# INPLASY PROTOCOL

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# Treating asthma patients with probiotics: A systematic review and meta-analysis

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**Review question / Objective:** To evaluate the role of probiotics in the treatment of asthma patients by meta-analysis.

Condition being studied: Asthma is a common chronic inflammatory respiratory disease, with high morbidity and mortality. Studies have shown that the proportion of children aged 13 - 14 and children aged 6 – 7 suffering from asthma increases by 0.28 % and 0.18 % annually. Due to the high incidence of asthma and the great economic pressure to treat asthma, it has attracted more and more attention from all walks of life in the past. The etiology and pathogenesis of asthma have not been fully elucidated, which may be related to various factors such as genetics, bacteria, viruses, immunity, nutrition, and environment. Asthma is mainly treated by inhaled corticosteroids, long-acting β-receptor agonists, leukotriene antagonists, and other drugs . Recently, the efficacy of probiotics in allergic diseases has received special attention. Experiments have shown that probiotics have a clear effect on allergic diseases such as allergic rhinitis and eczema . However, the current meta-analysis showed that Lactobacillus supplementation had a positive effect on asthma prevention, while other probiotics had no significant effect on asthma prevention and treatment . This is inconsistent with the conclusions of some experiments . In this study, Meta-analysis was used to study the efficacy of probiotics in the treatment of asthma and evaluate it, so as to provide reference for the selection of treatment options for asthma patients.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 July 2022 and was last updated on 16 July 2022 (registration number INPLASY202270076).

## INTRODUCTION

**Review question / Objective:** To evaluate the role of probiotics in the treatment of asthma patients by meta-analysis.

**Rationale:** PubMed, Embase, The Cochrane Library, Web of Science, and other databases were searched by computer, and the relevant literature on the treatment of asthma by probiotics that met the inclusion criteria was screened by manual retrieval. Meta-analysis was performed using Revman 5. 4 software and the combined effect was evaluated by odds ratio (OR) or (MD) and 95 % confidence interval (CL).

Condition being studied: Asthma is a common chronic inflammatory respiratory disease, with high morbidity and mortality. Studies have shown that the proportion of children aged 13 - 14 and children aged 6 -7 suffering from asthma increases by 0.28 % and 0.18 % annually. Due to the high incidence of asthma and the great economic pressure to treat asthma, it has attracted more and more attention from all walks of life in the past. The etiology and pathogenesis of asthma have not been fully elucidated, which may be related to various factors such as genetics, bacteria, viruses, immunity, nutrition, and environment. Asthma is mainly treated by inhaled corticosteroids, long-acting βreceptor agonists, leukotriene antagonists, and other drugs . Recently, the efficacy of probiotics in allergic diseases has received special attention. Experiments have shown that probiotics have a clear effect on allergic diseases such as allergic rhinitis and eczema . However, the current metaanalysis showed that Lactobacillus supplementation had a positive effect on asthma prevention, while other probiotics had no significant effect on asthma prevention and treatment. This is inconsistent with the conclusions of some experiments . In this study, Meta-analysis was used to study the efficacy of probiotics in the treatment of asthma and evaluate it. so as to provide reference for the selection of treatment options for asthma patients.

## **METHODS**

Search strategy: We searched PubMed, Embase, The Cochrane Library and Web of Science databases to collect randomized controlled trials that met the inclusion criteria until July 2022. References for the included studies were also searched to supplement access to relevant information.

Participant or population: The inclusion of subjects is not limited by age, gender, etiology, or ethnic group.Asthma diagnosis

is consistent with the Global Asthma Initiative 2014 ; There was no significant difference in age, gender, course of disease among the groups, and they were comparable; the experimental group was treated with probiotics (unlimited strains, doses, and courses of treatment), and the control group was treated with placebo.

Intervention: The experiment uses one or more Fractional exhaled nitric oxide(FeNO), Forced expiratory volume in the first second(FEV1), FEV1/FVC (%), asthma symptom inflammation degree, Childhood Asthma Control Test CACT, and the number of exacerbations to evaluate the experimental results.

**Comparator:** FeNO ,Asthma symptom severity,CACT,The number of acute episodes of asthma,FEV1,FEV1 / FVC (%).

Study designs to be included: Literature screening and data extraction Two researchers independently screened literature, extracted data and crosschecked them. If there are differences, they are solved through discussion or consultation with the third party. In literature screening, we first read the topic, and after excluding the obviously irrelevant literature, we further read the summary and full text to determine whether it is included. Contact the author of the original study by email or telephone, if necessary, to obtain undetermined but important information for this study. Data extraction included: research topics

Eligibility criteria: The inclusion of subjects is not limited by age, gender, etiology, or ethnic group.Asthma diagnosis is consistent with the Global Asthma Initiative 2014 ; There was no significant difference in age, gender, course of disease among the groups, and they were comparable; the experimental group was treated with probiotics (unlimited strains, doses, and courses of treatment), and the control group was treated with placebo. The experiment uses one or more Fractional exhaled nitric oxide(FeNO), Forced expiratory volume in the first second(FEV1), FEV1/FVC (%), asthma symptom inflammation degree, Childhood Asthma Control Test CACT, and the number of exacerbations to evaluate the experimental results.Exclusion criteria : Diseases with liver, gastrointestinal, kidney, endocrine, neuronal, cardiovascular, or psychiatric disorders or malignant tumors that may affect the results of the study Active upper respiratory tract infection conference papers, reviews, case reports, summaries of experiences, and repeated literature. The information contained in the literature is incomplete and cannot be obtained through other information ; low quality of literature (Cochrane Handbook < 2)

**Information sources:** PubMed, Embase, The Cochrane Library, Web ofScience.

Main outcome(s): The use of probiotics in patients with asthma can improve lung inflammation and asthma symptoms, reduce the number of asthma attacks, and have no effect on lung function.

Quality assessment / Risk of bias analysis:

Two commentators independently analyzed the included literature according to the Cochrane bias risk assessment criteria, and the inconsistencies were reached through discussion. The evaluation contents include: 1, the generation of the random allocation scheme; 2, the concealment of the allocation scheme;3 the implementation of the blind method; 4 the integrity of result data; 5, non-selective report of results; 6, other biases. "Low risk" means low risk of bias, " High risk " means high risk of bias, " Unclear risk " means that literature does not provide sufficient or uncertain information for bias assessment.

Strategy of data synthesis: Statistical analysis was performed using RevMan 5.4 software. For the enumeration data, relative risk (RR) and 95% confidence interval (95% CI) were used as efficacy analysis statistics. When there is statistical homogeneity among the studies (P>0.1, I2<50%), a fixed effect model is used for meta-analysis; if there is significant heterogeneity among the studies (P50%) ), further analyze the source of heterogeneity, and perform subgroup analysis on factors that may lead to heterogeneity. A random effects model was used for analysis. The funnel plot was used to judge whether there was publication bias in the included literature, and Egger's test could be used when there were at least 10 studies. Inspection level  $\alpha = 0.05$ .

Subgroup analysis: None.

Sensitivity analysis: The funnel plot was used to judge whether there was publication bias in the included literature, and Egger's test could be used when there were at least 10 studies. Inspection level  $\alpha = 0.05$ .

Language: The inclusion of subjects is not limited by age, gender, etiology, or ethnic group.

Country(ies) involved: China.

Other relevant information: The inclusion of subjects is not limited by age, gender, etiology, or ethnic group.

Keywords: probiotics, asthma, meta.

#### **Contributions of each author:**

Author 1 - Xie Qiwei. Author 2 - Yuan Jiatian. Author 3 - Wang Yaoweng.