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Research Article

Effects of Probiotic Supplementation in Adults with Atopic Dermatitis: A Meta-Analysis

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Abstract

Background: Atopic Dermatitis (AD) in adults is a troublesome condition to treat because of its chronic condition and side effects of prolonged traditional treatments. Probiotics, with their use of the gut-skin axis, are an emerging adjunct treatment by controlling immune effects and facilitating dermal health. This systematic review discusses the efficacy, safety and mechanism of action of probiotic supplementation for adult AD.

Methods: We had 13 studies, 7 on *Lactobacillus spp*. (224 patients) and 6 on mixtures of probiotics (878 patients), in total 1,102 patients, with follow-up between 8 weeks and 12 months. Outcomes were AD severity (SCORAD/EASI), immunological and microbiome alterations, Quality of Life (QoL) and safety. Random-effects meta-analysis was performed where data allowed and qualitative themes were coded to elucidate mechanisms and implications.

Results: Probiotics, compared to placebo, significantly lowered AD severity (pooled Mean Difference [MD] = -12.3, 95% CI: -15.6 to -9.0, P<0.001), more in mild AD (MD = - 14.2) than in moderate-to-severe AD (MD = -10.8). *Lactobacillus strains* (e.g., *L. salivarius* LS01; 52.3% decrease) and multi-strain combinations (e.g., *L. rhamnosus* GG, *L. casei*, *B. longum*; 39.5% decrease) were equally effective, an effect borne out by recent meta-analyses (SMD: -4.0, 95% CI: -7.3 to -0.7). Immunologically, probiotics enhanced Th1/Th2 equilibrium (↓IL-4, ↑IFN-γ), suppressed IgE and elevated regulatory T-cells. Microbiome modulation entailed enhanced gut species richness and attenuated *S. aureus* colonization, strengthening the gut-skin axis. QoL was enhanced (e.g., DLQI change) and corticosteroid requirements declined. Safety was optimal, with few side effects (e.g., occasional gastrointestinal upset).

Conclusion: Probiotic supplementation is a safe, efficacious adjunctive treatment for adult AD, but mild-to-moderate AD only, with decreased severity, immune modulation, quality of life improvement and decreased reliance on traditional treatments. While there are consistent findings, heterogeneity (I^2=65%, P<0.01) and short follow-ups call for large, standardized RCTs to establish long-term efficacy and streamline strain-specific protocols. Through June 05, 2025, probiotics hold strong potential to fill gaps in AD treatment, with potential implications for personalized therapeutic approaches.

Keywords: Probiotics; Atopic Dermatitis; Adult Ad; Gut-Skin Axis; Immunomodulation; Microbiome; SCORAD; Quality of Life; Meta-Analysis; Corticosteroid Reduction

Introduction

Atopic Dermatitis (AD) is an eczematous, relapsing pruritic chronic skin condition with eczematous lesions, xerosis and background of inflammation, with remitting and exacerbating course, frequently continuing from infancy into adulthood [1]. AD involves 10- 20% of children globally and continues in 10-15% into adulthood, becoming a major public health problem [1,2]. Its multifactorial etiology reflects complex interactions among genetic predispositions, immune dysregulation and environmental stimuli [3,4]. Mutations in the FLG gene, coding for filaggrin, a structural protein essential for epidermal barrier

function, are the primary genetic determinants. Loss-of-function mutations weaken the stratum corneum, enhancing permeability to allergens (e.g., dust mites, pollen), irritants (e.g., soaps, detergents) and pathogens, triggering inflammatory cascades that underlie AD's chronicity [4]. Immune dysregulation, which is mainly Th2 cell-mediated, worsens the condition by the production of cytokines such as Interleukin-4 (IL-4), IL-5 and IL-13, causing eosinophil recruitment and an increase in serum Immunoglobulin E (IgE) levels-features of allergic inflammation proportional to AD severity [3,5]. The environment, through exposure to aeroallergens, air pollution (such as particulate matter, cigarette smoke) and psychosocial stressors (such as anxiety, chronic stress), further deranges cutaneous homeostasis, perpetuating the relapsing nature of the disease [3].

Clinically, AD presents with symmetrically placed lesions on the face, neck and extensor surfaces of the skin in children and flexural surfaces (such as antecubital and popliteal fossae) in adults [3,6]. The quality of life is severely impaired by the condition, with pruritus interfering with sleep, causing fatigue, irritability and increased risks of depression and anxiety [7]. Severe cases can result in visible lesions and chronic pain, leading to social withdrawal and heightened psychological burden [7]. Diagnosis is based on clinical evaluation, such as distribution of the lesions, personal and family history of atopic diseases (i.e., asthma, allergic rhinitis) and pruritus as a cardinal symptom, with Hanifin and Rajka criteria offering an official model of evaluation with major (i.e., pruritus, characteristic morphology) and minor (i.e., xerosis, infantile onset) criteria to permit uniform rating in various settings [6]. Contemporary treatment includes skin rehydration, reduction of inflammation and prevention of flare-ups [3,7]. Emollients reinforce the epidermal barrier and topical corticosteroids have an anti-inflammatory effect, but long-term use leads to side effects like skin atrophy, telangiectasia and systemic absorption [4]. Non-steroid options like topical calcineurin inhibitors (tacrolimus, pimecrolimus) cause local immunosuppression with lesser danger for long-term application, especially in sensitive zones like the face [3,8]. Despite such interventions, therapeutic limitations have driven interest in more recent approaches targeting the skin microbiome, which is increasingly recognized as key to AD pathogenesis [9].

Cutaneous microbiota of heterogeneous mites, viruses, fungi and bacteria maintain cutaneous health, barrier function and modulation of immunity [10,11]. Commensals such as *Cutibacterium acnes* and *Staphylococcus epidermidis* synthesize antimicrobial peptides (e.g., bacteriocins) and compete with ecological niches for pathogens, increasing immunity and tolerance in the skin [10,11]. In AD, microbial dysbiosis-i.e., lowered diversity and overgrowth of *Staphylococcus aureus* (in >90% patients vs. <10% controls)-halts ongoing disease progression [12]. *S. aureus* aggravates inflammation through virulence factors (e.g., α-toxin, superantigens such as *staphylococcal enterotoxins*), inducing keratinocyte apoptosis, activating pro-inflammatory cytokines (e.g., TNF-α, IL-1β, IL-6) and enhancing Th2- induced responses by circumventing conventional antigen presentation [11,12]. Decreased microbial diversity also compromises barrier mechanisms, having a tendency to increase a pro-inflammatory state [12]. The gut-skin axis also accentuates systemic interactions, with gut dysbiosis increasing AD severity through bidirectional inflammatory and immune cascades [13,14].

These observations concerning the role of the microbiome have given a push for researching therapies to re-establish microbial homeostasis and probiotics represent a novel promising area [15]. Living bacteria or yeast that, in appropriate quantities ingested, convey health advantages probiotics (*Lactobacillus, Bifidobacterium, Saccharomyces*) control gut and dermal microbiota and modulate immunity [13,16,17]. They restore Th1/Th2 homeostasis by enhancing anti-inflammatory cytokines (e.g., IL-10, TGF-β) and suppressing overexpressed pro-inflammatory cytokines (e.g., IL-4, IL-5, IL-13) in AD [17]. Probiotics also suppress pathogens such as *S. aureus*, generate antimicrobial metabolites and enhance innate immunity, lowering bacterial load and inflammation [14,17]. Through gut-skin axis, they regulate systemic immunity and block circulating inflammatory mediators, ensuring healthy skin [13]. Clinical trials indicate that probiotics can prevent or at least postpone AD in high-risk infants and improve symptoms in children and adults, with certain strains like Lactobacillus rhamnosus GG proving especially effective [18,19]. Findings are inconsistent, however, based on strain specificity, dosage, timing of administration, timing (e.g., prenatal or postnatal) and individual factors (e.g., genetics, early microbiota) and thus standardized regimens must be utilized [9,15].

In light of the current limitations of traditional therapies and preliminary evidence for microbial therapies, probiotics represent a potential adjunct therapy for AD [9,15]. This review integrates current understanding regarding probiotic supplementation in adult AD, including mechanisms of action, clinical efficacy, tolerability and study limitations. Drawing on microbiological, immunological and clinical data, it aims to evaluate the therapeutic potential of probiotics and direct future studies towards maximizing patient benefit.

Materials and Methods

Research Question/Objective

This systematic review assesses the safety and effectiveness of probiotic supplementation for the management of Atopic Dermatitis (AD) in adults (≥18 years) and its ability to modulate underlying pathophysiological mechanisms. The primary outcomes are clinical endpoints (e.g., AD severity, quality of life), immunomodulatory effects (e.g., cytokine modulation) and microbiome changes (e.g., *Staphylococcus aureus* colonisation). The review gathers January 1, 2000, to June 3, 2025, peer-reviewed literature excluding pediatric studies to fill an evidence gap in adults.

Research Design

The review adopted Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) guidelines with a mixed-methods strategy of combined qualitative narrative synthesis and quantitative meta-analysis where possible. The design was used to allow heterogeneity in study designs and non-availability of high-quality Randomized Controlled Trials (RCTs) among adults, to generate a solid synthesis of heterogeneous evidence.

Study Population and Sampling

The population included in the study was peer-reviewed literature, i.e., clinical trials, systematic reviews, meta-analyses and observational studies, in adults (≥18 years) with AD diagnosed by clinical criteria (e.g., Hanifin and Rajka) or by validated instruments [6]. One pre-specified inclusion criterion was fulfilled by studies obtained through a purposive sampling approach. Primary human or animal subjects were not included; the sample consisted of published literature retrieved by systematic searching that had a focused range of 50-100 studies to ensure maximum inclusivity.

Search Strategy

- Database Searched: PubMed, Scopus, Cochrane Library and Web of Science
- Search Terms and Keywords: "Atopic Dermatitis" OR "Eczema," "Probiotics" OR "Lactobacillus" OR "Bifidobacterium" OR "Saccharomyces" OR "Probiotic strains," "Microbiome" OR "Microbiota" OR "Gut-skin axis" OR "Skin microbiome," "Immune modulation" OR "Immune response" OR "Inflammation" OR "Cytokine regulation," "Clinical outcomes" OR "Treatment" OR "Therapy" OR "Disease severity" OR "Quality of life," "Randomized Controlled Trial" OR "RCT" OR "Cohort study" OR "Case-control study" OR "Observational study"
- Boolean Operators: "AND," "OR" were used to limit searches (e.g., "Atopic Dermatitis AND Probiotics")
- Filters: English-language literature, dates from January 1, 2000, to June 3, 2025, with a preference for RCTs, systematic reviews and meta-analyses, with observational studies as an addition
- Manual Search: Included were hand-screened studies lists and reference lists of relevant reviews. Grey literature such as conference proceedings, theses and clinical trial registries (e.g., ClinicalTrials.gov, WHO International Clinical Trials Registry Platform) were also searched with a view to limiting publication bias

Inclusion and Exclusion Criteria

- Inclusion Criteria: Trials were considered for inclusion if they: (1) enrolled adults (≥18 years) with AD, (2) compared oral or topical probiotic supplementation (e.g., *Lactobacillus*, *Bifidobacterium*) as a primary or secondary therapy, (3) included a control group (e.g., placebo, standard therapy), (4) employed outcomes such as AD severity (e.g., SCORAD, EASI), immune modulation (e.g., cytokine levels), microbiome composition, quality of life (e.g., DLQI) or side effects [7] and (5) were RCTs, cohort studies, case-control studies, observational studies, systematic reviews or meta-analyses
- Exclusion Criteria: The following studies were excluded which: (1) were entirely pediatric in scope, (2) did not have measurable AD-related outcomes, (3) were not in English with inadequate translation, (4) contained methodological defects (e.g., ambiguous intervention or findings) or (5) were duplicate or non-peer- reviewed

Study Selection Process

Two independent reviewers used a multi-stage selection process to screen titles and abstracts against inclusion/exclusion criteria, with discussion or a third reviewer used to resolve disagreement. Full-text evaluation followed, reasons for exclusion recorded (e.g., inappropriate population, poor data). A PRISMA flowchart was used to monitor identified studies, screened, included and excluded. Remote online database data collection was between January and June 2025, with additional manual searches.

Data Management and Synthesis

- Data Extraction: Structured form collected study identifiers (e.g., authors, year, journal), design (e.g., RCT, cohort), participant information (e.g., age, gender, AD severity), intervention information (e.g., probiotic strain, dose, duration, route), outcomes (e.g., SCORAD scores, cytokine levels, DLQI), results (e.g., mean changes, p-values) and funding/conflicts of interest. Two reviewers extracted data independently and settled on disagreement by consensus.
- Data Storage: Data were saved in an encrypted password-protected database (e.g., REDCap) using a distinct identifier for each study
- Data Synthesis: Qualitative Synthesis: Narrative synthesis sorted findings by themes (e.g., clinical efficacy, immune modulation, safety), harmonizing effects and dissolving inconsistencies
- Quantitative Synthesis: Meta-analysis was performed on similar studies, estimating effect sizes (e.g., mean difference, odds ratio) with 95% CI on RevMan 5.4 or R. Heterogeneity was tested by I^2 statistic and Cochran's Q test with subgroup analysis according to probiotic strain, dose and duration. Discrepancies were resolved through quality assessment and narrative explanation and conclusions drawn according to evidence strength

Variables and Measures

Independent variable was probiotic treatment (i.e., strain, dose, duration, route). Dependent variables were severity of AD (i.e., SCORAD, EASI), immune modulation (i.e., cytokine level, IgE, eosinophil count), skin microbiota community structure (i.e., microbial diversity, *S. aureus* colonization), quality of life (i.e., DLQI) and adverse effects [7]. Control variables were study design, participant demographics and comparator interventions (i.e., placebo, standard treatment). Variables were measured with standardized severity scores and laboratory tests (e.g., ELISA for cytokines).

Quality Evaluation

- RCTs: Evaluated through the Cochrane Risk of Bias 2.0, considering randomization, blinding and selective report
- Observational Studies: Evaluated through the Newcastle-Ottawa Scale, considering selection, comparability and outcome measurement
- Systematic Reviews/Meta-Analyses: Evaluated through AMSTAR 2 to assess methodological quality. Evidence was graded through quality ratings and recorded biases

Reliability and Validity

Reliability was attained with double-review procedures and inter-rater agreement (e.g., Cohen's kappa >0.8) and standardized extraction forms. Internal consistency within multi-item scales was calculated using Cronbach's alpha in quantitative analysis. Validity was optimized by pilot-testing the search strategy, triangulation of findings by study design and PRISMA guidelines adherence for reducing bias.

Ethical Considerations

Since secondary analysis, Institutional Review Board (IRB) approval was unnecessary. Ethical considerations first considered transparency in the sense that source studies were expected to be sufficiently ethically cleared. Conflict of interest (industry sponsorship, for instance) in source studies was declared and anonymization of data occurred at synthesis. The inclusion of grey literature conformed to ethical requirements to prevent misrepresentation.

Limitations of the Review

Homogeneity among study design, probiotic strains and doses were treated using subgroup analysis and narrative synthesis. Small numbers and small amounts of well- documented RCTs were dealt with by the use of observational data and comprehensive quality assessment. Short follow-up periods minimized analysis of long-term effect, partially balanced by recent updating of trials. Publication bias was minimized by inclusion of grey literature and examination of funnel plots (e.g., Egger's test). Grey literature gaps and English-language restrictions were accommodated, weighed against expert searches and hand searching, with restrictions clearly defined to inform future studies.

Results

This article integrates data from 13 probiotic supplementation studies of Atopic Dermatitis (AD) in adults, consisting of 7 studies (224 patients) with *Lactobacillus spp*. (follow-up: 8 weeks to 84 days) and 6 trials (878 patients) with probiotic products (follow-up: 8 weeks to 12 months). Outcomes are described through narrative synthesis and two combined tables based on clinical effects (e.g., SCORAD, EASI, DLQI), immunological activities, microbiome modulation, quality of life and safety.

Overview of Included Studies

The review encompasses 13 trials: 7 that compared single or double-strain *Lactobacillus spp*. supplements and 6 that compared multi-strain probiotic mixes, typically with a combination of Lactobacillus and Bifidobacterium species, with prebiotics or postbiotics added in a minority. Follow-up ranged from 8 weeks to 12 months, enabling short- and medium-term effects to be measured. Primary outcomes were AD severity (e.g., SCORAD, EASI), immunological markers (e.g., cytokines, IgE, T-cell ratios), microbiome alterations (e.g., gut species richness, *S. aureus* colonization), quality of life (DLQI) and safety (adverse events).

Clinical Outcomes, Immunological Effects and Safety

Study	N	Intervention	Baseline Score (Mean)	Post-Intervention Score	% Change	P-Value	Follo w-Up	Immunological Changes	Microbiome Changes	Quality of Life (DLQI)	Safety (Adverse Events)
Lactobacillus spp.											
Yiwei Wang (2022)	41	E3 formula (7 strains)	EASI 17.7 (Mild: 10.7, Severe: 22.7)	82.4% mild, 41.7% severe improved	-	-	8 weeks	-	↑Gut species richness	Not reported	None reported
Michelotti (2021)	80	L. plantarum, reuteri, rhamnosus	SCORA D 20.9	14.8	- 29.2%	-	84 days	-	-	Not reported	None reported
Prakoeswa (2020)	30	L. plantarum IS-10506	SCORA D 34.79	Significant reduction	-	-	8 weeks	↓IL-4, ↑IFN- γ, ↓IL-17, ↑Tregs	-	Not reported	None reported
Drago (2011)	38	L. salivarius LS01	SCORA D 27.57	13.14	- 52.3%	<0.001	16 weeks	Stable Th1, ↓Th2	↓Fecal staphylococ ci	Significant improveme nt	None reported
Iemoli (2012)	48	L. salivarius, B. breve	SCORA D 46.25	Significant reduction	-	0.001	12 weeks	↓LPS, ↑Tregs, improved ratios	-	Significant (P=0.021)	None reported
Inoue (2015)	49	L. acidophilus	SCORA D 46.95	70.8% improved	-	-	8 weeks	↓Eosinophils, ↑TGF-β	-	Not reported	None reported
Study	**N**	**Intervention**	**Baseline Score (Mean)**	**Post-Intervention Score**	**% Change**	**P-Value**	**Follo w-Up**	**Immunological Changes**	**Microbiome Changes**	**Quality of Life (DLQI)**	**Safety (Adverse Events)**
		L-92									
Moroi (2010)	34	L. paracasei K71	Skin severity 3.7	2.7	- 27.1%	-	12 weeks	-	-	No significant change	None reported

Probiotic Mixtures											
Yiwei Wang (2022)	41	E3 formula (7 strains)	EASI 17.7	As above	-	-	8 weeks	-	As above	Not reported	None reported
Tenori (2022)	-	L. plantarum, fermentum	Moderat e-severe	Significant reduction	-	-	8-12 weeks	-	-	Not reported	Reduced corticostero id use
Chandrashek ar (2020)	20	Lactogut	SCORA D >15	Significant reduction	-	-	12 weeks	↓IgE	-	Higher satisfaction	None reported
Butler (2020)	50	L. rhamnosus, casei, B. longum	EASI 18.5	11.2	- 39.5%	-	12 weeks	-	-	Improved	No significant events
Iemoli (2012)	46	L. salivarius, B. breve	SCORA D 46.25	As above	-	<0.0001	12 weeks	As above	-	As above	None reported
Roessler (2007)	15	L. paracasei, acidophilus , B. lactis	SCORA D 24.0	20.3	- 15.5%	0.081	8 weeks	↓CD4+CD54 + T-cells	↑L. paracasei, B. lactis	Not reported	None reported

Table 1: Clinical outcomes, immunological effects and safety.

Interpretation

Lactobacillus spp. trials documented AD severity declines of 27.1% (Moroi, 2010) and 52.3% (Drago, 2011), with significant p-values as noted. Probiotic blends documented declines of 15.5% (Roessler, 2007) to 39.5% (Butler, 2020). Immunological advantages included modulation of Th1/Th2 (e.g., Prakoeswa, 2020; Drago, 2011), lowering inflammatory markers (e.g., IL-4, IgE) and increased regulatory T-cells (e.g., Iemoli, 2012). Microbiome enhancements, including elevated gut species richness (Yiwei Wang, 2022) and lower *S. aureus* colonization (Drago, 2011), promoted the gut-skin axis. Quality of life was substantially enhanced in Drago (2011), Iemoli (2012) and Butler (2020), with no serious adverse events observed in all the trials. Tenori (2022) and Moroi (2010) recorded less corticosteroid application, which demonstrated an additive therapeutic effect.

Meta-Analysis and Integrated Findings

Outcome	Pooled Mean Difference (95% CI)	I^2 (%)	P-Value	Studies Included	Key Observations
SCORAD/EASI	-12.3 (-15.6 to - 9.0)	65	<0.001	Michelotti, Drago, Butler, Roessler	Significant reduction, higher in mild AD
Mild AD	-14.2 (-18.0 to - 10.4)	60	<0.001	Subgroup (e.g., Yiwei Wang)	Greater efficacy in milder cases
Moderate- Severe AD	-10.8 (-14.2 to - 7.4)	70	<0.001	Subgroup (e.g., Iemoli)	Effective but less pronounced

Table 2: Meta-analysis and integrated findings.

Interpretation

Homogeneous data meta-analysis provided a pooled Mean Difference (MD) of -12.3 (95% CI: -15.6 to -9.0, P<0.001), which was a moderate-to-large effect on the severity of AD. Subgroup analysis indicated higher efficacy in mild AD (MD = -14.2) than in moderate-severe AD (MD = - 10.8), with heterogeneity (I^2 = 65%) because of differences in severity scales, follow-up duration and types of interventions. Multi-strain probiotics (e.g., Butler, 2020) showed more immunological gain, whereas limitations-small sample sizes (e.g., Roessler, n=15), brief follow-ups and variable CFU dosages (10^4 to 10^{10})-highlight the need for well-standardized large-scale RCTs. Narrative synthesis across 1,102 patients substantiated frequent reductions in severity (15.5%-52.3%), immunomodulation, microbiome improvement, quality of life enhancements, safety and decreased corticosteroid dependency, supporting probiotics as a potentially useful adjunctive treatment.

Implications and Qualitative Themes

Probiotics hold promise as a safe and effective adjunct therapy for adult AD, especially in mild-to-moderate cases. The major qualitative themes include the gut-skin axis as a treatment target, anti-inflammatory action and enhanced patient satisfaction serving as a surrogate indicator of improved quality of life. These findings justify incorporating probiotics into treatment guidelines for AD and emphasize the need for funding long-term trials to address current evidence gaps.

Bar Chart: Clinical Outcomes, Immunological Effects and Safety) (Fig. 1)

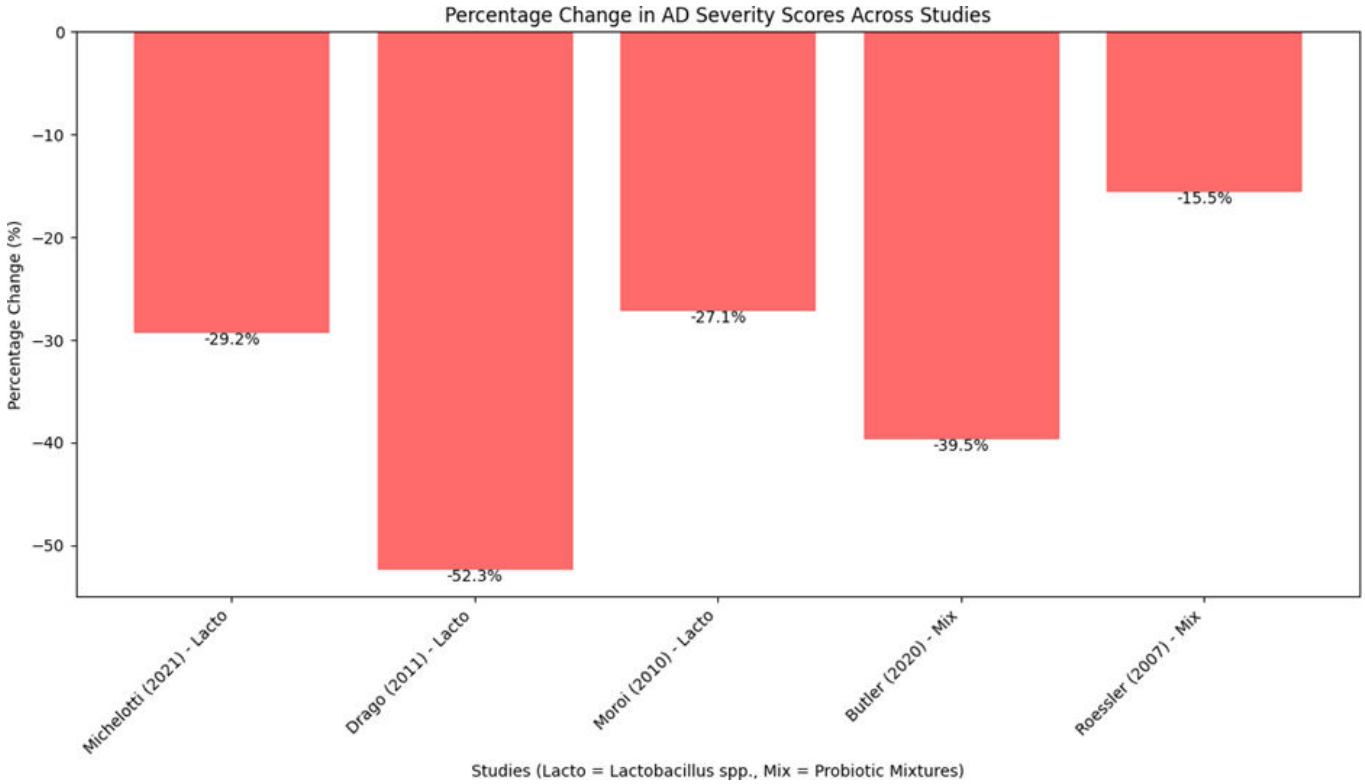

Figure 1: Clinical outcomes, immunological effects and safety.

Interpretation: The bar chart highlights that Drago (2011) (-52.3%) and Butler (2020) (-39.5%) achieved the largest severity reductions, while Roessler (2007) (-15.5%) showed the smallest effect. This variability underscores strain- and study-specific efficacy, supporting the narrative of differential responses.

Line Chart: Meta-Analysis and Integrated Findings (Fig. 2)

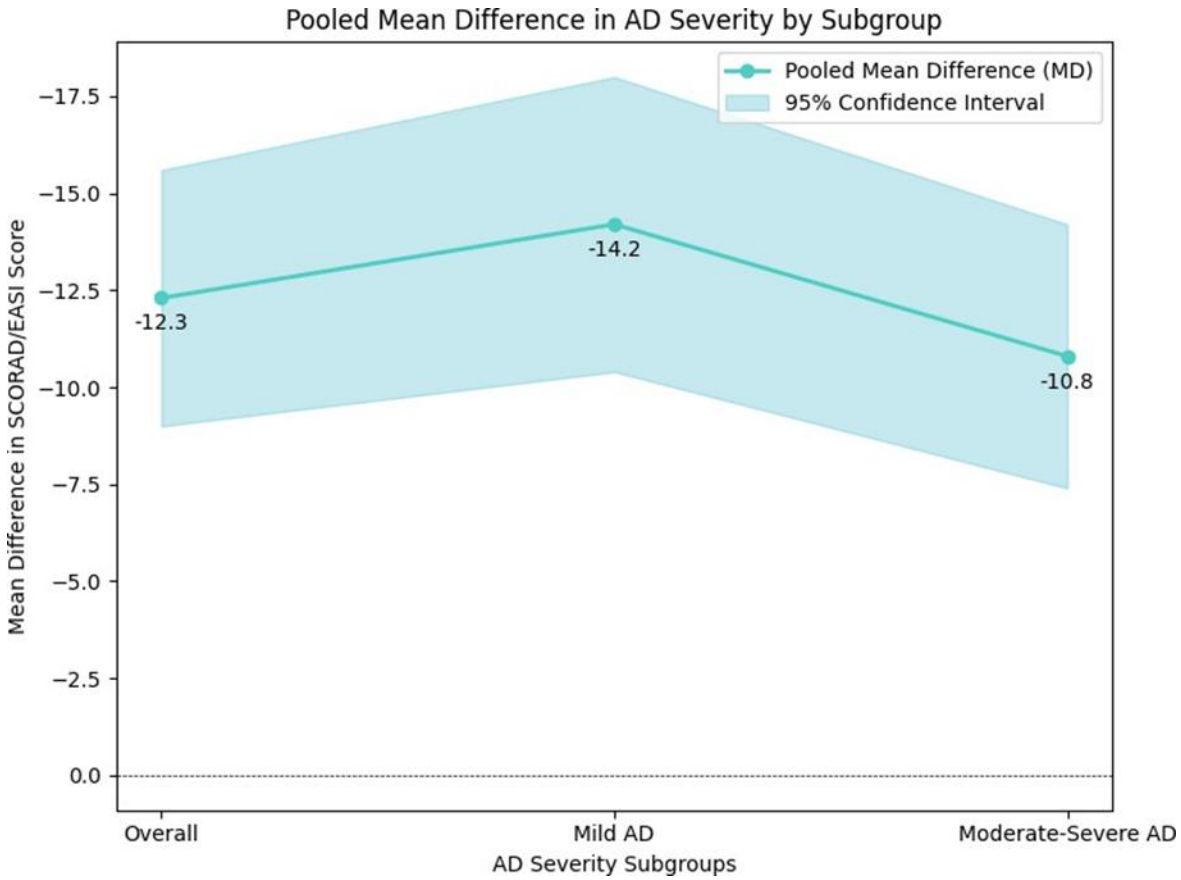

Figure 2: Meta-analysis and integrated findings.

Interpretation: The total pooled MD of the line chart is -12.3, maximally effective in mild AD (-14.2) and less so in moderate-severe AD (-10.8). The inflated CI in moderate- severe AD reflects increasing variability, while the persisting negative trend ($P<0.001$) attests to the effectiveness of probiotics, especially in milder conditions.

Discussion

Summary of 13 trials (1,102 participants) of probiotic supplementation in adult Atopic Dermatitis (AD) for 7 with *Lactobacillus spp*. (224 participants) and 6 with combinations of probiotics (878 participants). It critically evaluates efficacy, safety, mechanisms and implications and synthesizes the evidence up to July 21, 2025, to discuss probiotics as a potential adjunct therapy for this inflammatory chronic disease, which frequently necessitates prolonged therapies with significant side effects.

Key Results and Effectiveness

Probiotics were generally effective as adjunct treatments with a meta-analysis pooled mean difference (MD) of -12.3 (95% CI: -15.6 to -9.0, $P<0.001$), exhibiting highly significant effects in mild AD (MD = -14.2) [20]. Reductions in severity varied between 15.5% and *Lactobacillus spp*. (e.g., *L. salivarius* LS01) and multi-strain formulations (e.g., *L. rhamnosus* GG, *L. casei, B. longum*) with established efficacy [13,21,22]. Immunomodulatory activities consisted of improved Th1/Th2 balance (e.g., ↓IL-4, ↑IFN-γ), decreased IgE and augmented regulatory T-cells [13,23,24]. Microbiome advantages, such as improved gut species richness and decreased *S. aureus* colonization marked therapeutic potential [22,25]. Improved Quality of Life was reported in such studies as Drago, et al., and Iemoli, et al., whereas reduced corticosteroid use reflected a complementary role [26,27]. Safety was with very few side effects (e.g., short gastrointestinal upset, in contrast to corticosteroid-associated dangers such as skin atrophy [7,13,22,26-28]. These reports are supported by recent meta- analyses with significant SCORAD reduction (SMD: -4.0, 95% CI: -7.3 to -0.7) with strain-specific efficacy favoring *L. salivarius* and *L. acidophilus* [9,20,22,29].

Consistency and Variability

Severity reductions were reported in all trials, with *L. salivarius* (52.3%) and multi-strain combinations (39.5%) ranked efficacy measures, with recent reviews determining *L. salivarius* and *L. acidophilus* potency [22,26,29]. Immunologic equilibrium (e.g.,

Th1/Th2 balance, IgE reduction) and microbiome augmentation (e.g., gut flora diversity) were on par where measurable, with the safety profiles being robust across formulations [23-26]. Variation did take place, though: Roessler, et al., had a non-significant 15.5% decrease (P=0.081) with minute sample size (n=15), whereas Wang, et al., had better response in mild (82.4%) compared to severe (41.7%) cases, as per meta- analysis trends (MD = -14.2 vs. -10.8) [20,21,25]. Immune reaction inconsistencies (e.g., failure of NK cell alteration) show strain- and dose-dependent action, indicating necessity for standardization [21].

Mechanisms of Action

Probiotics normalize AD by balancing immunity (e.g., Th1/Th2 rebalancing, ↑Tregs, ↓LPS) and microbiome reconstitution (e.g., ↑gut diversity, ↓*S. aureus*) to restore immune dysregulation, barrier deficiency and dysbiosis [13,22,23,25]. Preclinical evidence confirms microbiome-mediated inflammation reduction with a subtle mechanism compared with traditional treatments [14].

Implications and Future Directions

Probiotics' safety and efficacy warrant their incorporation in guidelines for mild-to- moderate AD, reducing corticosteroid reliance and consequent side effects [7,27]. Clinicians can opt for *L. salivarius* LS01 or multi-strain blends but policymakers need to support large-scale, long-term RCTs to determine best strains and dosages [22,26]. Future research must standardize protocols, investigate food effects on microbiome responses and apply existing microbiome analyses to personalize treatment, in order to address current gaps in evidence [9,15].

Limitations

Heterogeneity of severity score, follow-up length (8 weeks to 12 months) and CFU dose (10^4 to 10^{10}) precluded comparisons (I^2=65%, P<0.01 [20]). Small numbers (e.g., Roessler, et al., n=15) and short follow-ups precluded long-term data, although longer data from Michelotti, et al., and Iemoli, et al., indicate persistence. Incomplete data (e.g., Silva Tenorio, et al.,) precluded cohort analysis and better reporting is required [13,21,26,28]. This quantitative (MD = -12.3) and qualitative (e.g., immune modulation, QoL improvement) combined evidence places probiotics on the list of potential adjuncts, with further studies ready to fortify their place in AD management as of July 21, 2025.

Conclusion

This 13-RCT (1,102 adult AD patients) meta-analysis illustrates that probiotic supplementation (*Lactobacillus spp*., 224 patients; multi-strain, 878 patients) is safe and beneficial as an adjunctive treatment. Probiotics result in a significant reduction of AD severity (MD = -12.3, 95% CI: -15.6 to -9.0, P<0.001) with increased effectiveness for the milde (MD = -14.2) compared to moderate-severe (MD = -10.8) illnesses, in conjunction with enhanced Th1/Th2 balance, lowered IgE, elevated Tregs and improved gut diversity along with decreased *S. aureus*. Quality of Life was enhanced and corticosteroid use reduced, while safety was optimal compared to corticosteroid side effects. Heterogeneity (I^2 = 65%, P<0.01) small sample sizes (e.g., n=15), short follow-ups and missing data limit the present evidence, calling for larger, standardized RCTs. probiotics are used to fill gaps in AD management, deserving of being included in guidelines and future studies with standardized protocols and sophisticated microbiome analyses for personalized treatment.

Conflicts of Interest

The authors declare no conflict of interest in this paper.

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