

# Effectiveness Probiotic Multistrain In Therapy Of Atopic Dermatitis : Systematic Review And Meta-Analysis

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## Abstract

Atopic dermatitis (AD) is a common chronic inflammatory skin condition in pediatric patients. Probiotics have been proposed as a potential adjunctive therapy for AD because of anti-inflammatory effects and can alleviate clinical symptoms of atopic dermatitis (AD) in children. However, the effectiveness of probiotic supplementation in pediatric patients with AD remains controversial. This study aimed to evaluate the clinical efficacy of probiotics for AD in children. We collected studies from several databases, including Pubmed, Cochrane, and ScienceDirect that were published from 2014 to 2024 with keywords “Atopic Dermatitis” OR “Eczema” AND “Pediatric” OR “Child” AND “Probiotic” OR “Lactobacillus” OR “Bifidobacterium” AND “Randomized Controlled Trial” OR “Clinical Trial”. Studies were assessed using Newcastle-Ottawa Scale (NOS). We performed a meta-analysis using a random-effect model in RevMan 5.4 with a 95% Confidence Interval (CI). A total of 3 published studies with a total number of 300 patients with Atopic Dermatitis (AD) were included. Most studies were concluded to have a low risk of bias based on NOS assessment. The pooled analysis showed there was significant improvement in SCORAD [-7.04(-14.44 to 0.37); 95% CI, p-value = 0.008; I<sup>2</sup>= 79%] in treatment of probiotic. However, the funnel plot showed a symmetrical figure, indicating low publication bias. Multistrain probiotic intervention was effective in reducing SCORAD index so it can reduce the rate of atopic dermatitis and promising therapy for AD.

*Keywords : Atopic Dermatitis, Pediatric ; Probiotic ; Multistrain ; Meta-analysis*

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## Introduction

Infants and pediatric are frequently affected with atopic dermatitis (AD), chronic inflammatory skin disease marked by itching and recurrent eczematous lesions. In general, it raises the risk of mental health problems, allergies, and asthma. In developed countries, 10-15% of babies and children suffer from AD, a disease that has become more common worldwide in recent decades. To control the condition, a variety of nonpharmacological therapies (such as moisturisers and bathing routines) and topical pharmacotherapies (such as topical corticosteroids, calcineurin inhibitors, and antihistamines) have been used frequently as first-line treatments. On the other hand, nonpharmacological therapies are utilised to treat minor diseases with the primary goal of decreasing transepidermal water loss and raising skin hydration. Additionally, the concerns regarding safety associated with long-term usage of topical corticosteroids (the first-line topical medication in the treatment of AD) are becoming more and more popular, particularly when the patients are young. Antihistamines are among the other medications that have been investigated for AD treatment, but sadly, they have not shown much promise. It is important to find novel therapeutics with promising results and safety for use in both prevention and treatment of AD, given the high prevalence of AD, possible long-term health implications, and safety issues surrounding present AD drugs. The hygiene theory states that early childhood infections may be minimised, which could lead to the development of allergy illnesses. Furthermore, several

researchers have discovered that children with and without AD have different gut microbiota compositions . This data bolsters the theory that the stomach should be appropriately colonised by microorganisms. may lessen the chance of contracting atopic illnesses. Living bacteria known as probiotics, which have been shown to benefit the host when ingested in sufficient quantities, are gaining popularity as a treatment for some gastrointestinal disorders, such as necrotising enterocolitis and diarrhoea. There have been mixed findings from research on the prevention and management of AD in children , several relevant meta-analyses were published; however, these studies focused on probiotics' ability to cure AD or prevent the disease. Performing a comprehensive assessment of the literature and a meta-analysis of randomised controlled trials was our goal. studies looking into how oral probiotics can help prevent and treat childhood AD.

## **Methodology**

### *1.1. Study Design*

A meta-analysis, following the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) protocols, was conducted to determine the Clinical Efficacy of multistrain probiotic to prevent Atopic Dermatitis. This research was to compare between the effect of multistrain probiotic and placebo. To formulate a comprehensive comparison, the relevant articles were collected and the information of interest was extracted to compare better results between Multistrain probiotic in decrease SCORAD in dermatitis atopic. We included all RCTs evaluating the effect of probiotics on AD, for either prevention or treatment of the disease. Participants in the study were under 18 years of age, and probiotics were administered orally with the species, dosage, and duration of administration clearly documented. The control group received either a placebo or another alternative intervention, excluding prebiotics and synbiotics. The primary endpoint was assessed at the first follow-up after the intervention, and studies with extended follow-up periods from the same population were excluded. For prevention trials, the incidence of atopic dermatitis (AD) was evaluated, while in treatment trials, the severity of AD was measured using the Scoring Atopic Dermatitis (SCORAD) index. AD diagnosis followed standard, searchable criteria. Conference abstracts, letters, and comments were excluded, as they did not provide sufficient information for a thorough evaluation of the study.

### *1.2. Search Strategy*

This systematic review and meta-analysis is reported according to preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline for network meta-analysis . By reading the study's full text and abstract as well as the title, the search process was established. For the purpose of determining if a study was acceptable, the authors conducted a thorough investigation. A study that was considered eligible was included in this meta-analysis study. When there are any differences in study selection, the author analyzes them. We created the search keyword using medical subject heading and terms relating to the target condition as follows: "Atopic Dermatitis" OR "Eczema" AND "Pediatric" OR "Child" AND "Probiotic" OR "Lactobacillus" OR "Bifidobacterium" AND "Randomized Controlled Trial" OR "Clinical Trial". We searched on Cochrane Library, PubMed, and ScienceDirect last ten years

### 1.3. Study Selection

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### 1.4. Data Extraction and Management

Data extraction and methodological quality assessment were conducted meticulously to ensure the reliability of our findings. 3 independent reviewers extracted relevant data from the included studies, focusing on study characteristics, participant demographics, intervention details, and outcomes. This process ensured consistency and minimized the risk of errors. The methodological quality of each study was assessed using the Newcastle-Ottawa Scale (NOS), which evaluates selection, comparability, and outcome ascertainment. Studies with higher NOS scores were deemed to have lower risk of bias. The extracted data were then synthesized and analyzed using a random-effects model in RevMan 5.4, with results presented within a 95% Confidence Interval (CI) to account for variability and provide robust conclusions

### 1.5. Quality Assessment

Quality assessment was done with Newcastle-Ottawa Scale (NOS) from Review Manager version 5.4.1 and done by 1 member of the authors and discrepancies were resolved with discussion. NOS has 4 dimensions including selection, comparability and exposure, for each item is explained to assess the study. for each item is explained to assess the study. After being explained, a star system is used for semi-quantitative assessment of the quality of learning so that studies of the highest quality are given a maximum of one star for each item with the exception of items related to comparability that allows the assignment of two stars.

### 1.6. Statistical Analysis

The statistical analysis for this systematic review and meta-analysis was conducted using RevMan 5.4. A random-effects model was employed to account for potential heterogeneity among the included studies. The primary outcome measured the decrease in SCORAD following placebo or multistrain probiotic. Effect sizes were calculated and presented with 95% Confidence Intervals (CI) to provide a precise estimate of the treatment effects. Heterogeneity was assessed using the  $I^2$  statistic, with values above 50% indicating substantial heterogeneity. Subgroup analyses and sensitivity analyses were performed to explore sources of heterogeneity and test the robustness of the results, ensuring the reliability and validity of the conclusions drawn from the meta-analysis.

## Result

The general characteristics of included studies in this meta-analysis are presented in **Table 1**. These studies were published from 2014 to 2024. A total number of 300 patients were screened for Atopic Dermatitis. Wang's 2015 study, a randomized controlled trial, involved children aged 1 to 18 years with atopic dermatitis. Patients were given an oral multistrain probiotic or a placebo, with a sample size of 51 children receiving the probiotic and 53 receiving the placebo. Cuckrowska's 2021 study, also a randomized controlled trial, involved children under the age of 2 with atopic dermatitis. Participants were given an oral mixture of probiotics, including *Lactobacillus casei*, *Lactobacillus rhamnosus* and *Lactobacillus rhamnosus*. A total of 66 children received the probiotic treatment, while 68 received the placebo. Rodriguez's 2023 study, another randomized controlled trial, involved children aged 4 to 17 years with atopic dermatitis. Patients were administered an oral mixture of *Bifidobacterium animalis subsp. lactis*, *Bifidobacterium longum*, and *Lactobacillus casei*. In this study, 32 children received the treatment and 30 received the placebo. The study highlights the role of multistrain probiotics in reducing SCORAD scores in children with atopic dermatitis.

The meta-analysis included 3 studies. The pooled analysis showed there was significant improvement in SCORAD [-7.04(-14.44 to 0.37); 95% CI, p-value = 0.008; I<sup>2</sup> = 79%] in treatment of probiotic. However, the funnel plot showed a symmetrical figure, indicating low publication bias

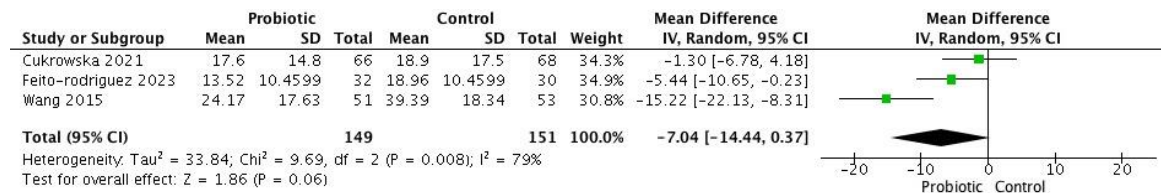


Fig. 1. Forest Plot efficacy of probiotics vs. placebo in reducing the severity of AD

Table 1. Characteristics of included RCTs for meta-analysis

Author, Year	Country	Study Design	Age	Intervention	Sample size	Outcome	Evaluation Outcome Therapy
Wang, 2015	Taiwan	RCT	1-18 years	1 x PO ((LP, LF (2x10 <sup>9</sup> colony forming units (cfu) qd.), an LP and LF mixture (4x10 <sup>9</sup> cfu qd.)) and Placebo	51 patient with intervention and 53 with placebo	SCORAD, Children's Dermatology Life Quality Index (CDLQI), and Family Dermatology Life Quality Index (FDLQI), bacterial fecal count	3 months

Cukrowska, 2021	Poland	RCT	<2 years	(1 × 10 <sup>9</sup> ) CFU 50% of <i>Lactobacillus casei</i> LOCK 0919, 25% of <i>Lactobacillus rhamnosus</i> LOCK 0908, 25% of <i>Lactobacillus rhamnosus</i> LOCK 0900 and maltodextrin	66 patient with intervention and 68 with maltodextrin	SCORAD	3 months, 9 months
Rodriguez, 2023	Spain	RCT	4-17 years	1 x (Bifidobacterium animalis subsp. lactis CECT 8145, Bifidobacterium longum CECT 7347 and Lactobacillus casei) CECT 9104 at a concentration of 1 × 10 <sup>9</sup> cfu and maltodextrin	32 patient with intervention and 30 patient with maltodextrin	SCORAD, number of days that each patient required topical corticosteroid administration over the 12 weeks of the study; total dose of topical corticosteroids used during the intervention; number of subjects with improvement in Investigator Global Assessment (IGA) scale score of 1 point or greater from baseline; and number of adverse events by group.	3 months

## Discussion

The skin microbiota is an ecosystem made up of several microbial species that interact with host epithelial cells and immune cells. By promoting the skin's vital processes and preventing pathogen colonization, the microbiota helps the host's health. But an imbalance of microbes can cause dysbiosis and exacerbate skin conditions like atopic dermatitis (AD). The systematic review showed that probiotics have a positive effect on children AD. This finding is further supported by a meta-analysis, which demonstrates that probiotics help reduce SCORAD scores, a measure of AD severity. However, due to the heterogeneity across studies, it is difficult to determine the exact degree of this reduction. This heterogeneity is due to the types of probiotics used, doses, treatment durations, and the subjectivity of the SCORAD scale in assessing AD severity.

The differences in population characteristics between studies also affected the subgroup analysis, which did not yield clear results, except for the observation that probiotics are more effective when administered for 3 months. A systematic review update by Lopez et al. similarly supported the use of probiotics, review

included 20 studies that did not focus on multistrain probiotics. While the result found probiotics reduced SCORAD scores.

Navarro-López et al showed that in this 12-week randomized clinical experiment, 50 children were given a combination of probiotics or a placebo. The results showed a substantial decrease in SCORAD and topical steroid use in the probiotic group when compared to the placebo group.

Huang et al. conducted another systematic review, concluding that more evidence was needed before probiotics could be widely recommended. Their review included small, diverse populations, limiting its strength. In contrast, the present review analyzed a larger number of studies with larger populations. One limitation of this review is the limited of the journal, which may result in differing outcomes across studies.

Probiotics have been researched for many years, especially in relation to digestive system disorders. Considering the variety of probiotics available in our country, they could potentially be used as an adjunct treatment for atopic dermatitis (AD).

## Conclusion

Multistrain probiotic intervention was effective in reducing SCORAD index so it can reduce the rate of atopic dermatitis and promising therapy for Atopic Dermatitis (AD).

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