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Research methodology in acupuncture and moxibustion for managing primary dysmenorrhea: A scoping review

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ABSTRACT

Background: Acupuncture and moxibustion have promising effects in managing primary dysmenorrhea. However, some evidence from clinical trials remains controversial due to methodological flaws in study designs that involve acupuncture and its related modalities and require urgent attention and dialogue.

Methods: Allied and Complementary Medicine Database (AMED), Cochrane Library, Excerpta Medica database (EMBASE), PubMed, Web of Sciences, Chinese Biological Medicine (CBM), China National Knowledge Infrastructure (CNKI), VIP Database for Chinese Technical Periodicals (VIP), and Wanfang database were searched from their inception to July 2021. Data were extracted based on the types of study design, primary outcome measures, adverse events (AEs), and participants' subjective views.

Results: Most studies (n = 282, 93 %) were published in Chinese and 21 (7 %) in English. Among these, there were 209 (69 %) randomized controlled trials (RCTs), 39 (13 %) non-randomized controlled trials (nRCTs), 30 (10 %) case-series reports, 15 (5 %) cohort studies, and 10 (3 %) case reports. The most frequent reported outcome was pain, followed by emotion, sleeping quality, quality of life, skin temperature, changes in brain function, uterine and ovarian blood flow, and reproductive endocrine level. AEs were reported in 37 studies with mild events, and all recovered without actions taken; 31 trials reported no AEs; 235 failed to report any AEs. One RCT found that the satisfaction rate of the intervention group was statistically significantly higher than the control group.

Conclusion: Clinical studies on acupuncture and its related modalities face methodological challenges and require urgent attention. RCT with blinding and sham control might be the gold standard trial design. However, it may not be the most suitable research method for these modalities. We recommend using pragmatic RCTs in this field, where trial protocol registration on the trial registry platforms and detailed safety reporting should be mandatory.

1. Introduction

Primary dysmenorrhea (PD) is painful periods without pelvic pathology, characterized by recurrent, crampy, and lower abdominal pain during menstruation.[1] Evidence shows that prevalence rates of PD vary, ranging from 50 % to 90 %.[2] PD is the most common reason for gynaecological visits, where associated pain is mainly described as moderate to severe,[2] which greatly influences the quality of life and work productivity.[3] Nonsteroidal anti-inflammatory drugs (NSAIDs) are considered first-line treatment for PD[4,5]; however, the therapeutic superiority of any individual NSAID has not been demonstrated due to commonly reported side effects.[6] Therefore, there is a compelling need

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to find effective non-pharmacological options for PD management.

Acupuncture and moxibustion have been practised as complementary and alternative therapies in China for thousands of years. Previous studies[7–10] have confirmed the beneficial effects of acupuncture and moxibustion for relieving PD-related pain. Acupuncture analgesia has already been demonstrated in many pathways.[11,12] However, recent randomized controlled trials (RCTs) on acupuncture and moxibustion in managing PD have raised methodological issues, including selection bias, non-blinding and insufficient objective outcomes.[13–16] A belief has also emerged that acupuncture is equivalent to a placebo, which has even been named "mega-placebo".[17–19] Moreover, a previous study [20] has identified misunderstandings and misuse of the concept of "randomization" in acupuncture and its related modalities, and many researchers have misnamed their non-RCTs as RCTs.[21] Clinical trials and systematic reviews have shown a lower application rate of blinding, misuse of randomization, and nonstandard outcome reporting.[22,23] A study[24] found that published RCTs had high proportions of positive results, which may contribute to reporting bias. In addition, researchers have noted acupuncture related research methodology to be poor, lacking in medium and long-term follow-up and qualitative data, and adverse events (AEs) have also been poorly reported.[25]

This review aims to analyse and evaluate research methodologies used in existing literature using acupuncture and moxibustion to manage PD, therefore, providing insight into its methodological challenges and opportunities in this field.

2. Methods

Following the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) guideline and framework,[26] the review questions have been established as follows:

(a) What research designs were applied in studies using acupuncture and moxibustion to manage PD?
(b) What are the primary outcome measures in studies using acupuncture and moxibustion to manage PD?
(c) What is the evidence of AEs when using acupuncture and moxibustion to manage PD?
(d) What are participant attitudes, beliefs, and experiences when managing PD with acupuncture and moxibustion?

2.1. Eligibility criteria

We searched nine electronic databases, including English: Allied and Complementary Medicine Database (AMED), Cochrane Library, Excerpta Medica database (EMBASE), PubMed, and Web of Sciences, and Chinese: Chinese Biological Medicine (CBM), China National Knowledge Infrastructure (CNKI), VIP Database for Chinese Technical Periodicals (VIP), and Wanfang database. In addition, manual searching of the references in this paper was also included. To avoid reporting bias, Cochrane recommended the inclusion of trials in languages other than English[27]; also, most RCTs in acupunctured related studies are published in Chinese.[28] Therefore, the searches were in English and Chinese from the inception date of databases to July 2021. We contacted authors to identify additional information when data was missing or incomplete. The following were the PICOs of this review:

2.1.1. Participants

Women aged 18–40 with clinically diagnosed PD were included. PD is defined as painful periods in the absence of pelvic pathology, characterized by recurrent, crampy, lower abdominal pain during menstruation.[1] Animal studies and secondary dysmenorrhea were excluded.

2.1.2. Intervention (s)

All types of acupuncture (manual, electro, or laser) and or, moxibustion (direct, indirect, electronic, or laser) were included. Wrist-ankle needle, auricular acupuncture, scalp acupuncture, fire needle, acupoint catgut embedding, and acupoint injection were excluded.

2.1.3. Comparator

Studies with or without control groups were included.

2.1.4. Outcomes

All types of outcomes related to PD and their used validated measurement tools.

2.1.5. Study type (s)

Any types of original studies involving acupuncture and or moxibustion as an intervention were included.

2.2. Search strategy

The search strategy was adapted to different database demands. The keywords in the search include "针刺", "针灸", "电针", "穴位", "灸法", "艾灸", "电子灸", and "激光灸" in Chinese; and "acupuncture", "moxibustion", "moxa", "wormwood", "laser moxibustion", "needle", "acupoint", "dysmenorrhea", "primary dysmenorrhea", "painful period", and "menstrual pain" in English. For example, the searching strategy on PubMed is shown in (Table 1).

2.3. Study selection

EndNote x9 software was employed to manage and screen the literature. PRISMA flow chart was used to present the process of study selection (Fig. 2). After removing duplicates, two reviewers screened the titles and abstract independently and excluded irrelevant articles. Next, they further screened the literature by reading the full text according to the inclusion and exclusion criteria. The third reviewer participated in consultation throughout this process to resolve conflicts and discuss any uncertainties related to study inclusion.

2.4. Data management

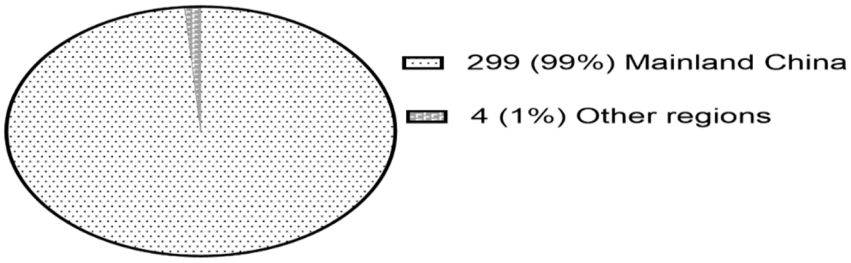
All data were entered into Excel spreadsheets (Microsoft Excel version 2019) by two entry personnel independently, after which the data manager cross-checked two data sets to ensure accuracy. This information of characteristics included author, publication year, country of publication, study design, interventions, primary outcome measures, and study related AEs. A narrative synthesis approach collated, summarized, and mapped the literature. Most data were descriptively analysed by calculating frequencies and percentages, where results were presented in tables, column charts, and pie charts using Microsoft Excel (version 2019). Qualitative data were presented descriptively.

Table 1
Searching strategy example.

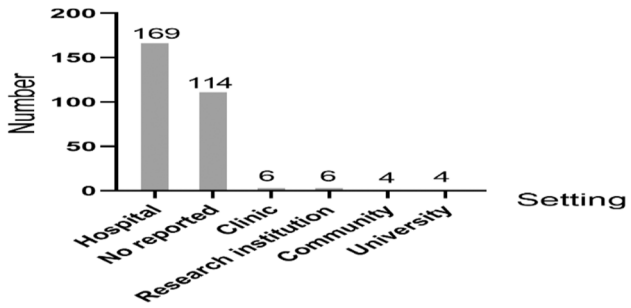
Items	Search Terms and Combinations
PubMed	
#1	("acupuncture" [Mesh]) OR ((needle [Title/Abstract]) OR (acupoint [Title/Abstract]))
#2	("Moxibustion" [Mesh] OR (((moxa [Title/Abstract] OR (wormwood [Title/Abstract])) OR (laser moxibustion [Title/Abstract]))
#3	#1 OR #2
#4	("dysmenorrhea" [Mesh]) OR (((((((primary dysmenorrhea [Title/Abstract]) OR (algomenorrhea [Title/Abstract])) OR (Painful period [Title/Abstract])) OR menstrual pain [Title/Abstract] OR (pain, menstrual [Title/Abstract])) OR (menstruation, painful [Title/Abstract] OR (painful menstruation [Title/Abstract]))
#5	#3 AND #4

3. Results

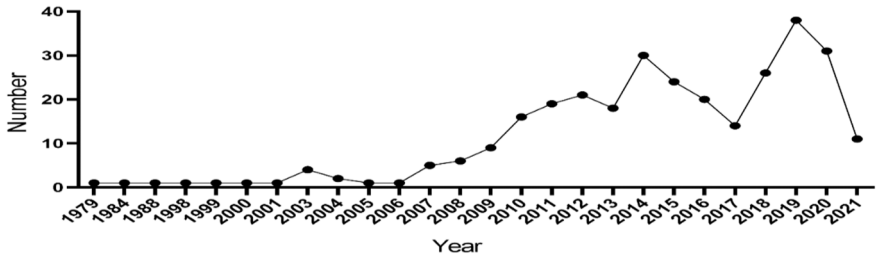
Across these searches, 10,619 records were retrieved. After de-duplication and screening titles and abstracts for relevance, 5728 and 1145 records remained, respectively. Screening by full-text, 303 articles met the inclusion criteria. A flowchart of this review process is shown in Fig. 2. The type of publications were journal articles (197, 65 %), thesis (100, 33 %), and conference papers (6, 2 %) in Chinese (282, 93 %) and English (21, 7 %). Most studies were conducted in Mainland China (299, 99 %). The rest of the studies originated from other regions, including



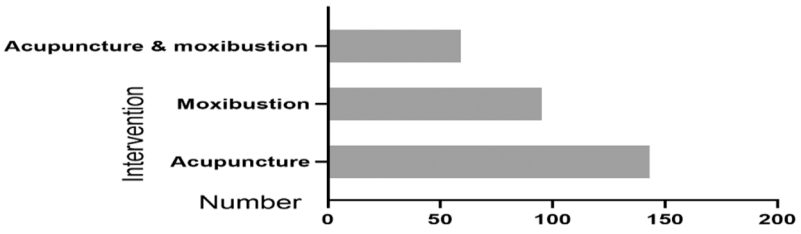
a) Location of included studies



b) Setting of included studies



c) Year of publications



d) Intervention of included studies

Fig. 1. Overview of the included studies: a) location of included studies: Mainland China and other regions; b) setting of included studies: hospitals, no reported, clinic, research institution (Scientist institute of traditional Chinese medicine, Research institutes of acupuncture and meridian, Laboratories), community, and university; c) year of publications: 1979–2021; d) intervention of included studies: acupuncture, moxibustion, and the combination of acupuncture and moxibustion.

Taiwan (n = 1), Iran (n = 1), and Thailand (n = 1) (Fig. 1a). The studies were published between 1979 and 2021. There was a significant hike from 2010, reaching the highest in 2019 (Fig. 1c). Most studies were conducted in hospitals (169, 56 %); followed by clinics (6, 2 %), research institutions (Scientist institute of traditional Chinese medicine, Research institutes of acupuncture and meridian, Laboratories) (6, 2 %), communities (4, 1 %), and universities (4, 1 %); more than 30 % studies (114, 38 %) did not specify the study setting (Fig. 1b). Interventions varied among acupuncture (145, 48 %), moxibustion (97, 32 %), and the combination of acupuncture and moxibustion (61, 20 %) (Fig. 1d).

3.1. Research design

There are two types of original studies: experimental studies and observational studies.[29] In the experimental study, 209 studies (69 %) were RCTs, while 39 (13 %) were nRCTs. Observational research were

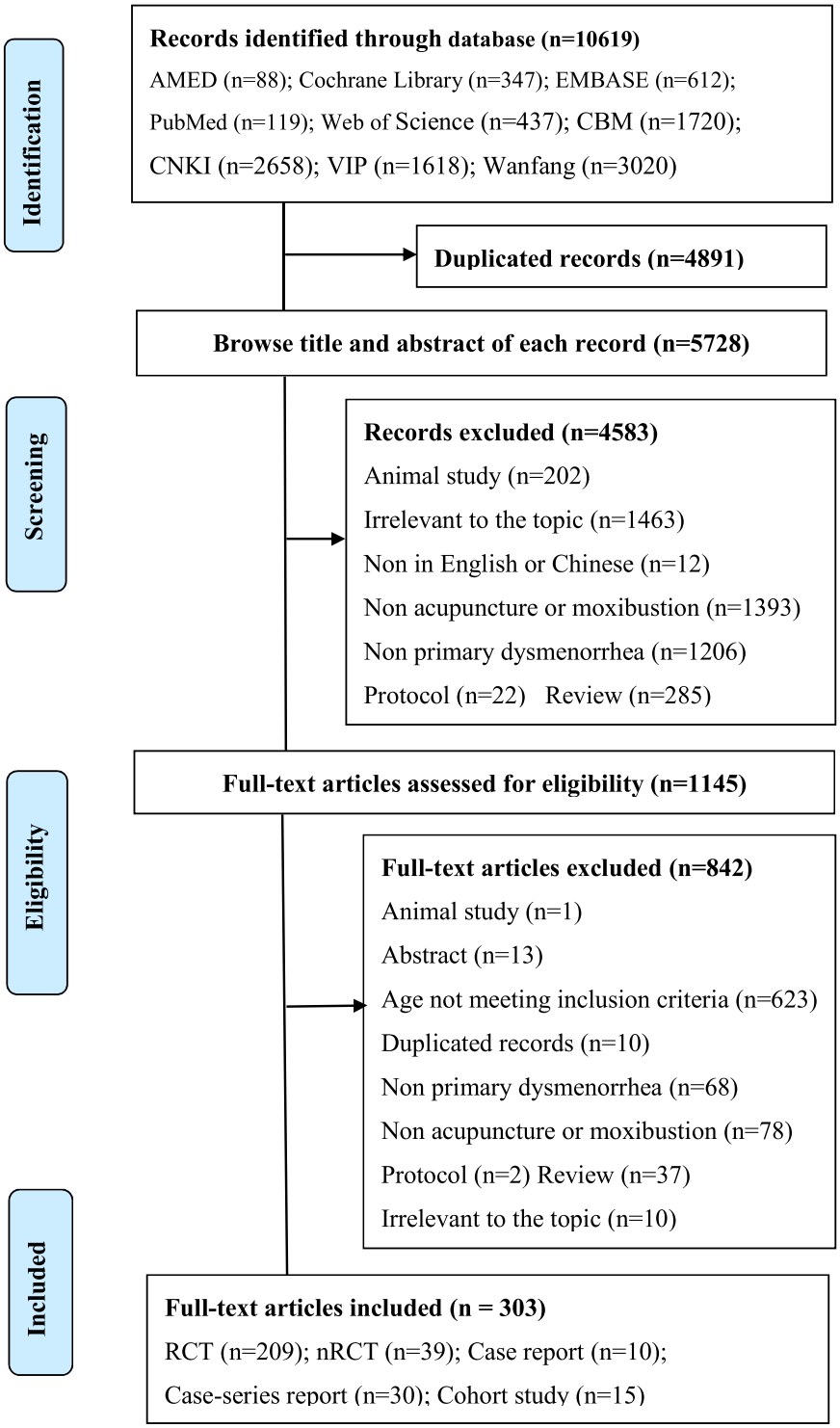


Fig. 2. Flow chart of the review process. Abbreviation: AMED: Allied and Complementary Medicine Database, EMBASE: Excerpta Medica database, CBM: Chinese Biological Medicine Database, CNKI: China National Knowledge Infrastructure, VIP: VIP Database for Chinese Technical Periodicals, Wangfang: Wangfang database; RCT: Randomized controlled trial, nRCT: non-randomized controlled trial.

case reports (10, 3 %), case-series reports (30, 10 %), and cohort studies (15, 5 %). The types of study design are shown in Fig. 3.

The interventions of RCTs included acupuncture (101, 48 %), moxibustion (61, 29 %), and the combination of acupuncture and moxibustion (47, 23 %). The control groups were no-treatment (22, 11 %), oral medications (66, 32 %), acupuncture and moxibustion (100, 47 %), sham acupuncture or moxibustion (16, 8 %), and others (5, 2 %). For the 16 (8 %) detailing sham acupuncture or moxibustion, there were 14 studies with sham acupuncture and two on sham moxibustion in the control groups, where sham acupuncture methods included real techniques on non-acupoint (9, 64 %), and sham techniques on real acupoints (5, 36 %). Meanwhile, sham moxibustion was operated on real acupoints, one of which used starch as a placebo-partitioned, and the other was a special sham moxibustion device, which stopped burning within three minutes.

3.2. Main outcome measures

Different instruments were applied in these studies to measure the efficacy of acupuncture and moxibustion for PD. The primary outcomes measured included pain, emotion, sleeping quality, quality of life, skin temperature, changes in brain function, uterine and ovarian blood flow, and reproductive endocrine level. There were five categories of approaches used, including 1) visual analogue scale (VAS), numeric rating scale (NRS), and verbal rating scale (VRS) for pain intensity assessment; 2) COX menstrual symptom scale (CMSS) and dysmenorrhea symptom score for symptom; 3) the total effective rate for efficiency index; 4) self-rating anxiety scale (SAS) and self-rating depression scale (SDS) for mental status; and 5) prostaglandin F2α (PGF2α), prostaglandin E2 (PGE2), and β-endorphin (β-EP) for lab test parameters and imaging data. As a pain evaluation scale, VAS was used in more than half of the studies (154, 51 %), and CMSS was identified 57 times. The total effective rate was also often used (159, 52 %), especially in case reports. Dysmenorrhea symptom score was reported 66 times, and fMRI examinations were reported 17 times. In addition, SAS and SDS were used 11 times, respectively. Thirteen (4 %) RCTs distinguished primary and secondary outcomes. The total effective rate was only used once for the primary outcomes, and then the others were pain-related indicators. Secondary outcomes included pain intensity, clinical symptoms, CMSS, syndrome score, sleep quality, lab test parameters, and so on. In addition, 17 studies calculated sample size using imaging indexes, total effective rate, abscission rate, CMSS, VAS, and treatment times as the basis. The measuring tools used more than ten times are shown in Fig. 4.

3.3. Adverse events (AEs)

AEs were mentioned in 68 (22 %) studies. Of those, 31 studies reported acupuncture and moxibustion as being safe with no AEs during the trials, whereas 37 reported mild AEs, including local and minor irritation, bleeding, hematoma, bruises, and blisters. These reactions were mild, where all participants recovered without any actions being taken, and they did not affect the participants or the trial. Disappointingly, 235 (78 %) studies failed to report any AEs (Table 2).

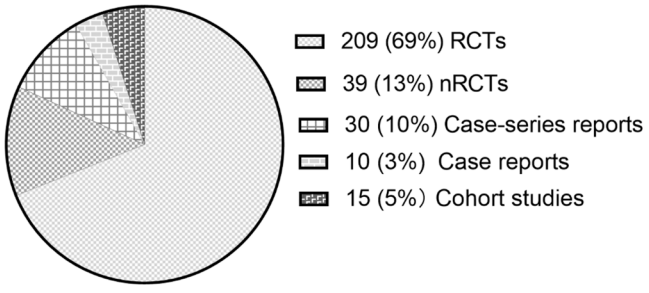


Fig. 3. Distribution of articles on original studies published between 1979 and 2021, by study design. Abbreviations: RCT: randomised controlled trial, nRCT: non-randomized controlled trial.

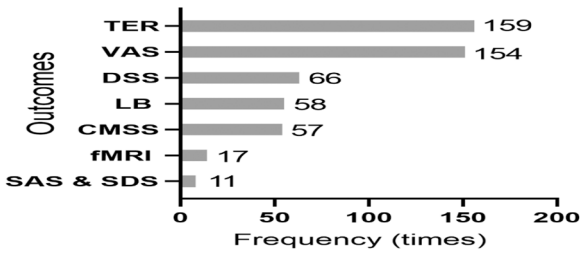


Fig. 4. Outcome measurement instruments and the usage frequency. Only those measuring tools used more than ten times are included in this figure. Abbreviations: TER: total effective rate; VAS: the visual analog scale; DSS: dysmenorrhea symptom scale; LB: lab test; CMSS: COX menstrual symptom scale; SAS: Self rating Anxiety Scale; SDS: Self rating Depression Scale.

3.4. Subjective data

This review aimed to investigate participant attitudes, beliefs, and experiences of participating in trials of using acupuncture and moxibustion to manage PD. However, we did not find enough available evidence. Only one RCT mentioned participant satisfaction rates after treatment.[30] This study found that the satisfaction rate of the intervention group with acupuncture and moxibustion was higher than that of the control group with oral ibuprofen (92.5 % and 62.5 %, respectively), and this difference was found to be statistically significant ($p < 0.05$).

4. Discussion

4.1. Methodological challenge in acupuncture related research

According to the essential concepts in the Clinical Research of Lancet,[29] the original research is divided into experimental and observational research. The clinical evidence of observational studies is lower than experimental studies because the former is subjected to information bias.[31] Observational studies consist of analytical (cohort study) and descriptive studies (case report and case-series report).[29] RCTs are the gold standard in clinical trials, reducing bias and improving the level of evidence, where this study type has been widely applied in the health field.[29,32,33] Therefore, it seems reasonable that RCTs accounted for a large proportion (69 %) in this review. A properly performed randomised trial is always superior and provides the highest quality data.[34] Any large, well-designed RCTs should evenly distribute known and unknown factors to minimise the potential for bias.[35]

Meanwhile, RCTs included in this review all presented positive results, affirming the efficacy of the intervention. Some researchers were concerned about the publication bias of the evidence due to the highly positive rate.[24] Determination of sample size is central to the design of RCTs;[36] only 17 (8 %) RCTs in this review reported the method of sample size calculation. Moreover, large scale RCTs were lacking, with only 38 (18 %) studies having a sample size of over 100, where 171 (82 %) studies were less than 100, and some studies[37–39] had only 12 participants.

Table 2
Adverse events related to interventions.

AEs	Number (n)	Percentage (%)
No reported	235	78 %
No adverse events	31	10 %
AEs including irritation, bleeding, hematoma, bruises, and blisters	37	12 %

Abbreviations: AEs: adverse events.

The use of blinding in RCTs is regarded as one of the key standards for evaluating the quality of trials. A study has shown that trials exaggerate the therapeutic effect by about 15 % without double-blinding compared with trials with double-blinding.[40] However, we did not find any RCTs with double-blinding in this review because the method is not often possible in this field. Randomization is the premise of RCT, whereas there was a misunderstanding and misuse of the concept of "randomization" in acupuncture related modalities trials.[20] Some authors were vague about randomization or simply noted "randomization"; however, they did not use this method in their trials. Methodological studies have shown that failure to conduct appropriate randomized concealment trials may exaggerate efficacy by 30~50 %.[41]

Only 13 (6 %) RCTs divided the outcomes into primary and secondary outcomes. The most frequent tool used to measure the primary outcome was the total effective rate, which scored the symptoms of dysmenorrhea according to *the clinical guiding principles of new traditional Chinese medicine*,[42] and then divided them into "cure", "remarkable effect", "improvement", and "failure", where the total effective rate was the proportion of the sum of the first three. However, this principle was formulated based on the model of new Chinese herbal, which cannot exactly reflect the efficacy of acupuncture and moxibustion intervention. Researchers[43–45] have found that the principle of outcome selection should focus on the purpose of the study and the disease, and then consider the characteristics and advantages of the interventions to help researchers to solve the main and valuable clinical questions. In addition, this process was conducted by *The Ministry of The Health of China* in 1993, which is outdated and has not been internationally recognized.

Few AEs (68, 22 %) in this review were reported, with 37 studies reporting irritation, bleeding, hematoma, bruises, and blisters, where all of these were mild and recovered with no actions taken; 31 with no AEs; and another 235 trials failing to report any AEs. There were apparent flaws in these data. Some studies did not report AEs, and some studies did not specify the type of AEs, although the authors have reported them, while some studies did not explain the causes of AEs. A recent study found that the incompleteness and inconsistency of AEs reporting in primary studies hampered the drawing of firm conclusions on acupuncture safety.[46] This is in line with the shortcoming identified for reporting of AEs in previous acupuncture RCTs.[47]

Studies[48,49] reported that the evaluation of efficacy and safety is based on personal feelings and experiences, especially in acupuncture and its related modalities with emphasis on syndrome differentiation and treatment. Only one study reported the satisfaction rate of participants after treatment. This incomplete outcome data belongs to attrition bias, in accordance with the questions in the previous paragraph about AEs.

Researchers[50–52] have claimed no statistically significant difference between acupuncture treatment and placebo-controlled groups. Several factors cause methodological challenges in acupuncture related fields. Firstly, acupuncture related researchers excessively pursue to apply the concept of modern western medicine in explaining the mechanism of acupuncture and moxibustion, where some even wholly duplicate the scientific research methods of western medicine in acupuncture related research, resulting in many methodological problems. Secondly, there has been a misunderstanding of the theory of acupuncture. For example, some acupuncture related RCTs do not describe the specific acupuncture process, or mention acupoints and techniques. While they defined "De Qi" as a numb, radiating sensation, judging the effect of acupuncture.[51]

A total of 16 (8 %) RCT studies in this review used sham acupuncture as their control group, including stimulating the adjacent sham acupoint located near or just doing a minor stimulation on the acupoint without penetrating the skin. At present, there are three forms of sham acupuncture, including sham technique with sham acupoint, real technique with sham acupoint, and sham technique with real acupoint.[53] Researchers have found that sham acupuncture is not inert, whereas sham techniques can still activate pathways.[54–58] However, placebo treatments in clinical research must be inert. Therefore, sham acupuncture control is not recommended in clinical trials.[59]

4.2. Recommendations and conclusion

The modern clinical mode of simultaneous physical and psychological treatment is the commonly applied general trend,[60] as participant beliefs and experiences in acupuncture and moxibustion are also a part of the curative effect, where qualitative data from this aspect is currently missing and required. In conceptualising the acupuncture related method as a holistic modality, clinical trials in this field should maintain its unique nature and characteristics, applying an appropriate research methodology that is scientific and can complement trials focusing on laboratory examination and biochemical indexes.

Since sham control is a challenge in acupuncture and its related studies, we propose replacing sham-controlled studies with pragmatic trials to establish a new evaluation system aligned with acupuncture associated characteristics. We also recommend the registration of all RCTs on international trial registry platforms to promote transparency, reduce potential bias, and avoid unintended duplications. Future clinical trials should also focus on AEs reporting, an essential element in high-quality and well-designed studies, to prove the benefit of these modalities beyond a reasonable doubt.

In conclusion, this review has evaluated current research designs relevant to acupuncture and moxibustion for managing PD; discussed the limitations in study designs, intervention procedures, and outcome measures limiting the evidence on the therapeutic efficacy of these modalities.

Previous research focuses on the types of intervention but poorly reported the control group. In this review, we overcome this limitation by explaining the importance of the pragmatic trial using the characteristics of sham acupuncture. We have provided updated evidence of methodological limitations in the acupuncture and its related field, including selection bias, misuse of the concept of "randomization", and nonstandard outcome reporting, then working in all steps of the process from identifying research questions, selecting studies, charting data, collating, summarizing and reporting results in acupuncture and moxibustion for managing PD. Finally, this review provided updated evidence on the status of study methodological issues involving acupuncture and its related modalities. It aimed to draw more attention and stimulate further discussions and hopefully better solutions to address the discourse in this space. The findings can also offer insight and contribute to the improved study design, outcome measures, and safety reporting in future studies.

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Declaration of Competing Interest

The authors declared no potential conflicts of interest.

Data Availability

Data used to support the findings of this study are included within the article.

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References

1. Kho KA, Shields JK. Diagnosis and management of primary dysmenorrhea. *JAMA*. 2020;323(3):268–269. https://doi.org/10.1001/jama.2019.16921.
2. ACOG. Committee Opinion No. 760: dysmenorrhea and endometriosis in the adolescent. *Obstet Gynecol*. 2018;132(6):e249–e258. https://doi.org/10.1097/AOG.0000000000002978.
3. Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. *Hum Reprod Update*. 2015;21(6):762–778. https://doi.org/10.1093/humupd/dmv039. Epub 2015 Sep 7. PMID: 26346058.
4. Proctor M, Farquhar C. Diagnosis and management of dysmenorrhoea. *BMJ*. 2006;332(7550):1134–1138. https://doi.org/10.1136/bmj.332.7550.1134.
5. Ferries-Rowe E, Corey E, Archer JS. Primary dysmenorrhea: diagnosis and therapy. *Obstet Gynecol*. 2020;136(5):1047–1058. https://doi.org/10.1097/AOG.0000000000004096.
6. Marjoribanks J, Ayeleke RO, Farquhar C, Proctor M. Nonsteroidal anti-inflammatory drugs for dysmenorrhoea. *Cochrane Database Syst Rev*. 2015;2015(7), CD001751. https://doi.org/10.1002/14651858.CD001751.pub3.
7. Sriprasert I, Suerungruang S, Athilarp P, Matanasarawoot A, Teekachunhatean S. Efficacy of acupuncture versus combined oral contraceptive pill in treatment of moderate-to-severe dysmenorrhea: a randomized controlled trial. *Evid Based Complement Altern Med*. 2015;2015, 735690. https://doi.org/10.1155/2015/735690. Epub 2015 Aug 4. PMID: 26346199.
8. Yang M, Chen X, Bo L, et al. Moxibustion for pain relief in patients with primary dysmenorrhea: a randomized controlled trial. *PLoS One*. 2017;12(2), e0170952. https://doi.org/10.1371/journal.pone.0170952.
9. Gou CQ, Gao J, Wu CX, et al. Moxibustion for primary dysmenorrhea at different interventional times: a systematic review and meta-analysis. *Evid Based Complement Altern Med*. 2016;2016, 6706901. https://doi.org/10.1155/2016/6706901.
10. Cho SH, Hwang EW. Acupuncture for primary dysmenorrhea: a systematic review. *BJOG*. 2010;117(5):509–521. https://doi.org/10.1111/j.1471-0528.2010.02489.x. Epub 2010 Feb 17. PMID: 20184568.
11. Zhang X. Pain research in China. *Sci China Life Sci*. 2010;53(3):356–362. https://doi.org/10.1007/s11427-010-0065-9. Epub 2010 Apr 29. PMID: 20596931.
12. Qiao L, Guo M, Qian J, Xu B, Gu C, Yang Y. Research advances on acupuncture analgesia. *Am J Chin Med*. 2020;48(2):245–258. https://doi.org/10.1142/S0192415×20500135. Epub 2020 Mar 5. PMID: 32138535.
13. Zhang HR, Tu HY, Wang Y, et al. Effectiveness and safety of moxibustion robots on primary dysmenorrhea: a randomized controlled pilot trial. *Chin J Integr Med*. 2021;27(8):578–584. https://doi.org/10.1007/s11655-021-3287-8.
14. Liu LY, Li XJ, Wei W, et al. Moxibustion for patients with primary dysmenorrhea at different intervention time points: a randomized controlled trial. *J Pain Res*. 2020;13:2653–2662. https://doi.org/10.2147/JPR.S270698.
15. Zhao MY, Zhang P, Li J, et al. Influence of de qi on the immediate analgesic effect of SP6 acupuncture in patients with primary dysmenorrhea and cold and dampness stagnation: a multicentre randomised controlled trial. Acupuncture in medicine: journal of the British Medical Acupuncture. *Society*. 2017;35(5):332–338. https://doi.org/10.1136/acupmed-2016-011228.
16. Yang M, Chen X, Bo L, et al. Moxibustion for pain relief in patients with primary dysmenorrhea: a randomized controlled trial. *PLoS One*. 2017;12(2), e0170952. https://doi.org/10.1371/journal.pone.0170952.
17. McGeeney BE. Acupuncture is all placebo and here is why. *Headache*. 2015;55(3):465–469. https://doi.org/10.1111/head.12524. Epub 2015 Feb 6. PMID: 25660556.
18. Linde K, Niemann K, Schneider A, Meissner K. How large are the nonspecific effects of acupuncture? A meta-analysis of randomized controlled trials. *BMC Med*. 2010;8:75. https://doi.org/10.1186/1741-7015-8-75.
19. Solomon S. Acupuncture for headache. It's still all placebo. *Headache*. 2017;57(1):143–146. https://doi.org/10.1111/head.12975.
20. Liu J, Kjaergard LL, Gluud C. Misuse of randomization: a review of Chinese randomized trials of herbal medicines for chronic hepatitis B. *Am J Chin Med*. 2002;30(1):173–176. https://doi.org/10.1142/S0192415×0200017X.
21. Wu T, Li Y, Bian Z, Liu G, Moher D. Randomized trials published in some Chinese journals: how many are randomized? *Trials*. 2009 2;10:46. https://doi.org/10.1186/1745-6215-10-46.
22. Zhang D, Yin P, Freemantle N, Jordan R, Zhong N, Cheng KK. An assessment of the quality of randomised controlled trials conducted in China. *Trials*. 2008;9:22. https://doi.org/10.1186/1745-6215-9-22.
23. Jiang M, Yang J, Zhang C, et al. Clinical studies with traditional Chinese medicine in the past decade and future research and development. *Planta Med*. 2010;76(17):2048–2064. https://doi.org/10.1055/s-0030-1250456. Epub 2010 Oct 26. PMID: 20979016.
24. Vickers A, Goyal N, Harland R, Rees R. Do certain countries produce only positive results? A systematic review of controlled trials. *Control Clin Trials*. 1998;19(2):159–166. https://doi.org/10.1016/s0197-2456(97)00150-5.
25. Tang JL, Zhan SY, Ernst E. Review of randomised controlled trials of traditional Chinese medicine. *BMJ*. 1999;319(7203):160–161. https://doi.org/10.1136/bmj.319.7203.160.
26. Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. *Ann Intern Med*. 2018;169(7):467–473. https://doi.org/10.7326/M18-0850. Epub 2018 Sep 4. PMID: 30178033.
27. Furlan Andrea D, Malmivaara Antti, Chou Roger, et al. Updated method guideline for systematic reviews in the Cochrane back and neck group. *Spine (Philos Pa 1976)*. 2015;40(21):1660–1673. https://doi.org/10.1097/BRS.0000000000001061.
28. Wu XY, Tang JL, Mao C, Yuan JQ, Qin Y, Chung VC. Systematic reviews and meta-analyses of traditional chinese medicine must search chinese databases to reduce language bias. *Evid-Based Complement Altern Med: eCAM*. 2013;2013, 812179. https://doi.org/10.1155/2013/812179.
29. Schulz Kenneth F, Grimes David A. *HE LANCET Handbook of Essential Concepts in Clinical Research*. 2006.
30. Liu MP. Clinical study on external treatment of traditional Chinese medicine and acupuncture in the treatment of menstrual abdominal pain. *J Changsha Med Coll*. 2018.
31. MacMahon S, Collins R. Reliable assessment of the effects of treatment on mortality and major morbidity, II: observational studies. *Lancet*. 2001;357(9254):455–462. https://doi.org/10.1016/S0140-6736(00)04017-4.
32. Moher D, Schulz KF, Altman DG. The CONSORT statement: revised recommendations for improving the quality of reports of parallel-group randomised trials. *Lancet*. 2001;357(9263):1191–1194.
33. Altman DG, Schulz KF, Moher D, et al, CONSORT GROUP(Consolidated Standards of Reporting Trials). The revised CONSORT statement for reporting randomized trials: explanation and elaboration. *Ann Intern Med*. 2001;134(8):663–694. https://doi.org/10.7326/0003-4819-134-8-200104170-00012.
34. Emani VR, Goswami S, Nandanoor D, Emani SR, Reddy NK, Reddy R. Randomised controlled trials for COVID-19: evaluation of optimal randomisation methodologies-need for data validation of the completed trials and to improve ongoing and future randomised trial designs. *Int J Antimicrob Agents*. 2021;57(1), 106222. https://doi.org/10.1016/j.ijantimicag.2020.106222.
35. Frieden TR. Evidence for health decision making-beyond randomized, controlled trials. *New Engl J Med*. 2017;377:465–475. https://doi.org/10.1056/NEJMra1614394.
36. Clark T, Berger U, Mansmann U. Sample size determinations in original research protocols for randomised clinical trials submitted to UK research ethics committees: review. *BMJ*. 2013:346–f1135. https://doi.org/10.1136/bmj.f1135.
37. He M. Study on the mechanism of the effect of electroacupuncture on the functional connectivity of periaqueductal gray matter in patients with primary dysmenorrhea. *Chengdu Univ Tradit Chin Med*. 2016.
38. Luo Xiao. Central mechanism of instant analgesia effect of acupuncture to primary dysmenorrhea patients based on fMRI. *Chengdu Univ Tradit Chin Med*. 2015.
39. Wang YX. A rs-fMRI study on the central mechanism through acupuncture treatment in primary dysmenorrhea. *Chengdu Univ Tradit Chin Med*. 2016.
40. Jüni P, Altman DG, Egger M. Systematic reviews in health care: assessing the quality of controlled clinical trials. *BMJ*. 2001;323(7303):42–46. https://doi.org/10.1136/bmj.323.7303.42.
41. Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *JAMA*. 1995;273(5):408–412. https://doi.org/10.1001/jama.273.5.408.
42. Ministry of Health of the PRC. The clinical guiding principles of new traditional Chinese medicine;1993, pp. 263–266.
43. Clarke M, Williamson P. Core outcome sets and trial registries. *Trials*. 2015;16:216. https://doi.org/10.1186/s13063-015-0738-6.
44. Wuytack F, Smith V, Clarke M, Williamson P, Gargon E. Towards core outcome set (COS) development: a follow-up descriptive survey of outcomes in Cochrane reviews. *Syst Rev*. 2015;4:73. https://doi.org/10.1186/s13643-015-0060-0.
45. Chiarotto A, Terwee CB, Deyo RA, et al. A core outcome set for clinical trials on non-specific low back pain: study protocol for the development of a core domain set. *Trials*. 2014;15:511. https://doi.org/10.1186/1745-6215-15-511.
46. Bäumler Petra, Zhang Wenyue, Stübinger Theresa, Irnich Dominik. Acupuncture-related adverse events: systematic review and meta-analyses of prospective clinical studies. *BMJ Open*. 2021;11(9), e045961. https://doi.org/10.1136/bmjopen-2020-045961.
47. Capili B, Anastasi JK, Geiger JN. Adverse event reporting in acupuncture clinical trials focusing on pain. *Clin J Pain*. 2010;26:43–48. https://doi.org/10.1097/AJP.0b013e3181b2c985.
48. Cao HJ, Li X, Li XL, et al. Factors influencing participant compliance in acupuncture trials: an in-depth interview study. *PLoS One*. 2020;15(4), e0231780. https://doi.org/10.1371/journal.pone.0231780.
49. Fogarty S, Barnett R, Hay P. Safety and pregnancy massage: a qualitative thematic analysis. *Int J Ther Massage Bodyw*. 2020;13(1):4–12.
50. Xu M, Yan S, Yin X, et al. Acupuncture for chronic low back pain in long-term follow-up: a meta-analysis of 13 randomized controlled trials. *Am J Chin Med*. 2013;41(1):1–19. https://doi.org/10.1142/S0192415×13500018.
51. Diener HC, Kronfeld K, Boewing G, et al. Efficacy of acupuncture for the prophylaxis of migraine: a multicentre randomised controlled clinical trial. *Lancet Neurol*. 2006;5(4):310–316. https://doi.org/10.1016/S1474-4422(06)70382-9. Erratum in: Lancet Neurol. 2008 Jun;7(6):475. PMID: 16545747.
52. Scharf HP, Mansmann U, Streitberger K, et al. Acupuncture and knee osteoarthritis: a three-armed randomized trial. *Ann Intern Med*. 2006;145(1):12–20. https://doi.org/10.7326/0003-4819-145-1-200607040-00005.
53. Birch S, Alraek T, Kim KH, Lee MS. *Placebo-Controlled Trials in Acupuncture: Problems and Solutions*. Singapore: Springer; 2016. https://doi.org/10.1007/978-981-10-2290-6_4.
54. Asghar AU, Green G, Lythgoe MF, Lewith G, MacPherson H. Acupuncture needling sensation: the neural correlates of deqi using fMRI. *Brain Res*. 2010;1315:111–118. https://doi.org/10.1016/j.brainres.2009.12.019. Epub 2009 Dec 16. PMID: 20025853.
55. Dhond RP, Kettner N, Napadow V. Neuroimaging acupuncture effects in the human brain. *J Alter Complement Med*. 2007;13(6):603–616. https://doi.org/10.1089/acm.2007.7040.
56. Kawakita K, Shinbara H, Imai K, Fukuda F, Yano T, Kuriyama K. How do acupuncture and moxibustion act? - focusing on the progress in Japanese

acupuncture research. *J Pharmacol Sci.* 2006;100(5):443–459. https://doi.org/10.1254/jphs.crj06004x.
57. Lewith G, Barlow F, Eyles C, et al. The context and meaning of placebos for complementary medicine. *Forsch Komplementmed.* 2009;16(6):404–412. https://doi.org/10.1159/000259371. Epub 2009 Dec 4. PMID: 20090354.
58. MacPherson H, Green G, Nevado A, et al. Brain imaging of acupuncture: comparing superficial with deep needling. *Neurosci Lett.* 2008;434(1):144–149. https://doi.org/10.1016/j.neulet.2008.01.058. Epub 2008 Jan 31. PMID: 18294772.
59. Langevin HM, Wayne PM, Macpherson H, et al. Paradoxes in acupuncture research: strategies for moving forward. *Evid Based Complement Altern Med.* 2011;2011, 180805. https://doi.org/10.1155/2011/180805. Epub 2010 Oct 11. PMID: 20976074; PMCID: PMC2957136.
60. Enck P, Klosterhalfen S, Zipfel S. Acupuncture, psyche and the placebo response. *Auton Neurosci.* 2010;157(1–2):68–73. https://doi.org/10.1016/j.autneu.2010.03.005. Epub 2010 Apr 1. PMID: 20359961.