

## Meta Analysis of Clinical Efficacy of Acupuncture Combined with Medicine in the Treatment of Climacteric Insomnia

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### Abstract

**Objective:** to evaluate the clinical efficacy of acupuncture combined with medicine in the treatment of climacteric insomnia by evidence-based method. **Methods:** the randomized clinical trials published from February 2009 to December 2020 were searched by two independent reviewers using PubMed, CNKI, Wanfang database and VIP database. The literatures were screened and the data were extracted according to the criteria. Meta analysis was performed to evaluate the clinical efficacy of acupuncture combined with medicine in the treatment of climacteric insomnia. Meta analysis was carried out by Revman5.3 software. **Results:** a total of 10 randomized controlled trials were included, including 967 patients with climacteric insomnia. Meta-analysis showed that, compared with the control group, the total effective rate of acupuncture combined with medicine in the treatment of climacteric insomnia was higher than that of the simple treatment group [RR=1.10,95%CI (1.01, 1.20), 0.03]. **Conclusion:** the systematic evaluation shows that the combination of acupuncture and medicine is effective in the treatment of climacteric insomnia, can significantly improve the climacteric sleep quality and related symptoms, and there are no serious adverse reactions. However, due to the small sample size and low quality of the study, more high-quality randomized controlled trials are needed to verify it.

### Keywords

Combination of Acupuncture and Medicine; Climacteric Insomnia; Randomized Controlled Trial; Meta Analysis.

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### 1. Introduction

Menopausal insomnia, also known as peri-menopausal insomnia, peri-menopausal sleep disorders, menopause is a transitional period before and after menopause, during which women's physiology and endocrine will change greatly in a short period of time[1]. Because it is always accompanied by hot flashes, sweating, depression, insomnia, osteoporosis and many other complex symptoms [2], profound impact. After women enter menopause, with the gradual decrease of estrogen secretion and the degradation of ovarian function, the decline of physical quality will be accelerated, which can easily lead to the imbalance of intravascular environment, leading to a series of unavoidable "diseases" both mentally and physically. These "diseases" also tend to aggravate night awakening and sleep interruption, thus greatly affecting the sleep quality of patients [3]. Epidemiology shows that mental and neurological symptoms are the most common diseases in climacteric women, of which the incidence of insomnia accounts for 70.6%. Therefore, effectively solving the problem of insomnia in peri-menopausal women has become the focus of this study [4]. At present, western medicine mostly uses sedation therapy, hormone replacement therapy (HRT) and later psychological regulation and antidepressant methods to treat climacteric insomnia. At present, both single use and combination

therapy have a more definite effect in clinic, but the drugs need to be taken persistently and have certain dependence. Once stopped, the recurrence rate is high and the side effects are serious [5]. Traditional Chinese medicine in the treatment of climacteric insomnia is based on "adjusting Zang-fu organs, qi, blood, yin and yang". It has the advantages of simple clinical application, easy operation, wide adaptation, remarkable curative effect and less adverse reactions [6]. At present, a large number of studies have confirmed that the combination of acupuncture and medicine in the treatment of climacteric insomnia is more effective and safer than western medicine, and it can also avoid patients' dependence on western medicine and have more irreversible side effects. This study included a randomized controlled trial (RCT) of acupuncture combined with traditional Chinese medicine and western medicine or acupuncture alone in the treatment of climacteric insomnia. Revman5.3 analysis provided by Cochrane collaboration network was used to include the heterogeneity of the data, and a systematic review and meta-analysis were conducted to evaluate the clinical efficacy and safety of acupuncture combined with medicine in the treatment of climacteric insomnia, and to provide evidence-based medicine basis for the clinical rationality of acupuncture combined with medicine in the treatment of climacteric insomnia.

## **2. Materials and Methods**

### **2.1 Literature Retrieval Strategy**

We searched CNKI, WanFangData, VIP, PubMed and other databases, using a combination of subject terms, keywords, text words and synonyms. The Chinese keywords are "acupuncture", "traditional Chinese medicine", "menopause", "peri-menopausal insomnia", "menopausal insomnia", "perimenopausal insomnia", "insomnia" and "insomnia". The English search words are "combination of acupuncture and medicine", "menopause insomnia", "insomnia" and "perimenopausal insomnia". The time limit is from February 2009 to December 2020.

### **2.2 Inclusion Criteria**

#### **1.2.1 Research Type**

There are no language restrictions in the randomized controlled trials (RCTs) and semi-randomized controlled trials (CCTs) published at home and abroad about the combination of acupuncture and medicine in the treatment of climacteric insomnia.

#### **1.2.2 Research Object**

The diagnostic criteria of patients with climacteric insomnia are in accordance with the Chinese Classification and Diagnostic criteria of Mental Disorders (3rd Edition) and the Diagnostic and Therapeutic criteria of traditional Chinese Medicine (TCM), or the American Classification system of Mental Disorders (4th Edition) (DSM-4), or the guiding principles of Clinical Research of New drugs of traditional Chinese Medicine, or other diagnostic criteria that can be defined as climacteric insomnia at home and abroad, and secondary insomnia can be excluded.

### **2.3 Exclusion Criteria**

1) review articles, case reports, expert experience, mechanism exposition and non-human studies; 2) literatures that can not extract data; 3) subjects of study are climacteric insomnia with other cardiovascular diseases or serious complications; 4) clinical diagnosis is not clear (non-climacteric insomnia); 5) intervention measures are given acupuncture combined with traditional Chinese and western medicine treatment in the treatment group.

### **2.4 Intervention Measures**

The experimental group was treated with simple acupuncture combined with traditional Chinese medicine (acupuncture manipulation, location, acupoints are not limited), while the control group was treated with simple acupuncture or simple traditional Chinese and western medicine.

## 2.5 Outcome Index

1) total clinical effective rate; 2) Pittsburgh Sleep quality Index (Pittsburgh Sleep Quality Index,PSQI) score; 3) TCM syndrome score; 4) 4SPIEGEL scale,; 5) Kuppermen scale; 6) determination of serum sex hormones; 7) such as E2, FSH, LH and other serum endocrine hormones; 8) clinical symptom improvement score.

## 2.6 Literature Screening and Data Extraction

In the study, two reviewers were selected to independently screen the search results, and identify possible relevant studies according to their titles and abstracts. Data extraction was performed on Excel and Microsoft spreadsheets to extract all factors that might affect the efficacy evaluation, including author, journal source, publication time, course of disease, intervention measures, and cross-check, and differences were resolved through negotiation or by third-party reviewers.

## 2.7 Quality Evaluation Included in the Study

The risk of bias was assessed according to the guidelines for Cochrane randomized controlled trials. There are seven main areas of evaluation: 1) hidden sequence generation and distribution (selection bias); 2) blindness of participants and personnel (performance bias); 3) blindness of result evaluation (detection bias); 4) incomplete result data (loss deviation); 5) selective result reports (reporting deviations); 6) and other potential sources of bias. According to established standards, the risk of deviation is rated as low, unclear or high.

## 2.8 Statistical Analysis

The random effect model of Revman software (version 5.3; CochraneCollaboration of London, UK) was used for meta-analysis. Forest map was used to represent the effect and 95% confidence interval (CI), RR was used to represent binary variables, SMD was used to represent continuous variables, and I2 index was used to evaluate statistical heterogeneity. Although funnel charts may be a useful tool for investigating effects of small studies in Meta analysis, their ability to detect such effects is limited when there are few studies. Therefore, because we included a small number of studies in the experimental group, there was no funnel chart analysis.

## 3. Results

### 3.1 Literature Screening Process and Results

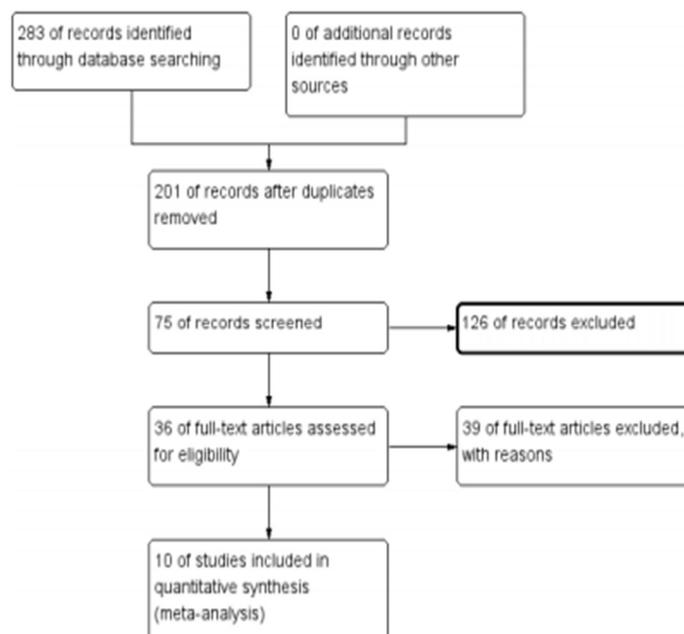


Figure 1. Document selection flow chart

A total of 283 related literatures were collected based on keyword search, including 258 in Chinese and 25 in English. After excluding repetitive articles, two reviewers read the topics and abstracts independently. Finally, according to the inclusion and exclusion criteria, 10 RCT were selected, including 967 patients with climacteric insomnia (first, 82 repetitive articles were excluded after reading abstracts, 126 non-RCT and CCT articles were excluded, 39 non-acupuncture and medicine therapy articles were excluded after reading the full text, and finally 10 articles were included. Figure 1 illustrates in detail the flow chart and exclusion reasons of the research selection process, and the main features of the study are included in Table 1.

**Table 1.** table of basic characteristics of the inclusion study

Included in the study	Stochastic method	Course of disease / month	Sample size / example	Intervention measures	Outcome index
	Experimental group / control group				
Chen Xia 2009	Random number table method	one	30/32/32	Traditional Chinese medicine + Acupuncture/Traditional Chinese medicine/Alprazolam	①
Wang Tiejun 2013	Random number table method	one	30	The traditional Chinese medicine Chai Gao Tang is flavored+Abdominal acupuncture/Body acupuncture group	①②
Wang Caixia 2014	Random number table method	one	32/30/32	Acupuncture and medicine/Traditional Chinese medicine/Acupuncture	①②
Tan Keping 2015	Unclear	one	63/63	Zishen Tiaogan decoction+Acupuncture/Acupuncture	①④
Zhao Jingjing 2016	Random number table method	one	32/32/32	Self-made prescription+The method of acupuncture is repeated in the classics/The method of acupuncture is repeated in the classics/Self-made prescription	① ② ③ ⑥
Du Jinli 2017	Random number table method	one	42/41/41/41	Modified Wumei Pill+Jin three needles/Ezzolam tablets/Jin's three-needle therapy/Modified Wumei Pill	① ② ⑤ ⑥
Yang Xiaolin 2017	Unclear	sixteen	46/46	Addition and subtraction of Yueju Pill+Shallow needle/Alprazolam	①
Guan Kevin 2018	Random drawing method	one	50/50	Self-made anshen decoction+Acupuncture/Estazolam tablets	①
Liu Huijun 2019	Random number table method	one	25/25	Addition and subtraction of Suanzaoren decoction+Acupuncture/Alprazolam	①⑤
Ye Meihua 2020	Simple randomization method	one	45/45	Traditional Chinese medicine+The acupuncture method of transferring to the governor/Traditional Chinese medicine	①②③

Note: ① total effective rate ②PSQI total score ③TCM syndrome score ④SPIEGEL scale⑤Kuppermen scale ⑥serum sex hormones

### 3.2 Results of Literature Bias Risk Assessment the Lack of Data Was not Described

in the included literature. most randomized controlled trials were not clear about the risk of selection and reporting bias, and all randomized controlled trials were rated as having a high risk of bias in areas where participants and people blinded. Based on the Cochrane bias risk assessment tool, we assessed the quality of the included literature, did not rule out the possibility of other biases, and published the bias risk in the included literature (see figure 2).

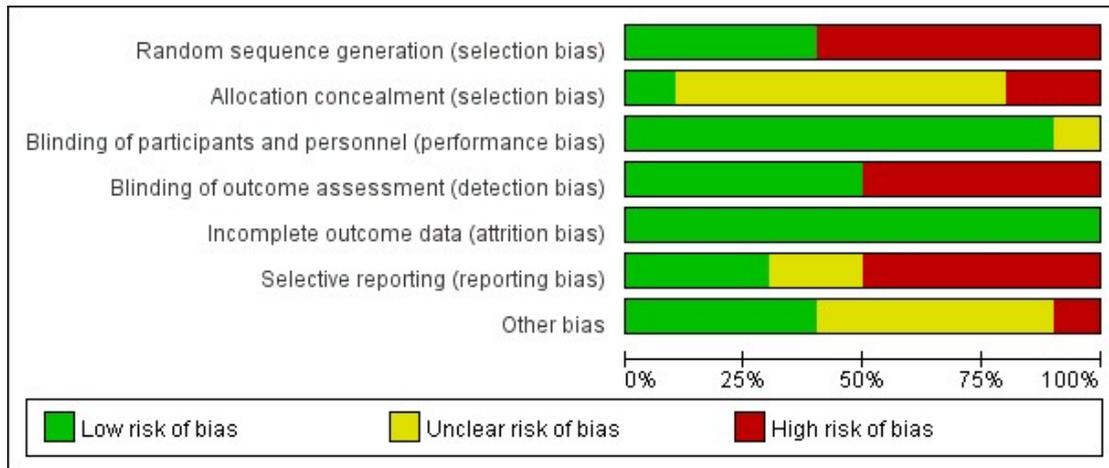


Figure 2. included in the bias risk assessment form of the study

### 3.3 The Results of Meta Analysis

#### 3.3.1 Efficiency Result Analysis

The nine randomized controlled trials included in this meta-analysis provide sufficient data for the evaluation of the total clinical effective rate of acupuncture combined with medicine in the treatment of climacteric insomnia. Compared with the control group, acupuncture combined with medicine is effective in the treatment of climacteric insomnia. The results showed that there was statistical heterogeneity among the studies [RR=1.10,95%CI (1.01), 0.03], Meta analysis showed that the difference was statistically significant. See figure 3.

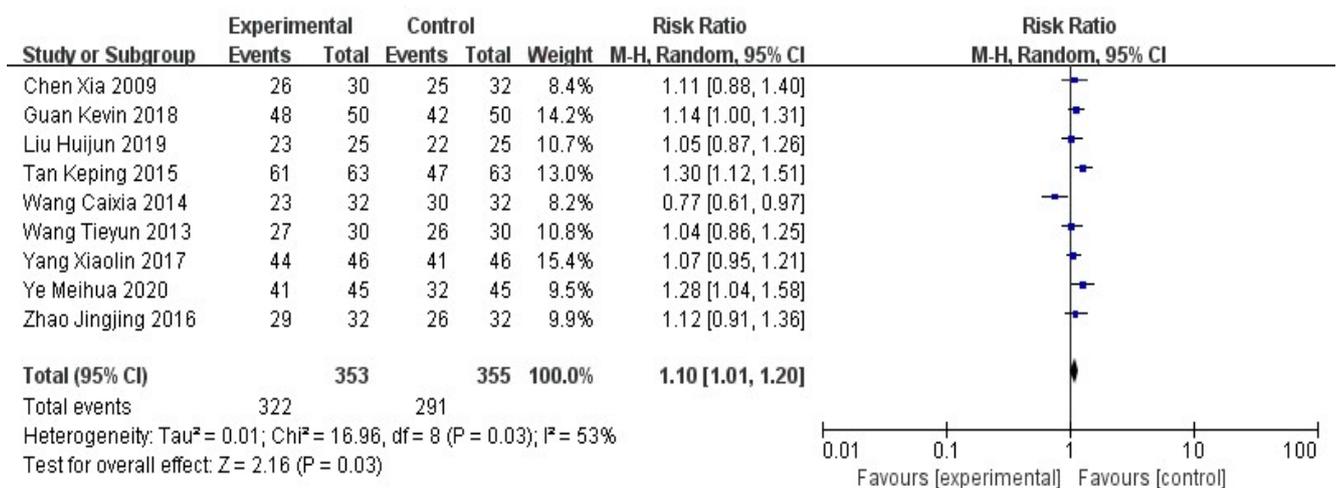
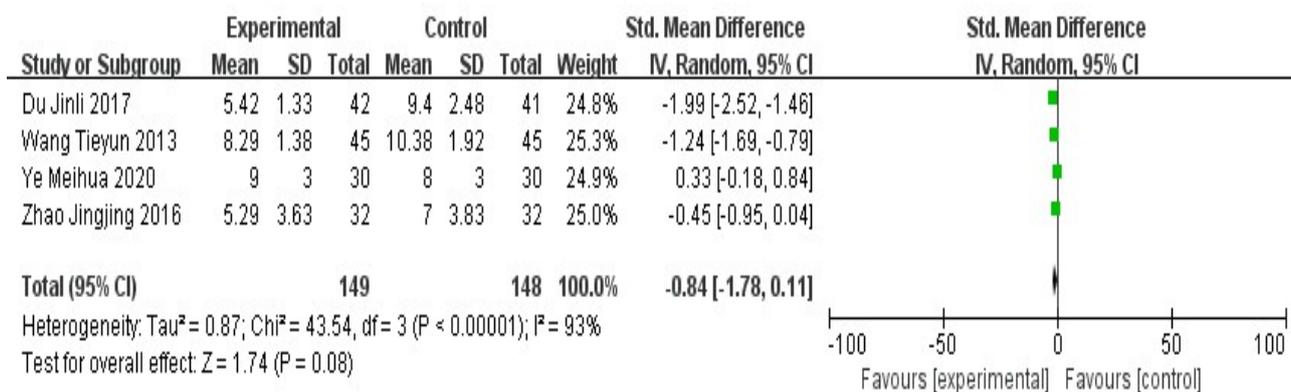


Figure 3. Meta analysis of the comparison of clinical effective rate between the acupuncture-medicine combination group and the control group after treatment.

#### 3.3.2 Comparison of PSQI Total Score

The four randomized controlled trials included in this meta-analysis provide sufficient data for the total PSQI score of acupuncture combined with medicine in the treatment of climacteric insomnia.

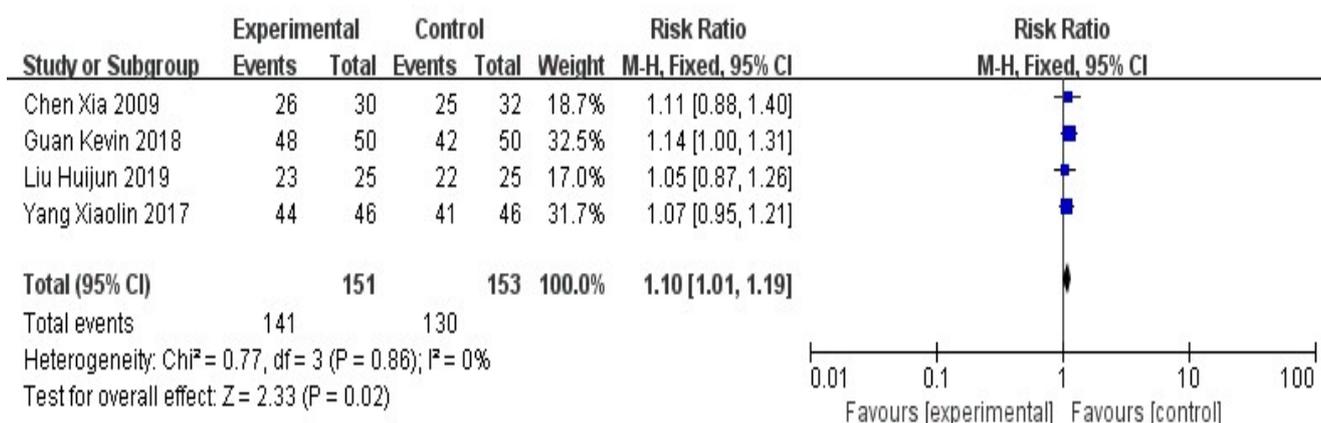
Compared with the control group, the use of acupuncture combined with medicine can significantly reduce the PSQI score and improve the sleep quality of patients with climacteric insomnia. The results showed that there was no statistical heterogeneity among the studies [SMD=-0.84,95%CI [- 0.78, 0.11], P < 0.00001]. Meta analysis showed that the difference was statistically significant. See figure 4.



**Figure 4.** comparison of the total PSQI score of the clinical effective rate between the acupuncture-medicine combination group and the control group after treatment.

### 3.3.3 Acupuncture Combined with Medicine Compared with Simple Western Medicine Group

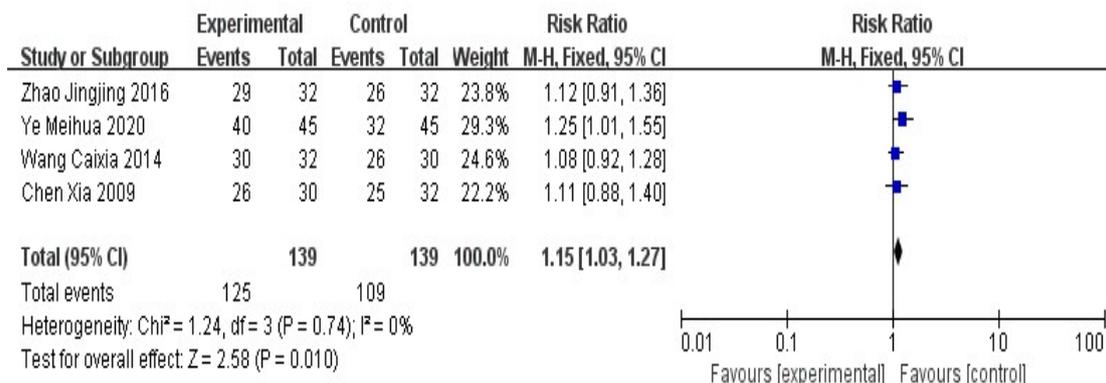
In this meta-analysis, the control group of 4 experiments used simple western medicine to treat climacteric insomnia, and there was no statistical heterogeneity among the results of each study (I<sup>2</sup> score 0.86). Fixed effect model was used for meta analysis. The comprehensive results showed that the effective rate of acupuncture combined with medicine in the treatment of climacteric insomnia was better than that of western medicine alone, [RR=1.10,95%CI (1.01, 1.19), P=0.02]. The difference was statistically significant. See figure 5.



**Figure 5.** Meta analysis of total effective rate between acupuncture-medicine group and simple western medicine group after treatment

### 3.3.4 Acupuncture Combined with Medicine Compared with Simple Traditional Chinese Medicine Group

In this meta-analysis, the control group of 4 experiments used simple traditional Chinese medicine for menopausal insomnia, and the results showed that there was no statistical heterogeneity among the results of each study (I<sup>2</sup> score 0.74); [RR=1.15,95%CI (1.03, 1.27), P=0.010], the difference was statistically significant. See figure 6.



**Figure 6.** Meta analysis of total effective rate between acupuncture-medicine group and simple traditional Chinese medicine group after treatment

### 3.3.5 Adverse Reaction

Of the 10 articles included, only 3 reported adverse reactions, and there were no adverse reactions in the experimental group. Among them, 26 cases in the control group had drowsiness and dizziness, 6 cases had mild mental tension before acupuncture, and 8 cases had gastrointestinal discomfort, but the follow-up statistical results were not affected, and the specific conditions of adverse reactions were not mentioned in the other 2 articles.

## 4. Discuss

In this study, by analyzing the total effective rate, PSQI sleep quality index and the effective rate of combined treatment compared with simple treatment, Meta analysis was used to systematically evaluate the clinical efficacy and safety of acupuncture combined with medicine in the treatment of climacteric insomnia. The results showed that the curative effect of acupuncture combined with medicine in the treatment of climacteric insomnia was better than that of simple treatment group. The total effective rate and reducing PSQI score of climacteric insomnia in acupuncture combined with medicine group were better than those of simple treatment group. Long-term treatment combined with acupuncture and medicine could significantly improve the sleep quality of patients with less side effects. Among them, acupuncture treatment is to stimulate the meridians and acupoints of the human body with needles to improve sleep by regulating the secretion of estrogen in the human body [7]. Acupuncture can also regulate the function of multiple organs, reconcile the whole body qi and blood, balance yin and yang, and achieve the purpose of treating insomnia[8]. Although the conventional acupuncture method is simple, safe and effective, and has a wide range of clinical application, the related clinical research and high-quality research are still relatively few [9]. In addition, a large number of studies have shown that oral Chinese medicine can significantly reduce the clinical symptoms of climacteric insomnia [10]. To sum up, the combination of acupuncture and medicine in the treatment of climacteric insomnia is a perfect combination for the benefit of the public and society, but considering the limitations of our systematic review and the low quality of the existing evidence, more high-quality randomized controlled trials are needed to confirm this discovery. In addition, it is still necessary to establish a more effective and low-recurrence evidence-based treatment program to provide more reliable evidence for the efficacy and safety of acupuncture combined with traditional Chinese medicine in the treatment of climacteric insomnia.

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