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REVIEW



## The maintenance effect of acupuncture on breast cancer-related menopause symptoms: a systematic review

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### ABSTRACT

**Background:** Acupuncture has been used for many breast cancer treatment-related problems, but how long the effect lasts is unknown. This meta-analysis aims to evaluate how long the effect of acupuncture on breast cancer-related hot flushes and menopause symptoms lasts.

**Methods:** The research design followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement, without language restrictions. Seven databases from inception through February 2019 were accessed; only randomized clinical trials (RCTs) that examined the maintenance effect of acupuncture on hot flushes or menopause symptoms after treatment were included. Cochrane criteria were followed and RevMan 5.2 software was used to analyze trials.

**Results:** In total, 943 patients from 13 RCTs were analyzed. The meta-analysis showed that acupuncture had no significant long-term maintenance effect on the frequency or severity of hot flushes ( $p=0.29$ ;  $p=0.34$ ), but had a significant 3-month maintenance effect of ameliorating menopause symptoms at 3 months after treatment ended ( $p=0.001$ ). No adverse events were reported.

**Conclusions:** Acupuncture significantly alleviated menopause symptoms for at least 3 months, but not hot flushes. Breast cancer patients concerned about the adverse effects of hormone therapy could consider acupuncture as an alternative. Additional acupuncture at 3 months after the initial treatment course could be considered. A large-scale study may help to define the optimal guideline for this issue.

### ARTICLE HISTORY

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### KEYWORDS

Acupuncture; breast cancer; hot flushes; menopause symptom; systematic review

## Introduction

As hormone therapy and chemotherapy are crucial in breast cancer treatment, some patients suffer from treatment-related menopause syndrome, such as hot flushes, insomnia, anxiety, and other symptoms. The prevalence of menopause-related symptoms in breast cancer is as high as 60–70%<sup>1–3</sup>. Furthermore, one study indicated that women with breast cancer have vasomotor symptoms for much longer compared with the general population<sup>4</sup>. Although hot flushes and menopause symptoms are known to be related to estrogen withdrawal, physicians usually do not prescribe hormones since this population may already have taken hormone therapy such as tamoxifen or aromatase inhibitors, and estrogen supplements will interfere with the disease status and treatment. Therefore, many patients seek alternative therapy such as herbal medicine, yoga, or acupuncture for symptom relief or improvement in their quality of life<sup>5</sup>.

Acupuncture, a widely adopted, ancient medical technique, has proven efficacy in pain control<sup>6,7</sup>, improving neuro-related problems<sup>8,9</sup>, and ameliorating the level of anxiety and insomnia<sup>10</sup>, since it works through adjusting the neurohormone

axis<sup>11</sup>. Evidence shows that acupuncture can stimulate the secretion of endorphin and substance P, which contribute to pain relief<sup>12</sup>; acupuncture may also regulate autonomic nervous activity and thereby improve neurological or other symptoms such as insomnia and anxiety, based on the autonomic-humoral theory<sup>13,14</sup>. From the viewpoint of Traditional Chinese Medicine, acupuncture reconciles the imbalance between the Yin–Yang meridians and returns a harmonious state to the body. In the real world, acupuncture has been widely adopted in western countries based on its results, whatever the mechanism. Above all, patients with breast cancer tend to choose it as a safe treatment option with few side effects.

As a previous study advocated that acupuncture may ameliorate vasomotor symptoms by raising the serotonin level, which alters the temperature set point in the hypothalamus<sup>15</sup>, some clinicians prescribe acupuncture for breast cancer-related symptoms, including hot flushes, menopause-related symptoms, or even aromatase inhibitor-related musculoskeletal symptoms<sup>16</sup>. Although studies show a positive effect of acupuncture on menopause-related symptoms, including hot flushes<sup>17,18</sup>, opponents argue that the small

sample size of most studies prevents a definite conclusion<sup>19</sup>. While advocates claim that acupuncture is effective and safe, the placebo effect should be considered and some find that the effect is only short term<sup>20,21</sup>. Therefore, studies have been designed to evaluate whether the efficacy of acupuncture could be maintained after patients complete their course of acupuncture treatment. Most studies chose 3 and 6 months as an acceptable followed interval. Some studies even followed the participants for up to 2 years. So far, no systematic reviews have investigated how long the effect of acupuncture may persist, a question that will affect the schedule of an acupuncture course of treatment. Accordingly, this systematic review aims to investigate the relevant randomized clinical trials (RCTs), which had collected the relevant data, to determine whether the effect of acupuncture is maintained after its use to treat breast cancer-related hot flushes and menopause symptoms.

## Methods

### Data sources and search strategy

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement<sup>22,23</sup> to ensure transparent and complete reporting. The structured strategy was developed for seven databases – Embase, MEDLINE (Ovid), Cochrane Central Register of Controlled Trials (CENTRAL), Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus with Full Text, Web of Science Core Collection, Index to Taiwan Periodical Literature System, and the World Health Organization International Clinical Trials Registry Platform (ICTRP) – without language restrictions, from the inception date of each database until February 2019. The reference lists of relevant articles were also checked to identify additional studies.

The key concepts – hot flush, menopause symptoms, breast cancer, and acupuncture – used in the search included their 78 synonyms in total and controlled vocabulary (12 Emtree terms, 11 MeSH terms, etc.). We applied highly sensitive search filters to identify RCTs. The [supplementary online appendix 1](#) displays the full search strategy.

### Eligibility criteria

All eligible studies examined women with breast cancer and measured the frequency or severity of hot flushes and menopause symptoms. We enrolled studies which used real or electro-acupuncture as an experimental arm, excluding studies which adopted transcutaneous electrical nerve stimulation, ear acupressure, or stimulation of other acupoints. To achieve consistency, only studies that measured the frequency and severity of hot flushes and the Kupperman index (an international menopause rating scale)<sup>24</sup> in the follow-up phase were subjected to meta-analysis.

### Study and data extraction

A total of 612 potential articles were identified from the seven databases and additional sources. Two reviewers (T.-J.C. and C.-Y.L.) independently examined the study titles and abstracts of those articles which fulfilled the inclusion criteria, and the full texts of articles that met these criteria were obtained. Final decisions on inclusion were made by consensus after examination of the full manuscripts. In cases of duplicate publications, the most recent and complete versions were selected. For studies with only conference abstracts available, we contacted the authors to confirm the complete data (Figure 1).

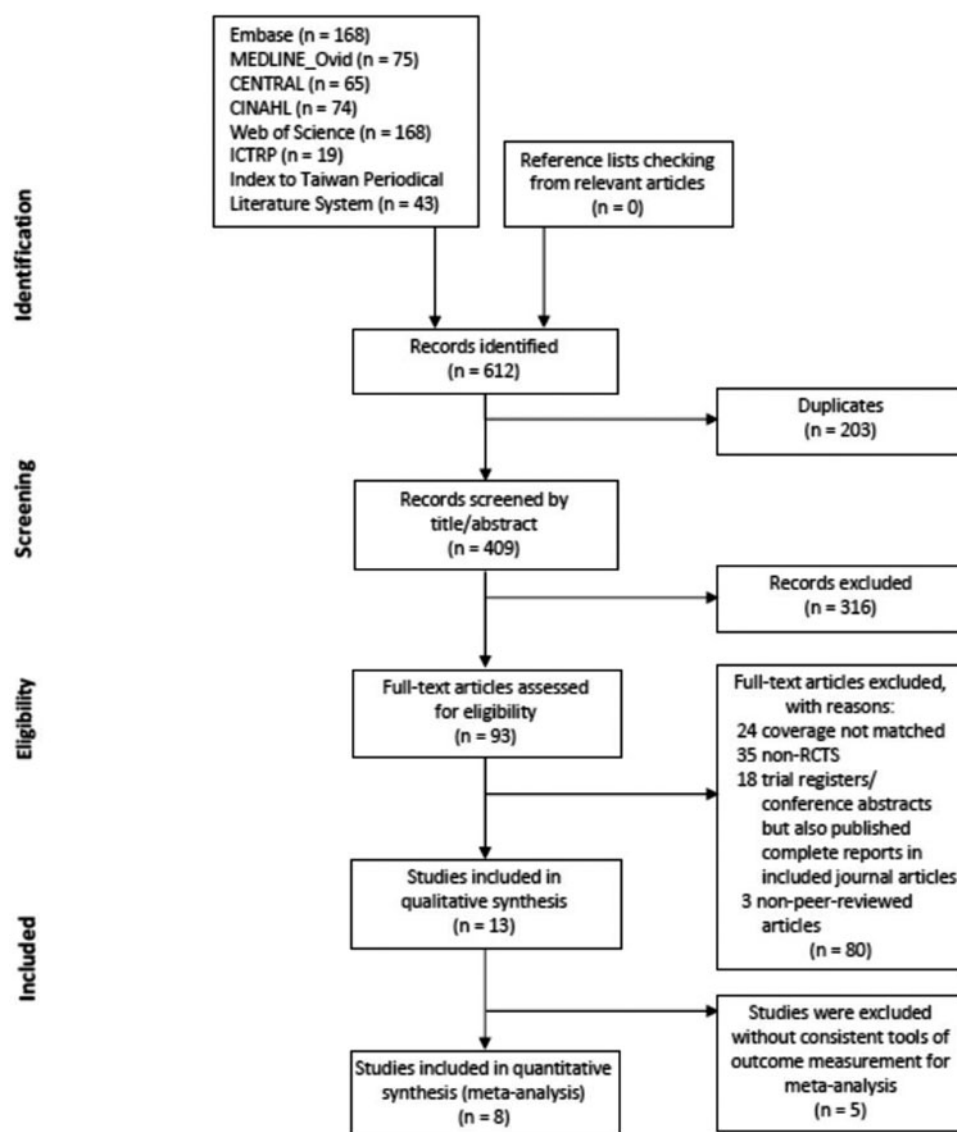
Thirteen studies were ultimately included. Four of these followed the effect of acupuncture at 3 months after the end of treatment (Bao *et al.*<sup>25</sup>; Hervik and Mjaland<sup>26</sup>; Bokmand and Flyger<sup>27</sup>; and Walker *et al.*<sup>28</sup>); one study follow the efficacy in terms of vasomotor symptoms at 18 weeks (Liljegren *et al.*<sup>21</sup>); seven studies checked the maintenance effect in 6-month intervals following treatment (Lesi *et al.*<sup>29</sup>; Hervik and Mjaland<sup>30</sup>; Walker *et al.*<sup>28</sup>; Deng *et al.*<sup>31</sup>; Nedstrand *et al.*<sup>32</sup>; Nedstrand *et al.*<sup>33</sup>; and Mao *et al.*<sup>34</sup>); and three studies evaluated the effect at 2 years after the end of treatment (Frisk *et al.*<sup>35</sup>; Frisk *et al.*<sup>36</sup>; and Hervik and Mjaland<sup>26</sup>).

### The risk of bias and quality assessment

The methodological quality of the including trials were examined following the *Cochrane Handbook for Systematic Reviews of Interventions*, version 5.1.0<sup>37</sup>. We used the six elements of the modified Jadad scale to assess the quality of the included studies: generation of randomization; allocation concealment; blinding of participants and personnel; blinding of outcome assessment; incomplete outcome data; and selective outcome reporting<sup>38,39</sup>. When trials met our criteria but the data were missing for meta-analysis, we also contacted the authors for additional methodological details.

### Data synthesis and statistical meta-analysis

To analyze the effects of acupuncture on the frequency and severity of hot flushes and menopausal symptoms in the period after treatment compared with baseline, we used the Cochrane Collaboration software Review Manager (RevMan) Version 5.2 for Windows (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark), estimating the weighted mean differences and 95% confidence intervals (CIs) from each study. For the weighted mean differences, we set a point estimation of zero to reflect 'no effect', and less than zero to reflect 'favored acupuncture stimulation'. The statistic heterogeneity was assessed using the chi-square test ( $p < 0.1$ ) and calculating the  $I^2$  statistic. We considered  $I^2 > 50\%$  an indication of significant heterogeneity across studies<sup>40</sup>. A random-effects model was adopted if significant heterogeneity was shown among trials. Otherwise, results were obtained from a fixed-effects model.



**Figure 1.** Study selection flowchart. CENTRAL: Cochrane Central Register of Controlled Trials; CINAHL: Cumulative Index to Nursing and Allied Health Literature; ICTRP: International Clinical Trials Registry Platform; RCT: randomized clinical trial.

## Results

### Study selection

Figure 1 illustrates the study selection flowchart. The searches led to the identification of 612 potentially relevant articles, from which 203 duplicates were removed. Based on the screening criteria, 316 additional titles/abstracts were excluded. After the full texts were assessed, 80 articles were excluded for the following reasons: 24 had non-matched coverage, 35 were non-RCTs, 18 were trial registries/conference abstracts that duplicated published complete reports in our included articles, and three were non-peer-reviewed articles. Finally, 13 unique studies were included in the systematic review, of which eight were included in the meta-analysis.

### Quality and descriptions of the included trials

Figure 2 shows the quality assessment of the 13 included RCTs using the modified Jadad scale<sup>38</sup>. All were of medium-

to-high quality. Figure 3 summarizes the risk of bias of the included RCTs. More than 80% of the included trials reach the criterion of low risk of bias.

Table 1 presents the characteristics of the 13 included perspective RCTs. These differed in their control arms, which included sham acupuncture (seven trials), self-care (one trial), hormone therapy (four trials), and applied relaxation (three trials). A total of 943 patients were enrolled in the systematic review; the average age of the participants was 56 years (range 51–60 years); the sample sizes ranged from 38 to 190 participants. To reduce bias, only studies using the Kupperman index to measure menopause symptoms are included in the meta-analysis. The meta-analysis of hot flashes included only those studies that measured frequency and severity.

### The maintenance effect of acupuncture on the frequency and the severity of hot flashes

The funnel plots of the effect of acupuncture on hot flashes (Figure 4(a)) and menopausal symptoms (Figure 4(b)) were

relatively symmetrical. Although the number of studies included in the meta-analysis was less than 10, the effect of each individual study was shown by its plotted position.

We observed significant between-study heterogeneity in the effect of acupuncture on hot flushes and menopausal symptoms ( $I^2 = 67%$ , and  $76%$ , respectively). For the four trials that reported data on the frequency of hot flushes in the

3 months after intervention, no significant reduction in the frequency of hot flushes was observed in subjects treated with acupuncture ( $-1.47$ ,  $95\% \text{ CI: } -4.18, 1.24$ ,  $p = 0.29$ ; Figure 5(a)) as compared with control subjects. For the two trials that reported data in the 3-month maintenance effect of the severity of hot flushes, no significant reduction in the severity of hot flushes was also observed in subjects treated with acupuncture ( $-6.08$ ,  $95\% \text{ CI: } -18.62, 6.47$ ,  $p = 0.34$ ; Figure 5(b)) as compared with control subjects in the period after treatment.

### The maintenance effect of acupuncture on menopausal symptoms

In the five trials that reported data on the 3-month maintenance effect of acupuncture on menopausal symptoms, as measured by the Kupperman index, a significant reduction in menopausal symptoms was observed in subjects treated with acupuncture ( $-3.47$ ,  $95\% \text{ CI: } -6.11, -0.84$ ,  $p = 0.01$ ; Figure 5(c)) as compared with control subjects in the period after treatment.

### Discussion

Acupuncture, although increasing in popularity, is still viewed as a kind of complementary therapy. Whether its effect is maintained over time is in doubt. Actually, patients report immediate symptom relief for pain-related problems, such as arthralgia, muscle strain, or anxiety; however, how long the effect can be maintained is still uncertain. Most acupuncture-related trials investigate the effect of acupuncture over the short term. In terms of hot flush and menopause symptoms after breast cancer treatment, most studies show that acupuncture is effective, yet the optimal length of treatment still lacks consensus. Because insurance may not cover acupuncture therapy or may limit its use, knowing how long acupuncture treatment will be effective is important in the design of cost-effective acupuncture treatment regimens. We

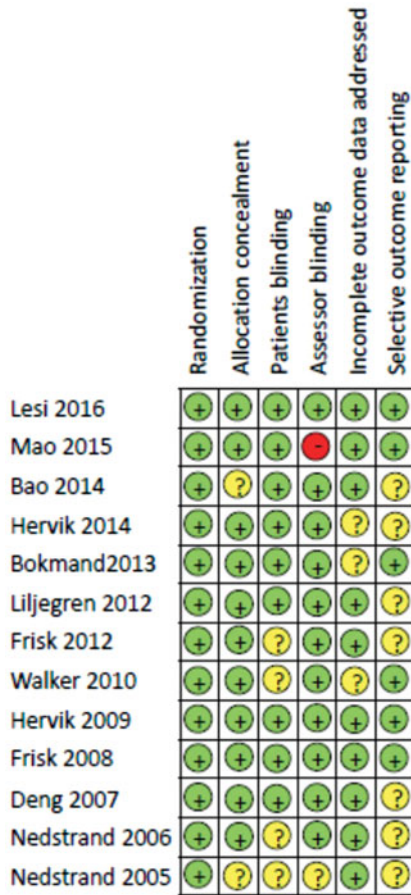


Figure 2. Risk of bias in the included trials.

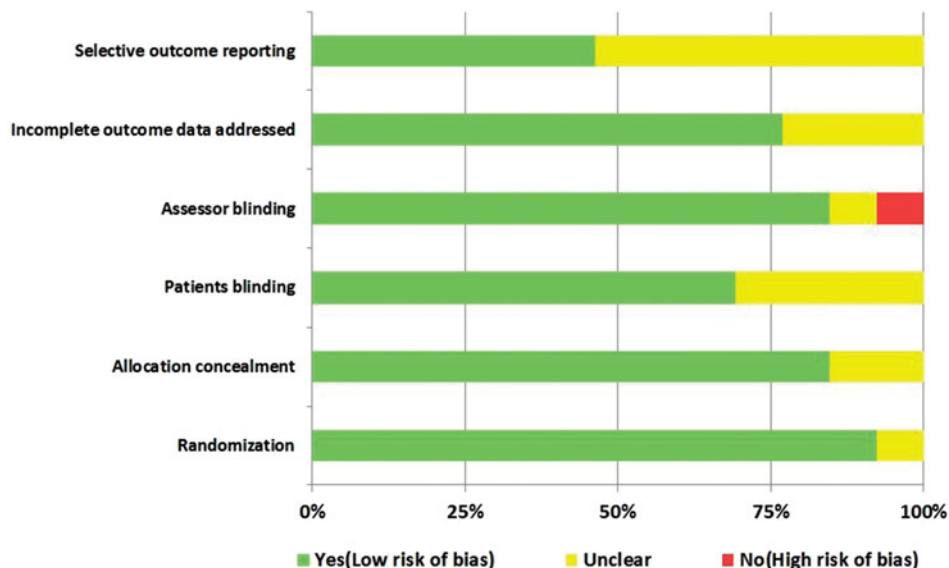


Figure 3. Summary risk of bias.

Table 1. Characteristics of the Included Randomized Controlled Trials.

Author <sup>[ref]</sup> , year	Sample	Study design exp:control	Acupuncture protocol	Primary acupoints	Measuring outcomes	Conclusion
Lesi <i>et al.</i> <sup>[29]</sup> , 2016	105:85	RA:SC	10 acupuncture sessions once per week; 12 weeks (following 6 months)	SP6, LI11, CV4	<ul style="list-style-type: none"> <li>Hot flush score</li> <li>Climacteric symptoms</li> <li>QoL</li> </ul>	Acupuncture significantly decreases hot flushes and climacteric syndrome, and improves QoL in following phase 6 months later
Mao <i>et al.</i> <sup>[34]</sup> , 2015	62:58	EA:Drug	Twice per week for 2 weeks, then once per week for 6 more weeks, for 8 weeks (following 6 months)	Not available	<ul style="list-style-type: none"> <li>Hot flush frequency</li> <li>Hot flush composite score (HFCS)</li> </ul>	In 6 months following treatment, hot flush reduction was greatest in the EA group, followed by sham acupuncture, placebo pill, and gabapentin
Bao <i>et al.</i> <sup>[25]</sup> , 2014	23:24	RA:SA	Weekly; for 8 weeks and 12 weeks	CV4, CV6, CV12; LI4; MH6; GB34; ST36; KI3; BL65	<ul style="list-style-type: none"> <li>NSABP</li> <li>CESD</li> <li>PSQI</li> <li>HADS</li> <li>Euro QoL</li> <li>HRFDI</li> </ul>	SA group has a significant change in flush frequency and severity, HFRDI, NSABP, and Euro QoL
Hervik and Mjaland <sup>[26]</sup> , 2014	33:28	RA:SA	A course of 15 acupuncture treatments for 10 weeks (following 3 months and 2 years post treatment)	Not available	<ul style="list-style-type: none"> <li>Kupperman index</li> <li>Plasma estradiol</li> </ul>	Acupuncture has a positive effect on health-related QoL in 3 months, yet loses significance 2 years later
Bokmand and Flyger <sup>[27]</sup> , 2013	31:29:34	RA:SA: no treatment	15-20 min weekly, for 12 weeks (following 3 months post treatment)	HC6, KI3, SP6, LR3	<ul style="list-style-type: none"> <li>VAS</li> <li>Estradiol level</li> </ul>	Significantly relieves hot flushes and sleep disturbance in 3 months post treatment; not correlated with estradiol level
Liljegren <i>et al.</i> <sup>[21]</sup> , 2012	42:42	RA:SA	20 min twice a week for 6 weeks (De-Qi required) (following in week 6 and week 18)	LI4, HT6, LR3, ST36, SP6, KI7	<ul style="list-style-type: none"> <li>Frequency</li> <li>Severity score</li> </ul>	Both true and CTRL reduce vasomotor symptoms in breast cancer patients treated with adjuvant tamoxifen
Frisk <i>et al.</i> <sup>[35]</sup> , 2012	27:18	RA:HR	As standards for Reporting Interventions in Clinical Trials of Acupuncture for 12 weeks (following 2 years)	Not available	<ul style="list-style-type: none"> <li>Hot flush scores</li> <li>PGWB</li> <li>WHO</li> <li>Men-QoL</li> <li>SF12</li> </ul>	Significant change of hot flushes in both HT and EA group at 12 months post treatment, the improvement level becomes less in month 24
Walker <i>et al.</i> <sup>[28]</sup> , 2010	25:25	RA:drug (non HR)	Twice-weekly for first 4 weeks, then weekly for 8 weeks (total 12 weeks) (following at post treatment 3, 6, 9, and 12-months)	BL23, KI3, SP6, Du14, 20, ST36, LI3, HE7	<ul style="list-style-type: none"> <li>Men-QoL</li> <li>SF12</li> </ul>	Both groups: significant decrease in hot flushes, depression and QoL. Hot flush frequency remained low between the 4-week and the 3-month visit for the acupuncture group
Hervik and Mjaland <sup>[30]</sup> , 2009	31:28	RA:SA	30 min twice-weekly for 5 weeks then weekly for following 5 weeks (total 10 weeks) (following 6 months)	LIV3, GB20, LU7, KI3, SP6, REN4, P7, LIV8	<ul style="list-style-type: none"> <li>Kupperman index</li> </ul>	Significantly improves flush frequency at 3-month follow up
Frisk <i>et al.</i> <sup>[36]</sup> , 2008	27:18	EA:HR	30 min twice-weekly for 2 weeks then weekly for 10 weeks (total 12 weeks) (following 2 years)	Not available	<ul style="list-style-type: none"> <li>Flush frequency</li> <li>Kupperman index</li> </ul>	Both groups noted significant change over flush frequency and depression, lasting up to 12 months
Deng <i>et al.</i> <sup>[31]</sup> , 2007	42:30	RA:SA	Twice-weekly for 4 weeks (following 6 months post treatment)	DU14, GB20, BL13, PC7, H6, K7, ST36, SP6	<ul style="list-style-type: none"> <li>Flush frequency</li> </ul>	TA has longer benefit in reducing hot flush than SA. The reduction in hot flush frequency persisted for up to 6 months after the completion of treatment
Nedstrand <i>et al.</i> <sup>[32]</sup> , 2006	19:19	RA:AR	30 min twice a week for 2 weeks then weekly for 10 weeks (De Qi required) total 12 weeks (following 6 months)	Not available	<ul style="list-style-type: none"> <li>VAS</li> <li>Mood scale</li> </ul>	In both groups, flushes per 24 hours (logbook) and climacteric symptoms (Kupperman index and VAS) decreased significantly between baseline and the 6-month follow-up
Nedstrand <i>et al.</i> <sup>[33]</sup> , 2005	19:19	RA:AR	30 min twice a week for 2 weeks then weekly for 10 weeks (De Qi required) (total 12 weeks) (following 6 months)	L15, 23, 32; HT7, SP6, 9, LR3, PC6, GV20	<ul style="list-style-type: none"> <li>Flush frequency</li> <li>Kupperman index</li> </ul>	Both groups have a significant change in flush frequency and Kupperman index after 6-month follow-up

AR, applied relaxation; EA, electroacupuncture; CESD, Center for Epidemiologic Studies Depression Scale; CTRL, control acupuncture; HADS, hospital anxiety and depression scale; HFRDI, hot flash-related daily interference scale; HR, hormone therapy; HT, hormone therapy; Men-QoL, menopause specific quality of life questionnaire; NSABP, National Surgical Adjuvant Breast and Bowel Project; PGWB, psychological and general well-being index; PSQI, Pittsburgh sleep quality index; QoL, quality of life; RA, real acupuncture; SA, sham acupuncture; SC, self-care; SF12, short form 12 health survey; TA, true acupuncture; VAS, visual analogue scale; WHO, World Health Organization.

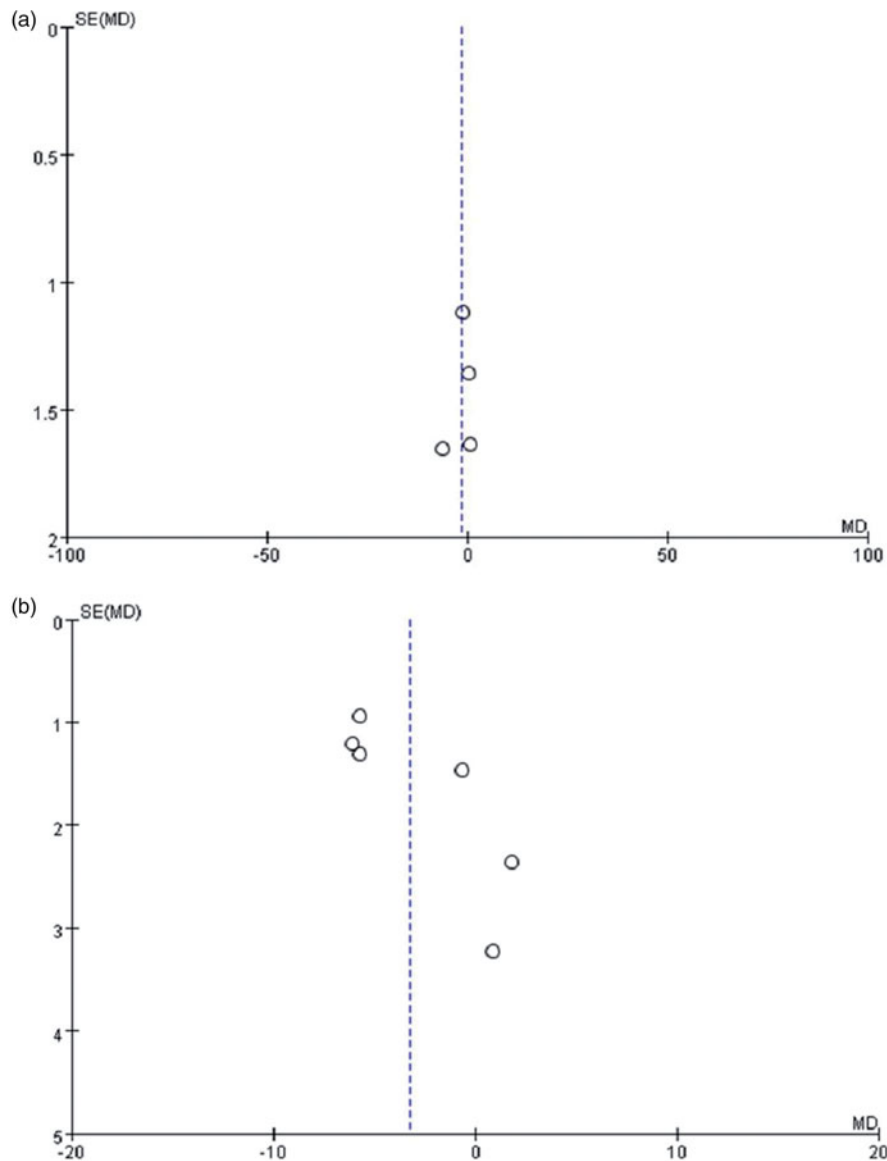


Figure 4. Funnel plot of comparison: (a) acupuncture for hot flushes; (b) acupuncture for menopausal symptoms. SE: standard error; MD, mean deviation.

therefore noted among the included trials that the follow-up time to test the treatment, namely, the post-acupuncture intervention, varied from 3 months to 2 years. The systematic review in our study collected data for 3 months after completing the acupuncture intervention for analysis. Although some trials provided data from 6 months following treatment, some patients are lost in following a much longer period and there are still other reasons affecting the results, such as that patients might adopt other methods to relieve their menopause symptoms after the study was completed or menopause symptoms would also be spontaneously resolved after a period of time of adapting to the menopause. Nevertheless, these results demonstrate that the effect of acupuncture indeed relieves menopause symptoms other than hot flushes for at least 3 months.

Due to the inconsistency of outcome measurements, only four and two studies analyzed the frequency and severity of hot flushes, and five studies included menopause symptoms

in the meta-analysis; the data available were from 3 months after the trial, which indicated that acupuncture had no maintenance effect on relieving hot flushes but a significant effect on ameliorating menopause-related symptoms except hot flush.

To further understand the issue, we note that the Kupperman index includes 11 elements (hot flushes, sweating, sleep disorders, irritability, depressed mood, dizziness, general weakness, joint pains, headaches, palpitation, and paresthesia). Hot flushes count for 4 of 21 points representative of menopause syndrome. Although acupuncture has an immediate effect, it has no maintenance effect on hot flushes; however, the systematic review did note a maintenance effect on menopause symptoms. As the included studies analyzed the Kupperman index instead of individual symptoms, we could not be sure which symptoms were improved most other than hot flushes. However, as the Kupperman index improved after 3 months of follow-up, the

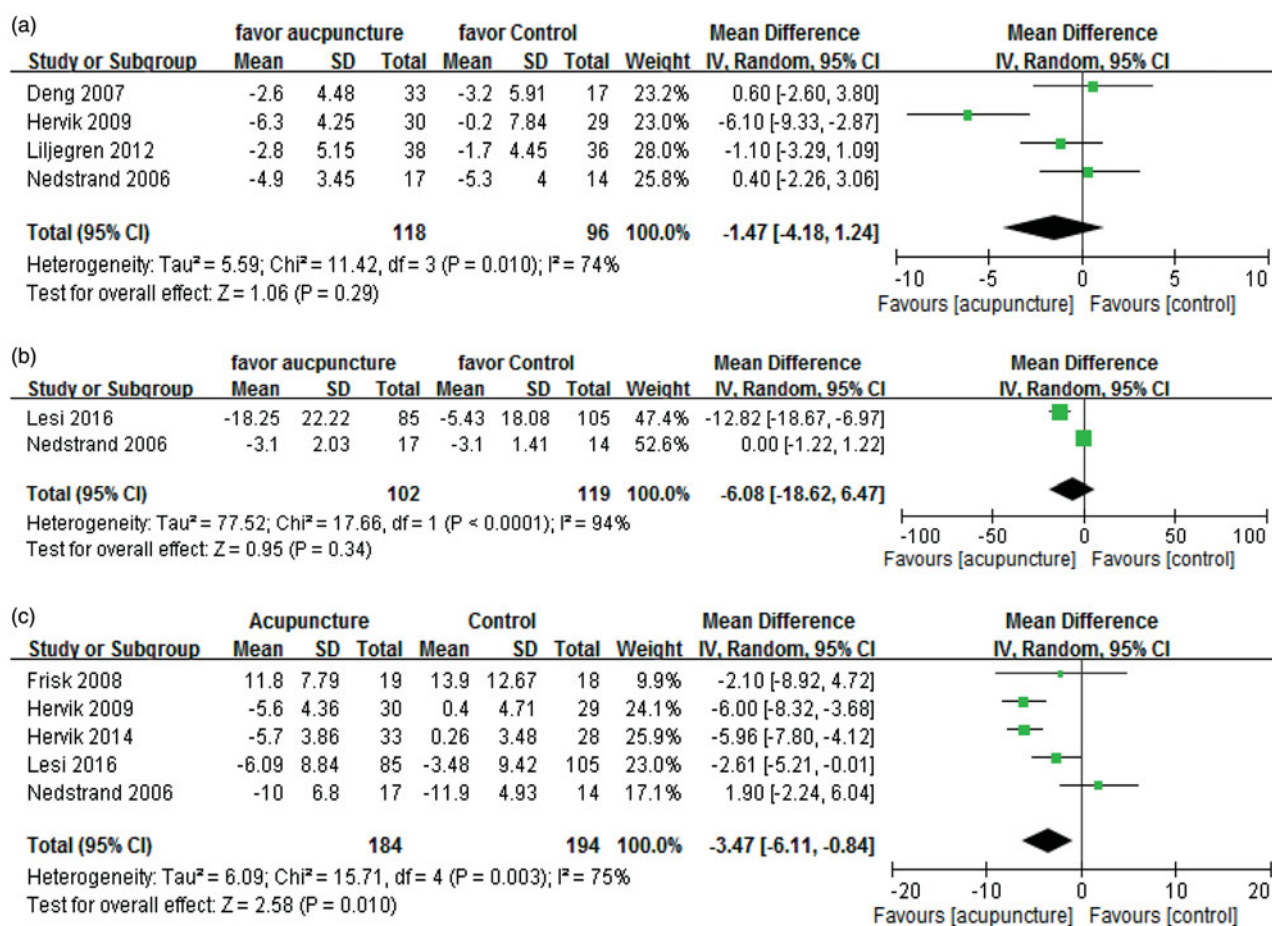


Figure 5. The 3-month maintenance effect of acupuncture on: (a) frequency of hot flushes in breast cancer; (b) severity of hot flushes in breast cancer; (c) menopause symptoms in breast cancer. CI: confidence interval; SD: standard deviation; IV, inverse variance.

results implied that acupuncture has an effect on menopause symptoms except for hot flushes, such as sleep disorder, arthralgia, headache, palpitation, and so forth, which in turn improves the quality of life in the menopause period. Actually, acupuncture has been proved to have efficacy in relieving arthralgia, sleep disorder, and autonomic dysfunction in previous studies<sup>10,16,41</sup>. The relevant mechanisms which have been reported include hormone regulation<sup>42</sup> or are related to the neurophysiologic response<sup>43,44</sup>. While it can be argued that acupuncture relieves hot flushes via increasing levels of  $\beta$ -endorphins and serotonin<sup>12,45</sup>, it may also act by reducing noradrenalin, which may affect the thermoregulatory set point and stabilize vasomotor activity<sup>46</sup>.

Whether acupuncture could alter the level of estrogen is unknown, but one of the included studies showed no change in serum estrogen levels after acupuncture<sup>27</sup>. However, opinions vary on this topic, with some arguing that acupuncture can stimulate estrogen production<sup>47</sup> whereas others have the opposite viewpoint<sup>48</sup>. The mechanism of hot flushes is complex, involving such elements as depletion of estrogen and narrowing of the thermoneutral zone, which result from activation of the sympathetic system<sup>49</sup>. Whether the neurohormone theory or the neurophysiologic theory plays a major role is unknown; yet, as acupuncture has no maintenance effect on hot flush control,

the effect on estrogen may be very small, a favorable element in breast cancer because therapies which change estrogen levels to relieve hot flushes are to be avoided in these patients. As many of these patients are under anti-estrogen or aromatase inhibitor treatment, modalities which trigger estrogen release should be used cautiously<sup>50</sup>.

On the other hand, the effect of acupuncture on the autonomic nervous system might be more profound, as it not only relieves pain (headache, joint pain<sup>51,52</sup>) but also stabilizes nervous or anxious mood<sup>53</sup>, leading to a more harmonious status<sup>13</sup>; as a result, an improvement in menopause symptoms was noted in the period after treatment ended<sup>54</sup>. From the viewpoint of Traditional Chinese Medicine, acupuncture can balance the Yin–Yang meridian and enhance the energy (Qi, 氣) which revitalizes the body<sup>55</sup>. This theory is compatible with the neurophysiologic feedback theory that acupuncture works by adjusting autonomic nervous activity<sup>56</sup> and thereafter alleviates many menopause or even physio-psychologic symptoms<sup>53,57</sup>. As shown by this meta-analysis, the maintenance effect of acupuncture on menopause symptoms may last 3 months or more, with some patients maintaining a stable status for up to 1 year. From this perspective, the most cost-effective acupuncture schedule may include a treatment-dense schedule for 2 months, followed by a maintenance treatment every 3 months thereafter.

To our knowledge, this is the first study to investigate the maintenance effect in acupuncture trials. The most chosen follow-up period was 6 months since it is difficult to collect information on patients in the months after they complete the acupuncture treatment course. Acupuncture has proven effects on migraine or low back pain lasting up to several months<sup>58,59</sup>, and a more rigorous study design will help clarify the optimal acupuncture treatment guideline for breast cancer patients<sup>60</sup>.

## Limitations

We noted some bias and limitations regarding the study. The first is that the measurement of hot flushes was not objective across trials, with researchers using self-reporting to evaluate the frequency and severity of hot flushes, rather than the more objective and reliable measurement of skin conductance or basal body temperature<sup>61,62</sup>. Artificial intelligence may contribute to increased objectivity, with new methods such as the digital hot flash phenomenology diary being used<sup>63</sup>. Second, an inherent bias lies in the lack of consensus in the acupoints chosen, the acupuncture schedule used, and the post-treatment time of observation. Moreover, the variety in control groups introduced some bias, especially with sham acupuncture, hormone therapy, and relaxation found to be effective in relieving menopause symptoms yet inferior to acupuncture in more than 80% of trials. Lastly, the sample was small compared with other multicenter trials, probably due to acupuncture being categorized as complementary and alternative therapy, rather than mainstream therapy. Yet, as more physicians are willing to let their patients adopt safe acupuncture, further large-scale trials should be encouraged.

## Conclusion

This is the first study to review the maintenance effect of acupuncture for breast cancer treatment-related menopause symptoms and hot flushes. The meta-analysis confirmed that patients who received acupuncture benefitted from a significant reduction in menopausal symptoms for at least 3 months, but no maintenance benefit in the frequency or severity of hot flushes after treatment. The at least 3-month maintenance effect demonstrates that the effect of acupuncture is not only a short-term or placebo effect. The mechanism is as yet unknown but, considering its safety relative to hormone therapy, acupuncture could be an alternative for breast cancer patients who suffer from menopause symptoms beyond hot flushes. Furthermore, a 3-month bolus therapy after the initial treatment schedule may well add cost-effective, long-term benefit. A large-scale study with a consistent acupuncture schedule design is expected to lead to consensus in developing an acupuncture treatment guideline.

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