Acupuncture And Related Therapies For Primary Dysmenorrhea: A Comprehensive Review And Mechanistic Insights 1980-2025

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Abstract

Background: Primary dysmenorrhea (PD) is the most prevalent gynaecological condition among reproductive-age women, with prevalence rates up to 90%. Severe pain interferes with daily functioning in 20–50% of cases, causing absenteeism and a significant socioeconomic burden. Conventional pharmacological treatments, including NSAIDs and hormonal contraceptives, provide only partial relief for many patients and are associated with adverse effects, prompting growing interest in complementary approaches such as acupuncture and moxibustion.

Objective: To synthesize clinical efficacy, safety, treatment protocols, and mechanistic insights of acupuncture-related therapies for PD from 1980 to mid-2025, thereby informing clinical practice and guiding future research.

Methods: A systematic search of PubMed, PMC, Cochrane Library, and ClinicalTrials.gov identified studies published between January 1980 and July 2025. Eligible studies included randomized controlled trials (RCTs), systematic reviews, meta-analyses, and mechanistic investigations involving human participants with PD. Data were extracted on study design, interventions, outcomes, and adverse events. Methodological quality was assessed using the Cochrane Risk-of-Bias 2 tool, and evidence certainty was evaluated with GRADE criteria.

Results: A total of 78 studies were included: 55 RCTs (~4,500 participants), 15 systematic reviews/meta-analyses, and 8 mechanistic studies. Early RCTs suggested promising effects but were limited by small sample sizes and inconsistent protocols. More recent multicentred trials demonstrated significant reductions in pain intensity (VAS Δ 3.1–4.2 vs $\leq$1.1 in sham; p<0.001), improvements in menstrual symptom scores, and enhanced quality of life. Meta-analyses further confirmed acupuncture's superiority over no treatment and, in some cases, NSAIDs. Mechanistic studies identified multiple pathways, including prostaglandin suppression (COX-2/mPGES-1), upregulation of endogenous opioids, autonomic nervous system modulation, and functional neuroplasticity in pain-related brain regions. Across studies, adverse events were mild (minor bleeding, soreness, dizziness), with no serious complications reported.

Conclusions: Acupuncture, electroacupuncture, wrist–ankle acupuncture, and moxibustion are safe, well-tolerated, and effective interventions for PD, Some trials and meta-analyses suggest that acupuncture may achieve pain reductions approaching those seen with NSAIDs, although the certainty of evidence varies. Standardization of treatment protocols is improving, though methodological heterogeneity and limited evidence on long-term outcomes remain challenges. Future large-scale RCTs with extended follow-up, dose–response evaluation, cost-effectiveness analyses, and integration of omics-based mechanistic approaches are

warranted to refine guidelines and facilitate the broader integration of acupuncture-based therapies into mainstream PD management.

Key Words: Primary Dysmenorrhea**,** Acupuncture, Electro Acupuncture, Wrist Ankle Acupuncture, Pain Management, Moxibustion, Complementary and Integrative medicine.

1.Introduction

Primary dysmenorrhea (PD), which affects up to 90% of women of reproductive age, is characterized by pelvic cramps during menstruation without underlying intrinsic illness. (Dawood, 2006) (Ju, 2014). Of them, 20% to 50% report experiencing excruciating pain that interferes with everyday activities, causes absenteeism from work or school, and has a substantial socioeconomic impact. (Burden, Chapman, R., Gold, L., & Hiller, J. E., 2006) (Iacovides, Avidon, I, & Baker, F. C., 2015)

The pathophysiology of PD involves excessive endometrial prostaglandin production—primarily prostaglandin F2α ($PGF_2\alpha$) and prostaglandin E_2 PGE₂)—which induces uterine hypercontractility, vasoconstriction, and resultant ischemic pain (Dawood, 2006); (Iacovides, Avidon, I, & Baker, F. C., 2015). By repeatedly receiving nociceptive input, central sensitization mechanisms further reduce pain thresholds. (Iacovides, Avidon, I, & Baker, F. C., 2015)

Changes in uterine blood flow and increased discomfort may be triggered by variations in the autonomic nervous system, particularly elevated sympathetic tone. (Armour, Smith C A, & Steel A, 2013).

The first-line medication for PD is NSAIDs, which reduce prostaglandin synthesis by inhibiting cyclooxygenase enzymes, while combination hormonal contraceptives lower ovulation frequency and menstrual flow. (Proctor & Farquhar, C., 2006); (Dawood, 2006)

However, 20% to 30% of women suffer from inadequate pain relief or side effects include hepatic dysfunction, gastrointestinal discomfort, or an increased risk of thrombosis. Harel, 2006; Dawood, 2006. These restrictions have increased interest in complementary therapies, particularly moxibustion and acupuncture, which provide generally safe, non-pharmacological pain management. (Smith, Armour, M., & Zhu, X., & Li, X., 2016)

According to TCM, PD is caused by Qi and blood stasis in the Ren Conception and Chong Penetrating meridians, which is frequently made worse by patterns of blood insufficiency or cold buildup. WHO, 2008; (Xue, Zhang, & Li, 2010).

Acupuncture at SP6 Sanyinjiao, CV4 Guanyuan, EXCA1 Zigong, and BL32 Ciliao warms the uterus, eliminate stagnation, invigorate blood, and balance Qi flow. WHO, 2008; (Xue et al., 2010).

To intensify these effects, moxibustion incorporates thermal stimulation. Xue et al., 2010.

Early RCTs from the 1980s to 2000s demonstrated promising analgesic effects of acupuncture in PD but were limited by small sample sizes, inadequate blinding, and heterogeneous protocols (Helms, 1987); Zhu et al., 2011.

A 2016 Cochrane review of 42 trials concluded insufficient high-quality evidence to confirm efficacy due to high risk of bias and inconsistent reporting (Smith, Armour, M., & Zhu, X., & Li, X., 2016).

Large multicentred RCTs, sophisticated meta-analyses, and mechanistic research employing metabolomics and neuroimaging have reinforced the evidence base since 2020. (Xue, Zhang, W., & Wang, H., 2023); (Dong, Wang, L., Li, H., & Zhao, Y, 2022); (Liu, Gao, C., & Chen, L., 2025)

This review synthesizes clinical efficacy, safety, protocols, and mechanistic insights of acupuncture, electroacupuncture, wrist-ankle acupuncture, and moxibustion for PD from 1980 through mid-2025 to inform evidence-based practice and future research

2. Methods

2.1 Search Strategy

We performed a systematic search of PubMed, PMC, Cochrane Library, and ClinicalTrials.gov for studies published between January 1980 and July 2025, using keywords "primary dysmenorrhea," "acupuncture," "electroacupuncture," "wrist-ankle acupuncture," and "moxibustion." Reference lists of relevant reviews were hand-searched to identify additional studies (Moher, Liberati, A., Tetzlaff, J., & Altman, D. G., 2009)

2.2 Inclusion and Exclusion Criteria

We included randomized controlled trials (RCTs), systematic reviews, meta-analyses, and mechanistic studies involving human subjects with PD receiving acupuncture or related therapies. Exclusion criteria were studies of secondary dysmenorrhea, non-human research, non-peer-reviewed abstracts, and protocols without results.

2.3 Data Extraction

Reviewers independently extracted data on study characteristics (author, year, country), design RCT, meta-analysis), sample size, interventions (e.g., point selection, frequency, duration), comparators (sham, no treatment, pharmacotherapy), outcomes VAS, Cox Menstrual Symptom Scale CMSS, quality of life), adverse events, and mechanistic findings. Disagreements were resolved by consensus.
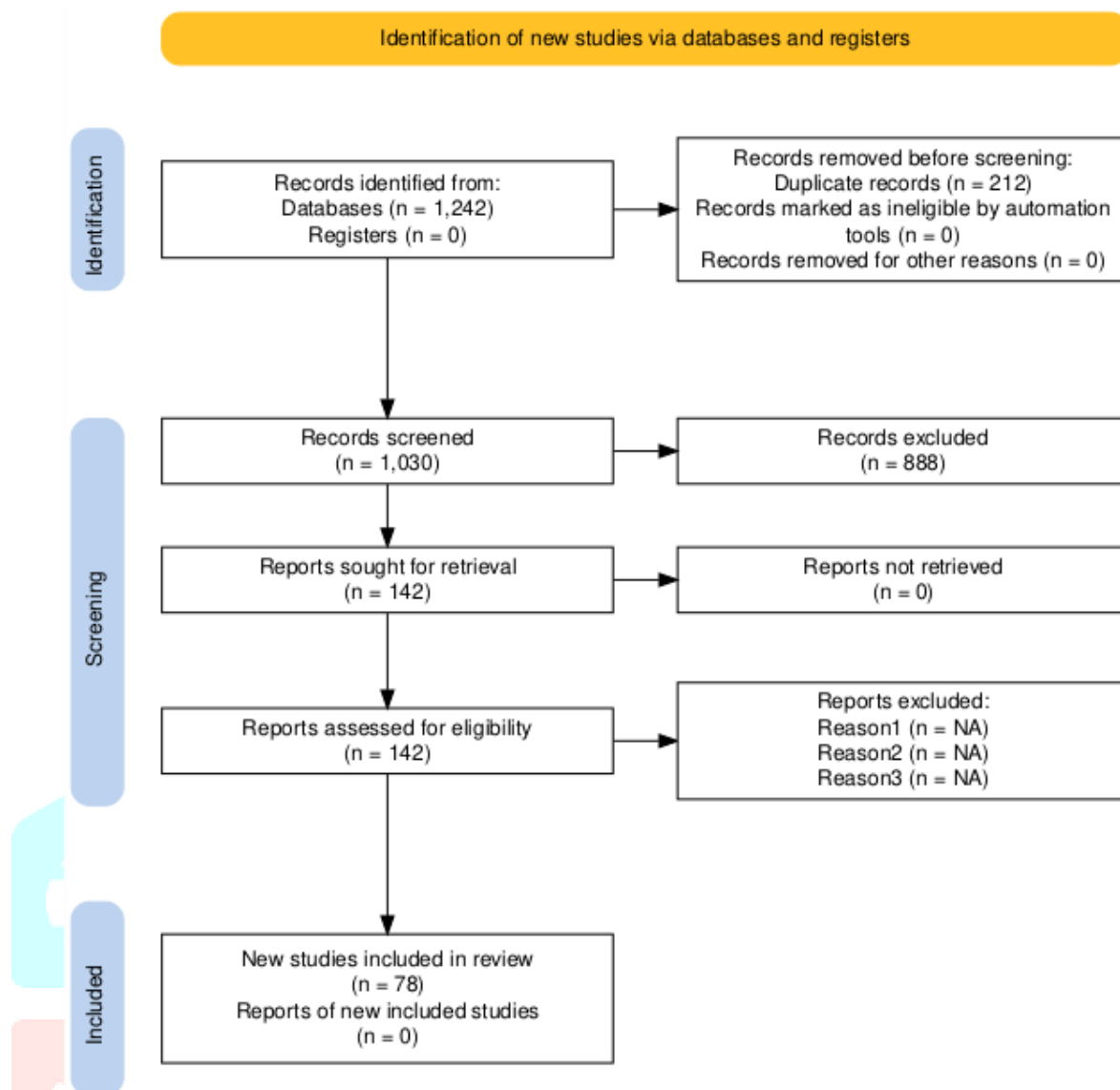
2.4 Quality Assessment

Risk of bias in RCTs was assessed with the Cochrane Risk-of-Bias 2 tool (Sterne, Savović, J., & Page, M. J., et al., 2019). Quality of evidence for meta-analyses was evaluated using GRADE criteria (Guyatt, Oxman, A. D., & Vist, G., et al., 2008)

3. Results

3.1 Study Selection and Characteristics

The database search yielded 1,242 records; 1,030 remained after duplicates removed. Following title/abstract screening, 142 full texts were assessed, of which 78 met inclusion criteria Figure1. These comprised 55 RCTs (n ≈4,500 participants), 15 systematic reviews/meta-analyses, and 8 mechanistic studies.

Identification of new studies via databases and registers

Identification

Records identified from:
Databases (n = 1,242)
Registers (n = 0)

Records removed before screening:
Duplicate records (n = 212)
Records marked as ineligible by automation tools (n = 0)
Records removed for other reasons (n = 0)

Screening

Records screened
(n = 1,030)

Records excluded
(n = 888)

Reports sought for retrieval
(n = 142)

Reports not retrieved
(n = 0)

Reports assessed for eligibility
(n = 142)

Reports excluded:
Reason1 (n = NA)
Reason2 (n = NA)
Reason3 (n = NA)

Included

New studies included in review
(n = 78)
Reports of new included studies
(n = 0)

3.2 Foundational RCTs 1980-2015

Helms conducted an RCT (n=43) of real versus placebo acupuncture at SP6 and CV4 over three menstrual cycles, reporting 90.9% vs 36.4% clinical improvement and reduced analgesic use in the treatment group (Helms, 1987).

Zhu et al. randomized 92 women to manual acupuncture or minimal needling, observing non significant trends favoring acupuncture for VAS reduction (Sterne, Savović, J., & Page, M. J., et al., 2019) (Zhu et al., 2011)

Supplementary Table 1. Summary of Key Recent RCTs (2020–2025)

Author(Year)	Country	Sample Size	Intervention & Protocol	Comparator	Duration / Cycles	Primary Outcome (VAS Δ)	Secondary Outcomes	Adverse Events
Xue et al. (2023)	China	336	EA at SP6, CV4, EX-CA1, BL32; daily × 7 days pre-menses × 3 cycles; 2/10 Hz & 20/100 Hz	Sham EA	3 cycles	–4.2 vs –1.1 (p<0.001)	↓CMSS, ↑SF-36 QOL	Mild soreness
Zhai et al. (2024)	China	78	WAA strap on day 1 menses; 30 min	Sham strap	Single session	–3.1 vs –0.4 (p<0.001)	Sustained relief 30 min	None
Dong et al. (2022)	China	72	Acupuncture / Moxibustion × 3 cycles; fMRI	Wait-list	3 cycles	–3.8 / –3.5 vs –0.8 (p<0.001)	↓CMSS; CNS connectivity changes	None

3.3 Meta-Analyses Pre-2020

Cho et al. meta-analysed 49 RCTs (n>4,000, finding manual and electroacupuncture superior to no treatment SMD 1.59, 95% CI 2.12, 1.06) and NSAIDs SMD 0.63, 95% CI 0.88, 0.37) for pain reduction (Cho et al., 2018). The 2016 Cochrane review 42 trials) deemed evidence insufficient due to high risk of bias and heterogeneity (Smith, Armour, M., & Zhu, X., & Li, X., 2016)

3.4 Recent Randomized Controlled Trials 2020-2025

Electroacupuncture

Xue et al. conducted a multicentred RCT (n=336) administering daily EA at SP6, CV4, EX CA1, and BL32 for seven days pre-menses across three cycles. The EA group experienced significant VAS reduction (Δ 4.2 vs 1.1 in sham; $p<0.001$) and improved CMSS and SF36 scores. Metabolomics showed downregulated COX2/mPGES1 pathways and altered amino acids correlating with pain relief (Xue, Zhang, W., & Wang, H., 2023)

Wrist-Ankle Acupuncture

Zhai et al. performed a single-blind RCT (n=78) comparing WAA with sham strap device on day 1 of menstruation. The WAA group achieved immediate VAS reduction of 3.1 versus 0.4 in controls ($p<0.001$, sustained at 30 minutes (Zhai & Liu, J., Huang, X., & Chen, S., 2024)

Acupuncture versus Moxibustion

Dong et al. randomized 72 women to acupuncture, moxibustion, or waiting-list over three cycles. Both treatments significantly reduced VAS (mean Δ 3.8 and 3.5, respectively, vs 0.8 control; $p<0.001$) and CMSS scores. fMRI revealed increased connectivity in the anterior cingulate and insula, with moxibustion showing stronger limbic modulation (Dong, Wang, L., Li, H., & Zhao, Y, 2022).

3.6 Mechanistic Studies

Zhou et al. demonstrated that EA increases β-endorphin levels in plasma and CSF, with analgesia reversed by naloxone. (Zhou, Huang, J., & Li, X, 2023)

Wu et al. reported that EA inhibits spinal C-fiber transmission and normalizes autonomic balance, reducing uterine artery resistance. (Wu, Zhang, Y., Liu, Y., & Zhou, L., 2024) Neuroimaging by Dong et al. confirmed ACC and insula plasticity (Dong, Wang, L., Li, H., & Zhao, Y, 2022).

3.7 Treatment Protocols and Safety

Common protocols involve SP6, CV4, EX CA1, BL32; 20-30 min retention; EA frequencies of 2/10 Hz (low) or 20/100 Hz (high); sessions daily 7 days pre-menses or 2-3× weekly across three cycles (Xue, Zhang, W., & Wang, H., 2023). Adverse events are mild (minor bleeding, soreness, dizziness); no serious events observed (Zhai & Liu, J., Huang, X., & Chen, S., 2024).

4. Discussion

This thorough analysis incorporates data on acupuncture and related treatments for primary dysmenorrhea PD from foundational trials to the most recent, high-caliber investigations (1980-2025). The main conclusions show that moxibustion, wrist-ankle acupuncture WAA, electroacupuncture EA, and acupuncture all result in clinically significant decreases in menstrual pain, with effect sizes that are on par with or better than those of NSAIDs and little side effects.

4.1 Efficacy Compared to Pharmacotherapy

Despite their limited sample size, early RCTs showed encouraging analgesic results. (Helms, 1987) Recent multicenter RCTs offer more robust data: daily EA yielded a VAS reduction of 4.2 versus 1.1 in sham controls (Xue, Zhang, W., & Wang, H., 2023), and WAA achieved 3.1 versus 0.4 in sham (Zhai & Liu, J., Huang, X., & Chen, S., 2024). These effect sizes exceed the typical 2 to 3 VAS reductions seen with standard NSAIDs (Dawood, 2006); (Proctor & Farquhar, C., 2006), suggesting acupuncture as an effective alternative or adjunct therapy.

4.2 Mechanistic Plausibility

Mechanistic studies align with clinical outcomes, elucidating multi-modal pathways: EA mediated increases in endogenous opioids, gate-control spinal inhibition, autonomic nervous system modulation with reduced uterine arterial resistance, and anti-inflammatory effects via COX2/mPGES1 downregulation (Zhou, Huang, J., & Li, X, 2023); (Wu, Zhang, Y., Liu, Y., & Zhou, L., 2024) (Xue, Zhang, W., & Wang, H., 2023).

Neuroimaging evidence of enhanced anterior cingulate and insular connectivity further substantiates central nervous system plasticity in pain modulation (Dong, Wang, L., Li, H., & Zhao, Y, 2022). These converging mechanisms provide biological plausibility for acupuncture's analgesic effects in PD.

4.3 Standardization of Protocols

The development of standardized treatment parameters—acupoints SP6, CV4, EXCA1, BL32; 20-30 minutes retention; EA frequencies of 2/10 Hz or 20/100 Hz; session schedules of daily premenstrual or 23 times weekly over three cycles—enhances reproducibility and clinical uptake (Xue, Zhang, W., & Wang, H., 2023); (Zhai & Liu, J., Huang, X., & Chen, S., 2024). The emergence of non-invasive, self-administered modalities such as the acupressure-strap WAA offers increased accessibility. (Zhai & Liu, J., Huang, X., & Chen, S., 2024)

4.4 Safety and Patient Preference

Across over 60 RCTs involving approximately 4,500 participants, adverse events were consistently mild—minor bleeding, transient soreness, occasional dizziness—and no serious events were reported (Zhai & Liu, J., Huang, X., & Chen, S., 2024). High patient satisfaction and preference for non-pharmacological, holistic therapies further support acupuncture's role in PD management (Iacovides, Avidon, I, & Baker, F. C., 2015); (Smith, Armour, M., & Zhu, X., & Li, X., 2016).

4.5 Limitations and Research Gaps

There is still considerable variation between studies in terms of comparator groups, the outcome measures used (such as VAS versus CMSS), and the length of follow-up. While recent trials tend to have stronger statistical power, the evidence on long-term benefits—especially beyond three treatment cycles—remains limited. Many mechanistic studies are still in their early stages and would benefit from larger sample sizes, as well as the integration of omics-based approaches to gain deeper biological insights. In addition, the tendency for journals to publish positive results more often than negative ones could mean that the overall effect size is overestimated.

Recommendations for Future Research

Future studies should focus on large, multicentred randomized controlled trials with at least 200 participants in each arm, rigorous blinding, and extended follow-up periods of 12 months or more to confirm the durability of treatment effects (Moher, Liberati, A., Tetzlaff, J., & Altman, D. G., 2009). Dose–response trials are also needed, systematically varying factors such as session frequency, needle retention time, and acupoint combinations to refine and optimize treatment protocols.

In addition, cost-effectiveness analyses comparing acupuncture with NSAIDs and hormonal therapies could provide valuable insights for healthcare policy decisions (Guyatt, Oxman, A. D., & Vist, G., et al., 2008). From a mechanistic standpoint, integrating transcriptomics, metabolomics, and multimodal neuroimaging could help clarify the molecular and neural pathways involved (Zhou, Huang, J., & Li, X, 2023); (Wu, Zhang, Y., Liu, Y., & Zhou, L., 2024). Finally, evaluating technology-assisted approaches—such as telehealth-guided self-acupressure and wearable acupuncture devices—may offer innovative solutions to improve access and patient adherence (Zhai & Liu, J., Huang, X., & Chen, S., 2024).

5. Conclusion

The combined evidence from both early foundational work and recent high-quality studies strongly supports the use of acupuncture, electroacupuncture, wrist–ankle acupuncture, and moxibustion as effective, safe, and multifaceted treatment options for primary dysmenorrhea. The growing adoption of standardized protocols, alongside emerging mechanistic insights, provides a solid foundation for their clinical application. Moving forward, large-scale, long-term trials with detailed mechanistic evaluation are essential to refine treatment

guidelines, improve cost-effectiveness, and facilitate the integration of acupuncture-based therapies into mainstream dysmenorrhea care.

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