

# INPLASY PROTOCOL

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**Conflicts of interest:**  
The authors have no conflicts of interest to declare.

## INTRODUCTION

**Review question / Objective:** Acute cerebral infarction (ACI) is a type of stroke with high incidence, recurrence and mortality, accounting for 69.6% to 70.8% of stroke cases in China. Chinese herbal

## Effectiveness comparisons of different Chinese herbal injection therapies for acute cerebral infarction: A protocol for systematic review and network meta-analysis

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**Review question / Objective:** Acute cerebral infarction (ACI) is a type of stroke with high incidence, recurrence and mortality, accounting for 69.6% to 70.8% of stroke cases in China. Chinese herbal injection (CHI) contains active ingredients of herbal medicine and is widely used in the adjuvant therapy of ACI. Due to the lack of randomized trials directly comparing the efficacy of various injections, it is still difficult to judge the relative efficacy. Therefore, we intend to conduct a network meta-analysis to evaluate the benefit among these CHI.

**Condition being studied:** Acute cerebral infarction (ACI) is a type of stroke with high incidence, recurrence and mortality, accounting for 69.6% to 70.8% of stroke cases in China. Chinese herbal injection (CHI) is widely used in the adjuvant therapy of ACI. But due to the lack of high-quality clinical studies, few direct comparison studies between drugs and insufficient evidence-based medicine, it has not been listed as a high-level recommendation in the guidelines, and the choice of clinical medication is not clear. We evaluated the efficacy and safety of CHI in promoting neurological function recovery based on NIHSS score, therapeutic efficacy and incidence of adverse reactions.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 June 2020 and was last updated on 23 June 2020 (registration number INPLASY202060087).

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meta-analysis to evaluate the benefit among these CHI.

**Rationale:** As a branch of traditional meta-analysis, network meta-analysis is an important evidence-based medicine tool that can indirectly compare interventions and give benefit ranking prediction.

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## METHODS

**Search strategy:** #1 "Brain Infarction"[Mesh] OR "cerebral infarction" OR "stroke" OR "brain embolism" OR "Ischemic stroke" OR "cerebrovascular disorders". #2 "Tanshinone type IIA sulfonate injection" OR "Die Mai Ling Injection" OR "Die-mailing injection" OR "Die-mailing zhusheye". #3"Ku die zi Injection" OR "Ku die zi zhusheye".#4"Safflower yellow injection". #5"Gegensu Zhusheye" OR "Puerarin Injection" OR "Gegensu injection".#6"Danhong injection" OR "Danhong zhusheye". #7"Shuxuetong injection" OR "Shuxuetong zhusheye". #8"Breviscapine injection" OR "Dengzhanhuasu Injection" OR "Dengzhanhuasu zhusheye". #9"Shuxuening injection" OR "Shuxuening zhusheye" OR "ginkgo biloba injection" OR "ginkgo leaf injection". #10"Tetramethylpyrazine injection" OR "Chuanxiongqin" OR "Chuanxiongqin zhusheye" OR "Chuanxiongqin injection" OR "Xuesaitong injection" OR "Xuesaitong

zhusheye". #11 randomized controlled trial OR controlled clinical trial. #12 #1 AND #2 AND #3 AND #4 AND #5 AND #6 AND #7 AND #8 AND #9 AND #10 AND #11.

**Participant or population:** As a systematic review and network meta-analysis, patients, and the public will not be directly involved in the design or planning of this study.

**Intervention:** Intervention measures: thrombolytic therapy, anti-platelet, anticoagulation, nutritional nerve and control of blood pressure, blood glucose, blood lipid as routine treatment. On this basis, the treatment group was given CHI, while the control group was given routine treatment or another CHI.

**Comparator:** Intervention measures: thrombolytic therapy, anti-platelet, anticoagulation, nutritional nerve and control of blood pressure, blood glucose, blood lipid as routine treatment. On this basis, the treatment group was given CHI, while the control group was given routine treatment or another CHI.

**Study designs to be included:** Type of study: Randomized controlled trials (RCTS) literature.

**Eligibility criteria:** Eligibility Criteria Type of study: Randomized controlled trials (RCTS) literature; Subjects: The diagnosis of ACI met the diagnostic criteria of cerebral infarction revised at the 4th National Conference on Cerebrovascular Diseases in 1995 or the Chinese Guidelines for diagnosis and Treatment of Acute Ischemic Stroke 2014 and 2018 editions, regardless of gender or age; Intervention measures: thrombolytic therapy, anti-platelet, anticoagulation, nutritional nerve and control of blood pressure, blood glucose, blood lipid as routine treatment. On this basis, the treatment group was given CHI, while the control group was given routine treatment or another CHI. Outcome indicators: the national Institutes of Health stroke Scale (NIHSS) score after treatment, the number of effective patients, and the

number of adverse reactions. Exclusion Criteria.

**Information sources:** According to the retrieval strategies, randomized controlled trials on the treatment of ACI with CHI were obtained from CNKI, WanFang, VIP, PubMed, Embase and Cochrane Library.

**Main outcome(s):** Outcome indicators: the national Institutes of Health stroke Scale (NIHSS) score after treatment, the number of effective patients, and the number of adverse reactions.

**Data management:** The network meta-analysis was carried out with Stata 14 and WinBUGS 1.4.3 software, and the results were included in cluster analysis to comprehensively evaluate drug benefits.

**Quality assessment / Risk of bias analysis:**

Two reviewers will be designated to assess the quality of included RCTs independently by utilizing the Cochrane risk of bias assessment tool. As specified by Cochrane Handbook V.5.1.0, the following sources of bias will be considered: random sequence generation, allocation concealment, participant blinding, outcome assessor blinding, incomplete outcome data, selective reporting, and other sources of bias. Each domain will be rated as high, low or unclear risk of bias as appropriate. The two reviewers will resolve any disagreements through discussion, and a third reviewer may be involved if no consensus is reached.

**Strategy of data synthesis:** Endnote 9.0 software was used for literature management. The dichotomous variables were calculated by the OR. Continuous variables were calculated by MD, and 95%CI (Confidence Intervals) was given. Draw network evidence diagram with Stata 14 software. Nonconformance testing is performed to evaluate the reliability of the model. Funnel plot was used to evaluate literature publication bias. WinBUGS 1.4.3 software was used for mesh meta-analysis. The stochastic effect model of Markov Chain Monte Carlo (MCMC) was used for Bayesian inference. The prior probability

was used to infer the posterior probability. The consistency model was used for data analysis, and 3 chains were set for simulation. The number of iterations was set to 100000. The first 10000 times were used for annealing to eliminate the influence of initial value, and the last 90000 times were used for sampling. Finally, Stata 14 software was used to analyze the mesh meta-analysis to observe the index ranking data, and the area under the curve (SUCRA) was used as the coordinate system for cluster analysis, and a scatter plot was drawn to comprehensively evaluate the efficacy and safety of drugs.

**Subgroup analysis:** If variability exists among the studies with regard to CHI types, subgroup analysis will be performed to investigate whether the results were significantly different.

**Sensibility analysis:** If necessary, sensitivity analysis will be performed to evaluate data reliability on the basis of the methodological quality.

**Language:** There will be no restriction on language.

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

**Keywords:** network meta-analysis; acute cerebral infarction; Chinese herbal injection; protocol.

**Contributions of each author:**

Author 1 - Runmin Li - Writing – original draft.

Author 2 - Ying Li - Writing – original draft.

Author 3 - Bingchen Li.

Author 4 - Haiyang Sun - Data curation.

Author 5 - Xinyu Liu - Data curation.

Author 6 - Xin Ge - Data curation.

Author 7 - Yuanxiang Liu - Writing – review & editing.

Author 8 - Jiguo Yang - Writing – review & editing.