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Review Article

Acupuncture-related therapies for protracted opioid abstinence syndrome:A systematic review and meta-analysis

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ABSTRACT

Background: An increasing amount of clinical evidence of acupuncture's effect on protracted opioid abstinence syndrome (POAS) has emerged in recent years. The aim of this study was to evaluating the evidence of efficacy of acupuncture for POAS. clinical and scientific research work.

Methods: Four English-language databases (PubMed, Medline, Embase, Cochrane Libraries) and three Chinese-language databases (CNKI, WanFang and VIP Libraries) were searched, with coverage from database inception to March 31, 2022. Randomized clinical trials (RCTs) evaluating the effects of acupuncture and acupuncture-related therapies for prophylaxis or treatment of POAS were included. Data were screened and extracted independently according to pre-set tabular formats. RCT quality was assessed using risk of bias tool in the Cochrane Collaboration. The primary outcome was opiate withdrawal scale. The secondary outcomes are depression, anxiety for assessing protracted symptoms. The scores on the above scales are proportional to the severity of the symptoms.

Results: Twenty-eight trials met the inclusion criteria and provided data for the meta-analysis. A total of only 3 studies (11%) were judged to be low-risk overall due to various biases in them. Acupuncture-related therapy showed statistical differences in improving protracted withdrawal symptom scores compared with sham acupuncture (5 studies, Standard mean difference (SMD), -1.85, 95% CI [-3.21, -0.50], $P = 0.007$), western medicine(7 studies, SMD, -0.72, 95% CI [-1.22, -0.21], $P = 0.005$)and no treatment(3 studies, SMD,-2.26, 95% CI [-3.82, -0.69], $P = 0.005$)with high heterogeneity.

Conclusions: Acupuncture maybe safe and effective in relieving POAS individuals' protracted withdrawal symptoms. However, the results of our review should be interpreted with caution because of the high risk of bias of the included trials.

Study registration: The protocol of this review has been registered at PROSPERO (CRD42022335505).

1. Introduction

According to the United Nations Office on Drugs and Crime World Drug Report 2022, about 300 million people worldwide will have used illicit drugs in 2021, a 22% increase from 2010. Opioids are the most widely used type of these drugs.[1] Opioid addiction has become a major public health and social problem plaguing human health and social development. Treatment for opioid-dependent patients is divided into three stages: detoxification, rehabilitation and return to society.[2] Addressing the high relapse rate after detoxification is the focus (and challenge) of current addiction treatment.[3] Protracted opioid abstinence syndrome (POAS) is a syndrome characterized by various long-term physical symptoms and mental disorders in opioid addicts after detoxification treatment.[4] These symptoms and disorders are an important cause of drug relapse.[5]

Opioid therapy is currently the classic detoxification therapy for POAS. However, the side effects of opioid therapy can emerge when dosage is reduced or discontinued, and patients are prone to sleep dis-

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turbance, depression, anxiety, pain, diarrhea and opioid cravings.[6,7] As such, there is an urgent need for a way to eradicate the series of protracted syndromes after detoxification.

Since the introduction of acupuncture for drug addiction in the 1970s, this therapy has spread throughout the world. The safety, minimal side effects, efficaciousness and other advantages have attracted the attention of addiction researchers.[8,9] Upon continuous in-depth research by many scholars, it has been found that not only is acupuncture effective for post-withdrawal symptoms, but also that transcutaneous electrical acupoint stimulation (TEAS), auricular acupressure, and warm moxibustion therapy have also produced promising experimental and clinical results.[10,11] This has confirmed that acupuncture-related therapies can reduce symptoms such as depression and anxiety in patients with opioid dependence, and effectively reduce patients' methadone doses.[12] However, few studies have focused on the POAS population, or paid sufficient attention to the heterogeneity of types of acupuncture. The improvement for specific withdrawal symptoms has also been overlooked.

In view of the increasing number of randomized controlled trials of acupuncture-related POAS treatment, yet the lack of a systematic study to integrate the data and the ensuing need for critical evaluation, we conducted a systematic review and meta-analysis of the available evidence. Our aim was to inform future clinical practice and scientific research.

2. Methods

This systematic review was registered in PROSPERO (CRD42022335505). This study was conducted according to the *Cochrane Handbook for Systematic Reviews of Interventions*.[13]

2.1. Data sources and search strategy

Four English-language databases (PubMed, Medline (via PubMed), Embase, Cochrane Libraries) and three Chinese-language databases (CNKI, Wanfang and VIP Libraries) were searched for RCTs published from database inception through March 31, 2022. To search more comprehensively, we queried ClinicalTrials.gov and China Clinical Trials Registry two major clinical trial databases; reference lists of included papers were also manually screened. The search was limited to publications in English and Chinese. The search strategy consisted of three components: clinical condition (opioid/heroin/morphine addiction, protracted withdrawal symptoms/syndrome), intervention(acupuncture-related therapy) and study type (RCTs). The detailed search strategy is shown in Supplement 1.

2.2. Study selection

Studies: We comprehensively examined RCTs evaluating acupuncture-related therapies for POAS. We excluded non-randomized uncontrolled trials, case reports or case series, systematic reviews and meta-analyses, comments or letters, conference papers, dissertations, technological achievements, scientific research projects, cell culture or animal experiments, as well as studies published as abstracts only and certain cross-sectional study design trial types.

Participants: Study participants were adults (≥18 years old) with POAS who met any of the diagnostic criteria, such as the Diagnostic Criteria for Opioid Dependence in the *International Classification of Diseases, 10th Edition* (ICD-10) subcategory of mental and behavioural disorders developed by the World Health Organization,[14] and several versions of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM) criteria for opiate dependence.[15,16] In addition, the diagnostic criteria for mental disorders caused by substance addiction in the *Chinese Classification and Diagnosis of Mental Disorders* (CCMD) are applied.[17] All patients had completed mandatory detoxification treatment (and generally had been detoxified for at least a month). There were no restrictions on participants' sex or race. Pregnant women and others with significant medical diseases were excluded, dependent on their actual clinical conditions.

Interventions: All types of acupuncture therapies are included in this study. According to the World Health Organization's definition, acupuncture includes literally piercing the corresponding acupuncture points with needles, and also the application of other types of stimulation to the acupuncture points, such as manual acupuncture(MA), electroacupuncture (EA), ear/auricular acupuncture (AA), auricular pressure, fire needling, scalp acupuncture(SA), laser acupuncture, transcutaneous electrical nerve stimulation (TENS), elongated needle, bee-sting therapy, catgut-embedding therapy, warming needle and acupoint injection.

The control group received either no treatment or a therapy other than acupuncture, such as sham acupuncture, conventional pharmacotherapy, psychosocial interventions, or other conventional interventions.

Outcome Measures: The primary outcome entails measuring persistent withdrawal symptoms' intensity, and generally incorporates the Heroin Persistent Withdrawal Symptom Scale.[18] Secondary outcomes were ratings of severity of anxiety, depression, sleep disturbance, cravings and other associated withdrawal symptoms. They generally used the HAMD/HAMA or SAD/SDS, or other tools suitable for the assessment of protracted symptoms, Pittsburgh Sleep Quality Index (PSQI), and Visual Analogue Scale/Score (VAS).

The exclusion criteria included duplicate publication, studies for which the full text was unavailable, or for which basic data from the study were not available after contacting the original authors.

2.3. Data extraction

All studies retrieved through the online database were imported into NoteExpress (software developed by the Guangzhou University of Chinese Medicine Library). Two reviewers (L. Ding and C. Li) independently identified studies by title and abstract according to the included and excluded criteria. Afterwards, the two authors independently screened through the full texts of the involved studies and cross-checked the results. The two reviewers (C. Chen and J. Zhan) extracted the characteristics of each eligible study (first author, year of publication, country, type of study, sample size, history of drug use, outcome indicators, Jadad score, and detailed descriptions of the intervention) independently according to predesigned forms. Any disagreements during screening or data extraction were resolved by discussion, or by a third investigator (L. M. L.) arbitrating the final decision when necessary.

2.4. Methodological quality assessment

Two of the authors (L. Ding and C. Chen) independently appraised the risk of bias for each included study with the Cochrane risk of bias assessment tool.[19] Any disagreements were resolved by discussion and consensus with another reviewer (L. M. L.). The assessment of risk of bias included six parts: selection bias (random sequence generation, allocation concealment), blinding bias (blinding of participants and personnel), detection bias (blinding of outcome assessment), attrition bias (incomplete outcome data), reporting bias (selective reporting) and other bias. We considered funding sources, baseline imbalances, and other potential study design problems as other sources of bias. Each part in the assessment was judged as either low, unclear, or high risk of bias. When more than half of the evaluation entries were judged to be high-risk, the study could be judged as being low-quality overall.

2.5. Data synthesis and analysis

Data from included studies were analyzed by RevMan v. 5.4 (The Nordic Cochrane centre The Cochrane Collaboration, Copenhagen). Considering that AA and other acupuncture-related therapies are based

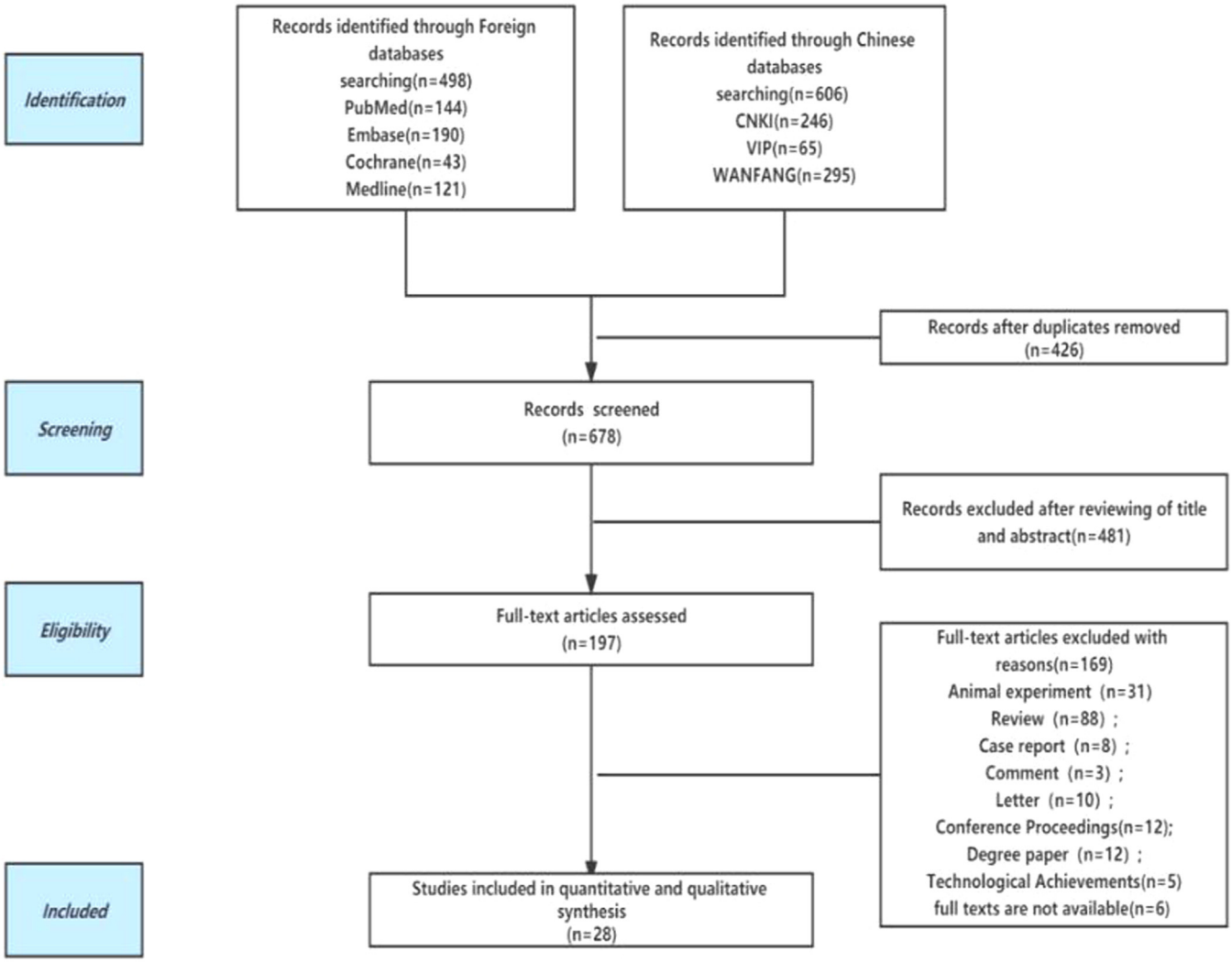

Fig. 1. The flow diagram.

on different treatment theories, we conducted a meta-analysis of auricular acupuncture data separately. For continuous variables, Mean Difference (MD) or Standard Mean Difference (SMD) was used for analysis. If data are reported at multiple points in time, the data reported immediately after the intervention is used. When the outcome indicator is measured by different assessment tools, the data is analyzed by SMD with 95% CIs; if the same assessment tool was used to measure the outcome, the data is analyzed by MD with 95% CIs.[13]

χ^2 test was used to analyze the heterogeneity among the included study results, and I^2 was used to quantitatively judge the heterogeneity.

Subgroup sensitivity analysis was used to explore potential sources of heterogeneity if the data were sufficient. Our initial planned subgroup analysis plan was based on different acupuncture methods.

A funnel plot was used to assess publication bias when the included study in one meta-analysis was more than 10.[13]

We also performed sensitivity analyses of the studies to test the robustness of their findings. If there was a significant difference in the studies' risk of bias assessment, we would perform an exclusion analysis for these studies.

3. Results

3.1. Quantity of studies available

A total of 1104 potential studies were identified through the database search, from which 427 duplicates were removed and 472 were excluded after reading the titles and abstracts because they did not meet the inclusion criteria. An additional 169 studies were excluded due to not meeting the article type or unavailability of the full text. The remaining 28 studies were included in the systematic review and qualitative synthesis (Fig. 1).

3.2. Characteristics of the included studies

These 28 studies involved 2463 patients with POAS, 1353 in the trial group and 1110 in the control group. The sample size for each group of studies ranged from 20 to 121. Twenty-seven of the studies included in the meta-analysis were conducted in China and one was conducted in the United Kingdom. Among the studies that met the inclusion and exclusion criteria, the vast majority of studies had subjects diagnosed with POAS by DSM-IV, and 9 studies had subjects diagnosed with POAS by ICD-10. Four studies has subjects diagnosed with POAS by CCMD.

Among the 28 RCTs included, the intervention with the highest frequency of use in acupuncture group was EA[20-27] (n = 8), followed by AA[28-35] (n = 8, here we refer to auricular acupoint pressing and auricular acupoint acupuncture both regard as auricular acupuncture), 4 studies[36-39] using MA, and another 3[40-42] using acupoint electrical stimulation on acupuncture points. In the control group setting, 11 studies[27-30,34,36,37,40,43-45] used Western medical controls, 8 of which[27,34,36,37,40,43-45] were conventional pharmacotherapy, and 3 of which[28-30] were conventional psychotherapy. Another 8 studies[21-23,25,26,31,38,39,46] used a no-treatment control,

7[20–22,24,32,33,35,41,42] used a sham acupuncture, and 1[21] used both simulated acupuncture and no treatment control.

Fifteen studies[21,27,29-32,35-38,40,41,45-47] reported protracted withdrawal symptom total scores, 14[20,21,23,24,27,33,36,37,39,40,43–45,47] reported protracted anxiety scores, 6[21,24,26,43,44,47] reported protracted depression scores, 13[20,22,25–30,36,38,40,45,46] reported protracted sleep disorder scores, 7[26,29,30,38,40,45,46] reported protracted withdrawal somatic symptom scores, and 7[20,28,35–37,40,41] reported crave scores. These studies' characteristics are summarized in Supplement 2.

3.3. Acupuncture points

A total of 47 acupoints were used in 28 studies involving three types of acupuncture points: twelve meridian points, ear points, and head points, each of which was used between 1 and 16 times in different combinations. The number of acupoints used per POAS patient varied between 2 and 11 in the trials analyzed. The more frequently used meridian points were PC6, ST36, SP6, and HT7, and the most commonly used ear points were Shen Men, subcortical, and endocrine; the specific distribution of the other points is shown in Supplement 3.

3.4. Risk of bias of the included studies

The risk of bias in the included literature was assessed (Fig. 2A and B) as follows: (1) Random sequence generation: thirteen studies(46%) were rated as low risk due to the use of appropriate randomization methods, from which 9 used a random number table,[23,26,27,35-38,42,46] and 3 used the envelope method.[21,22,25] Four studies(14%) were rated high risk due to their use of odd-even numbers[40] and order of admission[30,41,45] as randomized methods. The remaining studies(39%) mentioned randomization, but did not describe the specific randomization method, so they were rated as unclear. (2) Allocation concealment: Four studies (15%) were rated as high-risk because they had determined participant assignment based on admission sequence and the odd-even numbering method.[30,40,41,45] The remaining studies did not mention allocation concealment, so they were rated as unclear. (3) Blinding of participants and outcome assessment: Four studies(15%) used blinding methods for both participants and outcome evaluators,[30,35,41,47] and 2 studies were only blinded to participants.[37,40] (4) Incomplete outcome data: eight studies (29%) reported case shedding and culling outcomes,[35-37,39,41,43,45,47] and the remaining studies did not mention study outcome completeness. (5) Selective reporting: All of the studies reporting complete outcome indicators were rated as low-risk. (6) Other bias: None studies had any information on other risks-of-bias. In summary, a study can be considered high quality only if more than half of the entries (> 3) are rated as low risk, so only three studies meet this condition.[35,37,41]

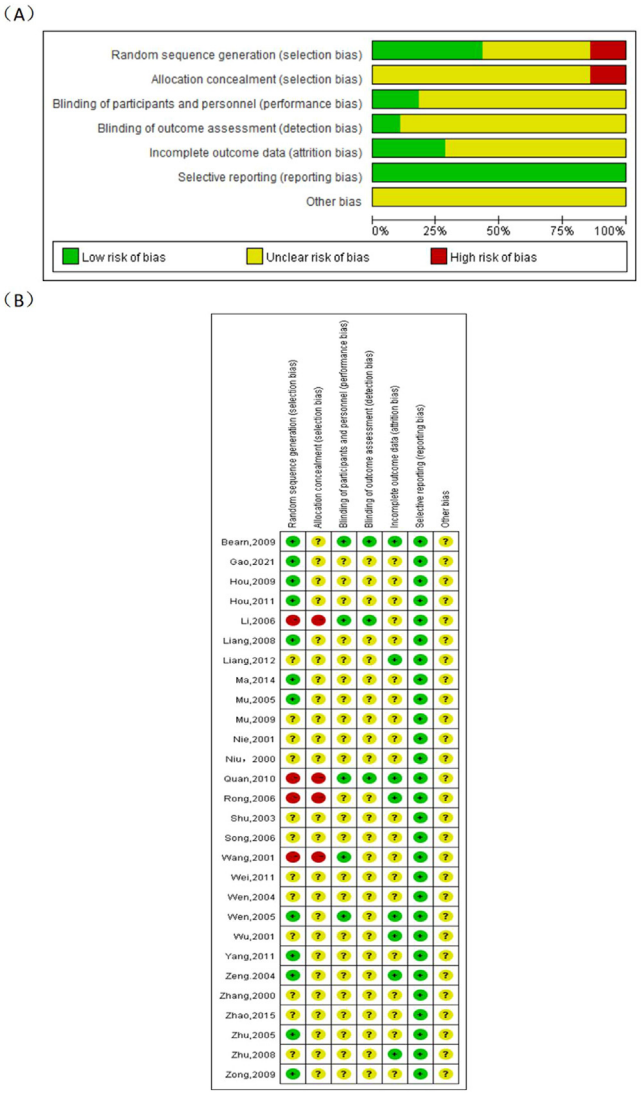

Fig. 2. The risk of bias in the included studies.

3.5. Effects of the intervention

3.5.1. Acupuncture vs. sham acupuncture

A total of 9 studies[20,21,24,32,33,35,41,42,47] used acupuncture versus sham acupuncture as control methods, and we conducted the following analysis according to the different outcome indicators.

3.5.1.1. Primary outcomes. Five studies assessed protracted withdrawal symptom scores. EA versus sham EA showed that EA was superior to sham acupuncture in improving protracted withdrawal symptoms (SMD=−1.85, 95% CI [−3.21, −0.50], P = 0.007, I^2=94%, Fig. 3A).[21,41,47] The results of AA[32,35] versus sham acupuncture showed that AA improved withdrawal symptoms more significantly than sham acupuncture (SMD=−0.19, 95% CI [−0.99, 0.62], P = 0.65, I^2=82%, Fig. 3B).

3.5.1.2. Secondary outcomes. Four studies[20,21,33,47] tested protracted anxiety symptom scores. The overall results showed that acupuncture-related therapy could significantly improve the symptoms of protracted anxiety compared with sham acupuncture (SMD=−1.66, 95% CI [−2.71, −0.62], P = 0.002, I^2=94%, Fig. 3C). We excluded these 4 studies one by one to find the source of heterogeneity, found that 1 study[47] was a major source of heterogeneity.

For crave scores, there were 3 studies mentioned.[20,35,41]The overall results showed that no significant difference between acupuncture-related therapy and sham acupuncture in reducing crave scores (SMD=−0.38, 95% CI [−2.50, 1.74], P = 0.73, I^2=99%, Fig. 3D).

3.5.2. Acupuncture vs. western medicine

A total of 11 studies[27-30,34,36,37,40,43-45] used acupuncture versus western medicine as control methods.

3.5.2.1. Primary outcomes. Seven studies assessed on protracted anxiety symptom scores. Five[27,36,37,40,45] used acupuncture-related treatments, and two[29,30] used AA. The overall results showed that acupuncture-related treatment improved protracted withdrawal symptoms better than western medicine (SMD=−0.72, 95% CI [−1.22, −0.21], P = 0.005, I^2=86%, Fig. 4A) Both MA (SMD=−0.78, 95% CI

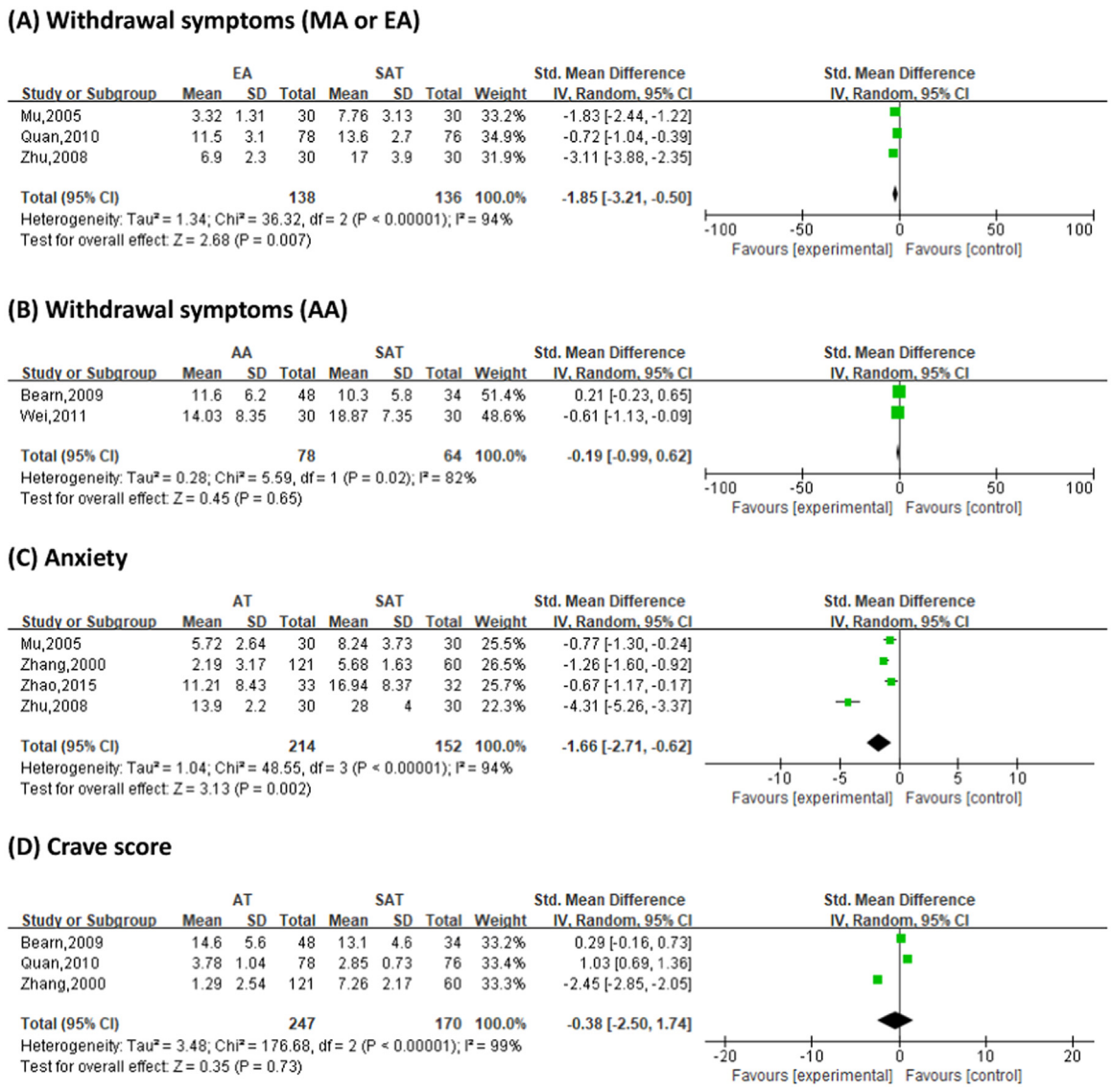

Fig. 3. Acupuncture vs. sham acupuncture of the effects of the intervention.

[−1.67, 0.10], $P = 0.08$, I^2=91%) and EA (SMD=−0.66, 95% CI [−1.40, 0.08], $P = 0.08$, I^2=81%) showed equvalent effects on this outcome compared with western medicine. The results showed that AA improved protracted withdrawal symptoms than western medicine (SMD=−5.97, 95% CI [−7.46, −4.48], P<0.00001, I^2=38%, Fig. 4B)

3.5.2.2. Secondary outcomes. Six studies tested the effects of acupuncture for protracted anxiety symptom scores. The overall results showed that acupuncture-related therapy could significantly improve the symptoms of protracted anxiety symptom scores compared with sham acupuncture (SMD=−0.64, 95% CI [−1.06, −0.23], $P = 0.002$, I^2=80%, Fig. 4C). MA showed superior effects compared to western medicine in improving protracted anxiety symptom score (SMD=−0.37, 95% CI [−0.59, −0.16], $P = 0.0007$, I^2=0%).[36,37,45] EA failed to show significant effects on the improvement of protracted anxiety symptom scores (SMD=−0.93, 95% CI [−1.96, 0.10], $P = 0.08$, I^2=91%).[27,40,43]

Two studies[43,44] evaluated protracted depressive symptom scores, and the result showed that EA was superior to western medicine in improving depressive symptoms (SMD=−0.95, 95% CI [−1.63, −0.26], $P = 0.007$, I^2=42%, Fig. 4D).

Six studies assessed the effects of acupuncture on protracted sleep disorder scores and showed that acupuncture-related therapy could significantly improve the symptoms of protracted sleep disorder scores compared with western medicine (SMD=−0.55, 95% CI [−1.05, −0.05], $P = 0.03$, I^2=77%, Fig. 4E). There were no significant difference in the improvement of protracted sleep disorder scores between MA and western medicine (SMD=−0.40, 95% CI [−0.93, 0.14], $P = 0.15$, I^2=75%, Fig. 4E).[27,36,45] AA could significantly improve the symptoms of protracted sleep disorder scores compared with western medicine (SMD=−2.04, 95% CI [−2.25, −1.82], P<0.00001, I^2=0%, Fig. 4F).[29,30]

Four studies showed that acupuncture-related therapy could significantly improve the symptos of protracted somatic scores with sham acupuncture (SMD=−0.66, 95% CI [−0.89, −0.43], P<0.00001, I^2=88%, Fig. 4G).[29,30,40,45]

The results of four studies showed no significant difference between acupuncture-related therapy and western medicine in improving craving (SMD=−0.17, 95% CI [−0.47, 0.12], $P = 0.26$, I^2=36%, Fig. 4H).[28,36,37,40]

3.5.3. Acupuncture vs. no treatment

A total of 9 studies[21-23,25,26,31,38,39,46] used acupuncture versus no treatment as control methods.

3.5.3.1. Primary outcomes. The results of three RCTs showed that acupuncture-related treatment improved protracted withdrawal symptoms better than no treatment (SMD=−2.26, 95% CI [−3.82, −0.69], P = 0.005, I^2=93%, Fig. 5A).[21,38,46]

3.5.3.2. Secondary outcomes. Three included studies showed that acupuncture-related treatment improved protracted anxiety symptom scores better than no treatment (SMD=−1.63, 95% CI [−2.17, −1.08], P<0.00001, I^2=55%, Fig. 5B).[23,24,39]

Three RCTs results showed that acupuncture-related treatment improved protracted depressive symptom scores better than no treatment (SMD=−2.31, 95% CI [−3.67, −0.95], P = 0.0008, I^2=92%, Fig. 5C).[21,24,26]

Five studies showed that acupuncture-related treatment improved protracted sleep disorder scores better than no treatment (SMD=−2.77, 95% CI [−3.64, −1.91], P<0.00001, I^2=84%, Fig. 5D).[22,25,26,38,46]

The results of three studies showed that acupuncture-related treatment improved protracted somatic symptom scores better than no

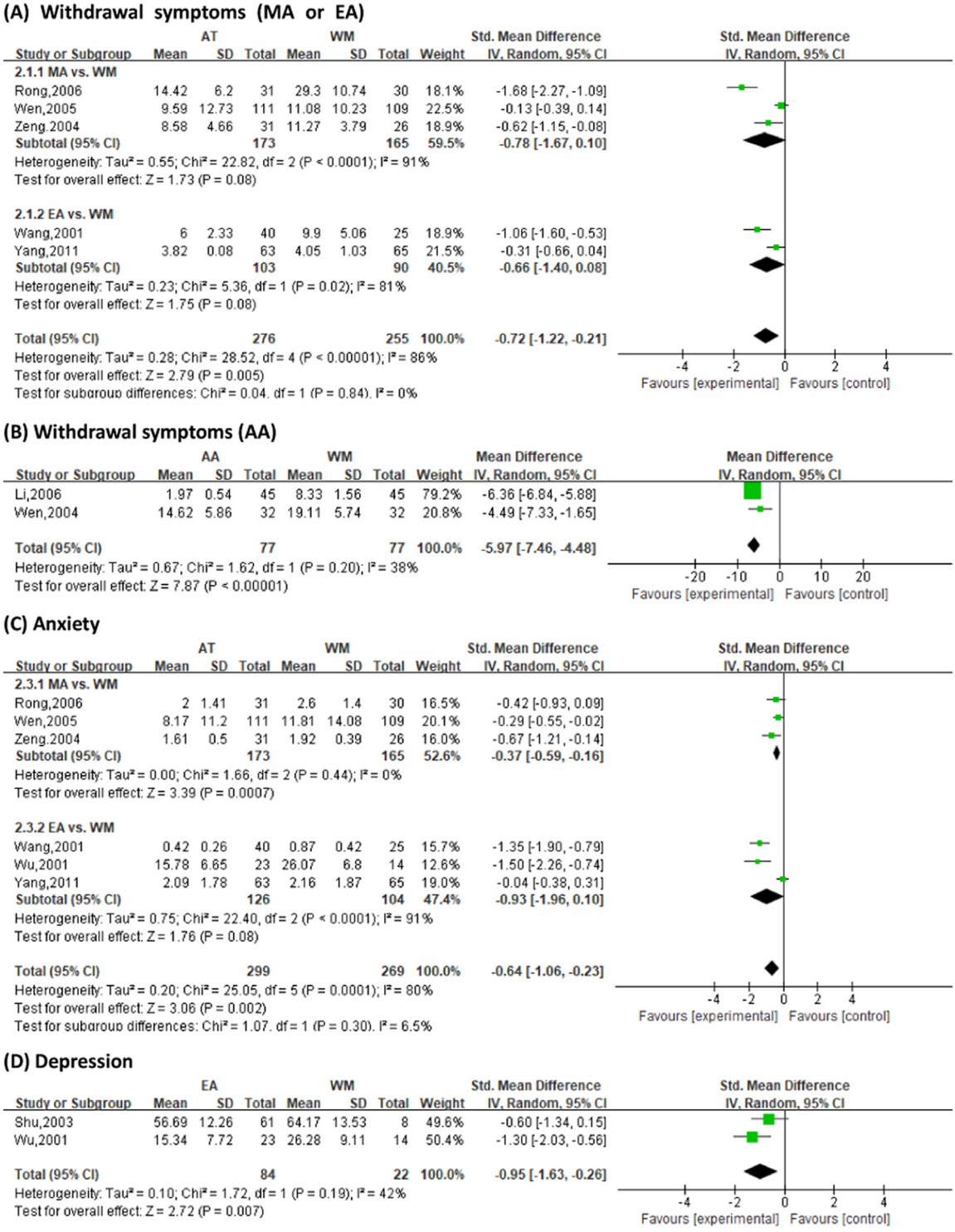

Fig. 4. Acupuncture vs. western medicine of the effects of the intervention.

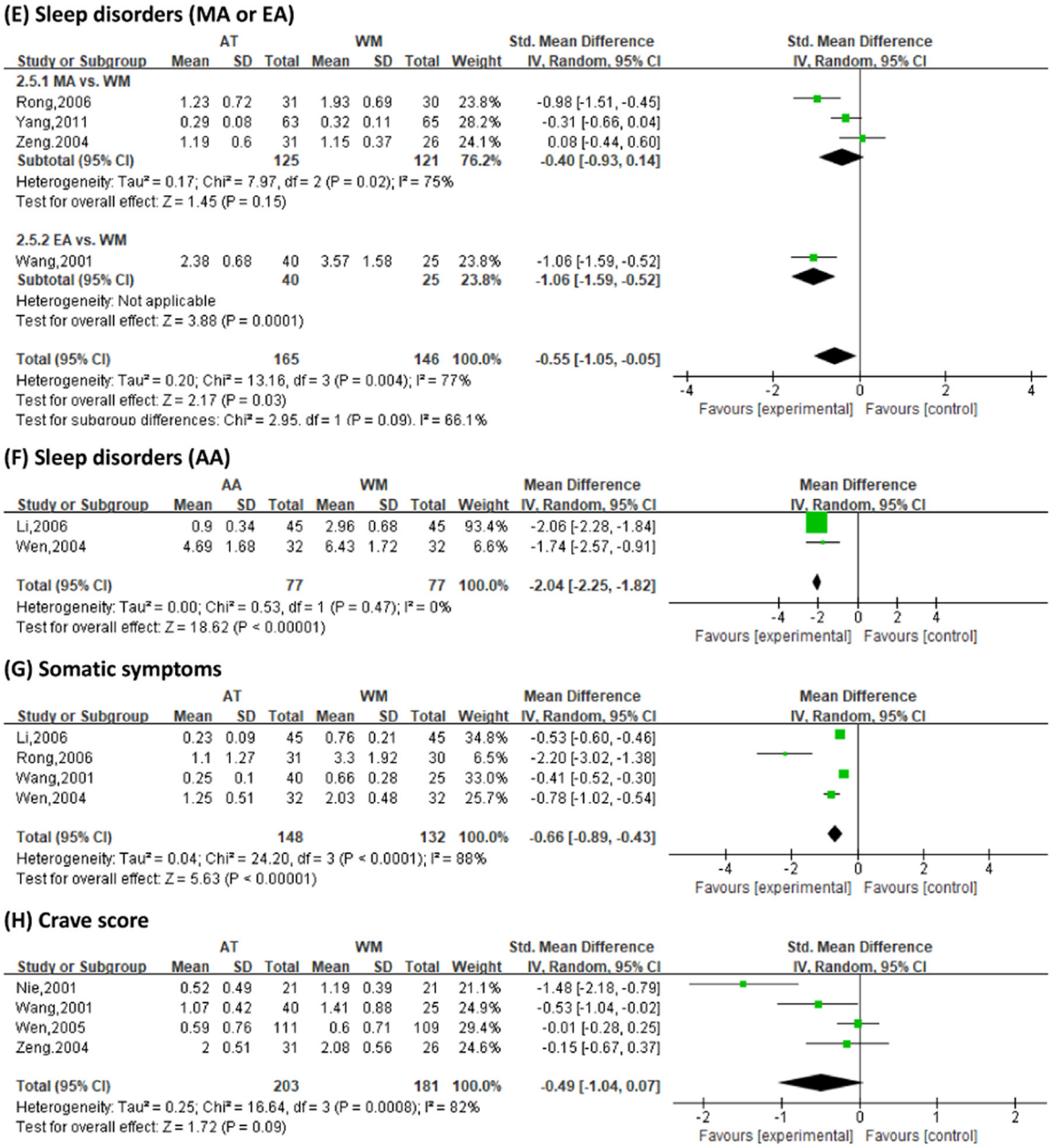

Fig. 4. Continued

treatment (SMD=−1.26, 95% CI [−1.68, −0.83], P<0.00001, I^2=32%, Fig. 5E). [26,38,46]

3.6. Sensitivity analysis

This review was evaluated based on the methodological quality of the included literature, and tested again after excluding low-quality literature. The findings showed that the results derived from this study's indicators were not affected by the methodological quality. This indicated that their combined results were generally stable and reliable.

3.7. Publication bias analysis

Because a funnel plot can only be applied if there are at least 10 included studies, however, less than 10 articles were included in the meta-analysis for each indicator in this paper, we did not conduct a publication bias analysis.

3.8. Adverse events due to acupuncture

No adverse events were reported in any of the included studies.

4. Discussion

4.1. Summary of results

Our review covered 28 RCTs involving 2463 patients with POAS. The results showed that acupuncture-related therapies might alleviate POAS patients' withdrawal symptoms. Significant evidence of efficacy was observed in the acupuncture group in improving anxiety, depression, sleep disorders, and somatic symptoms, compared to that in the control group. However, there was not enough evidence to support the idea that acupuncture mitigates cravings. This observation is generally consistent with the results of previous studies.[48-51]

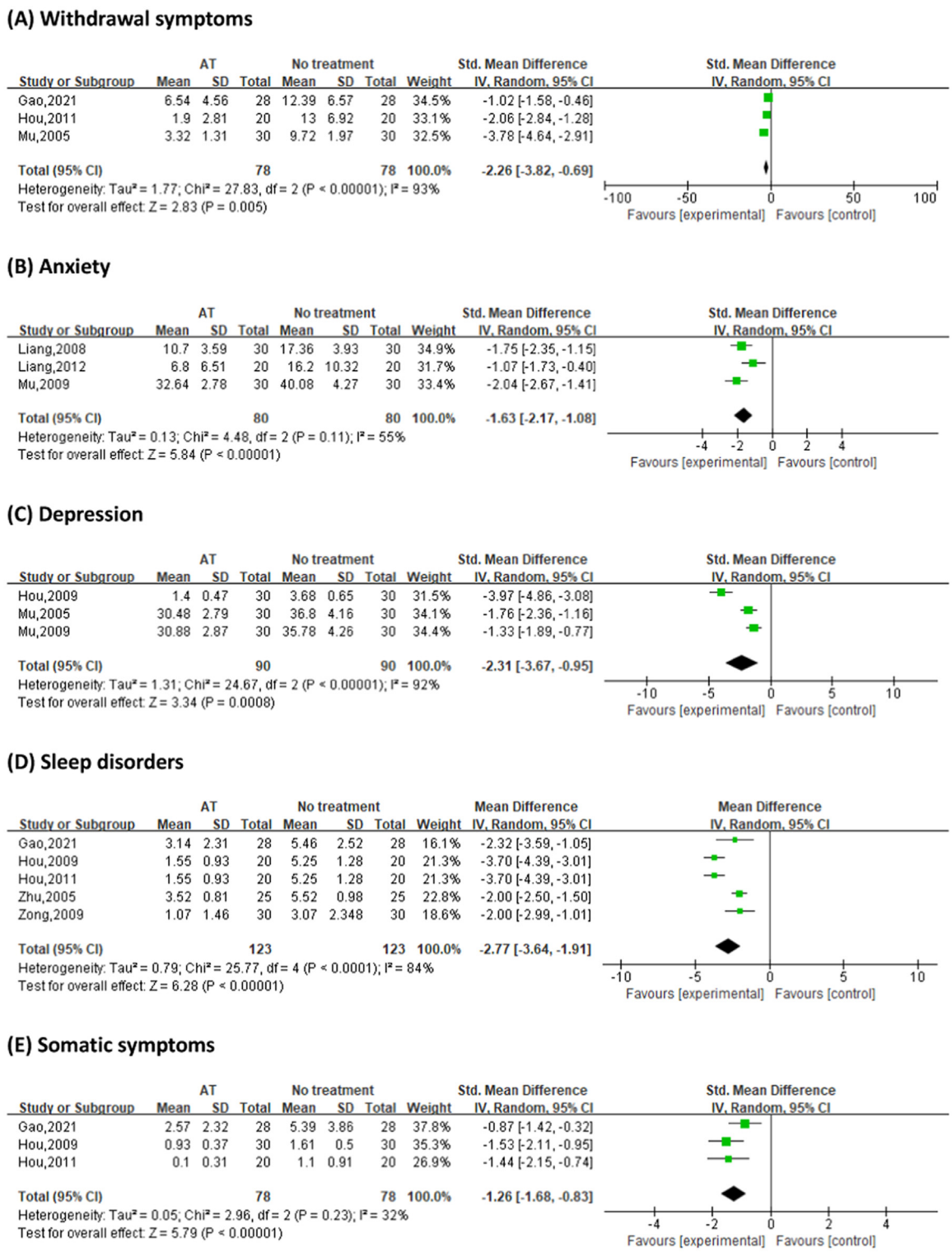

Fig. 5. Acupuncture vs. no treatment of the effects of the intervention.

4.2. Analysis of sources of heterogeneity

The heterogeneity in this study was generally higher than 50%, which we speculated was caused by some factors affecting the efficacy of acupuncture. It is generally accepted that the composition of an acupuncture protocol includes many factors which will affect the final effect such as the types of needle, the acupuncture points selected, the course of treatment, and the doctor's qualifications. Therefore, each of these factors served as a source of heterogeneity in the acupuncture meta-analysis. But further subgroup analysis was not feasible, due to the limited amount of literature.

4.3. Comparison to similar studies

The present study has shown considerable advantages over previous reviews on sample inclusion and bias assessment.[51-53] The first is

that this review update incorporates research from the years 2021 and 2022.[46] Secondly, we targeted patients with protracted withdrawal syndrome, rather than patients with opioid use disorder (OUD). When previous reviews used Jaded scores for quality assessment, the number and quality of trials were too low to draw valid conclusions about acupuncture's effectiveness in treating patients with psychological symptoms associated with opioid addiction; low-quality studies accounted for 62.5% of the total included studies 0.[53] However, in our study, low-quality studies with Jaded scores below 3 accounted for 46.4% (seen in Table 1 of Appendix 2). This confirms that study design has improved since the publication of the previous systematic review. However, the need to manually pierce acupuncture points during acupuncture treatment complicates the implementation of double-blind interventions. Although many sham-needle devices have been developed, there are still none that enable complete blinding of physicians and patients.

The treatment sessions in all studies were generally concentrated in a range of 20–30 days. Most studies using auricular acupressure or AA entailed treatment once per day; those using EA or MA entailed treatment of approximately 20/30 min per session, 3–5 times per week. MA focused on a treatment duration of about 2 weeks to show clinical effects. Although there are no guidelines for the frequency and duration of acupuncture treatment for POAS, it can be tentatively inferred from our meta-analysis results that a treatment duration of more than two weeks can be utilized as a crucial outcome in a standardized clinical treatment protocol.

By summarizing the frequency of acupuncture point use, we found that the acupuncture points selected for the treatment of POAS mainly reflected "up and down matching points", such as the most frequent ones: PC6, HT7, ST36 and SP6. The former two are located in the upper extremities, while the latter two are located in lower extremities. According to modern medicine, acupuncture stimulation of PC6, ST36 and other points can cause the release of Substance P (SP), locally and in brain areas. This activates the body's positive immunity, and because Substance P is related to opioid receptors,[54] dopamine and serotonin signaling pathways, acupuncture can improve POAS patients' protracted withdrawal symptoms and psychological dependence by regulating humoral-immune functions.[55,56]

4.4. Implications for clinical practice and future research

At present, the specific acupoint group and dominant acupoints in acupuncture treatment for POAS remain controversial. As such, multicenter, large-sample, high-quality, double-blind RCTs are needed to resolve these controversies. In addition, comprehensively judging the therapeutic effect of acupuncture treatment on POAS would require improved systematic study of psychological cravings and long-term recurrence rates in POAS patients treated by acupuncture.

4.5. Research strengths and limitations

To our knowledge, this is the first study to focus on lasting withdrawal symptoms in addiction patients, rather than covering the entire detoxification phase. This allowed us to conduct more stringent inclusion/exclusion criteria for our meta-analysis, and to provide a complete overview. Secondly, we cover a wide variety of acupuncture modalities that will inform clinical practice. This research will inject inspiration and ideas into the most difficult problem in drug rehabilitation work—relapse.

This study has several limitations. Firstly, there are large differences in the population characteristics of the literature included, mainly due to regional differences. Most of the literature is from China, which may have introduced regional bias. Second, all of the included studies covered topics pertaining to acupuncture in some fashion, such as EA, AA, and traditional body acupuncture, and were analyzed together without classification. More research on this is needed to comprehensively assess which acupuncture modality is most effective for POAS. Finally, previous reviews have shown that acupuncture can be effective in treating opioid use disorder; EA can alleviate cravings for opioids and depression, and TEAS can mitigate symptoms of insomnia and anxiety.[52] Given these findings, different acupuncture points and acupuncture techniques may have caused significant bias in this meta-analysis' conclusions. Due to the limited number of studies, we did not perform a subgroup analysis of the different acupuncture modalities, or of acupoint selection. However, the heterogeneous effects of different acupuncture techniques warrant consideration in practical clinical applications.

4.6. Conclusion

Recent evidence identified from this review suggests that acupuncture-related therapies can alleviate POAS patients' withdrawal symptoms. However, this review's conclusions are limited by the low quality of the included studies. Future multi-center RCTs with rigorous methodological quality are needed to elucidate acupuncture's role in improving withdrawal symptoms in patients with POAS.

Author contributions

All authors participated in its design. L. Ding and C. Li drafted the manuscript. L. M. Lu and P. M. Zhang revised it. L. Ding, C. Li, and C. Chen participated in designing the search strategies. L. Ding and C. Chen conducted the electronic search. L. Ding and C. Li completed the screening of all articles. C. Chen and J. Zhan participated in the data extraction. L. Ding and C. Chen assessed the risk of bias and the quality of the evidence. L. Ding, J. Zhan, and C. Chen participated in data analyses. LM. Lu arbitrated any disagreements in the process of the study. All authors read and approved the final manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

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Ethical statement

On account of the characteristics of systematic review and meta-analysis, ethical approval was not required.

Data availability

The data supporting this study's findings are available within the article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.imr.2023.100976.

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