

# INPLASY PROTOCOL

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

## INTRODUCTION

**Review question / Objective:** Adults more than 18 years of age; had an intervention duration not less than 8 weeks.

## Long-term Use of Different Kinds of Probiotics for the Management of Office and Ambulatory Blood Pressure: A Systematic Review and Meta-Analysis

Zhao, TX<sup>1</sup>; Zhang, L<sup>2</sup>; Zhou, N<sup>3</sup>; Xie, JH<sup>4</sup>; Xu, SK<sup>5</sup>.

**Review question / Objective:** The aim of this meta-analysis of randomized controlled trials is to evaluate the efficacy and safety of long-term use of different kinds of probiotics for the management of office and ambulatory blood pressure.

**Condition being studied:** Despite major advances in the identification of key pathophysiologic mechanisms and in treatment, hypertension remains one of the most important causes of acute and chronic cardiovascular diseases. Animal and human studies have shown that the imbalance in the abundance, diversity and evenness of certain microbiota species is associated with hypertension. However, the impact of probiotics on blood pressure and which kind of probiotics have the greatest impact on blood pressure are still uncertain. Thus, we conducted this meta-analysis to investigate the effect of long-term probiotic consumption (> 8 weeks) on blood pressure.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 February 2022 and was last updated on 23 February 2022 (registration number INPLASY202220097).

**Condition being studied:** Despite major advances in the identification of key pathophysiologic mechanisms and in treatment, hypertension remains one of the most important causes of acute and chronic cardiovascular diseases. Animal

and human studies have shown that the imbalance in the abundance, diversity and evenness of certain microbiota species is associated with hypertension. However, the impact of probiotics on blood pressure and which kind of probiotics have the greatest impact on blood pressure are still uncertain. Thus, we conducted this meta-analysis to investigate the effect of long-term probiotic consumption (> 8 weeks) on blood pressure.

## METHODS

**Participant or population:** Adults more than 18 years of age; had an intervention duration not less than 8 weeks.

**Intervention:** Long-term (>8 weeks) use of probiotics was the main intervention (e.g. Lactobacillus, streptococcus, bifidobacter). Also, probiotic products with live bacteria (e.g. capsules, fermented milk and bread) were included.

**Comparator:** The control group used drugs or foods that did not contain any probiotics.

**Study designs to be included:** Randomized clinical trials will be included irrespective of blinding, publication status or language.

**Eligibility criteria:** Eligible studies were included if they met the inclusion criteria: accessible full articles in English; a randomized controlled trial; included adults more than 18 years of age; used probiotic products with live bacteria in the intervention group, and used placebo products in the control group; had an intervention duration not less than 8 weeks. Inclusion criteria: adults more than 18 years of age; used probiotic products with live bacteria in the intervention group, and used placebo products in the control group; had an intervention duration not less than 8 weeks.

**Information sources:** We will search articles in three electronic database including PubMed, Embase, Cochrane Library and ClinicalTrials.gov databases for relevant studies. All the English publications until

October, 2021 will be searched without any restriction of countries or article type. Reference list of all selected articles will independently screened to identify additional studies left out in the initial search.

**Main outcome(s):** Mean change in office and ambulatory blood pressure from baseline.

**Additional outcome(s):** Mean change in glucose, lipid profile and arteriosclerosis from baseline.

**Data management:** Two authors will independently extract data. Any disagreement will be resolved by discussion until consensus is reached or by consulting a third author. The following data will be extracted: author, year of publication, country where the study was conducted, study period, original inclusion criteria, total number of people included in the study, probiotic type, doses of probiotics and changes of blood pressure from baseline.

**Quality assessment / Risk of bias analysis:** Assessment of risk bias was conducted by two separated authors based on the Cochrane Risk of Bias tool, which included: random sequence, allocation concealment, blinding of subjects and researchers, incomplete outcome data, selecting reporting of outcomes and other bias.

**Strategy of data synthesis:** The Stata software (Version 14.0) was used for data management and statistical analysis. The net effect of probiotics on BP was defined as the weight mean difference of changes between the probiotics and control group. We used Cochran's Q test and I<sup>2</sup> statistic to test the between-study heterogeneity. Because of the low variation between studies' population and BP analysis, we used the fixed-effect model for the pooled analyses. A P value <0.05 was considered statistical significant. In case of heterogeneity, subgroup analyses, sensitivity analyses and meta-regression were further inspected.

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**Subgroup analysis:** The studies were divided into three tertiles for further statistical analysis according to their initial age, baseline body mass index, treatment duration and systolic BP, respectively. We then performed tests for linear trend by entering the median value of each quartile as a continuous variable in the models. Subgroup analysis of the effects of different probiotics on blood pressure should also be carried out.

**Sensitivity analysis:** The Begg's funnel plots and Egger's regression tests were used to assess the potential publication bias at the  $P < 0.10$  level of significance. In case of heterogeneity, subgroup analyses, sensitivity analyses and meta-regression were further inspected.

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

**Keywords:** Meta-analyses; Blood pressure; Probiotics; Randomized controlled trials.

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