



Letter to the Editor

Evaluating the Effect of Acupuncture for Methadone Reduction: Insights from a Randomized Controlled Trial



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Dear Editors,

Opioid use disorder (OUD) is one of the major challenges facing global public health today. OUD not only leads to a decline in quality of life but also imposes a significant economic burden.¹ Opioid overdose increases the risk of death, and mortality rates remain high.^{2,3} Methadone maintenance therapy (MMT) is a key treatment method for OUD, showing considerable effectiveness in helping patients reduce their use of illicit opioids and receive necessary treatment.^{4,5} However, MMT has significant side effects that can affect various organ systems, including the cardiovascular, respiratory, endocrine, central nervous, neurobehavioral, gastrointestinal, and skeletal systems.⁶ Additionally, MMT may impair cognitive function.⁷

Given the unavoidable side effects of MMT, it is important to explore effective non-pharmacological rehabilitation programs. Recently, Professor Xu Nenggui's team from Guangzhou University of Traditional Chinese Medicine published a research paper titled *Randomized Controlled Trial of Acupuncture Intervention for Methadone Reduction* in the prestigious medical journal *Annals of Internal Medicine*.⁸ This research demonstrated that acupuncture can significantly reduce the maintenance dose of methadone and alleviate opioid cravings, while also improving sleep quality to some extent. Previous studies have suggested that acupuncture and moxibustion-related therapies can be effectively used to treat patients undergoing MMT, with manual acupuncture and moxibustion being particularly promising for opioid dependence.⁹ This research provides strong evidence supporting the use of acupuncture and moxibustion as an effective non-drug treatment method to help opioid-dependent patients reduce the dose of methadone. It represents the latest milestone in enhancing the contribution of acupuncture and promoting the internationalization of acupuncture.

This study employed a rigorous, multicenter, two-group, randomized, sham-controlled trial design. The acupuncture sites used

were *Dingshen-zhen*, *Sishen-zhen*, and *Shouzhi-zhen*. The study included 118 OUD patients who had been receiving MMT for at least six weeks in six MMT clinics in China. The therapeutic effects of the acupuncture group (n = 60) were compared with those of the sham acupuncture group (n = 58). Participants underwent a treatment regimen consisting of three sessions per week over an eight-week period. The results showed that, by the eighth week, more patients in the acupuncture group than in the sham acupuncture group had reduced their methadone dose by 20% or more compared with baseline (37 [62%] vs. 16 [29%]). The mean visual analogue scale score for opioid craving in the acupuncture group decreased significantly more than in the sham acupuncture group (16.2 vs. 4.5). These findings confirm that acupuncture was significantly more effective than sham acupuncture in reducing the maintenance dose of methadone and alleviating opioid cravings. The results are presented in [Figure 1](#).

This study provides strong evidence for the use of acupuncture as a non-pharmacological treatment to help opioid-dependent patients reduce their methadone dosage and opioid cravings. The results are not only statistically significant but also clinically meaningful, as a 20% reduction in methadone dosage is associated with significant clinical benefits and the prevention of relapse. Furthermore, the reduction in methadone dosage correlates with a decrease in reported opioid cravings, suggesting that acupuncture may reduce methadone maintenance doses by diminishing patients' cravings for opioids. The study's rigorous design, including random assignment, blinding, and the use of control groups, enhances the credibility of the findings. Additionally, the study assessed participants' sleep, anxiety, and depressive symptoms, indicating that acupuncture may have potential benefits in alleviating a range of symptoms associated with opioid withdrawal. This was also suggested in our previous study on electroacupuncture intervention for opioid-addicted patients.¹⁰ Electroacupuncture, according to the acupoint prescriptions (*bilateral Shenmen*, *Neiguan*, *Zusanli*, *Sanyinjiao*), was shown to reduce depression levels in patients. Biochemical analysis of serum revealed an elevated concentration of Noradrenalin in drug addicts subjected to genuine acupuncture therapy. Concurrently, a marked increase in the serum levels of brain-derived neurotrophic factor was observed in the same cohort of patients.

However, the study's limitations are also worth noting. For instance, the fixed acupuncture protocol may not account for indi-

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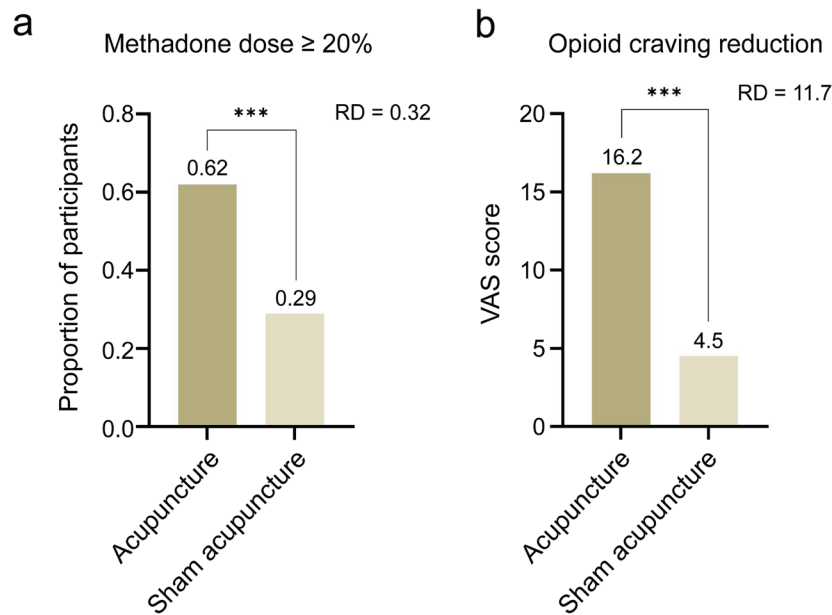


Fig. 1. Changes in methadone use and opioid cravings after eight weeks of acupuncture and sham acupuncture intervention compared with baseline. (a) Proportion of participants with $\geq 20\%$ reduction in methadone dose compared to baseline after eight weeks of acupuncture intervention. (b) Reduction in opioid cravings compared with baseline after eight weeks of acupuncture intervention. *** $p < 0.001$; RD, risk difference; VAS, visual analogue scale.

vidual differences, and the relatively short follow-up period may limit the assessment of the long-term effects of acupuncture. More importantly, the study does not explore the specific mechanisms by which acupuncture reduces methadone maintenance doses and opioid cravings. Therefore, based on this research, we propose the following future directions: First, we can investigate how acupuncture affects neurotransmitter and hormone levels in the brain, such as endorphins, enkephalins, adrenaline, norepinephrine, serotonin, and dopamine, which may play a role in reducing opioid cravings and improving withdrawal symptoms. Second, we can explore the effects of acupuncture on the pharmacokinetics and pharmacodynamics of methadone, including its potential impact on methadone metabolism and mechanism of action. Third, brain imaging technology can be used to further investigate how acupuncture regulates brain areas related to addiction and reward, such as the amygdala, prefrontal cortex, and nucleus accumbens. This will be important for studying the specific mechanisms by which acupuncture reduces methadone maintenance doses and opioid cravings. Overall, this research provides valuable insights into the application of acupuncture in treating OUD and offers directions for future research and clinical practice.

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Conflict of interest

None.

Author contributions

Study concept and design (JZH, RFW, QHH), drafting of the manuscript, and critical revision of the manuscript for important intellectual content (JZH). All authors have made significant contributions to this letter and have approved the final manuscript.

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