Clinical evidence of Chinese medicine therapies for depression in women during perimenopause and menopause

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ABSTRACT
Background: Depression is common in women during perimenopause and menopause. Complementary therapies such as acupuncture and Chinese herbal medicine (CHM) are often utilized by these women. However, the efficacy and safety of these treatments have not been systematically evaluated.

Methods: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs). Nine English and Chinese databases were searched and search terms included perimenopause, menopause, depression, Chinese herbal medicine, acupuncture, RCTs, and their synonyms. Methodological quality was assessed using the Cochrane Risk of Bias Tool.

Results: A total of 18 RCTs were identified (6 CHM, 11 acupuncture related therapies, 1 combination of CHM and acupuncture). For Hamilton Rating Scale of Depression (HRSD) and Kuppermans Index of Menopause, tuina-massage, combined therapy of CHM plus acupuncture showed significant benefits at end of treatment compared to antidepressants. Either CHM and acupuncture reduced HRSD scores, indicating less severe depression, showing comparable effects to antidepressants.

Conclusion: CHM and acupuncture treatment in perimenopause and menopausal women resulted in reduced severity of depression. Results should be interpreted with caution given the small number of studies included in this review and further RCTs are warranted to validate findings from this review.

1. Introduction

Perimenopause, the period before and after menopause, begins with endocrine, biological and clinical changes and ends 12 months after the final menstrual period. During these times of change, women often show clinical signs of physical, hormonal and psychological changes. Menopause symptoms include night sweating, hot flushes, vaginal dryness, breast tenderness, insomnia, migraines, and premenstrual dysphoria. Psychological symptoms include mood swings and depression.

Depression is characterised by depressed mood, or a loss of interest, or loss of pleasure in daily activities for more than two weeks. The onset of depression can occur at any stage of life. However, risk factors can be related to biological events such as menopause. Around menopause women with no history of depression are two to four times more likely to report depressed mood compared to premenopausal women, and the risk significantly increases in women with a history of depression.

In terms of treatment, hormone replacement therapy (HRT) may be effective for mild to moderate depression during perimenopause, but more severe depression requires antidepressant drugs. Although the combination of antidepressants and HRT are commonly prescribed during perimenopause and menopause, women often seek out complementary and alternative medicine, such as acupuncture and Chinese herbal medicine.

Complementary therapies are often sought to avoid side effects of HRT and antidepressants, as well as ongoing menopausal symptoms despite treatment. HRT increases the risk of venous thromboembolism and causes long term adverse effects on the uterus, breast and cardiovascular system. As for antidepressants, drugs such as selective serotonin reuptake inhibitors (SSRIs) have gastro-intestinal, stimulatory and sexual side effects. The long-term use of antidepressants in...
middle-aged women is limited by treatment emergent sexual dysfunction and weight gain. 16

Chinese medicine has a long history of recognizing and treating depression. The word “depression” is found in medical books written before CE 618, such as The Yellow Emperor’s Classic of Medicine (Huang Di Nei Jing). In this book it describes the negative effects emotions can have on one’s wellbeing. Depression in women was documented as early as CE 206 in the Medical Treatises of the Golden Chamber (Jin Gui Yao Lue). It is said that ‘woman with zang zao (a syndrome presented with sadness, tendency to cry, unstable mood and restlessness) feel sad, have a tendency to cry with no apparent cause, frequently yawn and should be treated with Gan mai da zao tang (a herbal formula).

To our knowledge, there are no systematic reviews on the effect of Chinese medicine for depression during menopause. This review systematically evaluates the safety and efficacy of Chinese herbal medicine and acupuncture therapies for depression and menopause related symptoms.

2. Methods

We implemented the methods outlined in the Cochrane Handbook for Systematic Reviews of Interventions S.1. 17 Nine databases were searched from their inception to February 2018. English databases were searched by JS, these included Allied and Complementary Medicine Database (AMED), Cochrane Central Register of Controlled Trials (CENTRAL) on The Cochrane Library, Cumulative Index of Nursing and Allied Health Literature (CINAHL), Excerpta Medica Database (EMBASE), and PubMed. Chinese databases were searched by LY, these included BioMedical Literature (CBM), Chinese National Knowledge Infra-structure (CNKI), Chongqing VIP (CQVIP) and Wanfang. Search terms were grouped into three blocks: 1) intervention (including acupuncture, Chinese herbal medicine, tuina, cupping); 2) clinical condition (including menopause, perimenopause, depression, depressive disorder, unipolar depression, major depression, major depressive disorder); and 3) trial design (including clinical trial, random, control). Complete lists of search terms are available from the authors. Reference lists of review articles were checked for additional references.

Randomized controlled trials of any duration published in English or Chinese were included. Trial participants were adult women during perimenopause or menopause, with a diagnosis of major depressive disorder based on clinical guidelines from the World Health Organisation, USA and China.4,18,19 Participants diagnosed with other types of depression, such as bipolar depression, dysthymia, depression or depressive symptoms caused by other mental disorders, physical disorders, another medical condition or the effects of a substance were excluded.

Included interventions were Chinese herbal medicine (CHM), acupuncture and tuina-massage. Comparators were antidepressants; studies were excluded if they did not specify which antidepressants were used. Pre-specified outcomes measures included clinician rated and self-rated depression severity scales, Kupperman menopausal index (KI), number of participants who relapsed or achieved remission, quality of life, functional capacity (eg, social adjustment scales), suicide rate and adverse events.

Search results were synthesized by removing duplicates, followed by screening of titles and abstracts by LY, YMD and JLS. Full texts were obtained and screened by two reviewers (LY and YMD). Eligible studies satisfying the inclusion criteria were extracted using EpiData software (EpiData Association, Odense, Denmark). LY and YMD extracted and double-checked the data from included articles to obtain information on authors, publication year, title, journal, location, study design, diagnostic criteria, sample size, dropouts, age, gender, intervention, control, treatment duration, outcome measures, and adverse events. Discrepancies were discussed with a third reviewer (JLS). Risk of bias was assessed independently by two reviewers (LY and YMD) using the risk of bias assessment tool from the Cochrane Handbook. 17 Disagreements were resolved by a third reviewer (JLS). Publication bias was assessed using funnel plots and Egger’s test in Stata 14 software. When necessary, included study authors were contacted by email or telephone to obtain additional data, if no response is received after four weeks, the unknown information was marked as not available.

Studies were grouped for pooling based on comparable interventions and controls. Meta-analysis was conducted in Stata 14 software using published data from the included studies.

Between group differences and within group changes were assessed using random effect model. Continuous outcome data was analysed with mean difference (MD) and 95% confidence intervals (CI). When different versions of Hamilton Rating Scale for Depression (HRSD) was reported, standardised mean difference (SMD) was used. For dichotomous outcome data, risk ratios (RR) and 95% CIs are reported. A formal test for heterogeneity using the I2 statistic is included for each meta-analysis. An I2 score greater than 50% was considered to indicate substantial heterogeneity. Pre-defined subgroup analyses included participant characteristics and study design, such as treatment duration, specific antidepressants, low risk of bias of sequence generation, and different versions of outcome measures. Frequently used herbs and acupuncture points are also reported to provide potential research direction for future studies.

3. Results

3.1. Characteristics of included studies

Database searches identified 30,733 citations. Based on our selection criteria, 18 studies were included.20–27 Six studies evaluated CHM, 11 evaluated acupuncture therapies, and one evaluated a combination of CHM and acupuncture (Fig. 1). All clinical trials were conducted in China and published from 2007 to 2017. Studies enrolled a total of 1,195 female participants and the sample sizes ranged from 30 to 240. Participants’ age ranged from 40 to 60 years old, all diagnosed with perimenopause or menopause. Treatment duration ranged from four to 12 weeks. Antidepressant controls such as SSRIs were fixed-dose recommended in clinical guidelines.38–40

All studies evaluated depression severity during perimenopause or menopause assessed by the HRSD, a clinician rated scale used to measure depression severity in adults.41 Severity of menopause symptoms was assessed by the KI in six studies.20,22,23,25,34,35 One study reported results from the Menopause-Specific Quality of Life (MENQOL) questionnaire.43 Other pre-specified outcomes were not assessed in the included studies. Adverse events were reported in 11 studies.

Five studies evaluated CHM alone compared to SSRIs and one study assessed CHM combined with SSRIs compared to SSRIs. Comparator SSRIs were fluoxetine21–23,25 and paroxetine.39 One study compared CHM plus fluoxetine to fluoxetine alone.24 All CHM treatments were orally administered decoctions and six distinct formulae were used. Herbal ingredients in the formulae overlapped in the included studies and common herbs used in three or more studies were Epimedium brevicornum Maxim. (Chinese name: Xian ling pi), Bupleurum chinense DC. (Chai hu), Curculigo orchioides Gaertn. (Xian mao), Angelica sinensis (Oliv.) Diels (Dang gui) and Anemarrhena asphodeloides Bge. (Zhi mu).

A total of 11 studies investigated the effect of acupuncture and tuina-massage (massage on acupuncture points or meridians). Eight studies compared acupuncture with SSRIs.26–32,36 Two RCTs compared acupuncture to HRT plus fluoxetine,33,35 and one study compared tuina-massage to HRT plus fluoxetine.37 The studies used 29 acupuncture points and frequently used points in four or more studies included BL18 Gan shu, BL23 Shen shu, DU20 Bai hui, BL15 Xin shu, SI shen cong, LR3 Tai cong, and BL20 Pi shu (Table 1).
3.2. Risk of bias

All 18 studies were described as randomized. However, only seven (38.9%) provided information on an appropriate method of sequence generation. One study (5.6%) described the method of allocation concealment, while 17 (94.4%) did not provide details and were judged to be at unclear risk of bias. Blinding of participants, personnel and assessors were judged at low risk of bias in one study and the remaining 17 studies were judged at high risk of bias, as the interventions were clearly different and no mention of blinding was mentioned. Outcome data were available for the included studies therefore they were assessed at low risk of bias for this domain. Selective outcome reporting was judged at unclear risk for all included studies because study protocols were not available. Risk of bias assessment is presented in Table 1.

3.3. Effects of intervention

3.3.1. Chinese herbal medicine

Five studies (380 participants) assessed the effects of CHM for depression compared to SSRIs.20–23,25 At the end of treatment (EoT), there was no significant difference between the CHM group and SSRIs in terms of HRSD scores (SMD -0.28 [-0.90, 0.34]; I² = 87.1%). Change scores within groups showed that both CHM and antidepressants improved HRSD scores when baseline data was compared to EoT (Table 2, Fig. 2).

KI was assessed by four studies (n = 320) and there was a significant difference between the CHM group and the antidepressant group at EoT (MD -5.02 [-8.33, -1.72]; I² = 82.3%). Change scores within groups were also significant in both groups.

One study including 72 participants assessed the effects of CHM plus fluoxetine compared to fluoxetine alone.24 HRSD scores were not significantly different between the groups (MD -0.46 [-0.93, 0.01]).

Of the three studies that reported on adverse events, there were no events in the CHM groups.21,22,24 Adverse events in the antidepressant groups included nausea, vomiting, indigestion, diarrhoea, headache, dizziness, disturbed sleep, fatigue, sexual dysfunction, difficulty breathing, dry mouth, breast tenderness and breakthrough bleeding.21,24

3.3.2. Acupuncture

Eight studies (743 participants) assessed the effects of acupuncture compared to antidepressants.26–32,36 When HRSD scores were assessed, there were no significant difference between the two groups (SMD -0.14 [-0.53, 0.25]; I² = 84.5%) (Fig. 3). Subgroup analysis of studies at low risk of bias for sequence generation, treatment duration (less than or equal to six weeks) or specific antidepressant (fluoxetine) did not show a significant difference of HRSD scores. Two studies (156 participants) with a treatment duration of 12 weeks showed significant difference in HRSD scores between the two groups (SMD -1.17 [-1.93, -0.40]; I² = 78.7%).28,29 Overall, within group analysis showed significant improvements in the acupuncture and antidepressant groups (Table 2). One study of 90 participants had a follow-up of 12 weeks, no significant difference was found between groups (MD 0.33 [-0.11, 0.77]).28 When compared with baseline, within group analysis showed significant improvement in both the acupuncture (MD -1.02 [-1.40, -0.64]) and antidepressant groups (MD -1.88 [-2.49, -1.27]).29

Two studies (n = 142) assessed menopause symptoms by KI.27,28 At EoT, acupuncture significantly improved KI scores compared to fluoxetine (MD -5.45 [-10.38, -0.52], I² = 89.7%). Significant change in scores was also observed within groups.

One study of 90 participants assessed quality of life using the MENQOL.29 No significant difference was found between acupuncture and escitalopram groups (MD -0.04 [-0.43, 0.35]). When compared to baseline, both group showed significant improvements in MENQOL scores at EoT. At 12 weeks follow-up, no significant difference was found between groups (MD -0.34 [-0.76, 0.08]). When compared with baseline, significant improvement was shown in both the acupuncture group (MD -0.89 [-1.25, -0.54]) and antidepressant group (MD -0.6 [-1.02, -0.18]).

Relapse rate was assessed in one study,28 after 12 weeks of treatment and 12 weeks of follow-up, results showed that acupuncture significantly reduced relapse rate compared to fluoxetine (RR 0.21 [0.05, 0.90]).

Five studies reported on adverse events.26,28–31 No adverse events were reported in the acupuncture group in two studies.26,29 A total of 11 adverse events in the acupuncture group were reported in three studies,28,30–32 including local bruising (2 cases), dizziness (3 cases), palpitations (2 cases), dry mouth (1 case) and nausea (3 cases). All studies reported AEs in the antidepressant group, there was a total of 108 AEs, including dizziness (11 cases), nausea (5 cases), vomiting (1 case), dry mouth (17 cases), indigestion (1 case), diarrhoea (1 case), fatigue (17 cases), headache (3 cases), trouble sleeping (7 cases), palpitations (7 cases), sweating (10 case) and skin problems (1).
### Table 1
Characteristics of included studies.

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Author, Year</th>
<th>No. of Participants (n, C)</th>
<th>Diagnostic criteria</th>
<th>Intervention (dose, frequency of intake)</th>
<th>Control (dose, frequency of intake)</th>
<th>Outcomes</th>
<th>Treatment duration</th>
<th>Risk of Bias (SG, AC, BPI, BPU, BQA, BID, SR, Other)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gao N 2010</td>
<td>82 (31:31)</td>
<td>ICSID-2</td>
<td>Le zhi tang (1000mg, p.o, b.i.d)</td>
<td>Paroxetine</td>
<td>HRSD, KI</td>
<td>12w</td>
<td>U, U, H, H, H, L, U, L</td>
</tr>
<tr>
<td>2</td>
<td>Li GY 2014</td>
<td>60 (30:30)</td>
<td>ICSID-2</td>
<td>Jiu wei er xian tang (500mg, p.o, b.i.d)</td>
<td>Fluoxetine</td>
<td>HRSD, KI</td>
<td>6w</td>
<td>U, U, H, H, H, L, U, L</td>
</tr>
<tr>
<td>3</td>
<td>Xu FQ 2013</td>
<td>164 (82:82)</td>
<td>ICSID-2</td>
<td>Bu shen xue gan hua ye tang (1000mg, p.o, b.i.d)</td>
<td>Fluoxetine</td>
<td>HRSD, KI</td>
<td>8w</td>
<td>U, U, H, H, H, L, U, L</td>
</tr>
<tr>
<td>4</td>
<td>Zeng HL 2008</td>
<td>30 (18:12)</td>
<td>ICSID-2</td>
<td>Shu ji tang (1000mg, p.o, b.i.d)</td>
<td>Fluoxetine</td>
<td>HRSD, KI</td>
<td>12w</td>
<td>U, U, H, H, H, L, U, L</td>
</tr>
<tr>
<td>5</td>
<td>Zhang Y 2013</td>
<td>64 (32:32)</td>
<td>ICSID-2</td>
<td>Bu shen xue gan hua ye tang (1000mg, p.o, b.i.d)</td>
<td>Paroxetine</td>
<td>HRSD, KI</td>
<td>8w</td>
<td>U, U, H, H, H, L, U, L</td>
</tr>
<tr>
<td>6</td>
<td>Zhang GQ 2009</td>
<td>72 (38:34)</td>
<td>ICSID-2</td>
<td>Zao ren bu xue tang jiu hua (1000mg, p.o, b.i.d)</td>
<td>Fluoxetine</td>
<td>HRSD, KI</td>
<td>4w</td>
<td>U, U, H, H, H, L, U, L</td>
</tr>
</tbody>
</table>

**Chinese herbal medicine studies**

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Author, Year</th>
<th>No. of Participants (n, C)</th>
<th>Diagnostic criteria</th>
<th>Intervention (dose, frequency of intake)</th>
<th>Control (dose, frequency of intake)</th>
<th>Outcomes</th>
<th>Treatment duration</th>
<th>Risk of Bias (SG, AC, BPI, BPU, BQA, BID, SR, Other)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>Dong J 2007</td>
<td>78 (39:39)</td>
<td>ICSID-2</td>
<td>BL23 Shenniu 惠象, BL18 Ganshu 血合, BL21 Pulou 脉合, G20 Baxia 谷合 (30 studies), EX-INSY 5Xian 5仙 (30 studies), EX-HN1 Shensong 身通, GV24 Shenting 神庭, PC9 Nogemu 内关</td>
<td>Fluoxetine</td>
<td>HRSD, KI</td>
<td>4w</td>
<td>U, U, H, H, H, L, U, L</td>
</tr>
<tr>
<td>11</td>
<td>Nina SX 2017</td>
<td>82 (41:41)</td>
<td>CCMD3</td>
<td>BL11 Feizhao 腹中, BL19 Ganshu 肝合, BL21 Shenniu 惠象, BL18 Ganshu 血合, BL21 Pulou 脉合, BL15 Xinshu 心合</td>
<td>Fluoxetine</td>
<td>HRSD, KI</td>
<td>6w</td>
<td>L, U, H, H, H, L, U, L</td>
</tr>
</tbody>
</table>

*(continued on next page)*
(2 cases), constipation (8 cases), sleepiness (2 cases), restlessness (1 case) and other unspecified symptoms (14 cases).

Two studies (318 participants) compared acupuncture to an antidepressant plus HRT. At EoT no significant difference was found in HRSD scores between groups (MD -1.13 [-3.22, 0.95], I² = 80.2%). Change scores in both the groups were significant at EoT compared to baseline (Table 2). At six months follow up, acupuncture improved HRSD scores (MD -0.74 [-1.11, -0.37]). Zheng SH 2010 also assessed
compared to antidepressants plus HRT. At EoT (2 cases) and tremor (1 case).

Vomiting (4 cases), sleepiness (3 cases), loss of appetite (5 cases), adverse events were reported, including: dizziness (9 cases), nausea and vomiting (4 cases), sleepiness (3 cases), loss of appetite (5 cases), diarrhea (3 cases), breast tenderness (3 cases), increased leucocorhoea (2 cases) and tremor (1 case).

One study (75 participants) assessed the effect of tuina-massage compared to antidepressants plus HRT. When acupuncture compared to antidepressant and HRT, there was no significant difference between groups. However, change in KI was shown in both groups after treatment. At 6 months follow-up, acupuncture significantly improved HRSD scores (MD -0.74 [-1.11, -0.37]) and KI scores (MD -3.7 [-4.98, -2.42]) compared to control.

Adverse events were reported in both studies. In the acupuncture group four cases of needle pain was reported. In the control group a total of 24 adverse events were reported, including: dizziness (9 cases), nausea and vomiting (4 cases), sleepiness (3 cases), loss of appetite (5 cases), diarrhea (3 cases), breast tenderness (3 cases), increased leucocorhoea (2 cases) and tremor (1 case).

One study (75 participants) assessed the effect of tuina-massage compared to antidepressants plus HRT. Significant improvements were also observed within groups when EoT scores are compared to baseline scores. This study also assessed KI. Tuina-massage significantly improved KI scores compared to antidepressant plus HRT (MD -6.09 [-8.33, -3.85]).

Acupuncture significantly improved HRSD (MD -1.43 [-1.94, -0.92]) compared to control. This study did not report on adverse events.

3.3.3. Chinese herbal medicine plus acupuncture

One study assessed the effects of Chinese herbal medicine combined with acupuncture compared to fluoxetine. A significant difference was found between groups (MD 12.67, [7.57, 17.78]). However, baseline imbalance was detected. Changes scores were significant for the control group but not the intervention group. There were no adverse events reported in the intervention group. Five adverse events were reported in the fluoxetine group including nausea, headache, dizziness and feeling feverish.

4. Discussion

Through systematic and comprehensive literature search, we found 18 RCTs that assessed the effects of CHM, acupuncture, or both administered simultaneously for depression in women during perimenopause or menopause. Overall, the results suggest that CHM and acupuncture is showed improvements post treatment in reducing depression severity during menopause and perimenopause. Our results show that CHM is well tolerated, with no reports of adverse events. Further, the incidence of adverse events of acupuncture is much lower than antidepressants, which is consistent with previous reviews.

There are currently no systematic reviews that assess the effect of Chinese medicine for depression during perimenopause or menopause. No previous reviews assessed the effect of CHM treatments for depression during perimenopause or menopause, the focus was on menopausal symptoms but not depression related to menopause. There are a few acupuncture reviews on acupuncture for depression during perimenopause and menopause women. Li 2014 evaluated the effectiveness and safety of acupuncture and moxibustion for perimenopausal depression based on 15 studies that involved 1,507 participants. Huang 2011 assessed the effect and safety of acupuncture in the treatment for peri menopausal depression, a total of 13 trials involving 1057 patients were included. Previous meta-analysis results showed that acupuncture plus medication (HRT, tibolone, antidepressants) or acupuncture alone is better than medication alone at both effective rate and curative rate. Both reviews reported on curative rate, however Li 2014 did not provide details on how it was calculated.

Within group comparison EoT:

**Comparison** | No. of studies (no. of participants) | Baseline balance | Between group comparison EoT: | Within group comparison EoT: | Between groups comparison FU: |
---|---|---|---|---|---|
CHM Vs. anti | 5 (380) | Yes | SMD -0.28 [-0.90, 0.34]; I² = 87.1% | SMD -2.48 [-3.42, -1.55]; I² = 91.0%; SMD -2.09 [-2.66, -1.51]; I² = 76.7% | NA |
Acup Vs. anti | 8 (743) | Yes | SMD -0.42 [-0.88, 0.04]; I² = 88.7% | SMD -2.88 [-3.43, -2.33]; I² = 85.3%; SMD -2.20 [-3.04, -1.36]; I² = 94.4% | NA |
Acup Vs. anti + HRT | 2 (318) | Yes | MD -1.13 [-3.22, 0.95]; I² = 80.2% | MD 13.90 [11.20, 16.60]; I² = 85.4%; MD 12.84 [8.74, 16.84]; I² = 93% | MD -0.74 [-1.11, -0.37] |

Abbreviation: Acup, acupuncture; anti, antidepressant; CHM, Chinese herbal medicine; EoT, end of treatment; FU, follow-up; therapy; NA, not applicable.

* statistically significant, p < 0.05.
inferior to antidepressant and HRT combined.

Limitations of this review
This review identified 18 studies with generally small sample sizes. The included studies have methodological limitations and thus provided low quality and inconclusive evidence, a consistent finding with previous reviews on depression during perimenopause. Heterogeneity was high, possibly arising from different herbs or acupuncture points used, dosage of herbs, different needle retention time and frequency, different treatment duration or depression severity.

Implications for future trials
We recommend future trials to follow rigorous methodology to improve overall quality including clearly describing methods of randomization, allocation concealment, methods of blinding and register the trial protocols in an internationally recognised registry.

One interesting observation was when acupuncture was compared to antidepressant plus HRT, the effect on HRSD and KI was not significant after three months of treatment but had significant long-term effects at six months follow-up. In our review, only four studies had a follow-up period, this can be incorporated into future trials to assess the long-term effect of CHM and acupuncture for depression during perimenopause and menopause periods. Therefore, it is worth assessing the long-term effects of acupuncture in the future. Further, depression is a lifelong disease and relapse often occurs, due to the nature of disease, therefore the long-term effect of Chinese medicine therapies on relapse rate should also be evaluated.

Only one included study evaluated the quality of life in this group of women. However, the results were not reported, so we cannot comment on its impact on the overall conclusions.
participants, this outcome should be incorporated into future trials as this may produce a significant benefit in addition to the improved physical and mental effects.

Implication for practice
We observed that formula and herbs identified our review focused more on treating menopause. Previous systematic reviews on Chinese herbal medicine for depression identified the most common formulæ used in the included studies being Xiao yao san, Chai hu Shu gan san more on treating menopause. Previous systematic reviews on Chinese physical and mental effects.

participants, this outcome should be incorporated into future trials as

Y.M. Di, et al. Provisonal Hospital of Traditional Chinese Medicine (Grant Number Chinese Medical Sciences, China with additional funding support from Research Centre for Chinese Medicine (CAIRCCM) - a joint initiative of follow rigorous methodology and reporting, using sufficient large

acupuncture for depression during perimenopause and menopause. Therapies have shown similar effect at reducing depression severity as

imply that the research on this topic using Chinese medicine therapies only treat menopause related symptoms but also improve depression.

5. Conclusion
The included studies were published in the last 10 years; this could imply that the research on this topic using Chinese medicine therapies started to emerge in the recent years. Although Chinese medicine therapies have shown similar effect at reducing depression severity as antidepressants, there is limited evidence on the efficacy of CHM or acupuncture for depression during perimenopause and menopause. Future well designed clinical trials on CHM and acupuncture should follow rigorous methodology and reporting, using sufficient large sample sizes with follow-ups.

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Conflicts of interest
The authors declare no conflicts of interest.

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