INPLASY PROTOCOL

To cite: Shao et al. Comparative efficacy and acceptability of traditional Chinese medicine for adult major depression : a network meta-analysis protocol. Inplasy protocol 2020100028. doi: 10.37766/inplasy2020.10.0028

Received: 09 October 2020

Published: 09 October 2020

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Support: **Medicine project (2019-0108).**

Review Stage at time of this submission: **Preliminary searches.**

Conflicts of interest:
We declare no conflicts of interest.

Comparative efficacy and acceptability of traditional Chinese medicine for adult major depression: a network meta-analysis protocol

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Review question / Objective: **Major depression disorder (MDD) is a severe health threat characterized by persistent depression, loss of interests, lack of initiative, and even suicidal tendencies. Traditional Chinese medicine (TCM) is well tolerated and effective in treating adult MDD. However, research on the evaluation of efficacy and acceptability of different TCM strategies for adult MDD is insufficient. Consequently, it is high time to evaluate the efficacy of TCM strategies for adult MDD. Meanwhile, the acceptability of different TCM strategies is worth exploring.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 October 2020 and was last updated on 09 October 2020 (registration number INPLASY2020100028).

INTRODUCTION

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adult MDD. Meanwhile, the acceptability of different TCM strategies is worth exploring.

Condition being studied: As a kind of severe emotional disorder, major depressive disorder (MDD) is characterized by low mood, lack of pleasure, and loss of interest, often accompanied by anxiety, cognitive impairment, psychomotor retardation, and even suicidal tendencies. Social and cultural factors have always had a significant role in the pathogenesis of MDD. However, the 12-month prevalence of MDD is almost the same in developed and non-developed countries, with the former being 5.5% and the latter being 5.9%. Therefore, MDD is not a simple consequence of an excessively fast pace of life or poor living conditions.Depression has sex-specific genetic effects. Depression is the most common mental disorder; about 350 million people worldwide suffer from MDD. The 12-month prevalence and lifelong morbidity are 6.6% and 16.2%, respectively, indicating that almost one in five people will suffer from MDD attacks at some point in their life. As of 2013, mental health conditions is added to the leading causes of disability list due to its destructive impacts, with a prediction that MDD will become the first cause ranked for disability by 2025. The tremendous healthcare costs of depression globally present a concern. It is estimated that the global costs of depression and anxiety reach $1.15 trillion per year.

METHODS

Participant or population: Participants are adults (older than 18 years old, regardless of gender and race) with a diagnosis of MDD according to The Diagnostic and Statistical Manual of Mental Disorders (DSM-V), International Classification of Diseases (ICD-10) and Chinese Classification of Mental Disorders (CCMD-3).

Intervention: The control group receives western medicine treatment alone. The experimental group uses western medicine at the same time as traditional Chinese medicine (TCM). Note that the western medicine used in the experimental group should be the same as the control group, and there is no limit on the dose and treatment time of TCM.

Comparator: The control group receives western medicine treatment alone.

Study designs to be included: The study included in the NMA is randomized controlled trials (RCTs) for adult MDD.

Eligibility criteria: The study included in the NMA is randomized controlled trials (RCTs) for adult MDD. The interventions in the NMA is to use western medicine at the same time as traditional Chinese medicine (TCM) in adult MDD. Note that the western medicine used in the experimental group should be the same as the control group, and there is no limit on the dose and treatment time of TCM. Participants are adults (older than 18 years old, regardless of gender and race)with a diagnosis of MDD according to The Diagnostic and Statistical Manual of Mental Disorders (DSM-V), International Classification of Diseases (ICD-10) and Chinese Classification of Mental Disorders (CCMD-3). We will exclude the following literature: participants with bipolar disorder, psychotic depression, or treatment-resistant depression; the treatment measures in the literature involve other treatments, such as psychological intervention, acupuncture and moxibustion, acupoint sticking, etc., which may affect the interpretation of causal relationship; literature with incomplete data; duplicate published literature.

Information sources: Cochrane Library,PubMed, Web of Science, Embase, CNKI Database, Wanfang Database, VIP Database, and CBM Database are the screened target database. The search time is limited from the establishment of each database to September 2020. No restriction will be applied for language and publication.

Main outcome(s): Primary outcome indicators: Effectiveness and acceptability. The efficacy is assessed using the

Hamilton Depression Scale (HAMD), and the HAMD score reduction rate ≥50% compared with the baseline is defined as effective. Acceptability is measured by the incidence of adverse reactions. Secondary outcome indicators: Hamilton Depression Scale (HAMD) score,Symptom Self-Assessment List (SCL-20) score, Beck Depression Inventory (BDI) score, Adverse Reaction Scale (TESS) score. Record the outcome index at 8 weeks of treatment. If there is no information at 8 weeks of treatment, the outcome index closest to 8 weeks will be recorded; if the time interval from 8 weeks is equal, we will use the results of long-term research.

Quality assessment / Risk of bias analysis: Two independent analysis for the risk of bias will be performed in strict accordance with the Cochrane Collaboration's risk of bias tool (Cochrane ROB) by two reviewers. Disagreement will be discussed and resolved by another reviewer. The assessment content mainly includes the following 6 aspects: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential bias. For each index, "low bias risk", "uncertainty of bias risk" and "high bias risk" are used to judge.

Strategy of data synthesis: We will select the random effect model. Markov Chain Monte Carlo (MCMC) algorithm will be used to conduct an NMA under the Bayesian framework. With the help of Winbugs 1.4.3 software, through Gibbs sampling, 3 Markov chains are generated, and the number of iterations permitted is 50,000 times (the first 20,000 times are used for the annealing algorithm, the last 30,000 times for sampling). Use STATA15.0 software to perform and present graphical analysis. Dichotomous outcomes use odds ratios (ORs) as the effect indicator, and continuous outcomes use standardised mean differences (SMD) as the effect indicator. Each effect size is given its point estimate and corresponding 95% confidence interval(CI). Calculate surface under the cumulative ranking area (SUCRA) and rank each treatment strategies according to the calculated values. A larger area under the curve indicates the better efficacy of a treatment strategy.

Subgroup analysis: The two methods are mainly used to perform the robustness test. We will use baseline depression severity, dose, dosage form, study duration, funding source, country for subgroup analysis.

Sensibility analysis: For sensitivity analysis, we will use an exclusion method to assess whether the heterogeneity changes with the deletion of a particular study. The excluded studies include the following types:studies with low methodologic quality, small sample size, only published data and unacceptable dosing dose.

Country(ies) involved: China.

Keywords: traditional Chinese medicine, major depression, protocol, systematic review.

Contributions of each author:
Author 1 - Yuze Shao - The author drafted the manuscript.
Author 2 - Jiaqiu Xi - The author provided statistical expertise.
Author 3 - Zhenyuan Jiang - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - Xiaowen Yu - The author read, provided feedback and approved the final manuscript.
Author 5 - Wenrong An - The author read, provided feedback and approved the final manuscript.
Author 6 - Yue Han - The author read, provided feedback and approved the final manuscript.
Author 7 - Zhonglin Wang - The author read, provided feedback and approved the final manuscript.