INPLASY

Efficacy and safety of Zhizi-Chi decoction (Gardenia and Fermented Soybean Decoction) for mental disorders: a systematic review and meta-analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

Support - Beijing University of Chinese Medicine.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 December 2025 and was last updated on 15 December 2025.

INTRODUCTION

Review question / Objective This review aims to evaluate the efficacy and safety of Zhizi-Chi decoction, used alone or in combination with Western medicine, for mental disorders compared with placebo or Western medicine, based on randomized controlled trials.

Condition being studied Mental disorders are a group of conditions characterized by disturbances in cognition, emotional regulation, or behavior that result in significant distress or impairment in functioning. Common mental disorders include depression, anxiety disorders, and sleep-related disorders, which are highly prevalent worldwide and impose a substantial burden on individuals and healthcare systems. Despite the availability of pharmacological and psychological treatments, many patients experience limited effectiveness or adverse effects, highlighting the need for complementary and alternative therapeutic approaches.

METHODS

Search strategy A comprehensive literature search will be conducted in the following electronic databases from inception to the search date: PubMed, Embase, Web of Science, the Cochrane Library, China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database, and SinoMed.
The search strategy will combine subject headings and free-text terms related to the intervention and condition, including “Zhizi-Chi decoction”, “Gardenia and Fermented Soybean Decoction”, “Zhi Zi Chi Tang”, “栀子豉汤”, and terms related to mental disorders (e.g., depression, anxiety, sleep disorders), together with terms related to randomized controlled trials. No language restrictions will be applied.

Participant or population Participants of any age or sex diagnosed with mental disorders will be included. Mental disorders will be defined according to recognized diagnostic criteria (such

as DSM, ICD, or CCMD) or validated clinical assessment scales. There will be no restrictions on ethnicity, nationality, or clinical setting.

Intervention The intervention of interest is Zhizi-Chi decoction (Gardenia and Fermented Soybean Decoction), including the original formula and modified formulations in which Zhizi-Chi decoction remains the core prescription. Zhizi-Chi decoction may be used alone or in combination with Western medicine. There will be no restrictions on dosage form, dosage, frequency, or duration of treatment.

Comparator Comparators will include placebo, no treatment, conventional treatment, or Western medicine used for the management of mental disorders. In trials where Zhizi-Chi decoction is administered in combination with Western medicine, the comparator must consist of the identical Western medicine alone.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria Studies will be considered eligible if they meet the following criteria:
(1) randomized controlled trials;
(2) participants of any age or sex diagnosed with mental disorders based on recognized diagnostic criteria or validated clinical assessment scales;
(3) interventions involving Zhizi-Chi decoction (Gardenia and Fermented Soybean Decoction), including the original formula or modified formulations in which Zhizi-Chi decoction remains the core prescription, used alone or in combination with Western medicine;
(4) comparators including placebo, no treatment, conventional treatment, or Western medicine, with the identical Western medicine alone used as the comparator in combination-therapy trials;
(5) studies reporting at least one relevant clinical outcome related to mental disorders.

Studies will be excluded if they are non-randomized studies, observational studies, case reports, reviews, animal experiments, or if the independent effect of Zhizi-Chi decoction cannot be clearly distinguished.

Information sources The following electronic databases will be searched from inception to the date of the final search: PubMed, Embase, Web of Science, and the Cochrane Library. Chinese databases including China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database, and SinoMed will also be searched.
In addition, the reference lists of included studies and relevant reviews will be manually screened to identify additional eligible trials. When necessary, corresponding authors of included studies will be contacted to obtain missing or unclear information.

Main outcome(s) The primary outcome will be the clinical efficacy of Zhizi-Chi decoction for mental disorders, assessed as change in symptom severity from baseline to end of treatment using validated rating scales. For depressive symptoms, scales may include HAMD or SDS; for anxiety symptoms, scales may include HAMA or SAS; and other standardized symptom scales will be considered where applicable.

Additional outcome(s)
Secondary outcomes will include:
(1) overall clinical effectiveness as defined by the original studies;
(2) changes in sleep-related symptoms assessed by validated scales such as the Pittsburgh Sleep Quality Index (PSQI), where reported;
(3) quality of life measured by standardized instruments;
(4) incidence of adverse events and treatment-related side effects.

Data management All retrieved records will be imported into reference management software for de-duplication. Two reviewers will independently screen titles and abstracts, assess full texts for eligibility, and extract data using a predefined data extraction form. Extracted data will include study characteristics, participant information, intervention and comparator details, outcome measures, and adverse events. Discrepancies will be resolved through discussion or consultation with a third reviewer. All extracted data will be stored securely and used solely for the purposes of this review.

Quality assessment / Risk of bias analysis The risk of bias of included randomized controlled trials will be assessed independently by two reviewers using the Cochrane Risk of Bias tool (RoB 2.0). The following domains will be evaluated: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. Any disagreements will be resolved through discussion or consultation with a third reviewer.

Strategy of data synthesis Quantitative synthesis will be conducted when sufficient data are available. Meta-analyses will be performed using a random-effects model to account for potential clinical and methodological heterogeneity. For continuous outcomes, mean difference (MD) will be

used when the same outcome scale is applied, and standardized mean difference (SMD) will be used when different scales are used, both with 95% confidence intervals (CIs). For dichotomous outcomes, risk ratios (RRs) with 95% CIs will be calculated.
Statistical heterogeneity will be assessed using the Chi-square test and the I^2 statistic. When substantial heterogeneity is detected, potential sources will be explored through subgroup or sensitivity analyses. If meta-analysis is not appropriate due to insufficient or highly heterogeneous data, a narrative synthesis will be conducted.

Subgroup analysis If sufficient data are available, subgroup analyses will be conducted to explore potential sources of heterogeneity based on the following factors:
(1) type of mental disorder (e.g., depression, anxiety disorders, sleep-related disorders);
(2) intervention mode (Zhizi-Chi decoction used alone versus Zhizi-Chi decoction combined with Western medicine);
(3) duration of treatment;
(4) type of comparator (placebo, Western medicine, or conventional treatment).

Sensitivity analysis Sensitivity analyses will be conducted to assess the robustness of the pooled results by excluding studies with high risk of bias, studies with small sample sizes, or studies with missing or incomplete outcome data. The impact of individual studies on the overall results will also be examined by sequentially removing one study at a time.

Language restriction No language restrictions will be applied. Studies published in any language will be considered eligible.

Country(ies) involved China.

Other relevant information This systematic review and meta-analysis will be conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Any amendments to the protocol after registration will be clearly documented and reported with justification.

Keywords Zhizi-Chi decoction; Gardenia and Fermented Soybean Decoction; mental disorders; depression; anxiety; randomized controlled trials; systematic review; meta-analysis.

Dissemination plans The results of this systematic review and meta-analysis will be disseminated through publication in a peer-reviewed academic journal and presentation at relevant academic conferences. The findings may also be shared with clinicians and researchers to inform evidence-based practice and future research.

Contributions of each author

Author 1 - Zhenzhen Li - Author 1 drafted the protocol.
Author 2 - Zhenxin Bao - Author 2 drafted the criteria.
Email: alcreminzb69@gmail.com
Author 3 - Dongying Liao - The author contributed to idea.
Author 4 - Liangsong Li - corresponding author.