INPLASY PROTOCOL

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Conflicts of interest:
None.

Non-pharmacological interventions in relapse prevention of unipolar depression: a network meta-analysis

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Review question / Objective: **Which is the most effective and whether non-pharmacological intervention can perform as effective as antidepressants in relapse prevention for unipolar depression?**
Condition being studied: **Relapse/recurrence of unipolar major depression in adults.**
Search strategy: **PubMed, EMBASE and PsycINFO will be searched. The search strategy will be adapted to each database. And we will screen the reference lists of all included studies and relevant systematic reviews to identify additional studies missed from the original electronic searches. English-language studies published or accepted for publication in peer-reviewed journals were included.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 April 2020 and was last updated on 13 April 2020 (registration number INPLASY202040072).

INTRODUCTION

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METHODS

Search strategy: **PubMed, EMBASE and PsycINFO will be searched. The search strategy will be adapted to each database.**

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Participant or population: Adults (aged 18+) who have had a major depressive episode and remitted. Depression in older adults (mean age older than 60 years old), depression in children/adolescents, pre- or postpartum depression, and depression secondary to physical disease or other mental disorders were excluded.

Intervention: Interventions in RCT should be at least one non-pharmachological, including various kinds of psychological interventions or neurostimulation techniques. Both monotherapy and comination therapy were included. Studies only including pharmacological treatments and placebo were excluded.

Comparator: Control group could be ADM, placebo, treatment as usual (TAU), care as usual (CAU), waiting list, clinical management, supportive psychotherapy or any other active non-pharmacological interventions.

Study designs to be included: RCTs with double-blind, single-blind, or open-label design were included. Studies with randomization during acute phase were excluded.

Eligibility criteria: RCTs investigating non-pharmacological treatment for relapse prevention in unipolar depression.

Information sources: PubMed, EMBASE and PsycINFO.

Main outcome(s): Relapse or recurrence.

Quality assessment / Risk of bias analysis: We will use the guidelines provided in the Cochrane Handbook for Systematic Reviews of Interventions for evaluating the methodology and risk of bias of the included trials. We will evaluate the following domains: · allocation sequence generation · allocation sequence concealment · blinding of participants and treatment providers · blinding of outcome assessors · incomplete outcome data · selective outcome reporting · other risks of bias Disagreements between the review authors over the risk of bias in particular studies will be resolved by discussion, with involvement of a third review author where necessary. We will assess a study at an overall low risk if unclear risk domains ≤ 3 and there is no high risk domain; at an overall high risk if high risk domains > 1; others at an overall moderate risk.

Strategy of data synthesis: To assess the heterogeneity, the posterior median of the between-study heterogeneity parameter (τ^2) will be monitored. The goodness of fit and model comparison assessments will be based on the residual deviance and the Deviance Information Criterion (DIC). To assess the inconsistency, we will compare DIC between consistency and inconsistency model. Global inconsistency will be assessed using a design-by-treatment interaction model and local inconsistency will be tested by a node-splitting method. To assess the transitivity, subgroup and meta-regression analyses will be performed by trial-level covariates. A single analysis with a shared between-trial heterogeneity parameter will be performed. Comparison-adjusted funnel plot will be constructed to detect publication bias and small study effect. This will be performed by netmeta package in R (3.5.3 version). We will assess the confidence in the interested results of network meta-analysis using CINeMA (https://cinema.ispm.unibe.ch/#general). There are four levels (high, moderate, low, and very low) for overall confidence rating, based on the following domains: Incoherence, Heterogeneity, Imprecision, Indirectness, Within-study bias and Across-study bias.

Subgroup analysis: Perform meta-regression or subgroup analyses by using the following moderators: mean age, female percentage, publication year,

number of previous depressive episodes (if available), and trial duration.

Sensibility analysis: Sensitivity analysis will be conducted by including trials with only at least 3 previous depressive episodes.

Country(ies) involved: China.

Keywords: Depression, relapse, recurrence, pyschotherapy.

Contributions of each author:
Author 1 - Author 1 drafted the manuscript.
Author 2 - The author provided statistical expertise.
Author 3 - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 5 - The author read, provided feedback and approved the final manuscript.
Author 6 - The author read, provided feedback and approved the final manuscript
Author 7 - The author read, provided feedback and approved the final manuscript.