


Acupuncture for premature ejaculation: a systematic review and meta-analysis

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Abstract

Background: Although acupuncture is widely used to treat premature ejaculation (PE), its effectiveness remains highly controversial.

Aim: To evaluate the efficacy and safety of acupuncture on PE.

Methods: According to the relevant keywords, 11 major English and Chinese databases were searched for randomized controlled trials (RCTs) of acupuncture alone or in combination with other treatments for PE. The quality of evidence across studies was assessed by the GRADEpro tool.

Outcomes: Study outcome measures included the intravaginal ejaculation latency time (IELT), the Premature Ejaculation Diagnostic Tool (PEDT), the Chinese Index of Premature Ejaculation–5 (CIPE-5), treatment success rate, and adverse events.

Results: Seven trials were included in this review for a total of 603 participants. A low quality of evidence suggests that it is not possible to determine whether acupuncture, as compared with a selective serotonin reuptake inhibitor, has an advantage in improving the IELT (standardized mean difference [SMD], -1.75 ; 95% CI, -6.12 to 2.63 ; $P = .43$, $I^2 = 98\%$), PEDT scores (SMD, 0.32 ; 95% CI, -0.68 to 1.32 ; $P = .53$, $I^2 = 85\%$), and treatment success rate (risk ratio, 0.69 ; 95% CI, 0.41 – 1.14 ; $P = .15$). However, participants receiving acupuncture had a lower CIPE-5 (SMD, -1.06 ; 95% CI, -1.68 to -0.44 ; $P < .01$). As compared with sham acupuncture, acupuncture significantly improved the IELT (SMD, 1.47 ; 95% CI, 1.01 – 1.92 ; $P < .01$, $I^2 = 0\%$) and PEDT scores (SMD, -1.23 ; 95% CI, -1.78 to -0.67 ; $P < .01$, $I^2 = 37\%$). When compared with other treatments alone, a combined treatment with acupuncture can significantly improve the IELT (SMD, 7.06 ; 95% CI, 2.53 – 11.59 ; $P < .01$, $I^2 = 97\%$), CIPE-5 (SMD, 0.84 ; 95% CI, 0.45 – 1.22 ; $P < .01$, $I^2 = 0\%$), and treatment success rate (SMD, 1.60 ; 95% CI, 1.18 – 2.16 ; $P < .01$, $I^2 = 53\%$).

Clinical Implications: The results suggest a significant effect of acupuncture in the treatment of certain important indicators of PE; however, this finding needs to be treated with caution because of the quality of the RCTs included.

Strengths and Limitations: Comprehensive inclusion of available RCTs has been performed. However, limitations include a low number of studies and a lack of detailed information to allow subgroup analysis.

Conclusion: The present systematic review and meta-analysis show that acupuncture has a significant effect on several subjective PE parameters, such as improving the feeling of control over ejaculation and distress, particularly when used in an integrated way. However, due to the low quality of evidence, acupuncture still needs larger well-designed RCTs to be confirmed.

Keywords: PE; acupuncture; systematic review and meta-analysis.

Introduction

According to the definition of the International Society for Sexual Medicine,¹ premature ejaculation (PE) is a male sexual dysfunction characterized by the following: (1) ejaculation that always or nearly always occurs before or within about 1 minute of vaginal penetration (lifelong PE) or a clinically significant and bothersome reduction in latency time, often < 3 minutes (acquired PE); (2) the inability to delay ejaculation in all or nearly all vaginal penetrations; and (3) negative personal consequences, such as distress, bother, frustration, and/or the avoidance of sexual intimacy. PE is a common sexual dysfunction in men, although its exact prevalence is difficult to assess: indeed, PE is a dysfunction that occurs only in the context of a couple and only when it is perceived as a source of distress.² When perceived as a sexual dysfunction, PE can seriously affect men's physical and mental health,^{3,4} as well as the couple's stability.² Several treatments have been

considered for the management of PE.⁵ Dapoxetine, a short-acting selective serotonin reuptake inhibitor (SSRI) derived from fluoxetine,^{6,7} is the gold standard of medical treatment for lifelong and acquired PE.^{5,8–10} In cases of acquired PE, treatment of the underlying contributing factor, when identifiable, is the priority (eg, by treating thyrotoxicosis or prostate inflammation).^{10–13} Local anesthetics have also been considered a possible alternative for lifelong PE.^{14,15}

Although such medications have proven effective to a large extent, several factors contribute to their limited success in clinical practice, such as their side effects, high sale price, and limited support given to manage patients' expectations.^{16–19} In a meta-analysis, treatments based on traditional Chinese medicine (TCM) theory were shown to be effective in improving PE.²⁰ Acupuncture is an important treatment method based on the theory of TCM and is applied in the treatment of many diseases.^{21–25} It was proven effective in basic and

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clinical studies^{21,22,26-28} and is widely used in the treatment of PE.²⁹⁻³¹ Based on TCM theory, acupuncture can extend ejaculation latency by regulating the balance of qi and blood. Moreover, studies have shown that acupuncture on acupoints Tianshu (ST25), Zusanli (ST36), and Taichong (LR3) can adjust neurotransmitter 5-hydroxytryptamine levels and reduce nerve sensitivity,³² a mechanism that can also be implicated for PE. However, since most clinical trials investigating acupuncture in the treatment of PE are based on small samples with a relatively low quality level of evidence, we aimed to meta-analyze published evidence to answer the following question: is it effective and safe to treat PE with acupuncture?

Methods

Inclusion and exclusion criteria

This study was conducted according to the PRISMA statement (Preferred Reporting Items for Systematic Reviews and Meta-analyses). Randomized controlled trials (RCTs) dealing with acupuncture were included in the treatment of PE, either alone or as a cotreatment. If the trial had been designed for crossover, only the precrossover data were used. Patients were men aged ≥ 18 years meeting the diagnostic criteria for PE,^{1,4,33,34} whether lifelong or acquired, excluding those who had PE from other known causes, such as prostatitis or mental illness, and those who were taking medication that may cause PE. Patients comorbid with other sexual dysfunctions were excluded to assess the efficacy of acupuncture specific for PE. Indeed, with PE being frequently comorbid with other sexual dysfunctions, especially erection (a clinical scenario better described as “loss of control of erection and ejaculation”),² it is not rare to “cure” PE by treating its comorbid disorder. However, this was not the scope of our meta-analysis, which instead focused on PE. Various forms of acupoint stimulation, such as acupuncture, electroacupuncture, and acupoint massage, with or without other drugs or therapeutic interventions, were included as long as the RCT protocol was based on direct stimulation of specific acupoints and met the following criteria:

- Acupuncture vs no treatment/Western medicine
- Acupuncture combined with another treatment vs the same other treatment

Considering the uncertain effect of acupoint injection, pharmacopuncture, embedding catgut, and bee needles were excluded.

Main outcomes

IELT: intravaginal ejaculation latency time³⁵

PEDT: Premature Ejaculation Diagnostic Tool³⁶

CIPE-5: Chinese Index of Premature Ejaculation-5³⁷

Secondary outcomes

Treatment success rate: defined as the percentage of effective cases in the total number of cases in the group; among them, *efficacy* refers to an IELT increase of at least 1 minute following treatment.

Adverse events: any adverse events related to drug use and acupuncture treatment, such as dizziness, nausea, local pain, bleeding at the acupuncture site, and visceral trauma.

Search strategy

Five English databases (PubMed, Scopus, Embase, Web of Science, Cochrane Central of Controlled Trials), 4 Chinese databases (National Knowledge Infrastructure, China Science and Technology Journal database, Wanfang Data, Sinomed), and 2 trial registration platforms (ClinicalTrials.gov, and Chinese Clinical Trial Registry) were systematically researched. In addition, related journals and conference abstracts were searched through research references and references from previous reviews. The end time was April 22, 2022, with no limit on the start time. A combination of subject headings and free words was used for retrieval. The search strategies are shown in Supplement 1.

Trial selection and data extraction

Two authors (H.Z. and E.C.) independently chose trials to be included in this review according to inclusion and exclusion criteria. Any disagreement was resolved through discussion or at the judgment of a final third-party reviewer (E.A.J.). The data were organized in a standardized table by author, publication year, country, trial design, age range of participants, sample size, experimental intervention, acupuncture points, control intervention, and outcome measures.

Assessment of risk of bias

Similarly, 2 independent reviewers (H.Z. and E.C.) assessed the risk of bias in each trial according to the criteria of the *Cochrane Handbook for Systematic Reviews of Interventions*.³⁸ Any disagreement was resolved through discussion between the reviewers and a third reviewer (E.A.J.), if necessary. For each trial, the evaluation criteria included 7 aspects: adequacy of generation of the allocation sequence, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data or not, whether selected reporting the results, and other possible biases (eg, imbalance of the baseline information). Each reviewer determined whether the corresponding entry was high risk, low risk, or unclear based on the characteristics of each trial. Trials were considered to have a low risk of bias when all items met the criteria and a high risk of bias when ≥ 2 items were deemed high risk.

Data synthesis

Studies with the same interventions were meta-analyzed. If the data were expressed as a continuous variable, the standardized mean difference (SMD) and 95% CI were calculated by using the score after treatment minus the score before treatment. If the result consisted of dichotomous data, the risk ratio and 95% CI were calculated. We pooled data with the random effects model.

If the changing mean and SD were not provided, the formula provided by the *Cochrane Handbook 5.1* for calculation was followed and is presented in Supplement 2. Groups of multiple doses were calculated according to the formula provided in Supplement 3. If all the data presented in the trial did not meet the criteria, the first author and/or the corresponding author was contacted by mail for original data. A specific trial was not included if original data could not be obtained. The statistical software R (version 4.1.3; R Core Team) was used for data analyses. The overall quality of trials was graded per the GRADE criteria (GRADEpro version 20; McMaster University).

Assessment of heterogeneity

To provide clinically significant conclusions, the I^2 statistic assessment was used to check whether the clinical and methodological characteristics of the trials were sufficiently similar. The heterogeneity among trial results was examined by overlapping confidence intervals. Poor overlap usually indicates statistical heterogeneity. The I^2 statistic is interpreted in the following way: 0% to 40%, low heterogeneity; 30% to 60%, moderate; 50% to 90%, substantial; 75% to 100%, considerable.³⁸

Heterogeneity was measured by examining individual trials and identifying subgroup characteristics.

Subgroup analysis

To explore possible sources of heterogeneity, a subgroup analysis related to the type of PE or region was performed.

Sensitivity analysis

Sensitivity analyses were performed on trials that satisfied double-blind sufficient hidden randomization to assess the stability of the results.

Assessment of reporting biases

If the number of trials was >10 , the potential publication bias was tested through a funnel plot.

The present systematic review and meta-analysis were registered with PROSPERO (CRD42022363469). Since the data collected in this study were drawn from previously published databases, approval from an institutional review board was not required.

Results

Trial selection

In total, 265 trials were retrieved, including 77 duplicated results. Overall 33 trials were excluded by keywords (rat model, novelty, meta-analysis, review, etc) and 127 by title and abstract. The remaining 28 trials were retrieved in full text. After a full-text search, 3 were excluded because of duplication,³⁹⁻⁴¹ 11 because they were non-RCTs,⁴²⁻⁵² 1 for inappropriate intervention,⁵³ 3 due to inappropriate comparisons,⁵⁴⁻⁵⁶ and 3 because there were no data available for analysis even after attempts to contact the authors.^{29,57,58} Therefore, 7 trials in total were included (Figure 1).^{30,59-64}

Description of trials

Seven RCTs were included in this study, involving 603 participants and all designed for parallel controls; sample sizes ranged from 60 to 120. The characteristics of the trials are shown in Table 1. With the exception of 1 study performed in Turkey and published in English,³⁰ all other trials were conducted in China⁵⁹⁻⁶⁴ and published in Chinese. Interventions involved acupuncture alone or in combination with Chinese herbal medicine, SSRIs, or other treatments. The controls included sham acupuncture, SSRIs, Chinese herbal medicine, and the other treatments. A summary of the acupuncture treatment plans is provided in Table 2. Participants in the trial received acupuncture for 4 weeks, 2 or 3 times per week in most cases, with a maximum of 25 times per month. The most commonly used acupoints were ST36 Zusanli, BL23 Shenshu, LR3 Taichong, and SP6 Sanyinjiao.

Assessment of risk of bias

Based on the research disclosures, 3 trials were at high risk of bias,^{59,61,64} and 4 were at low risk.^{30,60,62,63} Five trials that explicitly described the use of a random number table to generate a random sequence were rated as low risk.^{30,59-62} None of the trials reported a method for allocation concealment. Due to the unique nature of acupuncture, it is difficult to blind the actor and the subject simultaneously; while only 2 trials designed a sham acupuncture intervention,^{30,62} none mentioned blindness for evaluators. There were 5 trials in which participants dropped out, though the reports did not mention how the loss of participants was dealt with and these trials were rated as high risk.^{30,59,61,62,64} All 7 trials in this review lacked protocols; therefore, the selectivity bias reports were unclear. Other biases were mainly judged by the comparability of baseline data. Six trials reported comparability of baseline,^{30,59-63} stating that there were no statistical differences between groups at baseline, but no specific data were presented.⁶¹ In addition, trials that did not report baseline data but stated that they were comparable were assessed as high risk.⁶⁴ All bias risks in this review are shown in Figures 2 and 3.

Effects of interventions

We evaluated the impact of acupuncture on PE according to different comparison types (Table 2).

Acupuncture vs SSRIs

Five trials compared the effectiveness of acupuncture with SSRIs.^{30,59,61,62,64}

IELT.

Five trials compared the effects of acupuncture and SSRIs on IELT: 1 supported the superiority of acupuncture over SSRIs,⁶¹ and 4 supported the superior efficacy of SSRIs over acupuncture.^{30,59,62,64} However, the overall results showed that the treatment outcomes of acupuncture did not differ significantly from those of oral SSRIs (SMD, -1.75 ; 95% CI, -6.12 to 2.63 ; $P = .43$, $I^2 = 98\%$; 5 trial, 291 participants) (Figure 3).

PEDT.

Two trials compared the effects of acupuncture and SSRIs on the patient-reported outcomes obtained from the PEDT,^{30,62} reaching opposite conclusions, with 1 trial suggesting that acupuncture was equal to SSRIs in improving PEDT scores.⁶²

In contrast, another trial found that SSRIs were superior to acupuncture in improving patient-reported outcomes.³⁰ The overall results showed that the treatment outcomes of acupuncture did not differ significantly from those of oral SSRIs (SMD, 0.32 ; 95% CI, -0.68 to 1.32 ; $P = .53$, $I^2 = 85\%$; 2 trials, 124 participants) (Figure 3B).

CIPE-5.

One trial compared the effects of acupuncture and SSRIs on CIPE-5 scores,⁵⁹ showing that SSRIs had better therapeutic effect than acupuncture (SMD, -1.06 ; 95% CI, -1.68 to -0.44 ; $P < .01$; 1 trial, 46 participants) (Figure 3C).

Treatment success rate.

One trial comparing the effect of acupuncture and SSRIs on the treatment success rate showed no difference between the

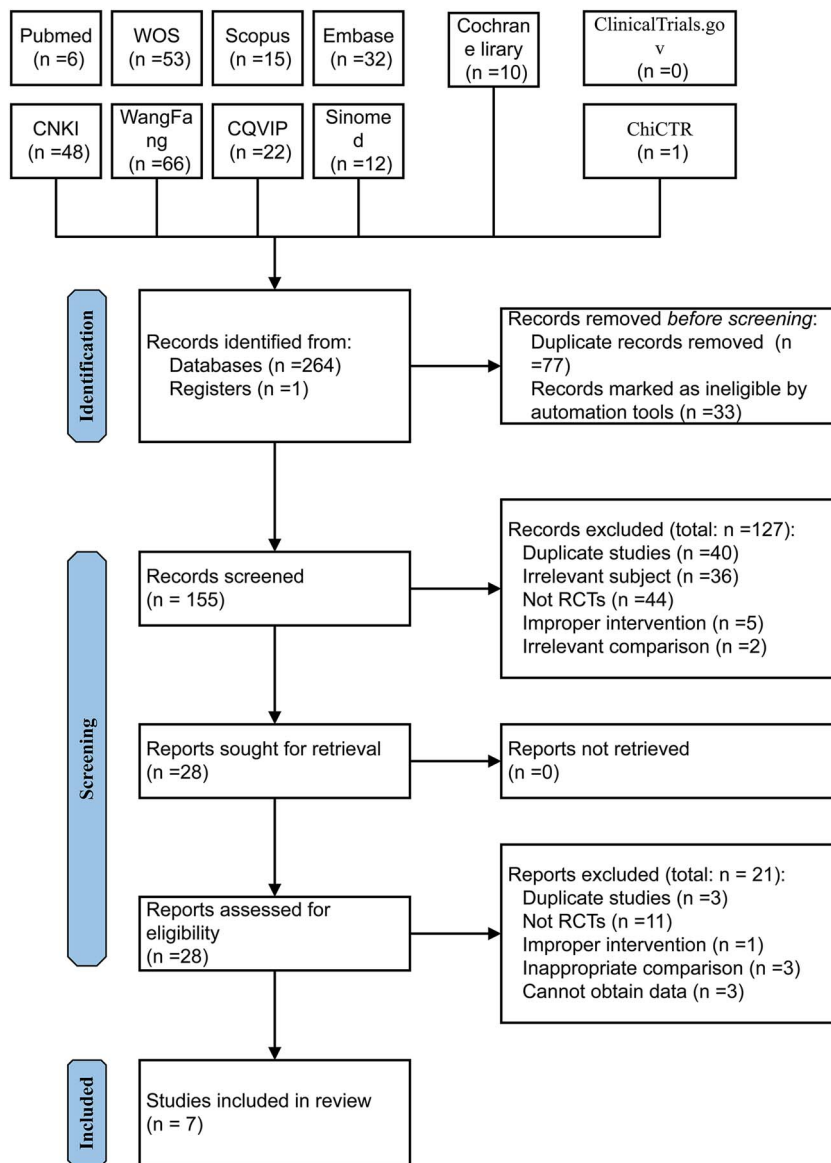


Figure 1. Study search. ChiCTR, Chinese clinical trial registry; CNKI, China National Knowledge Infrastructure; RCT, randomized controlled trial; VIP, Chinese science journal database; WOS, Web of Science.

acupuncture group and the SSRI group (risk ratio, 0.69; 95% CI, 0.41-1.14; $P = .15$; 1 trial, 46 participants) (Figure 3D).⁵⁹

Acupuncture vs sham acupuncture

Two trials compared the efficacy of acupuncture with that of sham acupuncture (acupoints next to conventional acupuncture points).^{30,62}

IELT.

These 2 trials compared the effects of acupuncture and sham acupuncture on IELT, and the results suggested that acupuncture treatment was superior to sham acupuncture (SMD, 1.47; 95% CI, 1.01-1.92; $P < .01$, $I^2 = 0\%$; 2 trials, 97 participants) (Figure 3E).

PEDT.

In addition to IELT, the 2 trials compared the effect of acupuncture and sham acupuncture on the PEDT scores of patients with PE, and the results suggested that acupuncture

was superior to sham acupuncture (SMD, -1.23 ; 95% CI, -1.78 to -0.67 ; $P < .01$, $I^2 = 37\%$; 2 trials, 97 participants) (Figure 3F).

Acupuncture plus other treatment vs the same other treatment

Four trials designed a comparison of acupuncture combined with other treatments vs the same other treatment.^{59-61,63}

IELT.

To investigate the difference in efficacy of acupuncture plus another treatment as compared with the same other treatment, Feng et al used sertraline hydrochloride and oral modified Jinkui Shenqi pills as the other treatment,⁶⁰ while Li et al used oral paroxetine⁵⁹ and Tang et al used oral Longdan Xiegan Tang.⁶¹ The result of each study supports that acupuncture combined with other treatments is better than other treatments alone (SMD, 7.06; 95% CI, 2.53-11.59; $P < .01$, $I^2 = 97\%$; 3 trials, 174 participants) (Figure 3G).

Table 1. Characteristics of the 7 trials^a

Study	Age, y, mean ± SD	Sample size	Treatment intervention	Acupoint	Control intervention	Outcome measures
Feng (2021) ^{60,b}	T: 33.41 ± 7.62 C: 32.03 ± 6.07	T: 34 C: 34	Warm acupuncture combined with Sertraline hydrochloride + Jiawei Jinkui Shenqi wan; warm acupuncture, 30 min each time, twice a week, 2 times as a course of treatment, 4 consecutive courses of treatment. Sertraline hydrochloride + Jiawei Jinkui Shenqi wan, same with C group.	ST36 Zusanli, BL23 Shenshu, BL20 Pishu, DU4 Mingmen, DU3 Yaoyangguan, SP6 Sanyinjiao, SP9 Yinlingquan	C: Sertraline hydrochloride (50 mg/d, 4 wk) combined with Jiawei Jinkui Shenqi pill (2 times/d, 4 wk)	IELT, CIPE-5, partner's satisfaction assessment, AEs
He (1999) ⁶³	T: 28.73 ± 3.27 C: 27.69 ± 4.12	T: 51 C: 51	Acupuncture (1 time/d, 2 groups of acupoints are used alternately, 2.5 times/mo, 2 mo) combined with self-formula decoction (1 time/2 d, 2 mo)	(1) RN6 Qihai, RN3 Zhongji, RN4 Guanyuan, SP6 Sanyinjiao, SP4 Gongsun, LR3 Taichong, LR2 Xingjian, KI3 Taixi, KI1 Yongquan, PC6 Neiguan, HT7 Shenmen, EX EM12 Annmian, DU20 Baihui. (2) BL23 Shenshu, DU4 Mingmen, SP6 Sanyinjiao, SP4 Gongsun, LR3 Taichong, LR2 Xingjian, KI3 Taixi, KI1 Yongquan, PC6 Neiguan, HT7 Shenmen, DU20 Baihui, EX EM12 Annmian	C: Self-formula decoction (1 time/2 d, 2 mo)	Treatment success rate
Li (2015) ⁵⁹	T: 27.98 ± 4.35 C1: 28.04 ± 4.56 C2: 23 ± 4.23	T: 23 C1: 23 C2: 23	Midfrequency EPAS, 4 min/acupoint/time, 3 times/wk, 8 wk.	BL23 Shenshu, RN6 Qihai, RN4 Guanyuan, SP6 Sanyinjiao, KI1 Yongquan	C1: Paroxetine, 20 mg/night, 8 wk. C2: Paroxetine plus EPAS, treatment combined with T and C1.	IELT, CIPE-5, treatment success rate, AEs
Sahin (2016) ^{30,c}	T: 32.90 ± 4.99 C1: 33.70 ± 6.97 C2: 33.20 ± 6.35 C3: 34.10 ± 6.48	T: 30 C1: 30 C2: 30 C3: 30	Acupuncture, 2 sessions/wk for a total of 8 sessions	BL30 Baihuanshu, BL52 Zhishi, ST36 Zusanli, LI4 Hegu, LR3 Taichong EX-HN3 Yintang, CV3 Zhongji	C1: Sham acupuncture. Punctures in the sham group were performed 1 cm to the left of each selected acupoint, with the same type of needles and with the same duration and frequency. The needles were not inserted as deep as the acupoints and did not penetrate the skin, and the sensation was a mere pricking rather than de qi. C2: Dapoxetine, 30 mg. Dapoxetine group was instructed to take the medication 1–3 h before engaging in sexual intercourse. C3: Dapoxetine, 60 mg. Usage is same with C2.	IELT, PEDT, AEs
Tang (2016) ⁶¹	NA	T: 30 C1: 30 C2: 30 C3: 30	Traditional acupuncture, 30 min/time, 5 time/wk, 4 wk	RN4 Guanyuan, RN3 Zhongji, LR2 Xingjian, GB43 Xiaxi, SP6 Sanyinjiao, BL18 Ganshu, BL32 Ciliao, BL28 bladder Shu	C1: Sertraline hydrochloride tablets, 50 mg/night, 30 d. C2: Longdan Xiegan decoction, twice/d. C3: Longdan Xiegan decoction (twice/d) combined with acupuncture (30 min/time, 5 times/week, 4 wk)	IELT, partner's satisfaction assessment, satisfaction of self-assessment rate, AEs
Tao (2012) ⁶⁴	33.5	T: 33 C: 31	Integrated psychotherapy + behavior therapy combined with acupoint low-frequency electrical stimulation, 4 min/acupoint, once per day, 24 times	ST25 Tianshu, RN6 Qihai, RN4 Guanyuan, BL23 Shenshu, BL52 Zhishi, SP6 Sanyinjiao, LR3 Taichong and KI3 Taixi alternately, ST36 Zusanli, KI1 Yongquan	C: Integrated psychotherapy + behavior therapy combined with fluoxetine hydrochloride, 20 mg/d, 4 wk	IELT, partner's satisfaction assessment, satisfaction of self-assessment rate, AEs
Wang (2013) ^{62,d}	T: 33.05 ± 4.27 C1: 32.45 ± 4.26 C2: 32.4 ± 3.86	T: 20 C1: 20 C2: 20	Acupuncture, 3 times/wk, 4 wk	LR3 Taichong, KI3 Taixi, SP6 Sanyinjiao, RN4 Guanyuan, DU20 Baihui	C1: 10 or 20 mg of paroxetine was taken in the morning or before going to bed, according to the patient's tolerance. C2: Sham acupuncture. Use of the point next to the acupoint as a control.	IELT, PEDT, AEs

Abbreviations: AE, adverse event; C, control; CIPE-5, Chinese Index of Premature Ejaculation-5; EPAS, electrical pulse acupoint stimulation; IELT, intravaginal ejaculation latency time; PEDT, Premature Ejaculation Diagnostic Tool; T, treatment. ^aEach study was conducted in China unless noted otherwise. Type of premature ejaculation could be determined in only 2 studies, as indicated. ^bType of premature ejaculation: acquired and lifelong. ^cStudy was conducted in Turkey. ^dType of premature ejaculation: lifelong.

Table 2. Effect estimates of the 7 trials.

Outcome of subgroup title	Studies	Participants	Statistical method	Effect size	P value ^a	Study
Acupuncture vs SSRIs						
IELT	5	291	MD (IV, random, 95% CI)	-1.75 (-6.12, 2.63), $I^2 = 98\%$	<.01	Li (2015) ⁵⁹ ; Tang (2016) ⁶¹ ; Wang (2013) ⁶² ; Sahin (2016) ³⁰ ; Tao (2012) ⁶⁴
PEDT	2	184	MD (IV, random, 95% CI)	0.32 (-0.68, 1.32), $I^2 = 85\%$	<.01	Wang (2013) ⁶² ; Sahin (2016) ³⁰
CIPE-5	1	46	MD (IV, random, 95% CI)	-1.0563 (-1.6765, -0.4360), $I^2 = \text{NA}$	NA	Li (2015) ⁵⁹
Treatment success rate	1	27	RR (M-H, fixed, 95% CI)	0.6875 (0.4148, 1.1395), $I^2 = \text{NA}$	NA	Li (2015) ⁵⁹
Acupuncture vs sham acupuncture						
IELT	2	97	MD (IV, random, 95% CI)	1.4661 (1.0137, 1.9185), $I^2 = 0\%$.72	Wang (2013) ⁶² ; Sahin (2016) ³⁰
PEDT	2	97	MD (IV, random, 95% CI)	-1.2283 (-1.7846, -0.6721), $I^2 = 37\%$.21	Wang (2013) ⁶² ; Sahin (2016) ³⁰
Acupuncture + other treatment vs same other treatment						
IELT	3	174	MD (IV, random, 95% CI)	7.06 (2.53, 11.59), $I^2 = 97\%$	<.01	Feng (2021) ⁶⁰ ; Li (2015) ⁵⁹ ; Tang (2016) ⁶¹
CIPE-5	2	114	MD (IV, random, 95% CI)	0.8385 (0.4541, 1.2229), $I^2 = 0\%$.54	Feng (2021) ⁶⁰ ; Li (2015) ⁵⁹
Treatment success rate	2	128	RR (M-H, fixed, 95% CI)	1.5962 (1.1781, 2.1626), $I^2 = 52.5\%$.15	Li (2015) ⁵⁹ ; He (1999) ⁶³

Abbreviations: CIPE-5, Chinese Index of Premature Ejaculation-5; IELT, intravaginal ejaculation latency time; IV, inverse variance; MD, mean difference; M-H, Mantel-Haenszel; NA, not available; PEDT, Premature Ejaculation Diagnostic Tool; RR, risk ratio; SSRI, selective serotonin reuptake inhibitor. ^aHeterogeneity.

CIPE-5.

Two trials described the effect of acupuncture on CIPE-5 scores, with the results showing that acupuncture combined with other treatments was superior to administering other treatments alone in improving CIPE-5 scores (SMD, 0.84; 95% CI, 0.45-1.22; $P < .01$, $I^2 = 0\%$; 2 trials, 114 participants) (Figure 3H).^{59,61}

Treatment success rate.

Two trials compared the difference in treatment success rate between the methods.^{59,63} Among them, He investigated the difference in efficacy of treatment using acupuncture with syndrome-targeted TCM herbal decoction as compared with treatment with TCM herbal decoction alone.⁶³ The results showed that the treatment success rate of the combined treatment group was better than that of the TCM herbal treatment alone (SMD, 1.60; 95% CI, 1.18-2.16; $P < .01$, $I^2 = 53$; 2 trials, 148 participants) (Figure 3I).

Adverse events

Adverse events were reported in 6 of the trials in this review.^{30,59-62,64} One trial cited 14 (20.3%) adverse events after paroxetine use, including dizziness, insomnia, and abdominal pain.⁵⁹ Another trial indicated similar adverse events—nausea, dizziness, diarrhea, insomnia, and headache—but the author did not report the exact number.³⁰ Feng's trial had 1 case (1.5%, based on the number of participants using the sertraline and Chinese herbal medicine decoction) of temporary fatigue in the drug combination group.⁶⁰ Tang reported 27 (22.5%) cases of adverse events: 8 cases of dizziness and fatigue after sertraline use; 5 cases of dizziness and hematoma after acupuncture; 7 cases of

stomach discomfort and diarrhea in participants using the Chinese herbal medicine decoction; and 7 cases of hematoma, dizziness, and stomach discomfort in the combined treatment group.⁶¹ Tao reported 6 (8%) cases of adverse events in the sertraline hydrochloride group; among them, dizziness with drowsiness was observed in 4 cases, dizziness in 1 case, and drowsiness in 1 case. No relevant findings were found in the acupuncture group.⁶⁴ Wang noted 1 (1.7%) patient who had an adverse reaction of nausea due to paroxetine.⁶²

Subgroup analysis

Acupuncture is one of the theoretical systems of Chinese medicine; therefore, the treatment of acupuncture should adopt different treatment strategies according to the type of TCM syndrome, which is the specific pattern of the disease. Indeed, in TCM, apparently different diseases (according to modern diagnostics) can share a common pattern (ie, syndrome) and be treated with the same formula,⁶⁵ while the same disease can be the expression of different syndromes and therefore be treated differently. Common syndromes related to PE are “damp invasion of lower energizer,” “fire excess from yin deficiency,” and “insufficiency of both spleen and kidney.”⁶⁶ This is a reason why the use and evaluation of disease-specific targets are not a reasonable approach to evaluate TCM's efficacy, which is rather based on the individual syndrome. Because of this, a subgroup analysis by type of PE and TCM syndrome was attempted. Most of the trials, though, did not report whether the patients in the trials had lifelong PE, acquired PE, or a TCM syndrome; hence, it was impossible to complete such an analysis. In addition, the cultural variability of the different regions in which the studies were conducted was taken into account, considering that these might be fundamental factors to consider. Therefore,

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Feng 2021	+	?	-	?	+	?	+
He 1999	?	?	-	?	+	?	+
Li 2015	+	?	-	?	-	?	+
Sahin 2016	+	?	+	?	-	?	+
Tang 2020	+	?	-	?	-	?	+
Tao 2012	?	?	-	?	-	?	-
Wang 2013	+	?	+	?	-	?	+

Figure 2. Risk of bias.

the studies were grouped by region in the acupuncture vs SSRI group. The results of the subgroup analysis showed that, while studies in China suggest that the effects of taking SSRIs are similar to those of acupuncture treatment, the study in Turkey shows that taking SSRIs is significantly better than acupuncture treatment in improving IELT (Analysis 1, Supplement 4). Unfortunately, due to the lack of relevant data, a detailed subgroup analysis could not be made.

Sensitivity analysis

A sensitivity analysis was attempted for the primary outcomes of the IELT, PEDT, and CIPE-5. However, because of the insufficient number of studies, we performed a sensitivity analysis of the IELT results only. This analysis was performed by one-by-one elimination, and the pooled data results obtained were similar to the original results, indicating that the pooled data results were robust (Analyses 2-4, Supplement 4).

Publication bias

A publication bias analysis was conducted on the trials, but the number of trials was insufficient to support the analysis.

Overall quality of evidence by GRADE

The overall quality of trials was evaluated by GRADE criteria. The quality of outcomes was mainly low or very low due to the deficiencies of the trials in blindness, allocation concealment, and heterogeneity (Table 3).

Discussion

Main findings

This review included 603 participants from 7 trials, most of which were conducted in China. Based on the available evidence from these collected studies, the effects of acupuncture were investigated in 3 comparisons: acupuncture vs SSRIs, acupuncture vs sham acupuncture, and combined other treatments with acupuncture vs the same other treatments without acupuncture.

According to the current evidence, acupuncture did not improve the IELT, PEDT, or treatment success rate as compared with SSRIs, and it was significantly inferior to SSRIs in improving the CIPE-5. From another perspective, acupuncture may be noninferior to SSRIs, and this may be a positive sign when considering the side effects associated with SSRIs. The beneficial effects of acupuncture were identified in the 2 other comparisons: first, acupuncture had an advantage in prolonging IELT and in improving PEDT scores when compared with sham acupuncture; second, acupuncture with other treatments over other treatments alone was beneficial in regard to all outcomes considered.

Interestingly, acupuncture was much more effective on the PEDT, a subjectively measured patient-reported outcome, than on the IELT, which is objectively measured with a stopwatch. PE is a tridimensional symptom where the timing appears less central with respect to the other 2 dimensions—specifically, the lack of control over ejaculation and the distress produced in the patient and in the partner.^{2,67} The evidence reviewed here shows that acupuncture is not inferior to SSRIs in improving the 2 subjective aspects of PE, although it is not as effective as SSRI in improving CIPE-5. Moreover, the few available data show that acupuncture is more efficient than sham in improving PE. The overall results, despite the exclusion of some unreliable indicators, must be viewed with extreme caution, being based on trials with some risk of bias and a relatively low quality of evidence.

It is important to note that 3 of the original trials also used “satisfaction” indicators (data not shown). First, they measured “partner’s satisfaction” with the 10th, 13th, and 14th items of the International Index of Erectile Function–15 (IIEF-15), asked directly to the patient’s partner.^{60,61,64,68} Two trials measured the effects of acupuncture directly on the patient’s self-reported satisfaction with the sixth, seventh, and eighth items of the IIEF-15.^{61,64,68} However, to our knowledge, no studies have validated the accuracy of the IIEF-15 in patients with PE and their partners; hence, the results of these indicators in the results were not reported because of substantial reliability concerns.

Another shortcoming of this study is represented by the noninclusion of a high-quality study by Sunay et al²⁹ that compared the effects of paroxetine, acupuncture, and a placebo on PEDT scores and IELT in patients with PE. In the study, acupuncture was inferior to paroxetine but significantly superior to placebo, similar to the results of our meta-analysis. Despite our attempts to meta-analyze this study, it could not be used as a source of data because only the mean, mean rank, and *P* values were provided in the text.

Implications for practice

Among the trials in this review, the main acupuncture points for treating PE were ST36 Zusanli, BL23 Shenshu, LR3 Taichong, and SP6 Sanyinjiao (Figure 4). In the theoretical

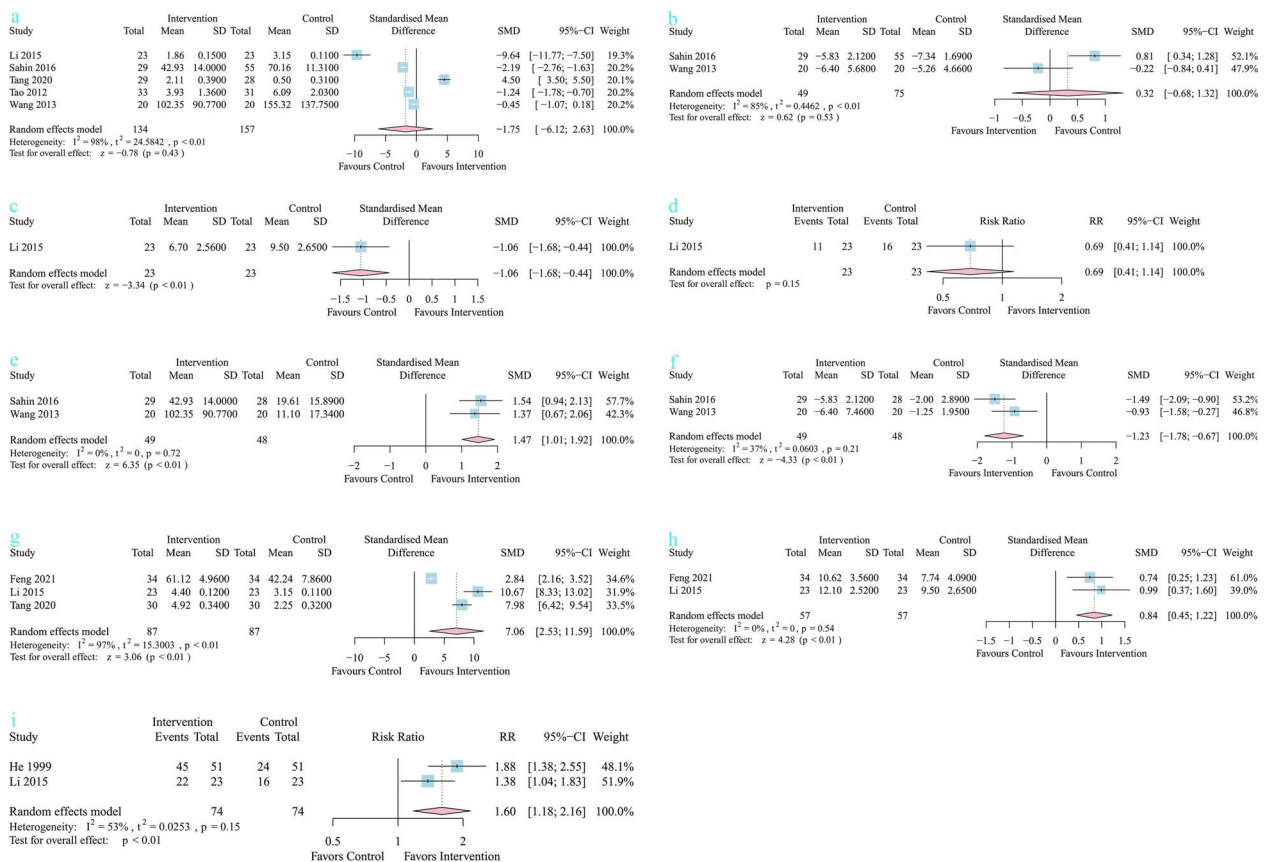


Figure 3. Forest plots comparing the effect of acupuncture vs SSRIs on (A) IELT, (B) PEDT, (C) CIPE-5, and (D) treatment success rate. Forest plots comparing the effect of acupuncture vs sham acupuncture on (E) IELT and (F) PEDT. Forest plots comparing the effect of acupuncture plus other treatment vs same other treatment on (G) IELT, (H) CIPE-5, and (I) treatment success rate. CIPE-5, Chinese Index of Premature Ejaculation-5; IELT, intravaginal ejaculation latency time; PEDT, Premature Ejaculation Diagnostic Tool; SMD, standardized mean difference; SSRI, selective serotonin reuptake inhibitor.

system of TCM, the causes of PE are complex, mainly concerning the heart, the liver, and the kidneys. In terms of TCM syndrome classification, PE can be related to numerous syndromes: damp invasion of lower energizer, fire excess from yin deficiency, nonconsolidation of kidney qi, deficiency of heart and spleen, depressed liver, and insufficiency of spleen and kidney, among others.⁶⁶ In TCM theory, the symptom is only a phenomenon of the disease, while the syndrome is the essence. Therefore, the same symptom and the same disease can be due to different syndromes, and depending on the syndrome, the same disease can even be treated in opposite ways. For example, in the treatment of PE, patients who have the damp invasion of lower energizer syndrome should be treated with the draining method, while patients who have the syndrome of deficiency of heart and spleen should be treated with the exact opposite method of tonification.⁶⁶ It should be noted that as the therapeutic effect of acupuncture greatly relies on the theory of TCM, the selection of acupoints should be chosen according to this theory. Of the 7 trials, only 2 were based on TCM theory regarding patients with PE who met the standard diagnosis.^{60,61} The rest of the trials did not differentiate types of PE in TCM. This aspect might be one of the reasons why heterogeneity is so prevalent among studies that investigate acupuncture, and it is worth the attention of acupuncture researchers.

It is likely that the greater attention given to the patient in the context of TCM, as compared with the simple

act of prescribing a drug treatment, might have some beneficial placebo effects. Indeed, an important part of PE treatment is the establishment of a good relationship, not only within the couple, but also between the doctor and the patient.^{5,19}

In juxtaposition to Western medicine, in China, the treatment is influenced by the patient-centered philosophy of Chinese medicine,⁶⁹⁻⁷¹ which may provide a unique path for the treatment of sexual function disorders.

Additionally, patients might be uncomfortable with being prescribed an SSRI (ie, a drug potentially affecting sexual function^{72,73}) resulting in a placebo effect.⁷⁴ This combination of factors can also affect the results of our meta-analysis and should be taken into consideration in clinical practice.

Implications for research

The quality of the data reviewed here suggests that robust conclusions on the effectiveness of acupuncture in PE cannot be drawn. This deficiency has several components, including the disunity of the evaluation system. Future research should use proven and validated tools to develop an acupuncture research proposal for PE, to support the consistency and interpretability of research results with strong evidence. The lack of long-term efficacy evaluation of PE is another shortcoming of the examined trials, which should be improved in future research.

Table 3. Overall quality by GRADE.

Outcomes	Participants (studies)	Quality of the evidence ^a	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with SSRIs	Risk difference with acupuncture (95% CI)
Acupuncture vs SSRIs					
IELT	291 (5)	⊕○○○ Very low ^{b-d} Due to risk of bias, inconsistency, indirectness, imprecision	NA		Mean IELT in the intervention group was 3.3 lower (5.57 to 1.02 lower).
PEDT	124 (2)	⊕○○○ Very low ^{b-d} Due to risk of bias, inconsistency, indirectness, imprecision	NA		Mean PEDT in the intervention group was 1.32 higher (0.46 to 2.18 higher)
CIPE-5	46 (1)	⊕○○○ Very low ^{b,d} Due to risk of bias, indirectness, imprecision	MD, -1.0563 (-1.6765, -0.4360)		Mean CIPE-5 in the intervention group was 2.8 lower (4.31 to 1.29 lower)
Treatment success rate	46 (1)	⊕○○○ Very low ^{b,d} Due to risk of bias, indirectness, imprecision	OR, 0.4 (0.12-1.34)	Study population: 696 per 1000 Moderate: 696 per 1000	218 fewer per 1000 (from 480 fewer to 58 more) 218 fewer per 1000 (from 480 fewer to 58 more)
Acupuncture vs sham acupuncture					
IELT	97 (2)	⊕⊕○○ Low ^{b,d} Due to risk of bias, indirectness	MD, 1.4661 (1.0137-1.9185)		Mean IELT in the intervention group was 25.74 higher (18.1 to 33.39 higher)
PEDT	97 (2)	⊕⊕○○ Low ^{b,d} Due to risk of bias, indirectness	MD, -1.2283 (-1.7846, -0.6721)		Mean PEDT in the intervention group was 4 lower (5.23 to 2.78 lower)
Acupuncture + other treatment vs same other treatment					
IELT	174 (3)	⊕○○○ Very low ^{b-d} Due to risk of bias, inconsistency, indirectness	NA		Mean IELT in the intervention group was 1.45 higher (1.39 to 1.51 higher)
CIPE-5	114 (2)	⊕⊕○○ Low ^{b,d} Due to risk of bias, indirectness	MD, 0.8385 (0.4541-1.2229)		Mean CIPE-5 in the intervention group was 2.71 higher (1.56 to 3.87 higher)
Treatment success rate	148 (2)	⊕⊕○○ Low ^{b,d} Due to risk of bias, indirectness	OR, 8.67 (3.45-21.81)	Study population: 541 per 1000 Moderate: 583 per 1000	370 more per 1000 (262 to 422 more) 341 more per 1000 (245 to 385 more)

Abbreviations: CIPE-5, Chinese Index of Premature Ejaculation-5; IELT, intravaginal ejaculation latency time; MD, mean difference; NA, not available; OR, odds ratio; PEDT, Premature Ejaculation Diagnostic Tool; SSRI, selective serotonin reuptake inhibitor. ^aGRADE Working Group grades of evidence. The basis for the assumed risk (eg, the median control group risk across studies) is provided in notes b-d. The corresponding risk (95% CI) is based on the assumed risk in the comparison group and the relative effect (95% CI) of the intervention. High quality: Further research is very unlikely to change our confidence in the estimate of effect. Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Very low quality: We are very uncertain about the estimate. ^bNone of the trials used adequate allocation concealment or blinding of participants or researchers. ^cDue to substantial heterogeneity, $I^2 > 75\%$. ^dRisk of bias unclear for some domains in most studies.

Finally, prospective registration on the clinical trial registry platform should be regarded as essential to improve the quality of trial design and transparent reporting.

Potential biases in the review process

Despite a comprehensive search strategy conducted by 2 reviewers simultaneously and without publication or language

restrictions, trials published in languages other than English and Chinese might have been missed.

The risk of publication bias might have been underestimated because <10 trials were included in this review, thus making it impossible to generate funnel plots. Subgroup analysis and sensitivity analysis were not conducted due to the lack of crucial information.

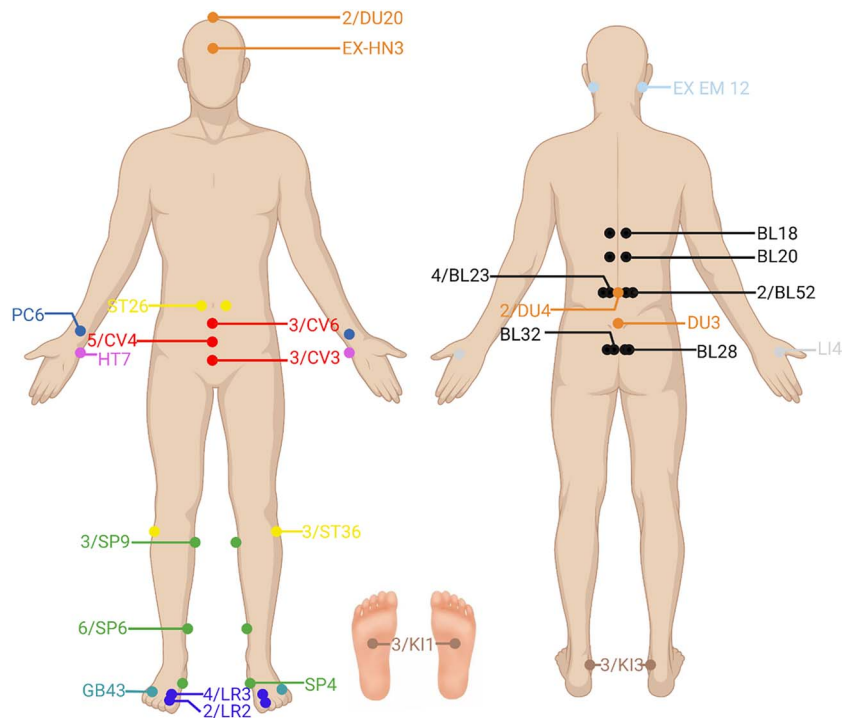


Figure 4. Main acupuncture points for treating premature ejaculation.

The authors of the missing trials were contacted to obtain these critical data, but none of the researchers responded, adding to the bias.

All of the trials except 1 were conducted on a Chinese population. As such, it should be noted that these findings may not be easily reproducible in a different population of patients, given the potential sociocultural impact of Chinese medicine within China as compared with other countries.

Conclusion

When compared with SSRIs, acupuncture did not provide an advantage in improving the IELT, PEDT, and treatment success rate, which means noninferiority effects. However, it was significantly inferior to SSRIs in improving the CIPE-5. As compared with sham acupuncture, the relatively low-quality evidence suggests that acupuncture has an advantage in improving IELT and PEDT scores. When compared with other treatments alone, combined treatment with acupuncture significantly improve the IELT, CIPE-5, and treatment success rate. To summarize, while positive results have been published, the promising effectiveness of acupuncture for PE needs to be fully demonstrated by larger, well-designed, registered trials due to the limited number of RCTs and lack of high-quality evidence.

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Supplementary material

Supplementary material is available at *Sexual Medicine* online.

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