INPLASY PROTOCOL

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

# Traditional Chinese Medicine for Kawasaki disease: A protocol for a systematic review and meta-analysis

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**Review question / Objective:** **This systematic review will evaluate the efficacy and safety of TCM for treating KD.**
**Condition being studied:** **Kawasaki disease (KD), also known as mucocutaneous lymph node syndrome, is an acute systemic vascular inflammatory disease which occurs in infants under 5 years old. Its clinical manifestations are complex, and in severe cases, myocardial ischemia, myocardial infarction and even sudden death may occur. At present, in developed countries, KD has become the main cause of acquired heart disease in children. As an important treatment method, traditional Chinese medicine plays an important role in the treatment of KD. The purpose of this study is to evaluate the efficacy and safety of Chinese medicine in treating KD**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 December 2020 and was last updated on 25 December 2020 (registration number INPLASY2020120066).

## INTRODUCTION

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## METHODS

**Participant or population:** Participants in the selected articles had no restrictions on gender, region, nationality, belief, race, origin and course of disease, except that the age was less than or equal to 5 years old.

**Intervention:** The experimental group was treated with traditional Chinese medicine on the basis of conventional western medicine. The use of traditional Chinese medicine is limited to prescription drugs and proprietary Chinese medicine. Prescription drugs require definite dosage, but there are no restrictions on drug composition, dosage form and dosage. The dosage forms can be soup, paste, pill or powder, etc. Acupuncture, massage and other traditional Chinese medicine treatment methods will be excluded.

**Comparator:** The control group was treated with conventional western medicine or surgery. Conventional western medicine generally includes oral aspirin, glucocorticoid or intravenous gamma globulin. Coronary artery bypass grafting, interventional catheterization and heart transplantation are commonly used in surgery. Specific drugs, doses and methods are not limited. The control group was excluded from traditional Chinese medicine treatment.

**Study designs to be included:** We will search all the studies that traditional Chinese medicine is used as the main intervention for KD. Non-randomized controlled trials (non-RCTs), quasirandomized controlled trials (qRCTs), summaries of personal experience, case reports, and crossover studies will be excluded. There are no language restrictions.

**Eligibility criteria:** Types of studies. We will gather all studies of TCM therapy in treating KD based on the method of RCT. Non-randomized controlled trials (non-RCTs), quasirandomized controlled trials (qRCTs), summaries of personal experience, case reports, and crossover studies will be excluded. There are no language restrictions. Types of participants. Participants in the selected articles had no restrictions on gender, regional, national, belief, ethnic, sources, and courses of disease, except that the age was less than or equal to 5 years old. Types of interventions. There is no requirement for the intervention course, the specific contents of the control group and the experimental group are as follows. Control interventional. The control group is treated with conventional western medicine or surgery. The specific drugs, dosages, and methods are not limited. If the patients in the control group are treated with traditional Chinese medicine, the research will be excluded. Experimental interventional. The experimental group was treated with traditional Chinese medicine on the basis of conventional western medicine. The use of traditional Chinese medicine is limited to prescription and Chinese patent medicines. Prescription drugs require definite dosage, but there are no restrictions on drug composition, dosage form and dosage. Acupuncture, massage and other traditional Chinese medicine treatment methods will be excluded.

**Information sources:** Ongoing experiments which have been registered on World Health Organization International Clinical Trials Registry Platform (ICTRP) or Chinese Clinical Trial Registry. Try to contact the researchers to inquire about the progress of the trial and provide the latest test data. As for grey literature, we will retrieve on the following websites: GreyNet International, SIGLE (The System for Information on Grey

Literature in Europe), Open Gery, Gery Literature Report.

**Main outcome(s):** Primary outcomes. The main results were clinical symptoms (fever, conjunctival membrane congestion, lip and oral manifestations, hand and foot symptoms, skin manifestations and cervical lymph node enlargement) and changes in coronary artery (coronary aneurysm, coronary artery stenosis or expansion). Secondary outcomes. The secondary evaluation criteria were: blood routine (WBC count, ESR, CRP), immunological indexes (Ab, blood circulation immune complex), ECG, chest X-ray and echocardiography. More importantly, the incidence of adverse reactions in the trial will also be recorded.

**Quality assessment / Risk of bias analysis:** Publication bias. If a result of a meta-analysis contains more than 10 articles, we will use a funnel plot to test the risk of publication bias. Quality of evidence. The quality of evidence for the main outcomes will also be assessed with the Grading of Recommendations Assessment, Development and Evaluation approach. The evaluation included bias risk, heterogeneity, indirectness, imprecision, and publication bias. And each level of evidence will be made “very low,” “low,” “medium” or “high” judgment.

**Strategy of data synthesis:** The meta-analysis in this review will use Revman 5.3 and stata13.0 software. Relative risk (RR) was used as the result index of the two categorical variables. The confidence interval (CI) of the mean difference (MD) or standardized mean difference (SMD) was 95% for the result indicators of continuous variables. Heterogeneity testing will be used for inclusion studies and tested by chi square test. When P¡Ý.10 and I2¡Ü50%,, there was no significant statistical heterogeneity or difference, then fixed effect model was used. If P < .10 and / or I2 > 50%, there is significant heterogeneity between studies, then the random effect model is used. Further analysis of the source of heterogeneity, if necessary, grouping analysis. There are differences in clinical and methodological aspects. Therefore, this paper will choose random effects model learning. Finally, funnel plot was drawn to evaluate publication bias.

**Subgroup analysis:** Subgroup analysis to explore the differences in age, gender, interventions, and course of disease/ treatment. We used funnel plots to identify whether there was small study bias if 10 or more studies were included. The asymmetry of funnel plots suggests the possibility of small study effects, and the results of analysis were explained cautiously.

**Sensibility analysis:** Sensitivity analysis will be performed to test the robustness of findings if there are sufficient studies included. The factors on effect are as follows: 1. Methodologic quality: analysis will be performed excluding studies of poor methodologic quality; 2. Published status: analysis will be performed excluding unpublished studies; 3. Sample size: analysis will be performed excluding small sample size studies; 4. Diagnostic criteria: analysis will be performed in studies of the same diagnostic criteria; 5. Race/ethnicity: analysis will be performed in studies of the same race or ethnicity.

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

**Keywords:** Kawasaki disease, protocol, systematic review, traditional Chinese medicine.

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