# INPLASY PROTOCOL

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

**Conflicts of interest:**
**None declared.**

# Chinese medicine intervention for autism spectrum disorders: A protocol for systematic review and network meta-analysis

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**Review question / Objective:** **This study will help patients recover better, provide clinical evidence for practitioners, and promote the use of TCM in ASD interventions.**
**Condition being studied:** **Autism spectrum disorder (ASD) is a neurodevelopmental disorder characterized by impairments in social communication and/or social interaction as well as restrictive and/or repetitive behaviors. TCM has been clinically practiced in the intervention of ASD, especially in mainland China where studies have shown promising efficacy. However, it remains to be further explored and elaborated. Therefore, the purpose of this study was to evaluate the effectiveness and safety of conventional treatment-based TCM intervention modalities for ASD.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 January 2022 and was last updated on 31 January 2022 (registration number INPLASY202210137).

## INTRODUCTION

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## METHODS

**Search strategy:** The study will be implemented from January 2022 and will be searched in the following electronic databases, including the Cochrane Library, Web of Science, PubMed, EMBASE Database, China Biological Medicine Database, Chinese Scientific Journals Database, Wan Fang databases, and China National Knowledge Infrastructure.

**Participant or population:** The age range of patients with ASD included in the study was 2-18 years, through early childhood to adolescence. All participants were diagnosed with ASD without regard to race and gender and were diagnosed according to relevant guidelines or consensus.

**Intervention:** Chinese medicine.

**Comparator:** Conventional intervention.

**Study designs to be included:** Randomized controlled trials of TCM interventions in ASD.

**Eligibility criteria:** The study will focus on all data-complete randomized controlled trials of TCM interventions in ASD, and all ethnic groups will be included in the study. However, language will be limited to studies published in English or Chinese only, and non-randomized controlled trials (e.g., sequential trials, systematic reviews, case reports, clinical experiences, conference abstracts, animal studies, cellular studies) will not be considered.

**Information sources:** Starting in January 2022, we will conduct comprehensive searches in the following databases: the Cochrane Library, Web of Science, PubMed, EMBASE Database, China Biological Medicine Database, Chinese Scientific Journals Database, Wan Fang databases, and China National Knowledge Infrastructure. The language will be limited to English or Chinese.

**Main outcome(s):** The main efficacy evaluation index needs to be the before-and-after results at the end of the intervention or at the end of the follow-up period to evaluate whether the intervention is effective. The efficacy, effectiveness, and ineffectiveness are evaluated according to the relevant forms or questionnaires; the evaluation forms are based on those commonly used in clinical practice, including ADOS or ADI-R or CARS, and one of the three is sufficient because ADOS and ADI-R are less commonly used in China due to the influence of copyright.

**Additional outcome(s):** Include some behavioral questionnaires, such as ABC, ATEC, etc., to evaluate the effect of TCM on the improvement of ASD symptoms in multiple dimensions, and may also include some symptom score scales, etc.

**Quality assessment / Risk of bias analysis:** The quality assessment will be conducted by two researchers (Yuxing Zhang and Hui Zhi) to independently assess the risk of bias in all included randomized controlled trials by applying the Cochrane Collaboration tool, which focuses on the following aspects: task concealment, random sequence generation, blinding of outcome assessors, participant and personnel blinding, selective reporting, completeness of outcome data, and other sources of bias. Each domain was classified as high risk, low risk, or unclear risk. Should disagreements arise during the study, they will be resolved through discussion with a third senior assessor.

**Strategy of data synthesis:** First of all, a conventional meta-analysis will be performed using Revman 5.3. (Cochrane Collaboration, Oxford, UK) for the direct comparisons. Secondly, considering the anticipated heterogeneity, the NMA within a Bayesian framework will be conducted by WinBUGS 1.4.3 (MRC Biostatistics Unit, Cambridge, UK) based on the random effect model for the results of the indirect

comparison. Besides, models will be calculated with Markov chain Monte Carlo algorithm: 4 chains will be employed for simulation analysis, the step size will be set to 10, the number of annealing times will be set to 20,000 for reducing the impact on arbitrary values, and the number of iterations will be set to 50,000.Additionally, the continuous outcomes will be measured by standard mean difference with 95% confidence interval for indirect comparisons, while binary variable selection relative risk and 95% confidence interval. Thirdly, the plot of surface under the cumulative ranking curve will be computed by STATA 14.0. (Stata Corporation, College Station, Texas) to forecast the possible ranking order. In our study, a higher surface under the cumulative ranking curve score represents the better TCM intervention for ASD.

**Subgroup analysis:** Not mentioned.

**Sensitivity analysis:** In general, differences between different kinds of evidence may be the main reason for inconsistency. Therefore, inconsistencies between indirect and direct evidence will be assessed by circular inconsistency tests and nodal splitting methods. In addition, Z-values will be calculated as well as the corresponding P-values, with P-values less than 0.05 showing significant differences. If significant heterogeneity is found, subgroup analyses will be performed according to possible sources of heterogeneity, such as severity of children with ASD, age stratification, evaluation forms, etc.

**Language:** Chinese and English.

**Country(ies) involved:** China.

**Keywords:** autism spectrum disorders, Traditional Chinese medicine.

**Contributions of each author:**

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Author 5 - Zhichao Gong - Data curation.
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