INPLASY PROTOCOL

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Review Stage at time of this update: **Data extraction.**

Conflicts of interest: **None.**

The effectiveness of electroconvulsive therapy, vagal nerve stimulation, and repetitive transcranial magnetic stimulation in the treatment of depression: a network meta-analysis

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Review question / Objective: **Electroconvulsive therapy (ECT), vagus nerve stimulation (VNS), and repetitive transcranial magnetic stimulation (rTMS) are three non-drug nerve stimulation treatments approved by the U.S. Food and Drug Administration for the treatment of major depressive disorder. However, previous studies have not compared the effectiveness of these three treatments. Therefore, this study plans to conduct this network meta-analysis to evaluate the effectiveness of these three treatment methods and provide evidence for the future development of treatment guidelines for major depressive disorder.**
Condition being studied: **Electroconvulsive therapy (ECT) is a physical therapy method that has a definitive cure for depression. It can quickly eliminate symptoms, reduce the risk of suicide, and limit recovery to the greatest extent possible. The vagus nerve stimulation (VNS) is a miniature implantable device that is used to assist in the treatment of drug-refractory epilepsy and depression. Repeated transcranial magnetic stimulation For more than 10 years, it has been increasingly used to treat various mental illnesses such as depression, and its efficacy and safety have been supported by a lot of evidence.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 April 2020 and was last updated on 06 July 2020 (registration number INPLASY202040173).

INTRODUCTION

Review question / Objective: **Electroconvulsive therapy (ECT), vagus nerve stimulation (VNS), and repetitive transcranial magnetic stimulation (rTMS) are three non-drug nerve stimulation treatments approved by the U.S. Food and Drug Administration for the treatment of major depressive disorder. However, previous studies have not compared the effectiveness of these three treatments.**

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METHODS

Search strategy: Search for the English literature related to electroconvulsive therapy, vagus nerve stimulation, repetitive transcranial magnetic stimulation, and depression up to 1st July, 2020.

Participant or population: Participants: (1) Patients who were first diagnosed (the first visit without any treatment). (2) Hamilton depression suppression scale (Hamil-ton Depresson Scale, HMD-24) score ≥ 20 points. (3) Diagnosed with the American Standard for Diagnoses of Mental Disorders and Statistics Manual 4th Edition Depression Diagnosis.

Intervention: Inclusion criteria: inpatient and/or outpatient, male and/or female, with unipolar or bipolar major depressive disorder per DSM-IV, DSM-5, ICD-10 or similar operational criteria. Exclusion criteria: secondary depressions or concomitantly to another psychiatric morbidity.

Comparator: The control group was given sham or blank.

Study designs to be included: Randomized controlled study.

Eligibility criteria: Randomized controlled study

Information sources: Search for the English literature in PubMed, Embase, Web of Science and Cochrane Library.

Main outcome(s): Response rates.

Additional outcome(s): Remission rates.

Data management: Two investigators independently extracted all data from each eligible study: first author's last name, year of publication, age, gender, response and remission data.

Quality assessment / Risk of bias analysis: Quality assessment was independently conducted using Modified Jadad Score(7-point).

Strategy of data synthesis: We will initially perform standard pairwise meta-analysis to estimate the available direct relative effects of the competing interventions using a random effects model in R language. Subsequently, we will perform network meta-analysis to synthesize the evidence from the network of trials by integrating direct and indirect evidence into a single summary estimate for every treatment comparison. These analyses will also be performed in R language using the approach of multivariate meta-analysis with the network package. Results will be presented as summary relative odds ratios for every possible pairwise comparison. We will estimate the ranking probabilities of the competing interventions and we will create the rankograms. The relative ranking of treatments will be estimated using the surface under the cumulative ranking curve (SUCRA), which expresses the effectiveness/acceptability of each treatment compared to a treatment that would be ranked first without uncertainty.

Subgroup analysis: A “low risk of bias” will include only studies presenting low risk in all categories or low risk in all categories

and unclear risk in allocation bias. An "intermediate risk" will include studies that present at least one unclear risk of bias, except for allocation bias risk. A "high risk" will include studies that present at least one high risk of bias.

Sensibility analysis: A sensitivity analysis will be performed according to the risk of bias. A "low risk of bias" will include only studies presenting low risk in all categories or low risk in all categories and unclear risk in allocation bias. An "intermediate risk" will include studies that present at least one unclear risk of bias, except for allocation bias risk. A "high risk" will include studies that present at least one high risk of bias.

Country(ies) involved: China and Brazil.

Keywords: ECT; VNS; rTMS; depression.

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