INPLASY PROTOCOL

To cite: Huang et al. Regulatory effect of traditional Chinese medicine on gut microbiota in patients with atherosclerosis：A protocol for systematic review and meta-analysis. Inplasy protocol 2020110056. doi: 10.37766/inplasy2020.11.0056

Received: 14 November 2020

Published: 14 November 2020

**Corresponding author:**
**Langlang Huang**

**1255283375@qq.com**

**Author Affiliation:**
**Jiangxi University of Traditional Chinese Medicine**

**Support:** **No.81660781.**

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

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

# Regulatory effect of traditional Chinese medicine on gut microbiota in patients with atherosclerosis：A protocol for systematic review and meta-analysis

Huang, LL[1]; Wang, JA[2]; Xu, R[3]; Liu, YW[4]; Liu, ZY[5].

**Review question / Objective:** **Atherosclerosis is the pathological basis of many cardiovascular and cerebrovascular diseases, and its pathogenesis is complex. Recent studies revealed a significant role of gut microbiota in the onset and development of atherosclerosis. Traditional Chinese medicine has rich clinical experience and unique advantages in the treatment of atherosclerosis. A large number of studies have proved that traditional Chinese medicine has the functions of reducing blood lipid, regulating gut microbiota and resisting inflammation. The aim of this systematic review is to observe the randomized controlled trial of traditional Chinese medicine in treating gut microbiota, so as to evaluate the effectiveness and safety of traditional Chinese medicine in treating atherosclerosis patients.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 November 2020 and was last updated on 14 November 2020 (registration number INPLASY2020110056).

## INTRODUCTION

**Review question / Objective:** **Atherosclerosis is the pathological basis of many cardiovascular and cerebrovascular diseases, and its pathogenesis is complex. Recent studies revealed a significant role of gut microbiota in the onset and development of atherosclerosis. Traditional Chinese medicine has rich clinical experience and unique advantages in the treatment of atherosclerosis. A large number of studies have proved that traditional Chinese medicine has the**

functions of reducing blood lipid, regulating gut microbiota and resisting inflammation. The aim of this systematic review is to observe the randomized controlled trial of traditional Chinese medicine in treating gut microbiota, so as to evaluate the effectiveness and safety of traditional Chinese medicine in treating atherosclerosis patients.

**Condition being studied:** Atherosclerosis (AS) is a chronic inflammatory disease related to lipid accumulation and changes in a blood vessel wall components. With the development of the social economy and the aggravation of population aging, its incidence rate increases, which causes higher mortality and social pressure in the world.This disease's pathogenesis is complex , neither theory can fully explain the formation mechanism of AS alone. There are more than 3,500 kinds of gut microbiota(GM) in normal human intestines. GM's stable composition and function play an essential role in maintaining the intestinal tract's normal physiological part and immune defense. More and more evidence shows that GM imbalance can lead to the formation of AS by participating in the regulation of cholesterol metabolism, oxidative stress, and inflammation; Moreover, GM produces metabolites to regulate the immunity and metabolism of host, thus affecting the occurrence and development of AS. Many studies have proved that Traditional Chinese medicine(TCM) has the functions of protecting vascular endothelial cells, resisting platelet aggregation, resisting inflammation, resisting oxidative stress, and regulating GM. Moreover, TCM can also play an anti-atherosclerosis role by regulating the metabolites of GM.

## METHODS

**Participant or population:** Patients who meet the diagnostic criteria for atherosclerosis will be included.

**Intervention:** The treatment group was treated with TCM or TCM combined with western medicine.

**Comparator:** The control group will receive western medicine treatment or without intervention and was not treated with TCM.

**Study designs to be included:** Randomized controlled trials (RCTs) on TCM intervention in treating atherosclerosis patients will be included in this review.

**Eligibility criteria:** (1)TCM combined with other non-drug adjuvant therapies(such as tai chi, acupuncture, and moxibustion); (2)Documents with similar original data and repeated publication; (3)Documents for which accurate data cannot be obtained; (4)Case report, conference papers, and summaries; (5)No RCT.

**Information sources:** We will search the following databases from their inception onwards to the October 2020: PubMed, Web of Science, Embase, the Cochrane Library, China National Knowledge Infrastructure, the Chongqing VIP Chinese Science and Technology Periodical Database, Wanfang Database, and China Biomedical Literature Database. We will also manually search the Chinese Clinical Trial Register, conference papers, and unpublished studies or references.

**Main outcome(s):** The lipid metabolism outcome indicators (TG, TC, HDL-C, LDL-C, HDL, LDL, ApoA1, ApoB) and gut microbiota and its metabolites (gut microbiota structure and diversity, TMAO, SCFAs, BA) are the primary outcome indicators of this study.

**Quality assessment / Risk of bias analysis:** According to the bias risk evaluation standard of randomized controlled trials provided by Cochrane Handbook, the literature quality evaluation is carried out, which includes the following six aspects: random sequence generation, allocation concealment, blinding of participants, caregivers, outcome assessors, incomplete outcome data, selective outcome reporting, and other bias. According to the specific scoring rules, the two researchers evaluated three types: "low risk," "high risk," and "uncertain risk." If there is any

difference in quality evaluation, discuss it with the third author.

**Strategy of data synthesis:** RevMan5.3.5 software will be used for this meta-analysis. According to the heterogeneity level included in the study, the fixed-effect model or the random effect model was selected. We will conduct a meta-analysis of at least three qualified standards. Otherwise, if only one or two studies met the inclusion criteria, meta-analysis will not be undertaken, but the descriptive analysis will be adopted. If more than 10 articles are included, the inverted funnel diagram is used to analyze publication bias.

**Subgroup analysis:** If heterogeneity is observed in the study, we will use subgroup analysis for research.

**Sensibility analysis:** We consider sensitivity analysis for methodological quality and test the results' robustness by excluding the risk of low quality and high bias.

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

**Keywords:** traditional Chinese medicine, gut microbiota, atherosclerosis, protocol, systematic review.

**Contributions of each author:**
Author 1 - Langlang Huang - Conceptualization, Data curation, Investigation, Methodology, Writing – original draft, Writing – review & editing.
Author 2 - Jianan Wang - Data curation, Formal analysis,Methodology, Software, Writing – original draft, Writing – review & editing.
Author 3 - Ri Xu - Data curation, Formal analysis, Methodology,Writing – review & editing.
Author 4 - Yanwei Liu - Formal analysis, Methodology, Software, Writing – original draft.
Author 5 - Zhongyong Liu - Conceptualization, Investigation, Supervision, Writing – original draft.