

# Traditional Chinese acupuncture and postpartum depression: A systematic review and meta-analysis

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## Abstract

**Background:** Acupuncture, a key component of traditional Chinese medicine, is a form of alternative medicine in which thin needles are inserted into the body commonly for pain relief. To date, the role of traditional Chinese acupuncture in mood disorders in the postpartum period is unclear. Thus, this study aimed to review the effectiveness of acupuncture in patients with postpartum depression (PPD).

**Methods:** We searched databases such as PUBMED, EMBASE, and Cochrane Controlled Trials Register until September 2018. Meta-analysis was performed using Comprehensive Meta-Analysis 2.0 software. The mean difference (MD) and risk ratio (RR) with 95% confidence intervals (CI) were calculated to evaluate the results of each comparison.

**Results:** A total of 887 PPD patients from 12 randomised controlled trials were included in the quantitative meta-analysis, with 443 patients in the treatment group and 444 patients in the control group. Patients in the acupuncture group had significantly better performances assessed by the Hamilton Depression Scale than those in the control group, and the pooled MD was  $-1.27$  (95% CI:  $-2.55$  to  $0.01$ ;  $p = 0.05$ ,  $I^2 = 83\%$ ) in the random-effect model. In addition, significantly better performance in the effective rate was observed in the acupuncture group than in the control group, and the pooled RR was  $1.20$  (95% CI:  $1.09$  to  $1.33$ ;  $p < 0.0001$ ,  $I^2 = 46\%$ ). However, in subgroup analysis for the acupuncture therapy alone, only effective rate showed a significantly better performance.

**Conclusion:** Traditional Chinese acupuncture seems to be effective in improving some symptoms of PPD, although the evidence is uncertain. Therefore, further studies following standardized guidelines with a low risk of bias are needed to confirm the effectiveness of acupuncture in the treatment of PPD.

**Keywords:** Acupuncture; Meta-analysis; Postpartum depression

## 1. INTRODUCTION

The theory of traditional Chinese medicine (TCM) comes from the summary of medical experiences and the theory of Yin-Yang and Five Elements in ancient China. The unique theoretical system of TCM has two basic characteristics: overall concept and differentiation of symptoms and signs.<sup>1-3</sup> The basic principle of TCM is a general summary of human life activities and disease changes.

Acupuncture is one of the treatment choices of TCM. Acupuncture includes needle manipulation and moxibustion therapy.<sup>4-6</sup> Needle manipulation is an important, but mostly overlooked, component of acupuncture therapy. Under the guidance of TCM theory, needles, such as filiform needles, are punctured into the body of the patient at a certain angle.

Subsequently, needling techniques, such as twisting, lifting, and inserting, are used to stimulate specific parts of the human body to achieve the purpose of treating diseases. The point of penetration is called human acupoint. Moxibustion therapy is a kind of heat therapy in which dried plant materials called “moxa” are burned on certain acupoints on the body surface to invigorate the flow of Qi in the body and dispel certain pathogenic influences.

Postpartum depression (PPD) refers to women's obvious depressive symptoms or typical depressive episodes in the puerperium period and may lead to puerperal psychiatric syndrome, postpartum restlessness, and postpartum psychosis. The incidence is 15% to 30% in new mothers. Typical PPD occurs within 6 weeks after delivery and can recover spontaneously within 3 to 6 months, but severe depression can last for 1 to 2 years. The recurrence rate of PPD in the second pregnancy is 20% to 30% in new mothers.<sup>7,8</sup> There is no significant difference in the clinical features between PPD and other depressive episodes. At present, the commonly used screening scales for PPD include Edinburgh Postpartum Depression Scale (EPDS) and Hamilton Depression Scale (HAMD). The primary treatment methods of PPD include psychological intervention, drug therapy, and physiotherapy.<sup>9,10</sup> Recently, acupuncture therapy has attracted considerable interests in the West medical community, and it has been shown to be effective in relieving postoperative pain, pregnant nausea, nausea and vomiting caused by chemotherapy, and toothache with

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very low side effects.<sup>11–15</sup> However, the role of acupuncture therapy in PPD remains unclear.<sup>16,17</sup> This study aimed to examine whether acupuncture has some advantages in improving degrees of depression compared with other therapies in PPD patients and to provide a new and useful treatment option for these patients.

## 2. METHODS

This study was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.<sup>18</sup>

### 2.1. Literature search

We retrieved all clinical studies (published before December 2018) evaluating the effect of acupuncture therapy on depression relief and control in patients with PPD. Retrieval databases included PubMed, Embase, Cochrane Library, Web of Science, and Chinese National Knowledge Infrastructure. The literature was searched using a combination of keywords including acupuncture, puncture, stitch therapy, moxibustion, traditional Chinese medicine, or TCM and PPD. Language is limited to English and Chinese. References were consulted for comprehensive retrieval.

### 2.2. Inclusion and exclusion criteria of literature

Studies were screened for eligibility using the following eligibility criteria: (1) Patients included in the analysis met the diagnostic criteria of PPD. It was noted that there was no unified criterion for the diagnosis of PPD, so the following two-step screening method was generally used in most of the included studies: identification of suspicious patients with screening scales and then diagnosis of patients using the diagnostic criteria; (2) The treatment group included all kinds of acupuncture methods, such as manual acupuncture, electro-acupuncture, or acupuncture methods accompanied by other therapies. The control group included placebos or any other types of TCM therapy, such as herb, drug, and psychological intervention; (3) The study types must be randomised controlled trial (RCT). The number of cases should be at least >30, and the baseline characteristics of acupuncture and control groups were comparable; (4) when duplicate publications were found, high-quality or the most recent publications from the same authors or teams were selected.

The following exclusion criteria were used in this study: (1) Unable to extract data or failed to find the full text of the literature; (2) non-RCTs, reviews, editorials, correspondences, comments, letters, practice guidelines, case reports, or editorials.

### 2.3. Data collection and quality evaluation

Two reviewers independently screened the titles, abstracts, and full texts of publications. Bias risks of data extraction and evaluation included in the study were cross-checked. In case of disagreement, the two reviewers discussed the issues or sought to use a third-party solution. The lack of essential data was supplemented by email and telephone contacts with the original authors. The following contents were extracted from the literature: (1) basic information included in the literature, such as the first author, year of publication, sample size, and age; (2) baseline characteristics and intervention measures of the subjects; (3) study types and critical elements of bias analysis and evaluation; (4) outcome indicators and outcome measurement data. The Cochrane Collaboration's "Risk of Bias" tool from the Cochrane Handbook for Systematic Reviews of Intervention was applied to evaluate the quality of included studies.<sup>19</sup>

The clinical indicators for extraction and analysis included authors, countries, study designs, sample sizes, specific interventions, treatment courses, and outcome measures in each study.

### 2.4. Outcome measures

The diagnostic scales of PPD were mostly conducted based on *The Diagnostic and Statistical Manual of Mental Disorders*, published by the American Psychiatric Association.<sup>20</sup> HAMD and EPDS were used to assess the PPD level quantitatively. HAMD is the most frequently used scale for clinical evaluation of the depressive state, and it comprises 24 items of depressive symptoms, which are scored in five grades. EPDS is the most widely used self-rating scale for primary health care screening and includes ten items. EPDS was conducted at 6 weeks postpartum to determine whether the patient has depressive disorders.

### 2.5. Statistical methods

Heterogeneity tests and effect values were analyzed using Comprehensive Meta-Analysis software (Computer program, Version 2.0).<sup>21</sup> First, the heterogeneity was assessed by two tests (test level:  $\alpha = 0.1$ ). If  $p > 0.1$  and  $I^2 < 50\%$ , the included studies were homogeneous. Meta-analysis was carried out using the fixed-effect model. If heterogeneity is observed among the studies, the random effect model was used for meta-analysis after the influence of obvious heterogeneity was excluded. Subgroup analysis, sensitivity analysis, or descriptive analysis was performed for the studies with obvious heterogeneity. Weighted mean difference (MD), risk ratio (RR), and the corresponding 95% confidence interval (CI) were used as combined statistics for continuous variables. The test significance level of meta-analysis was set at  $\alpha = 0.05$ . In the sensitivity analysis, the results of  $p < 0.10$  and  $I^2 > 50\%$  in the heterogeneity test were analyzed by the method of conversion between the fixed effect model and random effect model.<sup>22,23</sup>

## 3. RESULTS

### 3.1. Collection and selection of literature

Initially, we retrieved 298 publications in various databases using relevant search terms and strategies, of which seven were manually retrieved. After deleting duplicate 163 publications obtained from the major databases, we screened the titles and abstracts of the remaining 142 publications, of which 102 publications with unrelated or incomplete data were excluded from this study. We downloaded and reviewed the remaining 40 publications in full text, of which 26 publications that did not meet the inclusion criteria were subsequently excluded. Finally, 14 studies<sup>24–37</sup> were included in the meta-analysis.

### 3.2. Baseline characteristics

Table 1 shows the baseline characteristics of the included 14 RCTs published from 2004 to 2015. A total of 934 of PPD patients were included in the quantitative meta-analysis, with 465 patients in the treatment group and 469 patients in the control group. Acupuncture or electroacupuncture combined with other drug therapies and psychological treatments were used for PPD patients in the treatment intervention group, while anti-depressant drugs and other symptomatic and basic supportive therapies were applied for PPD patients in the control group. Treatment durations ranged from 4 to 12 weeks in the included RCTs. The depressive state was evaluated using HAMD and EPDS. Other assessment indicators included the rate of effective outcomes and the estradiol level.

The Cochrane Collaboration's "Risk of Bias" tool from the Cochrane Handbook for Systematic Reviews of Intervention

**Table 1****Baseline characteristics of the included studies**

Authors	Publication (year)	Study design	Sample size (treatment/control)	Interventions		Treatment duration (weeks)	Outcome measures
				Treatment	Control		
Xi et al <sup>24</sup>	2015	RCT	52/53	Acupuncture + PI	PI	6	HAMD, ER, E2
Yu et al <sup>25</sup>	2015	RCT	30/30	Acupuncture	Fluoxetine	4	HAMD
Zheng et al <sup>26</sup>	2015	RCT	24/24	Acupuncture + PI	Venlafaxine	6	HAMD, ER
Dong et al <sup>27</sup>	2014	RCT	30/30	Acupuncture	Fluoxetine	4	ER
Mi et al <sup>28</sup>	2014	RCT	37/37	Acupuncture + TCM	Citalopram	6	EPDS, ER
Ai et al <sup>29</sup>	2013	RCT	35/35	Acupuncture + PI	Citalopram	12	EPDS, HAMD, ER
Xu et al <sup>30</sup>	2013	RCT	50/50	Acupuncture + TCM	TCM	6	ER, E2
Xu et al <sup>31</sup>	2013	RCT	45/45	Acupuncture + TCM	TCM	6	ER, E2
Chung et al <sup>32</sup>	2012	RCT	8/10	Electroacupuncture	Sham acupuncture	4	EPDS
Zhang et al <sup>33</sup>	2012	RCT	43/43	Electroacupuncture	Venlafaxine	6	ER
Zhao et al <sup>34</sup>	2011	RCT	50/50	Acupuncture	Fluoxetine	6	ER
Chen et al <sup>35</sup>	2010	RCT	26/26	Acupuncture	Fluoxetine	6	HAMD, ER
Gong et al <sup>36</sup>	2010	RCT	21/21	Electroacupuncture	Paroxetine	8	HAMD
Manber et al <sup>37</sup>	2004	RCT	14/15	Acupuncture	Tuina	10	ER

EPDS = Edinburgh Postnatal Depression Scale; ER = effective rate; E2 = estradiol; HAMD = Hamilton Depression Rating Scale; PI = psychological intervention; RCT = randomized controlled trial; TCM = traditional Chinese medicine.

**Table 2****Quality assessment using the cochrane collaboration's "risk of bias" tool from the cochrane handbook**

Authors	Random sequence generation	Allocation concealment	Blinding of participant and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other bias
Xi et al <sup>24</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes
Yu et al <sup>25</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes
Zheng et al <sup>26</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes
Dong et al <sup>27</sup>	Unknown	No	Unknown	Unknown	Unknown	Yes	Yes
Mi et al <sup>28</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes
Ai et al <sup>29</sup>	Unknown	No	Unknown	Unknown	Unknown	Yes	Yes
Xu et al <sup>30</sup>	Yes	No	Unknown	Unknown	Yes	Yes	Yes
Xu et al <sup>31</sup>	Yes	No	Unknown	Unknown	Yes	Yes	Yes
Chung et al <sup>32</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes
Zhang et al <sup>33</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes
Zhao et al <sup>34</sup>	Unknown	No	Unknown	Unknown	Unknown	Yes	Yes
Chen et al <sup>35</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes
Gong et al <sup>36</sup>	Unknown	No	Unknown	Unknown	Unknown	Yes	Yes
Manber et al <sup>37</sup>	Yes	No	Unknown	Unknown	Unknown	Yes	Yes

was applied to evaluate the quality of the included studies.<sup>22</sup> As shown in Table 2, the criteria used for the assessment of included RCTs included random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessments, incomplete outcome data, selective reporting, and other sources of bias. The use of blinding was not available in the included studies. All study qualities were scored as medium to high.

### 3.3. Meta-analysis on HAMD, EPDS, and estradiol levels

A significantly better performance in the HAMD was found in the acupuncture group than in the control group, and the pooled MD was  $-1.27$  (95% CI:  $-2.55$  to  $0.01$ ;  $p = 0.05$ ,  $I^2 = 83\%$ ) in the random-effect model (Fig. 2A). The EPDS assessment method was only applied in two RCTs (Fig. 2B), and the analysis showed that the pooled MD had an obvious similar tendency in the acupuncture and control groups ( $p = 0.06$ ), and the difference was not significant (MD =  $-0.49$ ; 95% CI:  $-1.01$  to  $0.02$ ). We next evaluated the estradiol level. Acupuncture could significantly increase the estradiol level compared with controls, and the MD was  $63.99$  (95% CI:  $13.47$  to  $114.51$ ;  $p = 0.01$ ,  $I^2 = 98$ ) (Fig. 2C).

### 3.4. Meta-analysis on the effect rate

Further, we analyzed the incidence of the cases in which depressive outcomes were reported as recovery to normal mental status. As shown in Fig. 3A, acupuncture therapy showed a significantly better performance in the effective rate than did controls, and the pooled RR was  $1.20$  (95% CI:  $1.09$  to  $1.33$ ;  $p < 0.0001$ ,  $I^2 = 46\%$ ) in the random-effect model. Figure 3B displays the funnel plot for the publication bias assessment, and the plot is in asymmetry distribution, suggesting a lower publication bias for the effective rate outcomes.

### 3.5. Subgroup analysis

Specifically, we focused on the acupuncture therapy alone on the evaluated variables of PPD. Thus, the combined acupuncture therapies with other treatment strategies such as psychological intervention and traditional Chinese medicine were excluded from the subgroup analysis. Table 1, a total of eight RCTs<sup>25,27,32-37</sup> on the acupuncture or electroacupuncture alone were included in the pooled calculations. Figure 4A, showed when analyzed the acupuncture therapy alone, no significant difference was observed between the two groups (MD =  $-0.11$ , 95% CI:  $-1.09$ ,  $0.87$ ;  $p = 0.83$ ,  $I^2 = 74\%$ ) in HAMD scale. Similarly, Fig. 4B, in

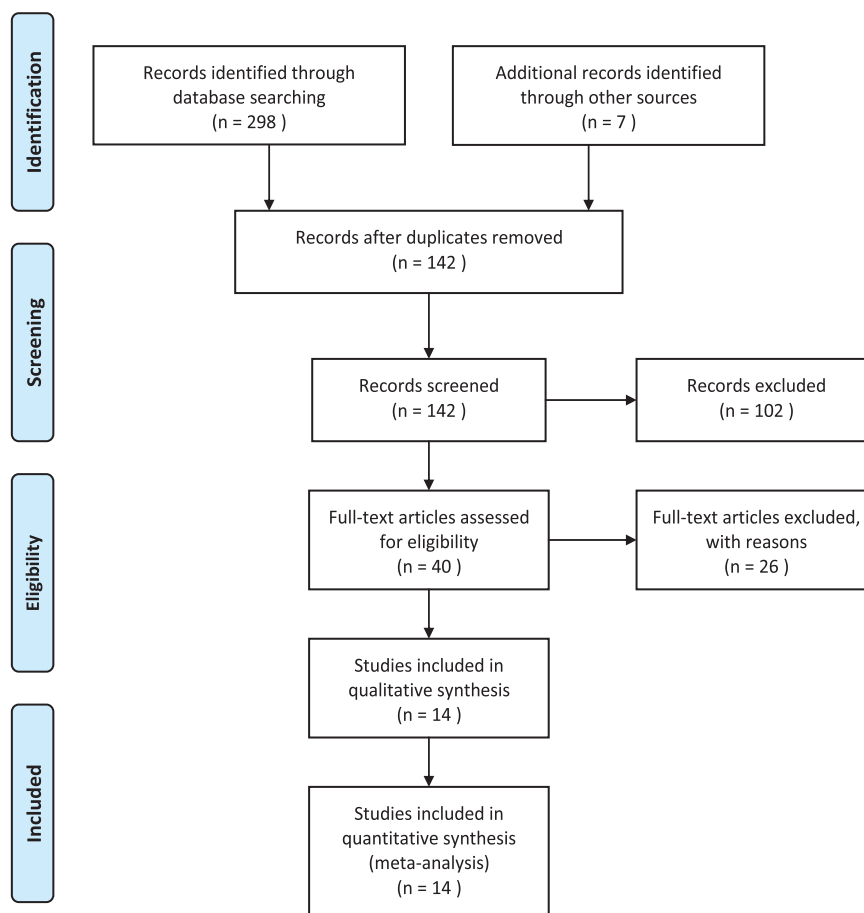


Fig. 1 Flowchart of selection process.

terms of EPDS scale, only one RCT has reported the outcome in EPDS in acupuncture alone, and no benefit was detected either ( $MD = -0.30$ , 95% CI:  $-4.64, 4.04$ ;  $p = 0.89$ ,  $I^2 = 0\%$ ). No available data on estradiol level was extracted in the subgroup analysis for acupuncture alone. Figure 4C, when pooled the combined outcome for effect rate in the acupuncture subgroup, again, a significantly better performance was observed in the acupuncture group, and pooled RR was 1.17 (95% CI: 1.03, 1.33;  $p = 0.01$ ,  $I^2 = 34\%$ ).

#### 4. DISCUSSION

The occurrence of PPD is the result of the interaction of multiple factors, and PPD has great harm to mother, infant, family, and society. In clinical practice, depression, anxiety, fear, irritability, lack of self-confidence, and lack of hope for life are the primary manifestations of PPD. Severe PPD patients may even have a suicidal tendency. Psychological, genetic, and social factors are the risk factors for PPD. The incidence of PPD ranges from 15% to 30% in new mothers. PPD usually occurs within 6 weeks and can recover spontaneously within 3 to 6 months, but severe PPD can last for one to two years. The recurrence rate in the second pregnancy is 20% to 30% in new mothers.

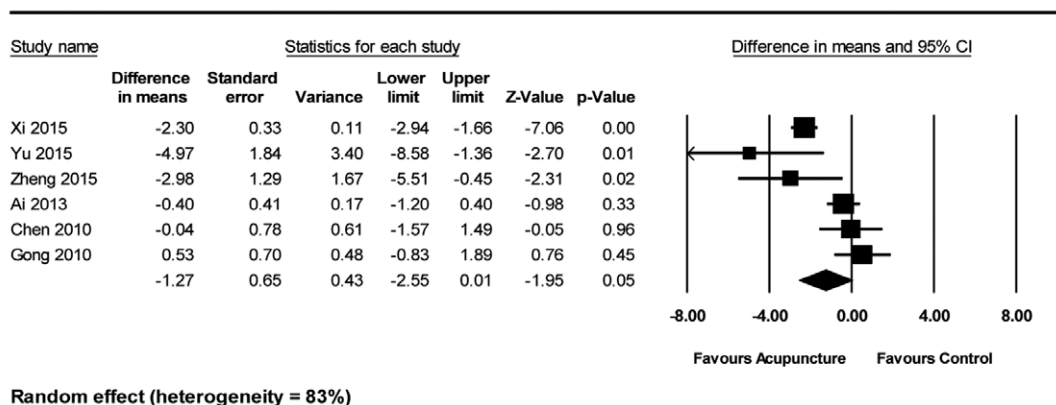
The following treatment methods for PPD are available recently: psychotherapy, routine therapy, drug therapy, physical therapy, and electroconvulsive therapy. However, these therapies are not effective and have many side effects; therefore, it is particularly important to find treatment with high

efficacy and safety. From the point of view of TCM, PPD is related to patients' emotional and visceral dysfunction. Acupuncture, a TCM treatment in China, enhances the input signal of the motor cortex by stimulating specific acupoints of the human body, increases the excitement of central nervous system, and might thus improve the depressive state of patients. Our systematic evaluation and meta-analysis suggest that acupuncture therapy is safe and effective in the treatment of PPD, as indicated by the traditional depression treatment scores (HAMD and EPDS) and the effective rate of treatment in PPD patients.

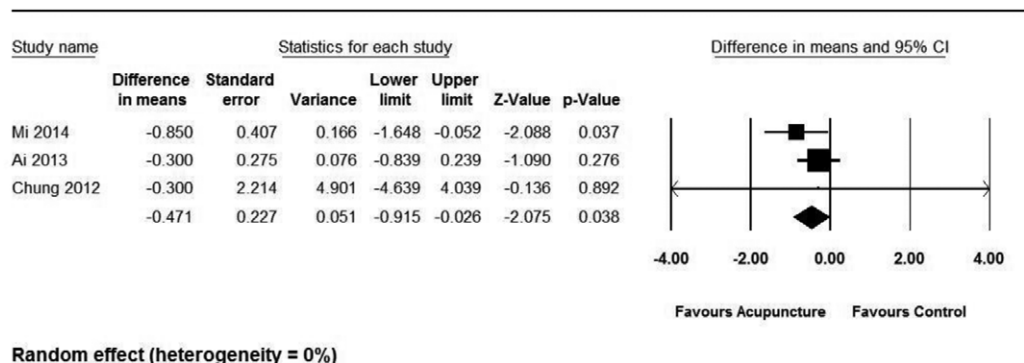
Drug therapy is the primary treatment for moderate PPD. At present, the first-line clinical antidepressants include selective serotonin reuptake inhibitors, 5-hydroxytryptamine and norepinephrine reuptake inhibitors, and other compounds with different mechanisms of action. Acupuncture combined with conventional drug therapy is superior to the conventional drug therapy alone. Although conventional drug therapy can improve patients' depressive state, long-term use can lead to drug resistance. Acupuncture can act not only on the skin but also on the subcutaneous muscular layer, thus enhancing the local blood circulation and tissue metabolism of the skin; it also causes the diffusion of inhibition function of the cerebral cortex and plays a role in sedation and antidepressant, which are the treatment goals of PPD.

At present, there are many hypotheses on the mechanism by which acupuncture improves PPD. According to the neuroendocrine disorder theory, acupuncture improves depressive

### A HAMD scale



### B EDPS scale



### C Estradiol level

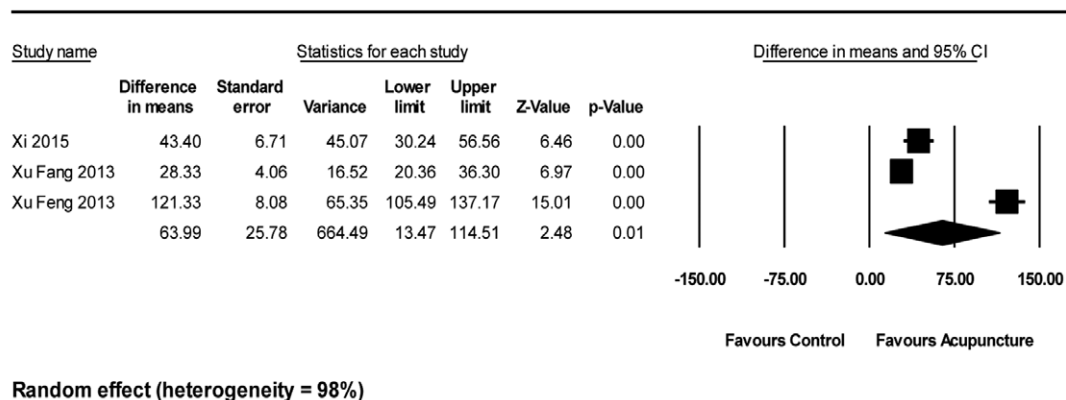
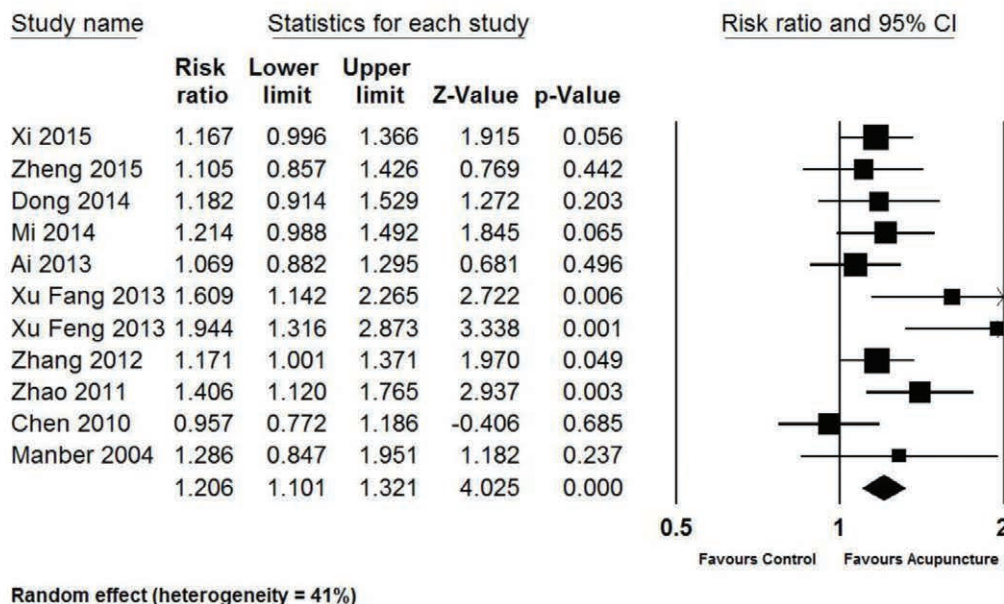


Fig. 2 Results of meta-analysis on HAMD (A), EPDS (B), and estradiol levels (C).

symptoms and exerts antidepressant effects through the hypothalamus-pituitary-adrenal axis and hypothalamus-pituitary-thyroid axis. According to the hypothalamus-pituitary-gonad axis theory, acupuncture might regulate the PPD status by improving sex hormone levels. This hypothesis is confirmed in our meta-analysis of estradiol levels. In addition, other hypotheses, including the neurotrophic and nerve regeneration dysfunction theory, hippocampal neuron alteration theory, and cell signal transduction theory, also have been used

to illustrate the mechanism of acupuncture-induced improved depressive symptoms. According to the theory of immune function changes, the proinflammatory cytokines, such as interleukin-1 (IL-1), IL-2, IL-6, and tumor necrosis factor  $\alpha$  (TNF $\alpha$ ), and interferon could induce psychiatric symptoms, such as apathy, depression, and delusion. It has been found that the serum levels of IL-2, IL-6, and TNF $\alpha$  were significantly higher in depressed rats than in healthy controls, but the levels of IL-2, IL-6, and TNF $\alpha$  significantly decreased

### A Effective Rate



### B Publication Bias

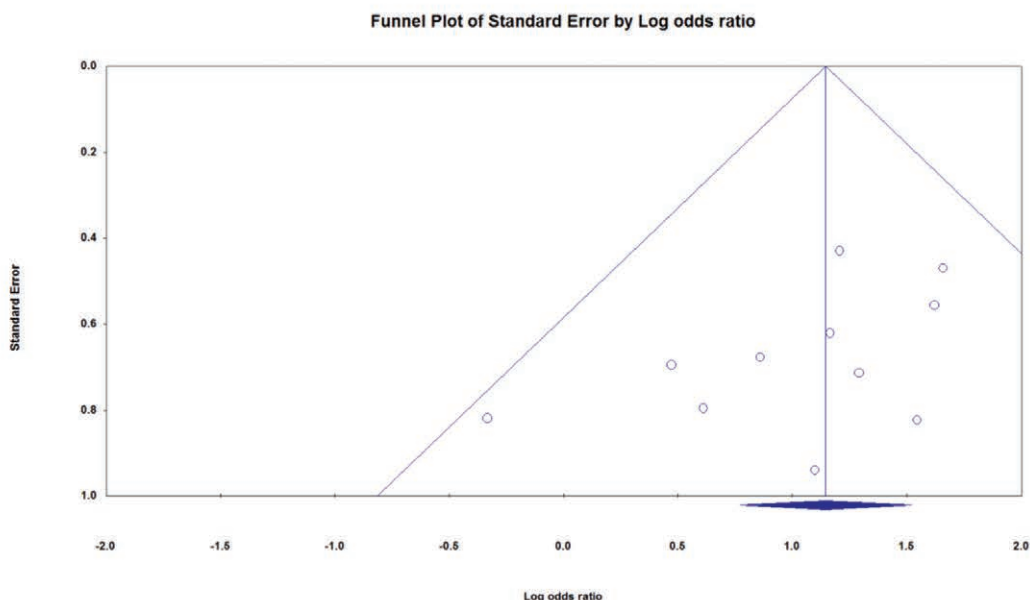


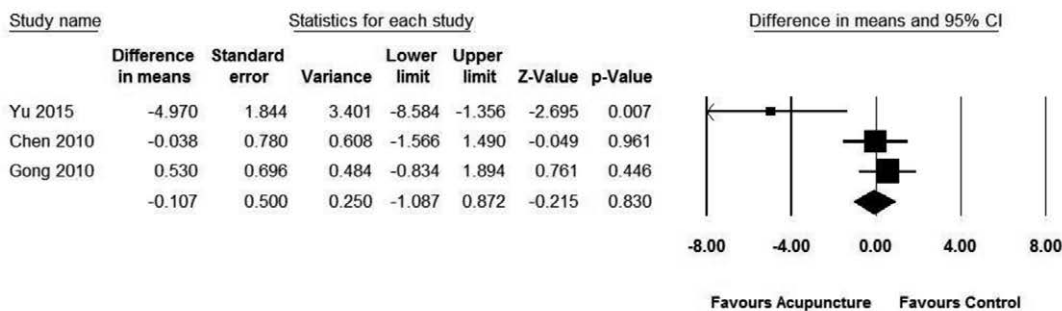
Fig. 3 Results of meta-analysis on the effective rate (A) and publication bias (B).

after needling Baihui and Taichong acupoints in the depressed rats.<sup>38</sup> Other studies have demonstrated that the combination of acupuncture and medicine attenuates the high expression of regulatory T (Treg) cells and improves depressive symptoms in depressed mice at an early stage. Therefore, acupuncture may regulate expression of Treg cells and thus improve the immunosuppressive state of depression.<sup>39</sup>

This meta-analysis has some limitations. Few studies have investigated the efficacy of the combined therapies, and the

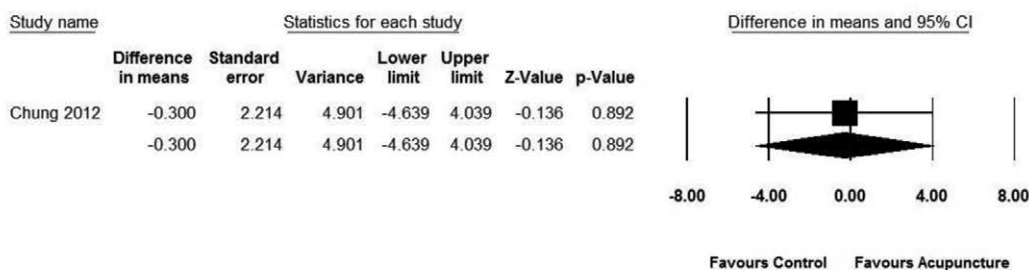
number of patients was small. The heterogeneity of various documents was considerable. Notably, this systematic review suggests that acupuncture is safe and effective in the treatment of PPD. Collectively, traditional Chinese acupuncture seems to be effective in the treatment for some symptoms of PPD, although the evidence is uncertain. Therefore, further studies following standardized guidelines with a low risk of bias are needed to confirm the effectiveness of acupuncture in the treatment of PPD.

### A HAMD



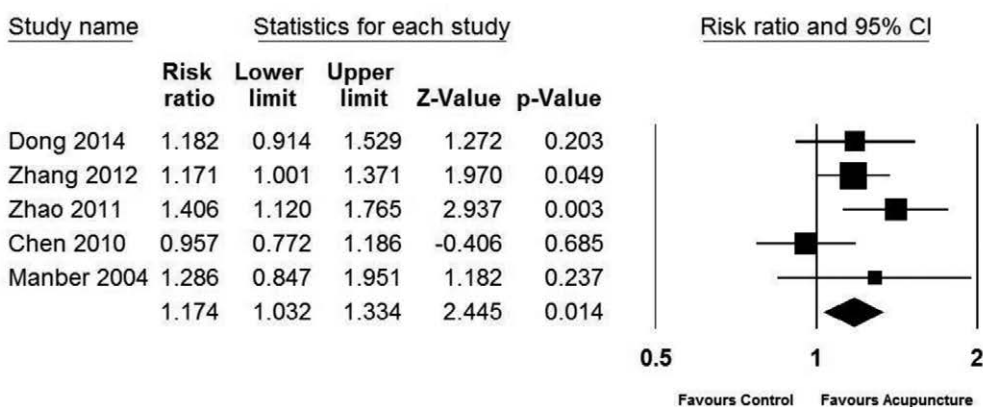
Random effect (heterogeneity = 74%)

### B EPDS



Random effect (heterogeneity = 0%)

### C Effective Rate



Random effect (heterogeneity = 34%)

Fig. 4 Results of subgroup analysis.

#### ACKNOWLEDGMENTS

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