition to acupoint stimulation.

Comparison

Placebo controls (sham acupuncture), blank controls (no acupuncture, usual care, or health education), or clinically recommended treatments (oral medicine) without acupoint stimulation.

Outcome Measures

Primary Outcomes

Visual Analogue Scale (VAS), effective rate and adverse reaction rate.

Secondary outcomes: dysmenorrhea symptom scores, Cox Menstrual Symptom Scale (CMSS), Pittsburgh Sleep Quality Index (PSQI), uterine hemodynamics, and serum prostaglandin contents.

Other Outcomes

Resting-State Scale (RSS), Verbal Rating Scale (VRS), Short Form - 36 Health Survey (SF-36), total pain duration, Self-Rating Anxiety Scale (SAS) and all reported outcomes.

Detailed descriptions of primary and secondary outcome variables, including reliability and validity of the scales, are provided in [Appendix 3](#).^{18,26-29}

Study Type

Inclusion criteria included randomized controlled trials (RCTs) in English or Chinese.

The exclusion criteria were studies of other types or languages, non-randomized allocation methods, animal experiments, and those with conflicts of interest.

Outcome Measures and Data Extraction

Title and abstract screening were independently conducted by two reviewers, and discrepancies were resolved through a consensus between them. Full-text screening for the inclusion of eligible studies was completed by two independent reviewers, and discrepancies were resolved through consensus. In case of any disagreement, a third researcher was consulted for the final adjudication. Following the completion of the screening process, the researchers extracted all data including the first author's name, year of publication, sample size, age of the participants, intervention measures, duration of treatment, control measures, and outcome measures. Short-term efficacy was evaluated within one day of treatment, whereas long-term efficacy was assessed after at least one menstrual cycle of treatment.

Quality Assessment

For each time point and each outcome eligible for meta-analysis of each study, we assessed the risk of bias using the revised Cochrane risk of bias, version 2 (RoB2) tool.³⁰ Two review authors independently judged whether each risk-of-bias criterion was adequately met. We used the Grade of Recommendations Assessment, Development and Evaluation (GRADE; Grade Pro version 3.6.1) to assess the quality of the evidence, which was categorized as high, moderate, low, and very low. We used Kappa scores to assess interrater agreements.

Data Synthesis and Statistical Analysis

Statistical analyses were conducted using Review Manager 5.4 and R studio 4.4.1. Considering the variety of treatment and duration, most effect pooling was conducted using a random effects model and presented with forest plots. For dichotomous variables, Relative Risk (RR) was used as the outcome indicator with Mantel-Haenszel method. For continuous outcomes, between-group differences were compared based on post-intervention values. The Mean Difference (MD) was used via inverse-variance. In cases where the units differed, Standardized Mean Difference (SMD) was adopted. We used Cohen's classification of SMD to assess the effect as small (SMD < 0.5), medium (SMD 0.5 to 0.8), or large (SMD > 0.8).³¹ When judging the effect size of pain intensity, we adopted a clinically important difference of 15 points on a 0 to 100 scale, 2 points on a 0 to 10 scale, or 30% change of the scores between two comparison groups.³² RR < 1.25 or RR > 0.8 was considered clinically significant. The level of significance was set at $\alpha = 0.05$.

Heterogeneity between studies was based on the results of I^2 , and an $I^2 > 50$ was considered to indicate high heterogeneity. Sensitivity, subgroup, and meta-regression analyses were performed to reduce heterogeneity. A sensitivity analysis was conducted using the leave-one-out method for each outcome. Results were considered unstable if exclusion of any single study altered the direction of the pooled effect size. For unstable cases, we calculated and reported all leave-one-out iterations in [Appendix 2](#) to identify potential sources of heterogeneity. For outcomes lacking standard deviation (SD) data, estimated SDs were used exclusively in sensitivity analyses to verify the robustness of primary results, with all such cases clearly flagged in supplementary materials. To explore potential sources of heterogeneity in cases where the sensitivity analysis suggested instability, we performed meta-regression analyses. Meta-regression analyses primarily based on treatment sessions.

For small samples (no more than 3) with poor stability, a Bayes analysis was performed. We chose a half-normal distribution with a shape parameter of 1.0, as the prior distribution when the heterogeneity was large ($\text{Tau}^2 > 0.4$), whereas when the heterogeneity was small ($\text{Tau}^2 < 0.4$), we selected a half-normal distribution with a shape parameter of 0.3 as the prior distribution.³³

For meta-analyses that included more than 10 studies, funnel plots were used to detect publication bias, whereas Egger's test was employed to detect potential publication bias.³⁴ The trim and fill method were used to adjust for publication bias.

Trial Registration

This systematic review was registered in the PROSPERO International Prospective Register of Systematic Reviews (registration number CRD42024586857). Preferred reporting items were used for systematic reviews and meta-analyses.

Protocol Amendments

All pre-specified outcomes from our registered protocol were reported. Outcomes with single-study data were quantitatively presented following PRISMA guidelines.³⁴

Results

Study Selection

Searches were performed on May 20, 2024, resulting in 9168 returns (PubMed: 309; Embase: 189; AMED: 383; CENTRAL: 385; Web of Science: 333; Scopus: 777; CNKI: 2400; WanFang: 2636; VIP: 1756). After excluding duplicate articles and briefly reviewing the titles and abstracts, 810 articles remained and the full texts were read. Twenty-six articles were initially selected based on the inclusion and exclusion criteria; a total of 26 articles were initially selected. However, three of these articles were excluded because of their low quality (two of them neglected the outcome indicators,^{35,36} one had an error in the sample size of the outcome,³⁷ and one trial had a duplicate reference,³⁸ resulting in the final inclusion of 22 articles.^{39–60} A flow diagram representing the flow of studies through the selection process is shown in Figure 1.

Study Characteristics

Twenty-two RCTs involving a total of 1955 participants (median of 89, with a range from 44 to 216) met our updated selection criteria. The characteristics of the included studies are presented in Tables 1 and 2, respectively. Four studies were published in English^{44,50,56,59} while the other 18 studies were published in Chinese. Three trials were published

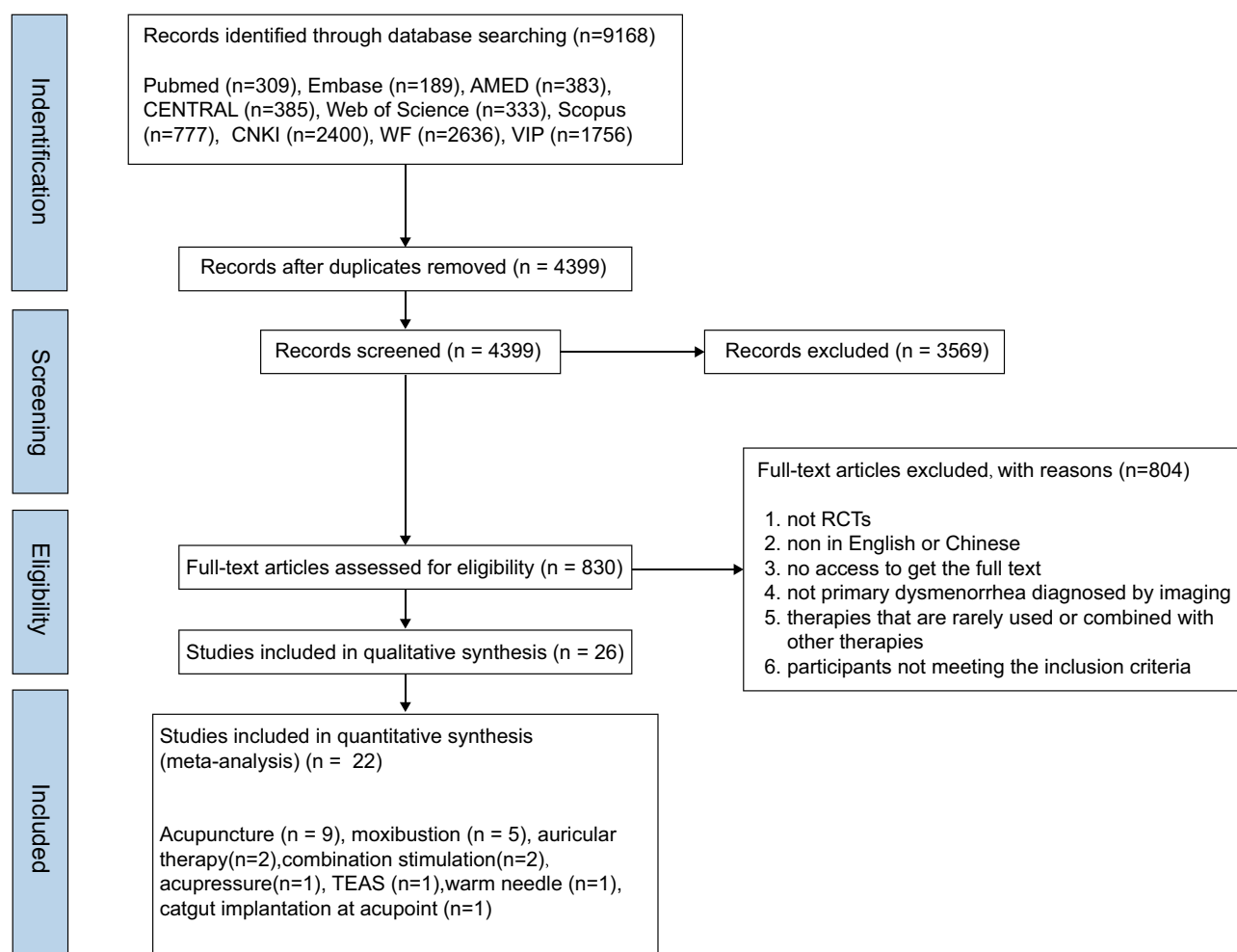


Figure 1 Flow diagram.

Table 1 Characteristics of Included Studies

| | Study | n | Intervention | Comparison | Course | Outcome |
|----|----------------------------------|-------------|--|--|--------------------|---------|
| 1 | Bi Y, 2014 ³⁹ | 35/35 | Staging acupoint catgut embedment | Ibuprofen | 3 menstrual cycles | ①②⑤⑨ |
| 2 | Han Y, 2015 ⁴⁰ | 30/30 | Acupuncture | Sham acupuncture | 3 menstrual cycles | ② |
| 3 | Huang ZQ, 2018 ⁴¹ | 30/30 | Herb-partitioned moxibustion | Compound paracetamol | 3 menstrual cycles | ①⑤ |
| 4 | Li Y, 2017 ⁴² | 33/34 | Moxibustion | Health education | 3 menstrual cycles | ②④⑥ |
| 5 | Liang RL, 2018 ⁴³ | 30/30 | Abdominal acupuncture | Ibuprofen | 3 menstrual cycles | ②⑤⑧⑨ |
| 6 | Liu CZ, 2011 ⁴⁴ | 49/49/48/48 | Electroacupuncture | Unrelated acupoint / non-acupoint / No treatment | 1 menstrual cycle | ②⑧⑪⑬ |
| 7 | Liu HQ, 2014 ⁴⁵ | 33/34 | Auricular plaster | Yuanhuzhitong tablets | 3 menstrual cycles | ② |
| 8 | Liu LF, 2022 ⁴⁶ | 30/30/30 | Transcutaneous electrical acupoint stimulation / percutaneous electrical nerve stimulation | No treatment | 3 menstrual cycles | ②⑦ |
| 9 | Liu X, 2020 ⁴⁷ | 50/50 | Abdominal acupuncture + moxibustion | Ibuprofen | 3 menstrual cycles | ①②③⑬ |
| 10 | Lu CX, 2021 ⁴⁸ | 30/30/30 | Auricular intradermal needle/ auricular plaster | Placebo needle | 3 menstrual cycles | ①②③④⑫ |
| 11 | Ma F, 2018 ⁴⁹ | 38/36 | Tuina + acupoint heat sensitive moxibustion | Yueyueshu Granule | 3 menstrual cycles | ①②⑤⑧ |
| 12 | Pouresmail Z, 2002 ⁵⁰ | 72/72/72 | Acupressure | Sham acupressure/Ibuprofen | 1 menstrual cycle | ② |
| 13 | Ren XL, 2013 ⁵¹ | 40/40 | Suspended moxibustion | Ibuprofen | 3 menstrual cycles | ①③ |
| 14 | Ruan CX, 2016 ⁵² | 52/49 | Drug-spreading moxibustion | Meloxicam | 3 menstrual cycles | ①⑦ |
| 15 | Shan BM, 2021 ⁵³ | 60/60 | Moxibustion + self-made patch | Ibuprofen | 3 menstrual cycles | ②④⑥ |
| 16 | Shi ZH, 2017 ⁵⁴ | 22/22 | Warm needle | Ibuprofen | 3 menstrual cycles | ①② |
| 17 | Wang HB, 2014 ⁵⁵ | 30/30/30 | Acupuncture/moxibustion | Ibuprofen | 3 menstrual cycles | ①②⑤ |
| 18 | Wang HJ, 2019 ⁵⁶ | 31/31 | Acupuncture | Ibuprofen | 3 menstrual cycles | ①②⑧ |
| 19 | Wei YH, 2019 ⁵⁷ | 38/37 | Acupuncture | Ibuprofen | 3 menstrual cycles | ②③⑧ |
| 20 | Xu SW, 2014 ⁵⁸ | 38/37 | Acupuncture | No treatment | 3 menstrual cycles | ①②⑩ |
| 21 | Yang Y, 2024 ⁵⁹ | 25/23/22 | Buccal acupuncture | Compound paracetamol/placebo | 3 menstrual cycles | ②④⑧ |
| 22 | Zhu XY, 2022 ⁶⁰ | 30/30/30 | Acupuncture/acupuncture + long snake moxibustion | Ibuprofen | 3 menstrual cycles | ①②③④ |

Notes: Outcome indicators: ① effective rate; ② VAS scores; ③ serum prostaglandin contents; ④ CMSS; ⑤ dysmenorrhea symptom scores; ⑥ PSQI; ⑦ uterine hemodynamics; ⑧ adverse reaction rate; ⑨ SF-36; ⑩ total pain duration; ⑪ RSS-COX; ⑫ SAS; ⑬ VRS; ⑭ β -EP.

Table 2 Detailed Characteristics of Included Studies

| | Study | Intervention Timing | Frequency | Stimulation Acupoint | Control Timing | Dose |
|----|------------------------------|---|--|--|---|-------------------------------|
| 1 | Bi Y, 2014 ³⁹ | Embed sutures once each in the 3 days before menstruation, and during menstrual cycle, specifically on days 12–14. | | Pre-menstrual period: Guanyuan (CV4) / Diji (SP8) / Zigong (EX-CA1) / Ciliao (BL32); Inter-menstrual period: Shenshu (BL23) / Ganshu (BL18) / Pishu (BL20); Additional points based on symptoms: Geshu (BL17) / Tianshu (ST25) / Shuidao (ST28) / Siman (ST27) / Xuehai (SP10) / Sanyinjiao (SP6) / Zusanli (ST36) | 3 days before menstruation until pain relief | 300mg, bid |
| 2 | Han Y, 2015 ⁴⁰ | Pain occurs and VAS \geq 4 | Once a menstrual cycle | Sanyinjiao (SP6) | The same timing | Once a menstrual cycle |
| 3 | Huang ZQ, 2018 ⁴¹ | Course 1: pain occurs, once a day for 6 times Treatment course 2/3: 3 days before menstruation, once a day for 6 times | | Guanyuan (CV4) / Zhongji (CV3) / Sanyinjiao (SP6) / Zigong (EX-CA1) | Pain occurs until pain relief | 1 tablet, tid |
| 4 | Li Y, 2017 ⁴² | Menstruation onset, 5 days continuously | Once a day | Sanyinjiao (SP6) | / | / |
| 5 | Liang RL, 2018 ⁴³ | 1 wk before menstruation until pain disappears | Once a day | Zhongwan (CV12) / Xiawan (CV10) / Qihai (CV6) / Guanyuan (CV4) / Huaroumen (ST24) / Wailing / Xiafengshipoint | Pain occurs until pain relief | 300mg, bid |
| 6 | Liu CZ, 2011 ⁴⁴ | 1 day before menstruation, 3 days continuously | Once a day | Sanyinjiao (SP6) | The same timing | Xuanzhong (GB39)/ nonacupoint |
| 7 | Liu HQ, 2014 ⁴⁵ | 1 wk before menstruation till 1 wk after menstruation | Replace patch every 4–7 days. Self-acupressure 3–4 times a day. | Ear acupuncture acupoints: Uterus / Endocrine / Sympathetic nerve / Shenmen / Liver / Upper tragic apex | Pain occurs until pain relief | 4 tablets, qd |
| 8 | Liu LF, 2022 ⁴⁶ | 1 wk before menstruation until the 3 rd day of menstruation | Twice a day | Zigong (EX-CA1) / Sanyinjiao (SP6) | Take Ibuprofen orally only when the pain is unbearable (VAS \geq 8) | |
| 9 | Liu X, 2020 ⁴⁷ | 1 wk before menstruation until pain disappear | Once a day | Acupuncture: Zhongwan (CV12) / Xiawan (CV10) / Qihai (CV6) / Guanyuan (CV4) / Huaroumen / Wanling / Xiafengshidian Moxibustion: Shenque (CV8) / Zhongji (EN3) / Qihai (CV6) / Guanyuan (CV4) / Zigong (EX-CA1) | Pain occurs until pain relief | 300mg, qd-tid |
| 10 | Lu CX, 2021 ⁴⁸ | 5 days before menstruation, replace every other day | 4 times a menstrual cycle self-acupressure for 3–4 times per day | Ear acupuncture acupoints: Internal genitalia / Endocrine / Shenmen / Kidney / Sympathetic nerve / Liver / Subcortex | The same timing | The same frequency |
| 11 | Ma F, 2018 ⁴⁹ | 1 wk before menstruation until the 1 st day of menstruation | Once a day | Tuina: Kidney Meridian of Foot-Shaoyin Mangshu (KI15) / Shenque (CV8) / Jueque (CV14) / Guanyuan (CV4) Heat-sensitive moxibustion: Guanyuan (CV4) / Zhongji (CV3) / Sanyinjiao (SP6) | The same timing | 10g, bid |

(Continued)

Table 2 (Continued).

| | Study | Intervention Timing | Frequency | Stimulation Acupoint | Control Timing | Dose |
|----|----------------------------------|--|------------------------|---|--|------------------------------|
| 12 | Pouresmail Z, 2002 ⁵⁰ | 1 day before menstruation | Once a menstrual cycle | Hegu (LI4) / Daheng (SP15) / Zusanli (ST36) / Sanyinjiao (SP6) / Taichong (LR3) | The same timing | 9 tablets (400mL) for 3 days |
| 13 | Ren XL, 2013 ⁵¹ | 3 days before menstruation, 6 days continuously | Once a day | Guanyuan (CV4) / Sanyinjiao (SP6) | Pain occurs until pain disappears | 400mg,tid |
| 14 | Ruan CX,2016 ⁵² | 5 days before menstruation until the 3 rd day of menstruation | Once every 3 days | Lumbar and sacral region: From Mingmen to the first lateral line of the GoveCVor Vessel and Bladder Meridian / Baliao; Lower abdomen: The meridian line area of the Conception Vessel from Shenque (CV8) to Zhongji (CV3) | 1 day before menstruation, 3 days continuously | 7.5mg,qd |
| 15 | Shan BM, 2021 ⁵³ | 1 wk before menstruation until onset of menstruation | Once a day | Guanyuan (CV4) / Sanyinjiao (SP6) | Pain occurs until pain disappears | 300mg,bid |
| 16 | Shi ZH, 2017 ⁵⁴ | 1 st day of menstruation | Once a menstrual cycle | Qihai (CV6) / Guanyuan (CV4) | Pain occurs once a menstrual cycle | 300mg,qd |
| 17 | Wang HB, 2014 ⁵⁵ | 3 days before menstruation until pain relief | Once a day | Guanyuan (CV4) / Sanyinjiao (SP6) | The same timing | 300mg,qd |
| 18 | Wang HJ,2019 ⁵⁶ | 5 days before menstruation until onset of menstruation | Once a day | Zhibian (BL54) / Shuidao (ST28) Additional points based on symptoms: Hegu (LI4) / Taichong (LR3) / Ciliao (BL32) / Xuehai (SP10) / Pishu (BL20) / Zusanli (ST36) | 5 days before menstruation until the 1 st day of menstruation | 300mg,bid |
| 19 | Wei YH, 2019 ⁵⁷ | The 1 st to 3 rd day of menstruation | Once a day | Baliao (Shangliao (BL31)/ Ciliao (BL32)/ Zhongliao (BL33)/Xialiao (BL34) | The 1 st day to 3 rd day of menstruation | 400mg,qd |
| 20 | Xu SW, 2014 ⁵⁸ | 1 wk before menstruation until onset of menstruation, Take Ibuprofen when the pain is unbearable | Once a day | Guanyuan (CV4) / Sanyinjiao (SP6) / Zhongji (CV3) / Dahe (KI12) / Ciliao (BL32) / Yinjiao (CV7) Additional points based on symptoms: Taichong (LR3)/Xuehai (SP10) or Dijii (SP8)/Yinlingquan (SP9) | Take Ibuprofen orally only when the pain is unbearable (VAS ≥ 8) | |
| 21 | Yang Y, 2024 ⁵⁹ | Every weekespecially the 1 st day of menstruation | Once a week | Based on symptoms:CA-7 / CA-8 / CA-4 / CA-3 / CA-2 | The 1 st to 3 rd day of menstruation | 1 tablet, tid |
| 22 | Zhu XY, 2022 ⁶⁰ | 7 to 10 days before menstruation until onset of menstruation | Once a day | Sanyinjiao (SP6) / Guanyuan (CV4) / Dijii (SP8) / Zigong (EX-CA1) / Zhongji (CV3) | Pain occurs until pain relief | 300mg,bid |

between 2002 and 2014,^{44,50,51} and 19 trials were published between 2014 and 2024. Sixteen studies were two-armed, five were three-armed^{48,50,55,59,60} and one was four-armed.⁴⁴ We attempted to contact the authors of one trial due to a lack of detailed data,⁴⁴ yet we did not obtain additional information from them. All trials used parallel-group designs; there were no crossover studies; 21 trials were performed in a single center, and one was a multi-center trial.⁴⁴

All participants were young, nulliparous females. The participants were 14–35 years old. Ten studies included minors under 18 years of age, whereas 12 did not. Acupoint stimulation interventions tested in the included trials varied significantly. Electroacupuncture was used in one trial,⁴⁴ manual acupuncture was used in nine trials, including body acupuncture,^{40,55–57,60} abdominal acupuncture,^{43,47} auricular acupuncture⁴⁸ and buccal acupuncture;⁵⁹ moxibustion was used in eight trials, including herb-partition moxibustion,^{41,47,52} heat sensitive moxibustion,⁴⁹ suspended moxibustion,^{42,51,55} ginger-partition moxibustion,⁵³ long snake moxibustion,⁶⁰ warm needle was used in one trial,⁵⁴ acupressure was used in one trial,⁵⁰ staging acupoint catgut embedment was used in one trial,³⁹ transcutaneous electrical acupoint stimulation was used in one trial,⁴⁶ and auricular plaster was used in two trials.^{45,48} Eighteen trials standardized acupuncture treatments (all participants were treated at the same points) and four semi-standardized treatments (either all participants were treated at some basic points and additional individualized points, or there were different predefined needling schemes depending on symptom patterns).^{39,56,58,59} Three trials chose to use the Sanyinjiao (SP6) acupoint alone.^{40,42,44} The most frequently used acupoints were Sanyinjiao (SP6, 13 trials) and Guanyuan (CV4, 11 trials). An overview of the acupoints that have been used more than once is presented in Figure 2. The course of most trials was three menstrual cycles, whereas two trials only treated participants for one menstrual cycle.^{44,50} Two trials were followed up for one menstrual cycle,^{47,48} six trials were followed up for three menstrual cycles^{39,43,46,49,57,58} and one trial was followed up for six menstrual cycles.⁵⁹ Nineteen trials conducted prophylactic treatment before the onset of menstrual pain, while three trials initiated treatment at the start of menstrual pain.^{40,42,54}

The comparator interventions tested in the included trials varied significantly between studies. Fourteen trials compared acupoint stimulation with NSAIDs treatment using ibuprofen,^{39,43,47,50,51,53–57,60} compound paracetamol^{41,59} or meloxicam.⁵² Two trials compared acupoint stimulation with Chinese medicine using Yuanhuzhitong tablets⁴⁵ or Yueyueshu Granule.⁴⁹ The techniques varied considerably in the six trials with sham controls. Two trials used “placebo” needles (telescopic needles with blunt tips not penetrating the skin).^{40,48} Two trials stimulated non-acupoints,^{44,50} and one

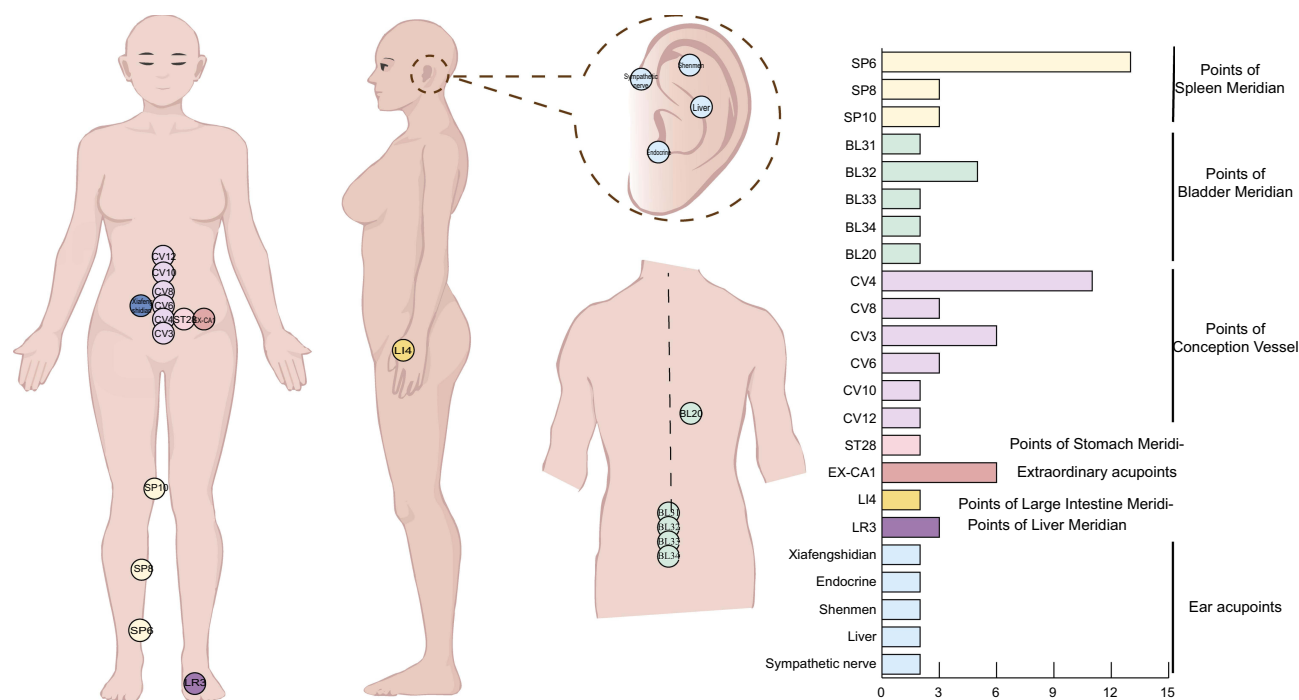


Figure 2 Acupoints used more than 2 times.

trial stimulated acupoints unrelated to the PD.⁴⁴ Another trial used a lactose pill (similar to the analgesic pill).⁵⁹ Four trials included a group that received treatment for acute attacks only or routine care.^{31,34,37,42,44,46,58}

Methodological Quality Assessment

The risk of bias in the included studies is shown in Figures 3 and 4, respectively. Most of the articles employed intention-to-treat (ITT) analysis, while 5 studies utilized per-protocol (PP) analysis.^{42,43,46,55,57} All 22 studies mentioned randomization. Fourteen trials used random number tables,^{39,40,42,43,45,47,52,53,55-60} while two trials used a computer-generated sequence.^{44,49} One trial used block randomization,⁴⁸ one trial used simple randomization⁵⁴ and one trial used “Envelope method”.⁵¹ Three trials were assessed as “some concerns” for the non-reported detailed method.^{41,46,50} Five studies reported appropriate allocation concealment^{40,44,49,56,59} using sealed envelopes, computer programs, and central telephone controls, which were considered to have a “low risk of bias”. However, most studies did not mention the allocation concealment strategy. Owing to the difficulty of blinding both participants and practitioners, only five studies tried blinding to avoid bias.^{40,42-44,56} The lack of blinding may introduce bias in subjective outcomes such as VAS scores; therefore these outcomes were rated as having “some concerns” in the “measure of the outcome” domain. Three studies

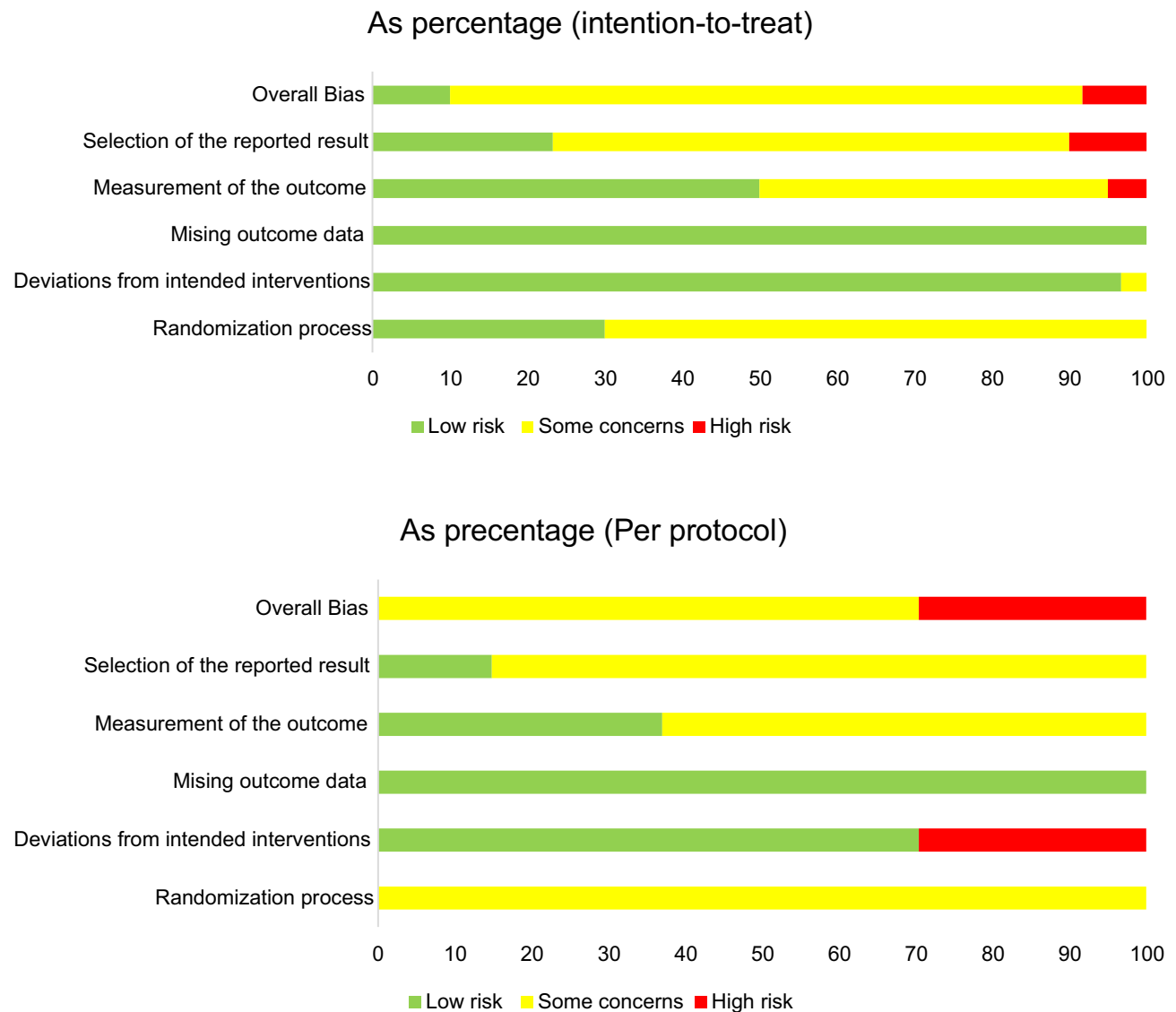


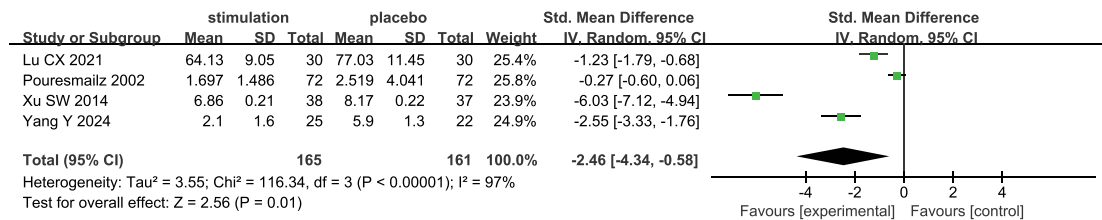
Figure 3 Risk of bias summary.

Table 3 GRADE Evidence Profile for Outcomes

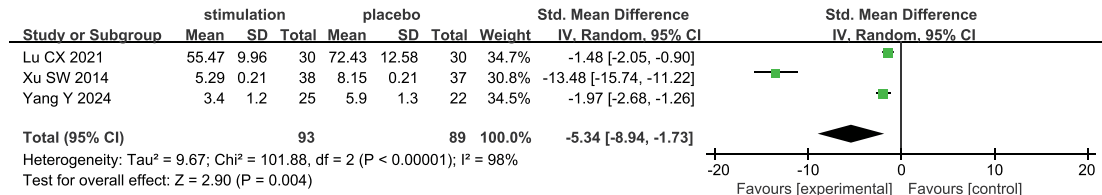
| Outcome | Quality Assessment | | | | | | Quality |
|---|--------------------|----------------------|---------------------------|-------------------------|---------------------------------|---|-----------------|
| | No of Studies | Risk of Bias | Inconsistency | Indirectness | Imprecision | Other Considerations | |
| Effective rate | | | | | | | |
| Non-invasive with medicine | 5 | Serious ¹ | Serious ² | No serious indirectness | Serious ³ | None | VERY LOW |
| Invasive with medicine | 6 | Serious ¹ | Serious ² | No serious indirectness | No serious imprecision | None | LOW |
| VAS scores | | | | | | | |
| 1 cycle medicine with stimulation | 5 | Serious ¹ | Very serious ⁴ | No serious indirectness | Serious ⁵ | None | VERY LOW |
| 1 cycle placebo with stimulation | 4 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| 2 cycles placebo with stimulation | 3 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| 2 cycles medicine with stimulation | 4 | Serious ¹ | Very serious ⁴ | No serious indirectness | Very serious ^{3, 5, 6} | Increased effect for RR ~1 | VERY LOW |
| 3 cycles placebo with stimulation | 6 | Serious ¹ | Very serious ⁴ | No serious indirectness | NO serious imprecision | Very strong association | MODERATE |
| 3 cycles non-invasive with medicine | 5 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| 3 cycles non-invasive with Chinese medicine | 2 | Serious ¹ | Very serious ⁴ | No serious indirectness | Very serious ^{3, 6} | Very strong association | VERY LOW |
| 3 cycles non-invasive with NSAIDs | 3 | Serious ¹ | Very serious ⁴ | No serious indirectness | Very serious ^{5, 6} | Very strong association | VERY LOW |
| 3 cycles medicine with stimulation | 11 | Serious ¹ | Very serious ⁴ | No Serious indirectness | No serious imprecision | Reporting bias very strong association | LOW |
| 3 cycles stimulation with NSAIDs | 9 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| 3 cycles stimulation with Chinese medicine | 2 | Serious ¹ | Very serious ⁴ | No serious indirectness | Serious ⁶ | Very strong association | LOW |
| 3 cycles invasive with medicine | 7 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| follow 1 cycle medicine with stimulation | 2 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| follow 3 cycles medicine with stimulation | 3 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| follow 3 cycles placebo with stimulation | 2 | Serious ¹ | Serious ² | No serious indirectness | No serious imprecision | Very strong association | HIGH |
| Immediate stimulation with NSAIDs | 2 | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | Very strong association | HIGH |
| 30 min placebo with stimulation | 2 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| 30 min medicine with stimulation | 2 | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ³ | None | LOW |
| Serum prostaglandin contents | | | | | | | |
| PGE2 after treatment | 3 | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | Strong association | HIGH |
| PGF2 α after treatment | 5 | Serious ¹ | Serious ² | No serious indirectness | No serious imprecision | None | LOW |
| CMSS | | | | | | | |
| CMSS total after treatment | 3 | Serious ¹ | Very serious ⁴ | No serious indirectness | Serious ⁵ | None | VERY LOW |
| CMSS severity after treatment | 2 | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | MODERATE |
| CMSS duration after treatment | 2 | Serious ¹ | Very serious ⁴ | No serious indirectness | No serious imprecision | Very strong association | MODERATE |
| Dysmenorrhea symptom scores | | | | | | | |
| 3 cycles medicine with stimulation | 4 | Serious ¹ | Serious ² | No serious indirectness | No serious imprecision | None | LOW |
| Follow 3 cycles medicine with stimulation | 2 | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | Very strong association | HIGH |
| PSQI | | | | | | | |
| PSQI after treatment | 2 | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | MODERATE |

| Uterine hemodynamics | | | | | | | |
|-----------------------|---|----------------------|--------------------------|-------------------------|------------------------|----------------------------|-----------------|
| Uterine artery PI | 2 | serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | none | MODERATE |
| Uterine artery RI | 2 | Serious ¹ | No serious inconsistency | No serious indirectness | No serious imprecision | None | MODERATE |
| Adverse reaction rate | | | | | | | |
| Adverse reaction rate | 6 | Serious ¹ | No serious inconsistency | No serious indirectness | Serious ¹ | Increased effect for RR ~1 | MODERATE |

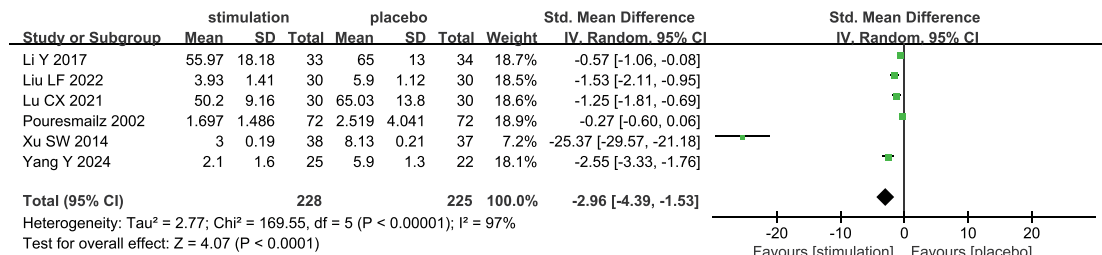
Notes: ¹ Inadequate allocation concealment and imperfect blinding. ² Considerable heterogeneity. ³ No significant benefit or harm. ⁴ Substantial heterogeneity. ⁵ The confidence interval crosses the equivalence margin. ⁶ Limited sample size.



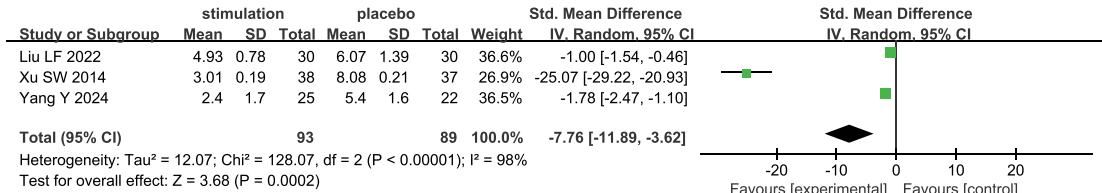
(A)



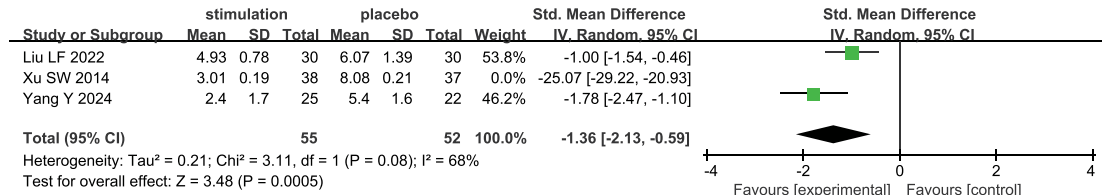
(B)



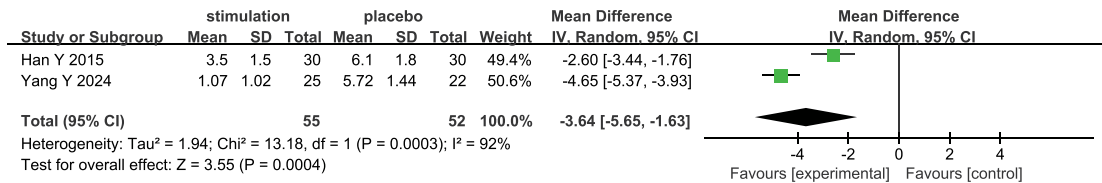
(C)



(D)



(E)



(F)

Figure 5 Forest plot of comparison: Acupoint stimulation vs no treatment or sham treatment, outcome: VAS (A) after one menstrual cycle; (B) after two menstrual cycles; (C) after three menstrual cycles; (D) after following three menstrual cycles; (E) after following three menstrual cycles (revised); (F) 30 minutes after the first session.

After two menstrual cycles of treatment (Figure 5B), the meta-analysis of pain intensity yielded a pooled SMD estimate of -5.34 (95% CI -8.96 to 1.73 , $P = 0.004$; 182 participants), indicating a statistically significant reduction in VAS scores for participants in the acupoint stimulation group compared to those in the sham treatment or no treatment group.^{48,58,59} The heterogeneity was high ($I^2 = 95\%$), suggesting considerable variation. The sensitivity analysis indicated that the results were stable.

After three menstrual cycles of treatment (Figure 5C), a meta-analysis of six studies yielded a pooled SMD estimate of -2.96 (95% CI -4.39 to -1.53 , $P < 0.0001$, $I^2 = 97\%$, 453 participants), indicating a statistically significant reduction in VAS scores for participants in the acupoint stimulation group compared to those in the placebo group or no treatment group.^{42,46,48,50,58,59} The sensitivity analysis confirmed that the results were stable.

Two studies assessed VAS scores for one menstrual cycle after the end of treatment. One showed that compared to the placebo group, both auricular intradermal needling ($P < 0.001$) and auricular point sticking ($P < 0.05$) were more effective.⁴⁸ Another showed that acupuncture was associated with a significant reduction in VAS scores compared to no treatment ($t = -10.69$, $P < 0.01$).⁵⁸ Three studies were followed for three menstrual cycles (Figure 5D).^{46,58,59} There was a trend toward lower acupoint stimulation scores, but the sensitivity analysis indicated that the results were unstable (Appendix 2A). The source of high heterogeneity may be the proportion of unreported use of emergency medications. We excluded Xu SW, 2014 (Figure 5E), resulting in a revised SMD estimate of -1.36 (95% CI -2.13 to -0.59 , $P = 0.0005$, $I^2 = 68\%$, 107 participants).

Immediately after the first session, a trial reported that acupoint stimulation had a trend toward lower VAS scores than placebo treatment ($F=87.12$, $P < 0.001$).⁵⁹ Two trials compared the VAS scores of acupoint stimulation and sham treatment 30 minutes after the first session.^{40,59} The meta-analysis (Figure 5F) yielded a pooled MD estimate of -3.64 (95% CI -5.65 to -1.63 , $P = 0.0004$, $I^2 = 92\%$, 107 participants), indicating a statistically significant reduction in pain intensity for participants in the acupoint stimulation group compared with those in the control group. The sensitivity analysis indicated that the results were stable. Another trial that did not mention standard deviation (SD) reported that repeated-measures analysis of variance at baseline, 5, 10, 30, and 60 minutes following the start of the first intervention revealed a treatment effect ($P < 0.001$) and a treatment * time interaction ($P < 0.001$), but no effect of time ($P = 0.267$).⁴⁴ The estimated SD was used as a sensitivity analysis with unstable results (Appendix 4), highlighting the need for more precise measurements and additional high-quality evidence to confirm the short-term efficacy.

Only two trials, including a control group that received sham treatment or no treatment, reported effective rates. One trial reported the effective rate of acupoint stimulation in sham treatment groups.⁴⁸ The total effective rates of the auricular intradermal needling group and auricular point sticking group were 93.3% and 80.0%, respectively, which were higher than that of the placebo group ($P < 0.05$). A trial reported that the effective rate of the acupuncture group was 100%, whereas the effective rate of the control group was not mentioned.⁵⁸

Comparison with Oral Medicine

Sixteen trials that compared acupoint stimulation with a control group receiving oral medical treatment were clinically heterogeneous. Among these, fourteen trials used NSAIDs, including using Ibuprofen,^{39,43,47,50,51,53–57,60} Compound paracetamol^{41,59} or Meloxicam.⁵² Sustained-release ibuprofen capsules were the most frequently used, with the most common dose being 300 mg twice a day. Previous research has suggested that NSAIDs are usually not required for more than two or three days if effective treatment is initiated with the onset of bleeding and/or associated symptoms.¹ However, one trial included a control group receiving ibuprofen sustained-release capsules only once per cycle, which may have exaggerated the effect in the intervention group.⁵⁴ Another trial started using ibuprofen sustained-release capsules five days before the onset of menstruation, lasting six days.⁵⁶ The prolonged treatment may have increased the rate of adverse reactions in the control group.

The meta-analysis compared the VAS scores of the acupoint stimulation and medicine groups after treatment and during the follow-up period, showing that acupoint stimulation may have a more rapid and long-lasting effect, especially in RCTs with invasive stimulation.

After one menstrual cycle of treatment (Figure 6A),^{43,47,50,57,59} non-significant differences between the two groups are present for acupoint stimulation and NSAIDs with a SMD of -0.29 (95% CI -1.18 to 0.61 , $P = 0.53$, $I^2 = 95\%$, 427 participants).

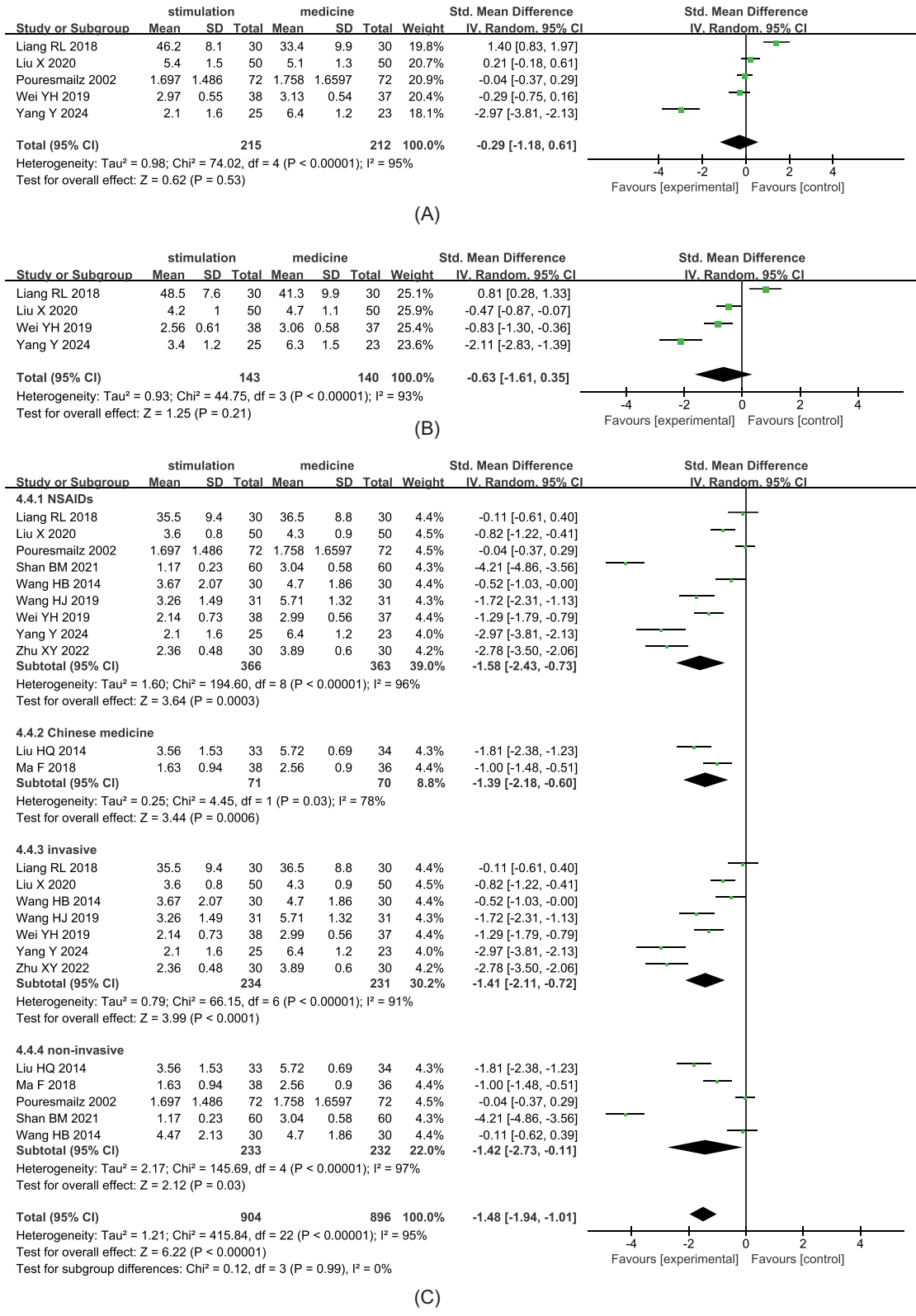


Figure 6 Continued.

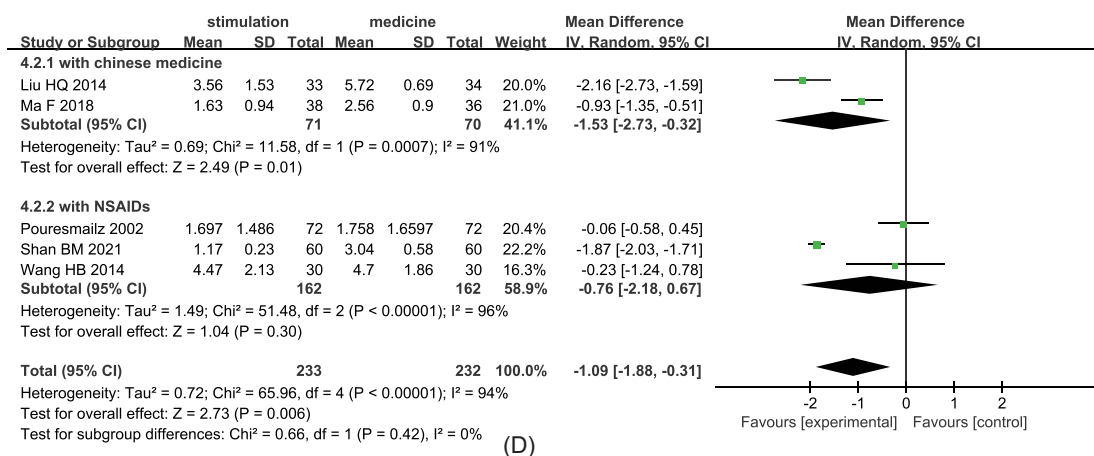


Figure 6 Forest plot of comparison: Acupoint stimulation vs oral medicine, outcome: VAS (A) after one menstrual cycle; (B) after two menstrual cycles; (C) after three menstrual cycles; (D) non-invasive stimulation after three menstrual cycles.

After two menstrual cycles of treatment, the VAS scores were not significantly different (SMD = -0.63 , 95% CI -1.61 to 0.35 , $P = 0.21$, $I^2 = 93\%$, 283 participants; see Figure 6B).^{43,47,57,59} However, the sensitivity analysis indicated that the results were unstable (Appendix 2B), possibly because of variations in acupoints. Subgroup analysis and meta-regression failed to reduce heterogeneity.

After three menstrual cycles of treatment, as shown in Figure 6C, acupoint stimulation was more effective than NSAIDs (nine RCTs, 699 participants, SMD = -1.58 , 95% CI -2.43 to -0.73 , $P = 0.0003$, $I^2 = 96\%$)^{43,47,50,53,55–57,59,60} and Chinese medicine (two RCTs, 141 participants, SMD = -1.39 , 95% CI -2.18 to -0.60 , $P = 0.0006$, $I^2 = 78\%$).^{45,49} Sensitivity analysis confirmed that the results were stable. Compared with medical treatment (all NSAIDs), invasive acupoint stimulation was more effective (seven RCTs, 465 participants, SMD = -1.41 , 95% CI -2.11 to -0.72 , $P < 0.00001$, $I^2 = 91\%$).^{43,47,55–57,59,60} As for non-invasive acupoint, there was a trend toward lower VAS scores for non-invasive acupoint stimulation with a SMD of -1.75 (5 RCTs, 465 participants, 95% CI -2.73 to -0.11 , $P = 0.03$, $I^2 = 97\%$),^{45,49,50,53,55} but the sensitivity analysis indicated that the results were unstable. Subgroup analysis (Figure 6D) showed that non-invasive acupoint stimulation reduced VAS scores more than Chinese medicine after treatment (two RCTs, 141 participants; SMD = -1.53 , 95% CI -2.73 to -0.32 , $P = 0.01$, $I^2 = 91\%$),^{45,49} yet the result did not meet the threshold for clinical significance. Moreover, compared to NSAIDs, the difference were not significant (three RCTs, 324 participants, SMD = -0.76 , 95% CI -2.18 to 0.67 , $P = 0.30$, $I^2 = 96\%$).^{50,53,55} Sensitivity analysis confirmed that the results were stable.

Two studies reported VAS scores after one menstrual cycle of follow-up (all treatment courses were 3 menstrual cycles). Results showed that (Figure 7A) after one menstrual cycle of follow-up, acupoint stimulation were still more effective than NSAIDs (SMD = -3.03 , 95% CI -5.16 to -0.90 , $P = 0.005$, $I^2 = 94\%$, 160 participants).^{43,47} The sensitivity analysis indicated that the results were stable. After three menstrual cycles of follow-up (Figure 7B), acupoint stimulation was more effective than medicine (SMD = -3.74 , 95% CI -5.57 to -1.90 , $P < 0.00001$, $I^2 = 93\%$, 183 participants).^{43,57,59} One trial followed up for six menstrual cycles, indicating that at six menstrual cycles follow-up, the differences in VAS scores between the observation (buccal acupuncture) and control (NSAIDs) groups were -3.92 , which were statistically significant ($P < 0.01$).⁵⁹

Immediately (within five minutes) after the first session, meta-analysis of VAS scores of two studies (Figure 7C) yielded a pooled MD estimate of -2.85 (95% CI -4.06 to -1.64 , $P < 0.00001$, $I^2 = 86\%$, 123 participants),^{57,59} indicating a statistically significant reduction in VAS scores for participants in the acupoint stimulation group compared to those in the NSAIDs group instantly. The sensitivity analysis indicated that the results were stable.

Three trials compared the VAS scores of acupoint stimulation and medicine after 30 minutes of the first session.^{54,57,59} Seemingly, non-significant differences between the two schedules were observed for acupoint stimulation and medicine (Figure 7D), but the sensitivity analysis indicated that the results were unstable (Appendix 2C). Shi ZH was excluded because the treatment received by the control group in this trial was irregular, which resulted in greater heterogeneity. The

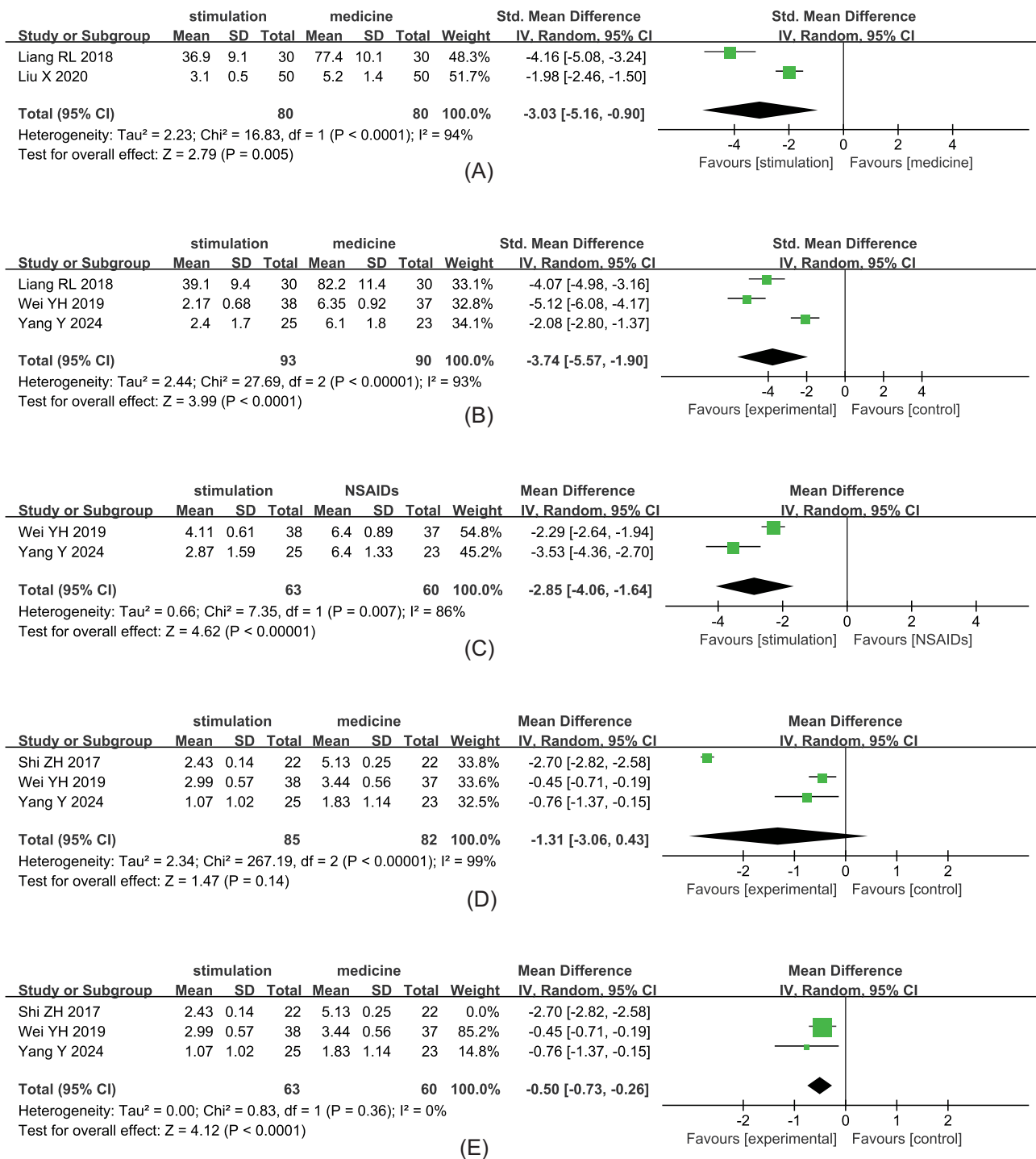


Figure 7 Forest plot of comparison: Acupoint stimulation vs oral medicine, outcome: VAS **(A)** after following one menstrual cycle; **(B)** after following three menstrual cycles; **(C)** immediately / 5 minutes after the first session; **(D)** 30 minutes after the first session; **(E)** 30 minutes after the first session (revised).

revised results indicated a trend toward lower VAS scores for acupoint stimulation (two RCTs, 123 participants; SMD = -0.50, 95% CI: -0.73, -0.26, P < 0.0001, I² = 0%, see [Figure 7E](#)), yet the result did not meet the threshold for clinical significance.⁵⁴

Shi Z H, 2017 reported VAS scores at other points.⁵⁴ The treatment group showed significant differences from the control group at all time points after 30 min of treatment ($P < 0.05$), with a faster onset (15 min vs 30 min) and an earlier peak analgesic effect (30 min vs 60 min), both lasting up to 180 min.

After treatment, 346 (89.18%) of the 388 participants receiving acupoint stimulation were more effective than 255 (72.24%) of the 353 participants receiving oral medicine treatment. The efficacy rate of the NSAIDs was 70.03%. As shown in **Figure 8A**, both invasive stimulation (6 RCTs, 396 participants; SMD = 1.29, 95% CI: 1.05 to 1.58, $P = 0.02$, $I^2 = 73\%$)^{39,47,54–56,60} and non-invasive stimulation (5 RCTs, 375 participants; RR = 1.14, 95% CI: 1.02 to 1.29, $P = 0.02$, $I^2 = 55\%$)^{41,49,51,52,55} were more effective than oral medicine. The efficacy rates of invasive and noninvasive stimulation were 87.89% and 90.53%, respectively. However, the results of the comparison between the non-invasive and medicine groups were not clinically significant. A study reported the efficacy rate in the follow-up period, which showed that the long-term efficacy of staging acupoint catgut embedding was superior to that of ibuprofen ($P < 0.01$).³⁹

Safety of Acupoint Stimulation

Six trials compared the adverse reaction rates of acupoint stimulation and control.^{43,44,49,56,57,59} The main adverse reactions to acupoint stimulation include faintness⁴⁴ and subcutaneous hemorrhage^{43,56} while those of the control groups include gastrointestinal irritation^{43,56,57} and dizziness.⁵⁷ The adverse reaction rate for acupoint stimulation was 4.74% (10 of 211).

Because there was data with a value of 0 in the two sets of studies, we conducted a continuity correction. There was a significant difference between the two group (**Figure 8B**), with an RR of 0.50 (95% CI 0.27 to 0.95, $P = 0.0332$, $I^2 = 0$), but the sensitivity analysis indicated that the results were unstable (**Appendix 2D**). The main source of heterogeneity was reported by Wang HJ, 2019).⁵⁶ We found that the number of adverse reactions reported in the control group (oral administration of ibuprofen, 300 mg/bid, from 5 days before menstruation until menstruation began) was significantly higher than that in the other groups (17 cases, all gastrointestinal reactions caused by ibuprofen). It is speculated that this bias may be due to longer treatment duration and excessive dosage. Therefore, this study was excluded from analysis.

A revised meta-analysis reported that non-significant differences between the two groups were present for acupoint stimulation and control (**Figure 8C**, with an RR of 0.94 (95% CI 0.26 to 3.33, $P = 0.9204$, $I^2 = 0$).^{43,44,49,57,59}

Secondary Outcomes

Objective Indicators

Serum Prostaglandin Contents

Three trials compared the serum levels of Prostaglandins E2 (PGE2) in the acupoint stimulation and control groups.^{47,48,60} As shown (**Figure 9A**), participants in the acupoint stimulation group had significantly higher PGE2 levels (SMD = 0.90, 95% CI 0.63 to 1.18, $P < 0.00001$, $I^2 = 0\%$, 220 participants). The sensitivity analysis indicated that the results were stable.

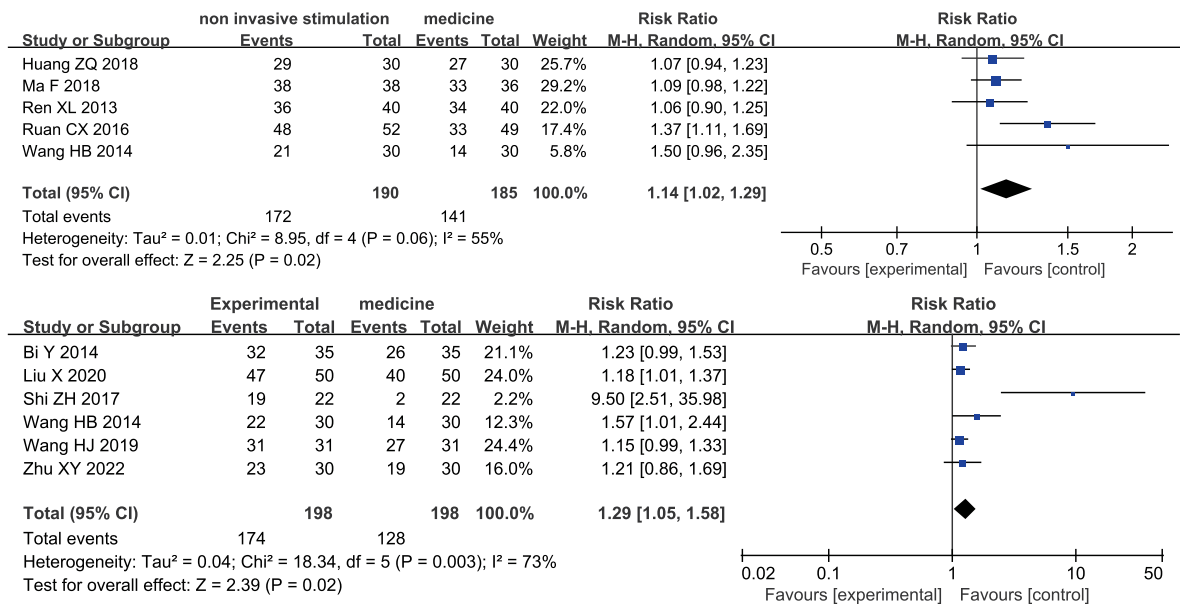
Five trials compared the serum levels of PGF2 α .^{47,48,51,57,60} The results (**Figure 9B**) showed that participants in the acupoint stimulation group had moderately lower Prostaglandins F2 α (PGF2 α) levels (SMD = -0.69, 95% CI -1.04 to -0.34, $P = 0.0001$, $I^2 = 63\%$, 375 participants). The sensitivity analysis indicated that the results were stable.

Uterine Hemodynamics

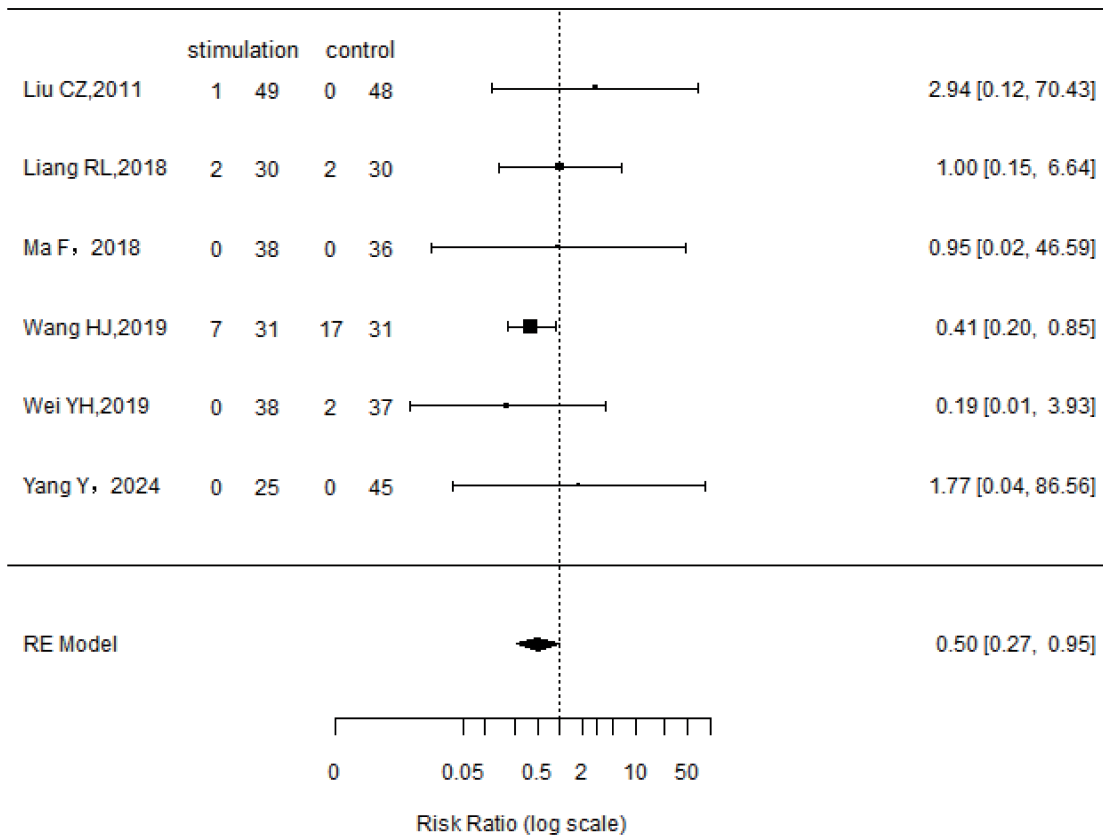
Two trials compared the uterine hemodynamics of acupoint stimulation and controls.^{46,52} The results showed that after treatment in the acupoint stimulation group, the uterine artery resistance index (RI) (**Figure 9C**, MD = -0.04, 95% CI -0.07 to -0.02, $P < 0.0001$, $I^2 = 0\%$, 181 participants) and pulsatility index (PI) (**Figure 9D**, MD = -0.37, 95% CI -0.57, -0.16, $P = 0.0005$, $I^2 = 0\%$, 181 participants) were significantly reduced compared to those in the control group, indicating that acupoint stimulation could improve uterine hemodynamics. Sensitivity analysis indicated that the results were stable.

Participant-Reported Outcomes

CMSS Three trials compared the total CMSS scores of the acupoint stimulation and control groups.^{48,59,60} The meta-analysis (**Figure 10A**) yielded a pooled MD estimate of -2.88 (95% CI -4.80 to -0.97, $P = 0.003$, $I^2 = 73\%$, 168 participants), but the sensitivity analysis indicated that the results were unstable. Treatment sessions of three trials were 8,



(A)



(B)

Figure 8 Continued.

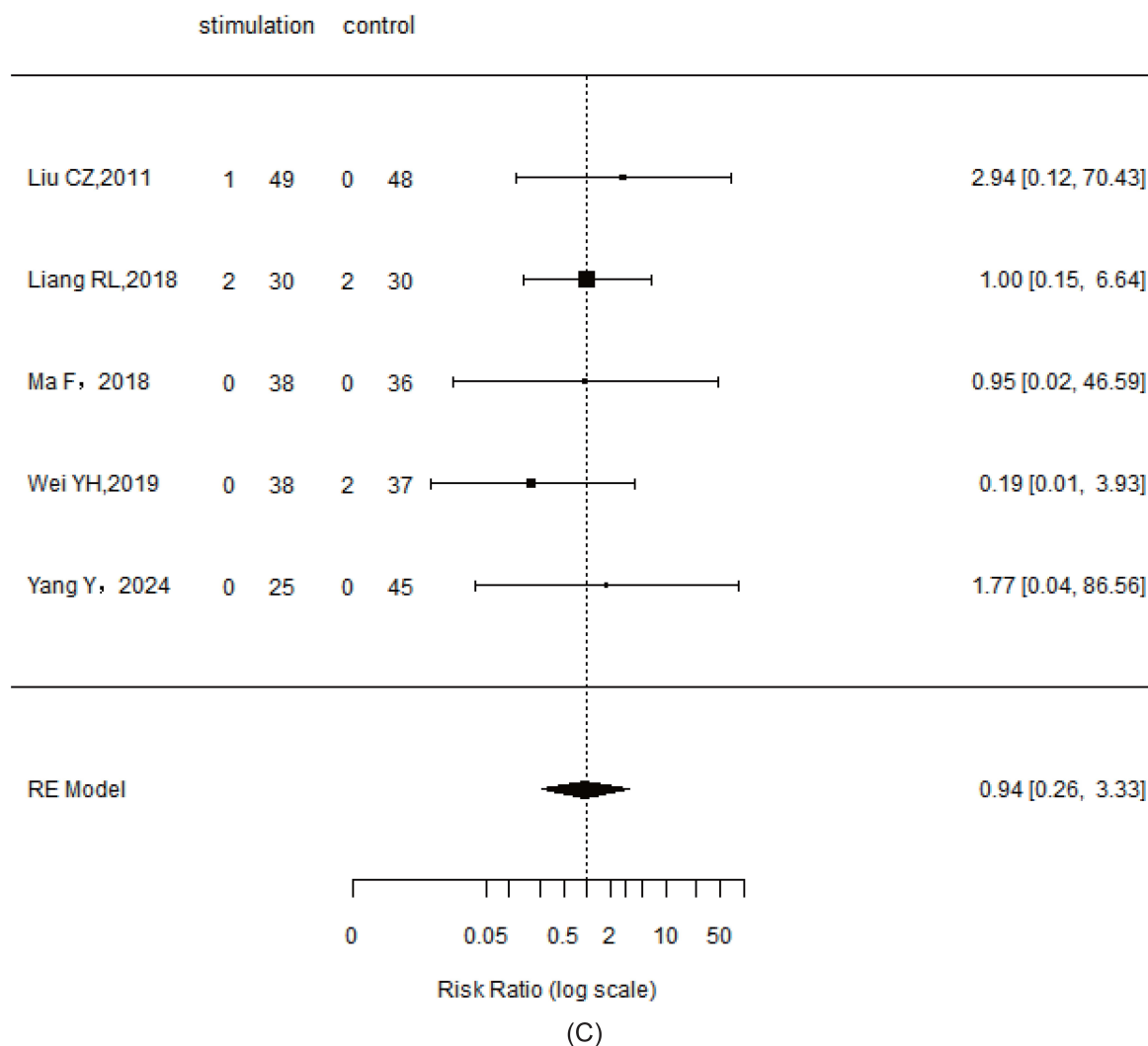


Figure 8 Forest plot of dichotomous variables (A) comparison: Acupoint stimulation vs oral medicine, outcome: effective rate; (B) comparison: Acupoint stimulation vs control, outcome: adverse reaction rate; (C) adverse effective rate (revised).

4, 8.5. The results of the meta-regression (Figure 10B) indicated that the total CMSS scores of CMSS significantly correlated with the treatment sessions ($P < 0.0001$).

A study reported the total CMSS after 6-months of follow-up, which supported that acupoint stimulation could still improve dysmenorrhea symptoms during the follow-up period ($MD = -13.92$, $P < 0.01$).⁵⁹

Two studies separately reported CMSS scores for each group in detail in terms of severity and duration.^{42,53} Compared with those in the control groups, participants in the acupoint stimulation groups had lower scores for severity (Figure 10C, $MD = -2.43$, 95% CI -3.28 to -1.59 , $P < 0.00001$, $I^2 = 0\%$, 187 participants) and duration (Figure 10D, $MD = -6.84$, 95% CI -10.05 to -3.62 , $P < 0.0001$, $I^2 = 60\%$, 187 participants). The sensitivity analysis indicated that the results were stable.

Dysmenorrhea Symptom Scores Four trials compared the dysmenorrhea symptom scores of acupoint stimulation and medicine after three menstrual cycles of treatment.^{41,43,49,55} Meta-analysis of dysmenorrhea symptom scores (Figure 10E) yielded a pooled MD estimate of -1.65 (95% CI -2.56 to -0.73 , $P = 0.0004$, $I^2 = 53\%$, 254 participants), indicating a statistically significant reduction in symptom scores for participants in the acupoint stimulation group. The sensitivity analysis indicated that the results were stable.

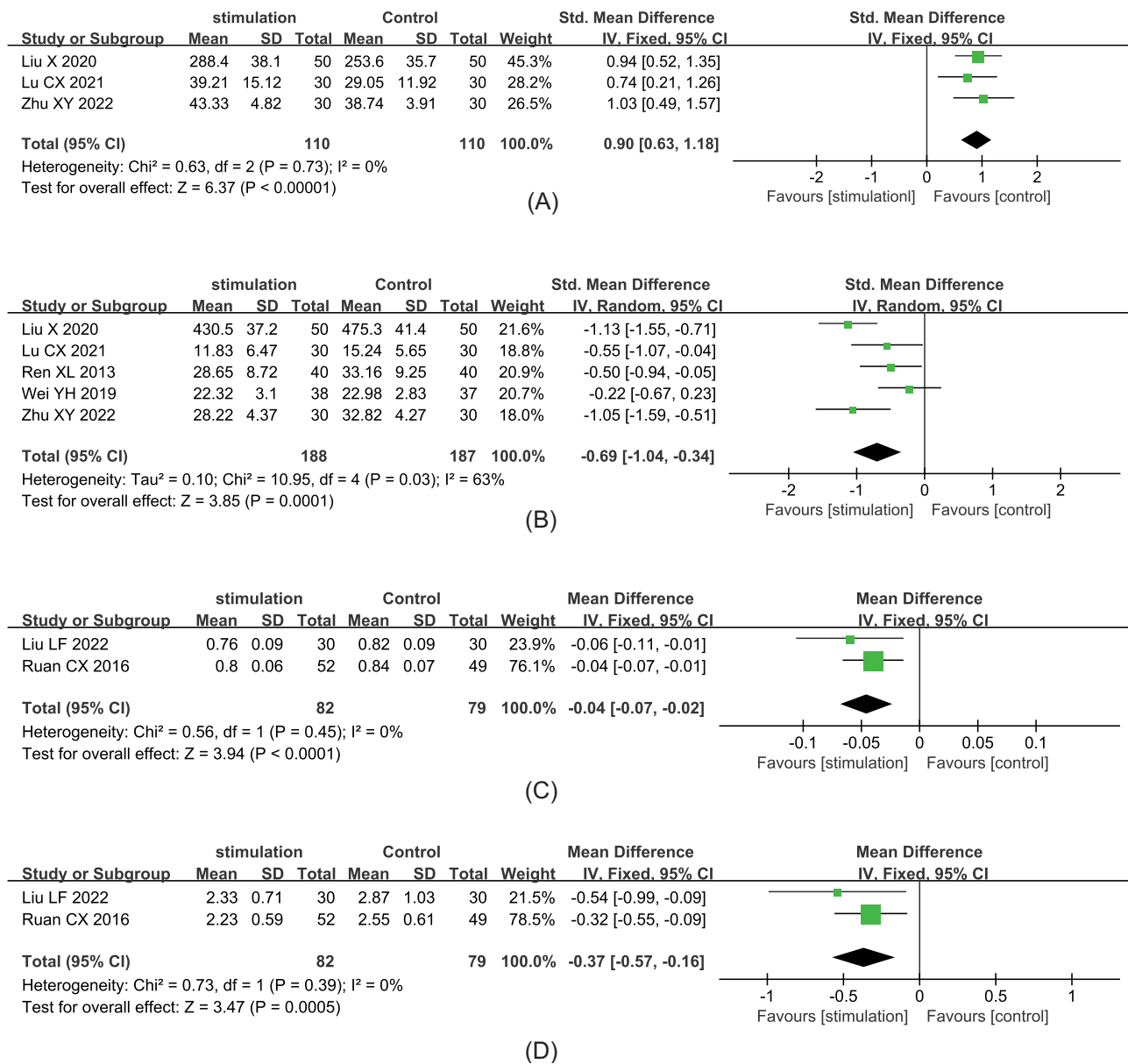
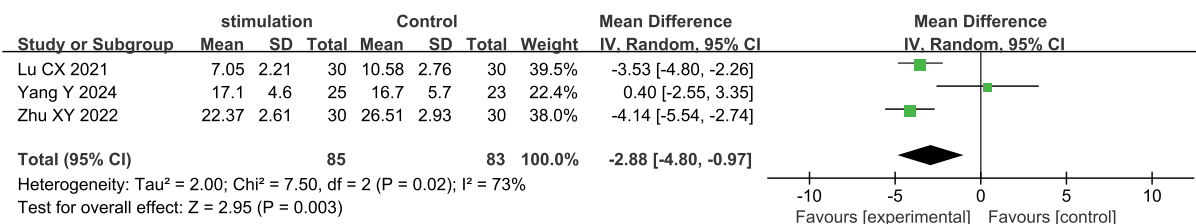


Figure 9 Forest plot of objective indicators **(A)** comparison: Acupoint stimulation vs control, outcome: PGE2; **(B)** comparison: Acupoint stimulation vs control, outcome: PGF2 α ; **(C)** comparison: Acupoint stimulation vs control, outcome: RI; **(D)** comparison: Acupoint stimulation vs control, outcome: PI.

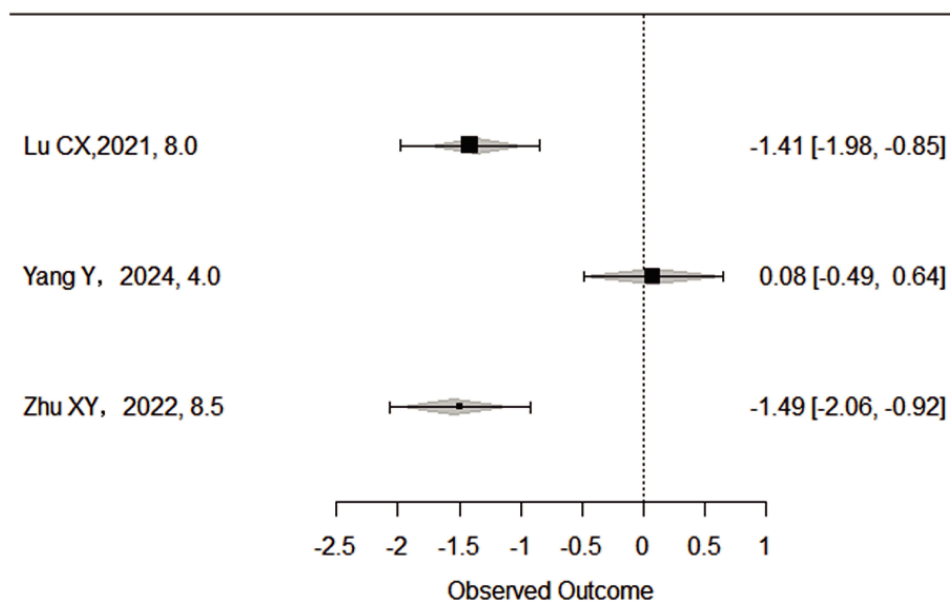
Two trials also compared the dysmenorrhea symptom scores for acupoint stimulation and medicine during the follow-up period.^{43,49} Meta-analysis of dysmenorrhea symptom scores (Figure 10F) yielded a pooled MD estimate of -3.77 (95% CI -6.92 to -0.61 , $P = 0.02$, $I^2 = 90\%$, 134 participants), indicating a statistically significant reduction in symptom scores for participants in the acupoint stimulation group compared to those in the medicine group. The sensitivity analysis indicated that the results were stable.

PSQI

Two trials compared the PSQI scores of acupoint stimulation and controls.^{42,53} There was a trend toward lower PSQI scores for acupoint stimulation (Figure 10G), but sensitivity analysis indicated that the results were unstable. Given the small sample size, we tried bayes to explain this, resulting in a posterior probability of MD of -0.516 (95% CI -0.978 to -0.049), which indicated a trend toward lower PSQI scores for acupoint stimulation.

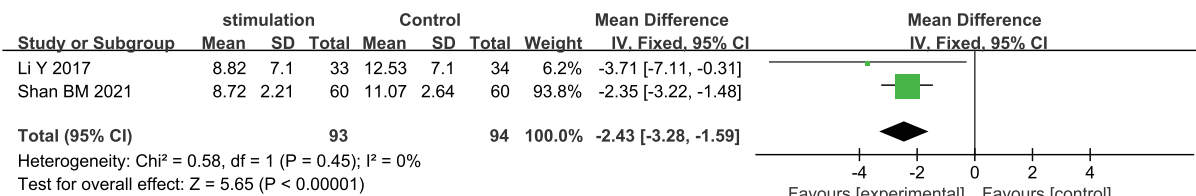


(A)

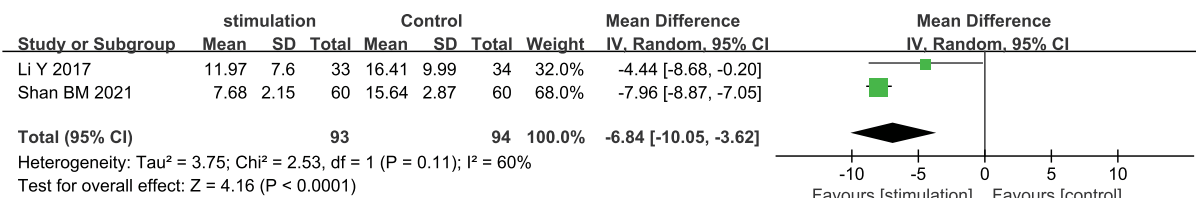


| | estimate | se | zval | pval | ci.lb | ci.ub | |
|----------|----------|--------|---------|--------|---------|---------|-----|
| intrcpt | 1.5038 | 0.5908 | 2.5454 | 0.0109 | 0.3459 | 2.6618 | * |
| medicine | -0.3580 | 0.0830 | -4.3113 | <.0001 | -0.5207 | -0.1952 | *** |

(B)



(C)



(D)

Figure 10 Continued.

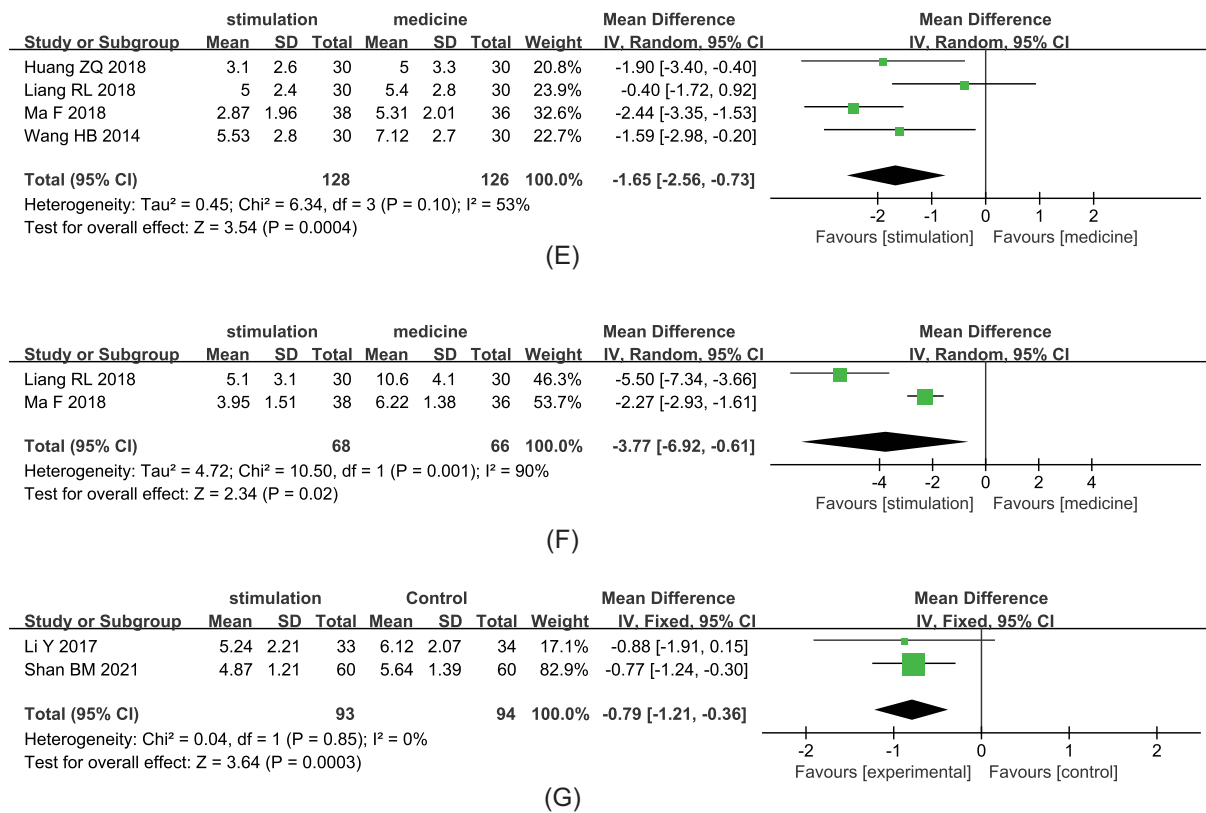


Figure 10 Forest plot of participant-reported outcomes (A) comparison: Acupoint stimulation vs control, outcome: CMSS; (B) meta regression: Acupoint stimulation vs control, outcome: CMSS; (C) comparison: Acupoint stimulation vs control, outcome: severity of CMSS; (D) comparison: Acupoint stimulation vs control, outcome: duration of CMSS; (E) comparison: Acupoint stimulation vs medicine, outcome: dysmenorrhea symptom scores after treatment; (F) comparison: Acupoint stimulation vs control, outcome: dysmenorrhea symptom scores during follow-up period; (G) comparison: Acupoint stimulation vs control, outcome: PSQI.

Other Outcomes

Short Form 36 Health Survey (SF-36)

Two studies collected the data of SF-36.^{39,43} This table consists of 36 items, each of which was assigned a different score. The higher the score, the better is the health status and quality of life represented. Bi Y, 2014 argued that both acupoint stimulation and fenbid could improve the health status and quality of participants ($t_{\text{stimulation after treatment}} = -6.41$, $t_{\text{stimulation during follow-up}} = -6.91$, $t_{\text{Fenbid after treatment}} = -3.92$, $P < 0.01$) and that acupoint stimulation performed better ($t_{\text{after treatment}} = 2.535$, $P < 0.05$; $t_{\text{follow-up}} = 4.667$, $P < 0.01$).³⁹ Liang RL 2018 argued that there were no differences between the two groups after treatment ($P > 0.05$); however, differences occurred during the follow-up period ($P < 0.05$) because of the reduction in the efficacy of ibuprofen ($P < 0.05$).⁴³ The efficacy of acupoint stimulation was higher ($P > 0.05$).

Resting State Scale (RSS)

A study collected RSS data.⁴⁴ The results showed that the RSS- COX1 score in the unrelated acupoint group (-2.847 mm, 95% CI -5.325 to -0.370 , $P = 0.025$) was lower than that in the non-acupoint group; however, there was no statistically significant difference in the RSS-COX2 scores among the four groups ($P > 0.05$).

Verbal Rating Scale (VRS)

A study showed that there was a non-significant difference in VRS among the different groups.⁴⁴

Total Pain Duration

A study compared the total pain duration of the participants.⁵⁸ The results of Xu SW,2014 showed that the total pain duration during treatment and follow-up was shorter in the acupuncture treatment group than in the blank control group ($t_{\text{one menstrual cycle of treatment}} = -2.72$, $P = 0.008$; $t_{\text{two menstrual cycles of treatment}} = -6.08$, $P < 0.01$; $t_{\text{three menstrual cycles of treatment}}$

= -10.64, $P < 0.01$; $t_{\text{one menstrual cycle of follow-up}} = -10.69$, $P < 0.01$; $t_{\text{two menstrual cycles of follow-up}} = -10.73$, $P < 0.01$; $t_{\text{three menstrual cycles of follow-up}} = -10.70$, $P < 0.01$). There was no significant difference between the data collected at 1–3 months follow-up and 3 months post-treatment in the treatment group, indicating that the therapeutic effect lasted for at least three menstrual cycles.

Self-Rating Anxiety Scale (SAS)

Anxiety was assessed using a 20-item scale, with five reverse-scored items rated on a 4-point scale (higher scores indicate greater anxiety). A study reported significant post-treatment reductions in SAS scores across all groups ($P < 0.05$); however, no significant differences were observed between time points within the groups ($n = 90$, $P > 0.05$), suggesting a potential placebo effect.⁴⁸

β -Endorphin (β -EP)

A study demonstrated that acupoint stimulation significantly increased β -endorphin (β -EP) levels, a neuropeptide involved in endogenous analgesia and reproductive endocrine regulation, compared to controls ($t = 5.828$, $P < 0.001$).⁴⁷ Reduced β -EP levels may impair uterine regulatory mechanisms.

Discussion

Summary of Main Findings

Current evidence suggests that acupoint stimulation may be effective for PD, with a total efficacy rate of 89.18% (346 of 388). Compared with the no-treatment or sham treatment groups, the acupoint stimulation group exhibited significantly reduced pain immediately after treatment and during the follow-up period. However, more RCTs are needed to confirm the transient efficacy. Compared with pharmacological treatment, acupoint stimulation may provide additional benefits such as rapid pain relief and potential long-term effects. Immediately after treatment, the acupoint stimulation group showed a greater reduction in pain intensity, yet this difference was of limited clinical significance at the 30-minute post-treatment assessment. After three menstrual cycles of treatment, there was no significant difference in pain levels between the two groups during the first two menstrual cycles. However, in the third menstrual cycle, the acupoint stimulation group experienced lower pain levels, and this trend persisted for at least three menstrual cycles during the follow-up period. This delayed but sustained effect suggests that acupoint stimulation may be particularly beneficial for long-term management of PD. Acupoint stimulation may serve as an effective alternative treatment for patients with PD without increasing the incidence of adverse reaction. The number of adverse reactions in the acupoint stimulation group was not significantly different from that in the control group, with an adverse reaction rate of 4.74% (10/211).

Other secondary indicators also supported the primary outcomes. Since pain intensity is a subjective indicator that may introduce bias, objective indicators such as serum prostaglandin levels and uterine hemodynamics were also examined. The results indicated that compared with the control group, acupoint stimulation significantly increased serum PGE2 levels and decreased PGF2 α levels in patients, with significant reductions in RI and PI of the uterine artery. Acupoint stimulation also improved the quality of life. Compared with the control group, the acupoint stimulation group showed significant reductions in CMSS and dysmenorrhea symptom scores after treatment and during the follow-up period; however, there seems to be no significant improvement in sleep quality.

Invasive and Noninvasive Stimulation

As in previous reviews, we also conducted subgroup analyses of invasive and noninvasive stimulation. However, the results were different. After three menstrual cycles of treatment, the pain intensity in the invasive stimulation group was significantly lower than that in the NSAIDs group, whereas the difference between noninvasive stimulation and NSAIDs was not significant. Nevertheless, the non-invasive stimulation group showed statistically significant but clinically insignificant lower pain intensity than the Chinese medicine group. This suggests that invasive stimulation offers superior pain reduction. Several factors could explain this discrepancy:

This difference may be attributed to the concept of “deqi” in traditional Chinese medicine. “Deqi” refers to the specific sensation experienced by the patient during acupuncture treatment, which occurs when the acupuncture needle

pierces through the skin and stimulates a particular acupoint, eliciting feelings such as soreness, numbness, distension, and heaviness. In both literature and clinical practice, the crucial importance of “deqi” in acupuncture therapy has been highly emphasized. The mechanism of “deqi” involves altering pain thresholds and temperatures at disease-specific acupoints, inducing a more stable and extensive activation of brain regions, enhancing the expression of opioid receptors in the midbrain and spinal cord, reducing the release of local inflammatory mediators, and improving uterine micro-circulatory disorders.⁶¹ Multicenter RCTs showed that “deqi” was associated with greater reduction of pain intensity.^{62,63} Consequently, noninvasive acupoint stimulation may result in weaker therapeutic effects because of the lack of “deqi”.

According to the previous review,²⁵ certain patients may fear invasive acupoint stimulation because they are afraid of needles, which may reduce their compliance. Invasive acupoint stimulation may more frequently lead to adverse reactions such as subcutaneous hemorrhage,⁵⁶ albeit these reactions are generally mild. In contrast, non-invasive acupoint stimulation offers better safety, causes less pain, and may be more acceptable to patients.

There are also some possible biases. Among the included studies, the majority contained intervention groups involving invasive acupoint stimulation (13 out of 22). Only five studies with noninvasive stimulation reported VAS scores after three menstrual cycles of treatment, and the heterogeneity in intervention methods was considerable, resulting in instability in the outcomes. The interventions for invasive stimulation were mainly acupuncture, whereas those for noninvasive stimulation was more diverse, including various forms of moxibustion, transcutaneous electrical acupoint stimulation (TEAS), and acupressure. All primary outcome measures in clinical trials in PD are participant-reported and most of trials were lack of blinding. It cannot be ruled out that participants allocated to invasive stimulation reported positively biased outcomes, whereas those allocated to non-invasive stimulation reported negatively biased outcomes. Additionally, the quality of acupuncture interventions in clinical trials is often disputed. It is argued that better acupuncturists would have achieved better results, but the studies included did not report acupuncture therapists' confidence in treatment.

Merits and Demerits of Acupoint Stimulation

Rooted in traditional Chinese medicine practice, acupoint stimulation represents a time-tested approach for primary dysmenorrhea, offering sustained efficacy and safety. Its analgesic mechanisms appear to involve both peripheral (microcirculation improvement, oxidative stress and inflammation modulation) and central (endogenous analgesic release) pathways,^{17–20} making it particularly suitable for pharmacotherapy-resistant cases. Additionally, acupoint stimulation avoids the gastrointestinal side effects associated with NSAIDs and the ovulation-suppressing adverse effects of COCs. However, these mechanisms depend on critical technical and adherence factors. The efficacy of acupoint stimulation shows significant correlation with both the proficiency and attentiveness of the acupuncture practitioner.⁶⁴ Furthermore, the intervention typically requires a minimum of three treatment cycles to achieve optimal therapeutic effects. Moreover, compared to the single-dose cost of NSAIDs, acupoint stimulation entails higher economic expenses per treatment session. The development of this modality is additionally constrained by needle phobia among certain patient populations, which limits acceptance of invasive stimulation techniques.

Limitations

We propose that acupoint stimulation is not intended to replace conventional pharmacological treatments but rather to serve as a complementary approach, given the following limitations in our study. The methodological quality of the included trials varied. The methods for sequence generation and handling of dropouts and withdrawals were adequate in the most recent trials. However, most trials lacked blinding and details regarding allocation concealment. Most studies used a subjective, self-reported index of treatment effects as the outcome measure, which may introduce bias; only seven trials included objective outcomes such as serum prostaglandin content and uterine hemodynamics. Moreover, the observed differences in treatment outcomes may also reflect cultural factors, as patients in Chinese populations may have higher expectations and confidence in traditional therapies such as acupuncture, potentially enhancing placebo effects. Most articles lacked publicly available clinical registration or protocols, which may introduce publication bias. The GRADE certainty of the most evidence ranged from low to moderate, owing to considerable risk of bias and high heterogeneity.

We are confident that we have identified a search as comprehensive as possible for existing clinical trials relevant to our question, but we cannot rule out the possibility that there are additional trials that are unpublished or published in sources not accessible to our search or published in other languages. Moreover, we did not include the most recent literature published after May 20, 2024, and variable treatment schedules may have obscured the optimal dosing. Due to the limited number of studies (fewer than 10) included in each meta-analysis, we were unable to conduct statistically meaningful assessments of publication bias. Owing to constraints in the sample size of the non-pharmacological control arm, we combined the sham treatment and no-treatment groups for analysis, potentially introducing some bias. However, subgroup analysis from our pilot study demonstrated no significant intergroup differences, suggesting that the efficacy of acupoint stimulation is not merely a placebo effect. Perhaps because some of the studies were published earlier, we could not access unpublished data. Because we included all types of acupoint stimulation, the results of the meta-analysis exhibited considerable heterogeneity, and even after conducting subgroup analyses, the heterogeneity remained relatively high.

Clinical Implications of the Study

The findings demonstrate that acupoint stimulation can effectively reduce pain intensity in patients with PD, particularly in terms of long-term efficacy, with a favorable safety profile. For clinicians, this review provides robust evidence supporting the therapeutic value of acupoint stimulation, making it a viable recommendation for PD patients who are resistant to pharmacological treatments. Regular acupoint therapy, such as acupuncture or electroacupuncture, could be integrated into clinical practice as an adjunct or alternative option. For patients, simple stimulation techniques like acupressure offer a convenient and accessible self-management strategy for PD symptom relief. For researchers, future studies should focus on standardizing intervention protocols, improving blinding procedures, and incorporating objective outcome measures such as serum biomarkers and imaging data to further validate the efficacy of acupoint stimulation for PD.

Conclusions

This systematic review incorporates the latest literature while applying rigorous inclusion criteria. Current evidence suggests that acupoint stimulation can effectively reduce pain intensity in patients with primary dysmenorrhea, especially the long-term efficacy. Compared with non-steroidal anti-inflammatory drugs, acupoint stimulation demonstrates comparable pain relief, with potentially faster onset during initial treatment and superior long-term analgesic effects, particularly notable with invasive stimulation techniques. The effective rate of acupoint stimulation reached 89.18%. The incidence of adverse reactions was minimal (4.74%) and all cases were mild, showing no significant difference from control groups. These findings indicate that long-term acupoint stimulation may serve as a safe and effective alternative management option for young nulliparous patients with intolerance or poor adherence to conventional medications. However, due to the limitations of the sample size and quality of the existing studies, the above conclusions still need to be further validated and supplemented by more large-sample, multicenter and high-quality randomized clinical trials with standardized protocols.

Abbreviations

PD, Primary dysmenorrhea; RCTs, Randomized controlled trials; Embase, Excerpta Medica Database; AMED, Allied and Complementary Medicine Database; CENTRAL, Cochrane Central Register of Controlled Trials; CNKI, China National Knowledge Infrastructure; SMD, Standardized Mean Difference; MD, Mean Difference; CI, Confidence Interval; RR, Relative Risk; GRADE, Grade of Recommendations Assessment, Development and Evaluation; ADHD, Attention Deficit Hyperactivity Disorder; NSAIDs, Non-steroidal Anti-inflammatory drugs; COC, Combined Oral Contraceptives; TENS, Transcutaneous Electrical Nerve Stimulation; Sinomed, Chinese Biomedical Literature Service System; MeSH, Medical Subject Headings; PICOS, participants, intervention, comparison, outcome, study type; VAS, Visual Analogue Scale; CMSS, Cox Menstrual Symptom Scale; PSQI, Pittsburgh Sleep Quality Index; RSS, Resting-State Scale; VRS, Verbal Rating Scale; SF-36, Short Form - 36 Health Survey; SAS, Self-Rating Anxiety Scale; Rob2, the revised Cochrane Risk of Bias, version 2; SD, Standard Deviation; SP6, Sanyinjiao acupoint; CV4, Guanyuan acupoint; ITT, intention-to-treat; PP, per-protocol; PGE2, Prostaglandins E2; PGF2 α , Prostaglandins F2 α ; β -EP, β -Endorphin; RI, Resistance Index; PI, Pulsatility Index; TEAS, Transcutaneous Electrical Acupoint Stimulation.

Declaration

During the preparation of this study, the authors used the generative artificial intelligence tool, ChatGPT 4.0, in the drafting of this paper for grammar and language refinement. Subsequently, the authors reviewed and edited the content and took full responsibility.

Data Sharing Statement

The authors confirm that data supporting the findings of this study are available within the article.

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 report no conflicts of interest in this work.

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