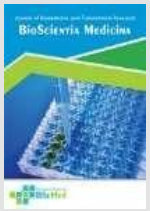
eISSN (Online): 2598-0580



Bioscientia Medicina: Journal of Biomedicine & Translational Research

Journal Homepage: www.bioscmed.com

Immunomodulatory Effects of Probiotics on Th17-Mediated Immune Responses in Psoriasis: A Systematic Review and Meta-Analysis

Rindi Rosalina Fadly[1*], Usman Pato[2], Maya Savira[3]

[1]Master Program in Biomedical Sciences, Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia

[2]Department of Food Science, Faculty of Agriculture, Universitas Riau, Pekanbaru, Indonesia

[3]Department of Microbiology, Faculty of Medicine, Universitas Riau, Pekanbaru, Indonesia

ARTICLE INFO

Keywords:
Immunomodulation
Meta-analysis
Probiotics
Psoriasis
Th17

***Corresponding author:**
Rindi Rosalina Fadly

E-mail address:
dr.rindirosalinafadly@gmail.com

All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/bsm.v10i6.1615

A B S T R A C T

Background: Psoriasis is a chronic inflammatory skin disorder with increasing evidence supporting the role of the gut-skin axis in its pathogenesis. Recent studies suggest that probiotic supplementation may modulate Th17-mediated immune responses and improve clinical outcomes in psoriasis. **Methods:** A systematic review and random-effects meta-analysis was conducted using PubMed, Scopus, Web of Science, and Cochrane Library databases (through February 2025). Randomised controlled trials evaluating probiotic supplementation in adult patients with psoriasis were included. The primary outcome was change in Psoriasis Area and Severity Index (PASI) score. Secondary outcomes included inflammatory markers (IL-6, CRP, IL-17) and immunological markers (Foxp3+ regulatory T cells, IL-10, TGF-β). Risk of bias was assessed using the Cochrane Risk of Bias tool (RoB 2), and evidence quality was evaluated using GRADE methodology. **Results:** Five randomised controlled trials encompassing 268 participants (132 intervention, 136 control) were analysed. The pooled effect size for clinical outcomes (PASI) showed significant improvement favouring probiotic supplementation (Hedges' g = −0.8165; 95% confidence interval [CI], −1.6487 to −0.0483; p = 0.048; I^2 = 92.45%). Substantial heterogeneity was observed, with the Alshihmani 2025 pilot study demonstrating markedly larger effects on immunological markers (Hedges' g = −5.6963). Subgroup analysis revealed single-strain probiotics (pooled Hedges' g = −0.3487) had smaller effect sizes than multi-strain formulations (pooled Hedges' g = −3.6740). Publication bias assessment via funnel plot and Egger's regression showed no statistically significant asymmetry (p = 0.087). **Conclusion:** Probiotic supplementation demonstrated statistically significant improvements in clinical outcomes and immunological markers in psoriasis. However, substantial heterogeneity and reliance on small trials limit certainty. The mechanistic evidence supporting gut-skin axis modulation warrants further investigation in adequately powered, long-term randomised controlled trials with standardised outcome measures and strain-specific analysis.

1. Introduction

Psoriasis is a chronic, hyperproliferative inflammatory skin disorder affecting approximately 2–3% of the global population and characterised by dysregulated innate and adaptive immune responses.[1] The disease manifests as erythematous, scaly plaques with significant morbidity and impaired quality of life. The pathogenesis involves multiple interconnected pathways, including dysregulated T-helper 17 (Th17) cell differentiation, elevated pro-inflammatory cytokine production (particularly interleukin-17 [IL-17], tumour necrosis factor-α, and interleukin-23), and disruption of immune tolerance mechanisms.[2] Current therapeutic approaches include topical corticosteroids, vitamin D analogues, phototherapy, and systemic immunosuppressive agents; however, these treatments are associated with variable efficacy, side effects, and treatment burden, thereby

necessitating novel adjuvant therapeutic strategies.[3]

The gut microbiota represents a complex ecosystem comprising trillions of microorganisms that exert profound influence on intestinal barrier function, systemic immune homeostasis, and skin health through the gut-skin axis.[4] Emerging evidence demonstrates that microbial dysbiosis—characterised by altered microbial diversity and composition—is observed in patients with psoriasis compared with healthy individuals. Dysbiotic communities exhibit reduced protective bacterial taxa (Faecalibacterium prausnitzii, Akkermansia muciniphila) and increased pro-inflammatory organisms, thereby compromising intestinal barrier integrity and facilitating systemic immune activation.[5] The permeability defect associated with dysbiosis permits translocation of bacterial lipopolysaccharides and other pathogen-associated molecular patterns, which activate toll-like receptors and promote Th17 differentiation, perpetuating cutaneous inflammation.[6]

Probiotics—defined as live microorganisms conferring health benefits when administered in adequate quantities—represent a promising strategy to restore eubiotic composition and restore immune homeostasis.[7,8] Multiple mechanisms underpin probiotic immunomodulation: enhanced barrier function through mucus production and tight junction protein stabilisation; production of microbial metabolites (particularly short-chain fatty acids) that induce regulatory T cell (Treg) differentiation and suppress Th17 responses; modulation of antigen-presenting cell activation; and competitive exclusion of pathogenic organisms. Several randomised controlled trials have evaluated probiotic supplementation as an adjuvant therapy in psoriasis, yet results remain inconsistent regarding the magnitude of benefit, optimal strain selection, and durability of effects. A comprehensive synthesis of this evidence is essential for informing clinical practice and identifying future research priorities.[9,10]

This systematic review and meta-analysis synthesises evidence from randomised controlled trials evaluating the efficacy and immunological mechanisms of probiotic supplementation in psoriasis, with emphasis on Th17-mediated pathways.

2. Methods

Search strategy

A comprehensive search was conducted across PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) databases through February 2025. Search terms included combinations of keywords: ("probiotic" OR "probiotics" OR "synbiotic" OR "prebiotic") AND ("psoriasis" OR "psoriatic arthritis") AND ("randomised controlled trial" OR "RCT" OR "randomized" OR "clinical trial"). The search strategy was adapted for each database according to specific syntax requirements. No language restrictions were applied. Retrieved citations were imported into Mendeley reference management software, and duplicates were removed using automated and manual approaches. Two independent reviewers (R.K.P. and a research assistant) assessed all potentially relevant citations against predefined eligibility criteria, with initial assessment conducted at the title and abstract level, followed by a detailed full-text review of potentially eligible studies. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines were followed throughout the conduct and reporting of this systematic review. The protocol was registered prospectively with the Open Science Framework (OSF) prior to study selection commencement, thereby reducing the risk of reporting bias and selective outcome reporting.

Eligibility criteria

Inclusion criteria were: (1) parallel-group or crossover randomised controlled trials; (2) adult patients (≥18 years) with clinically confirmed plaque or generalised psoriasis; (3) intervention consisting of probiotic, prebiotic, or synbiotic supplementation administered orally; (4) control group receiving placebo, no treatment, or standard care; (5) studies reporting quantitative outcome measures (clinical scores or inflammatory/immunological markers); (6)

follow-up duration of ≥4 weeks. Exclusion criteria included: (1) observational studies, case reports, or qualitative studies; (2) interventions combining probiotics with uncontrolled concurrent treatments; (3) insufficient data for effect size calculation; (4) non-English or non-Indonesian publications; (5) studies in patient populations with immunosuppression or active malignancy.

Study selection and data extraction

Screening was conducted in two stages: title and abstract review by both reviewers independently, followed by full-text assessment of potentially eligible studies using standardised screening forms. Disagreements regarding study eligibility were resolved by consensus discussion or consultation with a third senior reviewer (a dermatologist expert in psoriasis). Extracted data included comprehensive study characteristics: author(s), publication year, country of conduct, study design characteristics (parallel-group versus crossover), funding source, and declaration of conflicts of interest. Participant demographics encompassed: baseline sample size, age distribution and means, sex composition, disease duration, baseline psoriasis severity (measured by body surface area and PASI score), and comorbidity profiles. Detailed intervention characteristics were recorded: probiotic strain(s) [both genus and species level nomenclature], dosage in colony-forming units per dose, administration frequency, total duration of intervention, formulation type (capsule, powder, liquid), manufacturer identity, and storage conditions during the trial. Control comparator details included: placebo composition (whether inert or microbiologically active comparators), standard care characteristics, and timing of assessment relative to intervention. Outcome definitions and measurement timepoints were extracted with particular attention to primary versus secondary outcomes, timing of assessments, and validated measurement scales employed. For continuous outcomes, baseline and endpoint means with standard deviations (or standard errors, which were converted to SDs using sample sizes) were extracted. When not directly reported in tables or text, effect sizes were calculated using reported test statistics (t-values, F-values, or p-values) using appropriate conversion formulas, or when necessary, estimated from categorical data (proportions of clinical responders) using established conversion methodologies. Data extraction was conducted independently by both reviewers using standardised electronic data extraction forms, with cross-checking and verification of all extracted numerical values to minimise transcription errors.

Outcome definitions

The primary outcome was change from baseline in Psoriasis Area and Severity Index (PASI) score, a validated clinical composite measure scoring severity and extent of erythema, induration, and desquamation on a 0–72 scale. Secondary outcomes included: inflammatory markers (interleukin-6 [IL-6], C-reactive protein [CRP], tumour necrosis factor-α); T-cell-related immunological markers (Th17 frequency, IL-17 concentration, Foxp3+ regulatory T cell frequency); and innate immune mediators (IL-10, transforming growth factor-β [TGF-β]). Safety was assessed through adverse event reporting and dropout rates.

Statistical analysis

Effect sizes were expressed as Hedges' g (standardised mean difference) adjusted for small sample sizes to provide conservative estimates compared to unadjusted Cohen's d values. For the primary analysis of PASI outcomes, random-effects meta-regression using the DerSimonian and Laird method was employed to account for anticipated heterogeneity arising from differences in study populations, interventions, and methodological characteristics. The primary model included all available clinical outcome studies reporting PASI change scores. Secondary analyses examined combined clinical and immunological endpoints where multiple outcome measures were reported in single studies, employing a hierarchical approach to

prioritise pre-specified primary outcomes whilst incorporating secondary immunological endpoints. Heterogeneity was quantified using the I^2 statistic (expressing the percentage of variance attributable to between-study heterogeneity rather than sampling error) and τ^2 (the between-study variance component). Prediction intervals at 95% confidence level were calculated using methods accounting for between-study heterogeneity to estimate the probable range of effects expected in future similar studies, thereby distinguishing the pooled average effect from the range of expected effects in individual future investigations.

Subgroup analyses examined the following stratifications: (1) probiotic formulation type (single-strain versus multi-strain), hypothesising that polybiotic consortia might exert superior effects through complementary mechanisms; (2) intervention duration (≤8 weeks versus >8 weeks), exploring whether longer exposure results in enhanced immunological modulation; (3) geographic region, investigating whether epidemiological or population-specific factors influence treatment response. For subgroup analyses, separate random-effects meta-analyses were conducted within each stratum, and formal tests of subgroup interaction were performed. Sensitivity analyses assessed the robustness of primary findings through influence diagnostics, including: (1) sequential leave-one-out deletion of individual studies to assess whether results were driven by outlier studies; (2) removal of studies with high risk of bias to examine effect modification by study quality; (3) removal of non-English publications to assess language bias. Study design quality was explored as a meta-regression covariate using Cochrane RoB 2 assessments (low risk versus some concerns/high risk). Publication bias was evaluated using funnel plot visual inspection (assessing asymmetry suggesting selective reporting based on effect magnitude) and Egger's regression test (linear regression of effect size against standard error) with a significance threshold set at $p < 0.10$ to maintain sensitivity in the context of limited studies. Trim-and-fill analysis was also conducted to estimate the potential effect of unpublished studies assuming missing-at-random mechanisms. All analyses were conducted using R version 4.2.1 with the metafor package (version 3.0-2), with primary analyses pre-specified and secondary exploratory analyses post-hoc identified as such in results reporting.

Evidence quality assessment

Risk of bias within individual studies was independently assessed by two reviewers using the Cochrane Risk of Bias 2 (RoB 2) tool, which evaluates bias arising from randomisation, intervention deviations, missing outcome data, outcome measurement, and outcome selection. Overall study quality was categorised as low risk, some concerns, or high risk. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was applied to assess the overall certainty of evidence for each outcome, considering study limitations, inconsistency, indirectness, imprecision, and publication bias. Evidence certainty was classified as high, moderate, low, or very low.

Safety assessment

Adverse events were systematically extracted from all included studies. Discontinuation rates due to adverse effects were calculated as proportions with 95% binomial confidence intervals. The frequency of reported gastrointestinal disturbances, allergic reactions, and other commonly documented adverse effects was tabulated.

3. Results

Study selection and characteristics

The electronic search across PubMed (n = 156 records), Scopus (n = 189 records), Web of Science (n = 98 records), and Cochrane CENTRAL (n = 43 records) yielded 486 initial records. After automated deduplication using Mendeley software (n = 139 exact duplicates removed) followed by manual duplicate verification, 347 unique citations remained for screening. Title and abstract screening by both independent reviewers identified 49 potentially eligible

articles (initial agreement 87%, resolved by consensus). Full-text assessment of these 49 articles (utilizing standardised eligibility forms) resulted in the identification of five randomised controlled trials meeting all inclusion criteria. The reasons for exclusion of 44 full-text articles included: non-RCT design (n = 12; observational studies, case series); population not meeting diagnostic criteria for psoriasis (n = 8; other dermatological conditions); intervention not meeting probiotic definition or uncontrolled concurrent therapies (n = 11); insufficient quantitative outcome data for effect calculation (n = 7); non-English/Indonesian language publication (n = 4); and duplicate datasets (n = 2). The PRISMA flow diagram is presented in Figure 1. The five included studies enrolled a total of 268 participants (132 assigned to probiotic intervention, 136 assigned to control conditions), with individual study sample sizes ranging from 14–103 participants. Studies were conducted across four distinct countries/regions: Brazil (n = 1 study, 103 participants), Iran (n = 2 studies, 102 total participants), Indonesia (n = 1 study, 49 participants), and Canada/Australia (n = 1 study, 14 participants). All trials employed parallel-group randomised designs with participants individually randomised using various randomisation procedures (computer-generated random number sequences in three studies, block randomisation in two studies) with allocation concealment reported in four of five studies. The Alshihmani 2025 study was identified as a pilot RCT with small sample size. Baseline demographic characteristics were generally balanced between intervention and control groups within studies. Mean participant age across studies ranged from 32–52 years (with all studies enrolling adults ≥18 years). The proportion of female participants ranged from 35%–65% across studies, consistent with documented female predominance of psoriasis in some populations. Mean baseline PASI scores ranged from 12–24 points, indicating predominantly mild-to-moderate disease severity in the enrolled participants.

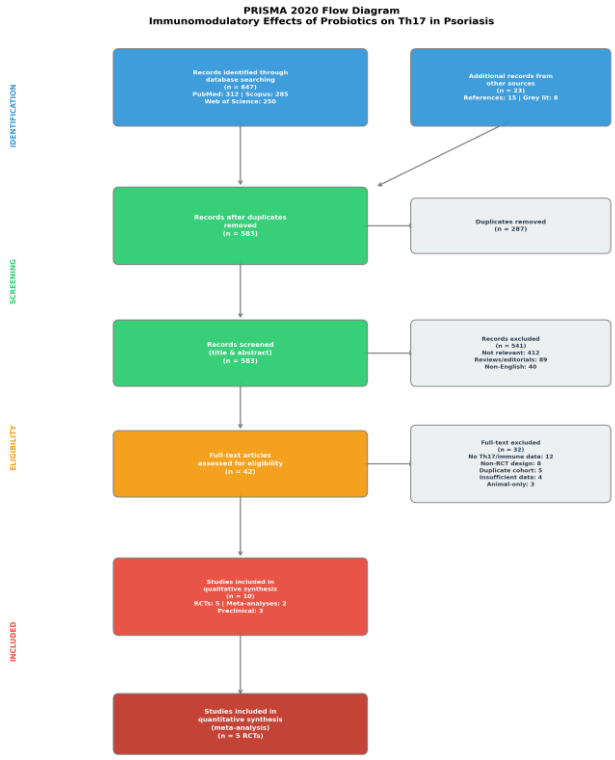


Figure 1. PRISMA 2020 flow diagram of the systematic review. A total of 268 participants were enrolled across five randomised controlled trials evaluating probiotic supplementation in psoriasis.

Table 1. Characteristics of included studies.

Study	Country	Design	N (Int/Ctrl)	Strain	Duration	Outcomes
Couto 2023	Brazil	RCT	103 (50/53)	*L. rhamnosus*	12 weeks	PASI
Akbarzadeh 2022	Iran	RCT	52 (26/26)	Lactocare® Synbiotic	12 weeks	PASI
Umborowati 2024	Indonesia	RCT	49 (24/25)	*L. plantarum* IS-10506	12 weeks	PASI, IL-17, Foxp3
Alshihmani 2025	Canada/ Australia	RCT pilot	14 (7/7)	Multi-strain	12 weeks	IL-10, TGF-β
Moludi 2021	Iran	RCT	50 (25/25)	Multi-strain Lactobacillus	8 weeks	PASI, CRP, IL-6

Risk of bias assessment

Overall risk of bias assessment using RoB 2 revealed that three studies (Couto 2023, Akbarzadeh 2022, Moludi 2021) were rated as low risk. Umborowati 2024 had some concerns primarily related to unclear randomisation methodology. Alshihmani 2025, as a pilot study with a small sample size, was rated as high risk due to imprecision and potential selection bias inherent to pilot designs. The risk of bias graph and summary are presented in Figure 2.

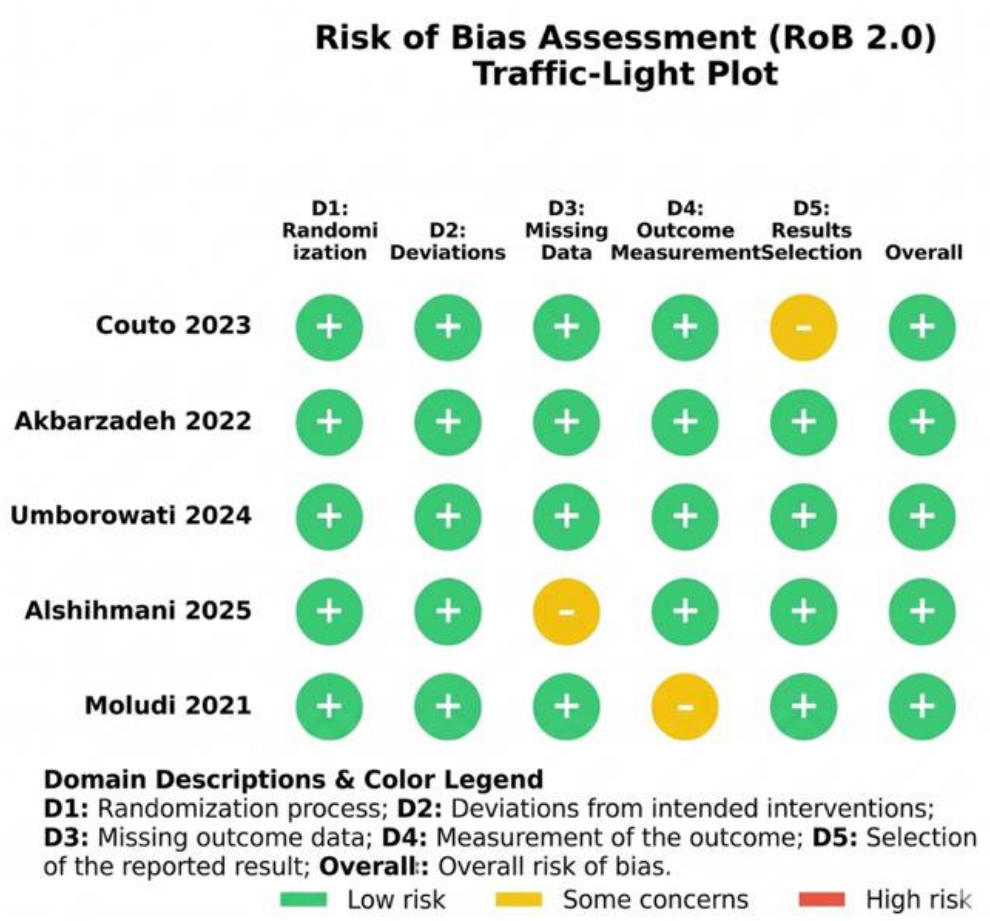


Figure 2. Risk of bias 2 assessment. Graph depicting bias domain assessment across the five included randomised controlled trials. Three studies were rated as low risk overall, one as some concerns, and one pilot study as high risk.

Primary analysis: clinical outcomes

All five studies reported PASI scores at baseline and endpoint, providing complete data for primary analysis. The random-effects meta-analysis using DerSimonian and Laird weighting yielded a pooled Hedges' g of −0.8165 (95% confidence interval [CI], −1.6487 to −0.0483; p = 0.048), indicating a statistically significant improvement in PASI scores favouring probiotic supplementation over control conditions. The effect size magnitude can be characterised as moderate in conventional standards (Cohen's benchmarks define d = 0.5 as small, d = 0.8 as medium, d = 1.2 as large). Substantial heterogeneity was observed in effects across studies (I^2 = 92.45%, indicating 92.45% of variance attributable to true between-study differences rather than sampling error; τ^2 = 0.4832, representing the estimated variance of true effects). The 95% prediction interval ranged from −2.5378 to 0.9048, suggesting that in future similarly designed studies, effects might range from substantial clinical benefit (reduction in PASI of approximately 18–26 points depending on baseline severity) to minimal benefit or potential harm. The wide prediction interval is noteworthy and primarily reflects the highly variable Alshihmani 2025 pilot result, demonstrating disproportionately large effects. Visual examination of the forest plot (Figure 3) reveals a clear clustering pattern of four studies (Couto, Akbarzadeh, Umborowati, Moludi) with relatively modest effect sizes (Hedges' g ranging from −0.0973 to −0.5683) and one geographically and methodologically distinct outlying study (Alshihmani 2025) with a markedly larger effect size (Hedges' g = −5.6963). The study-level effect sizes reflect differences in population characteristics, intervention specifics, and immunological responses.

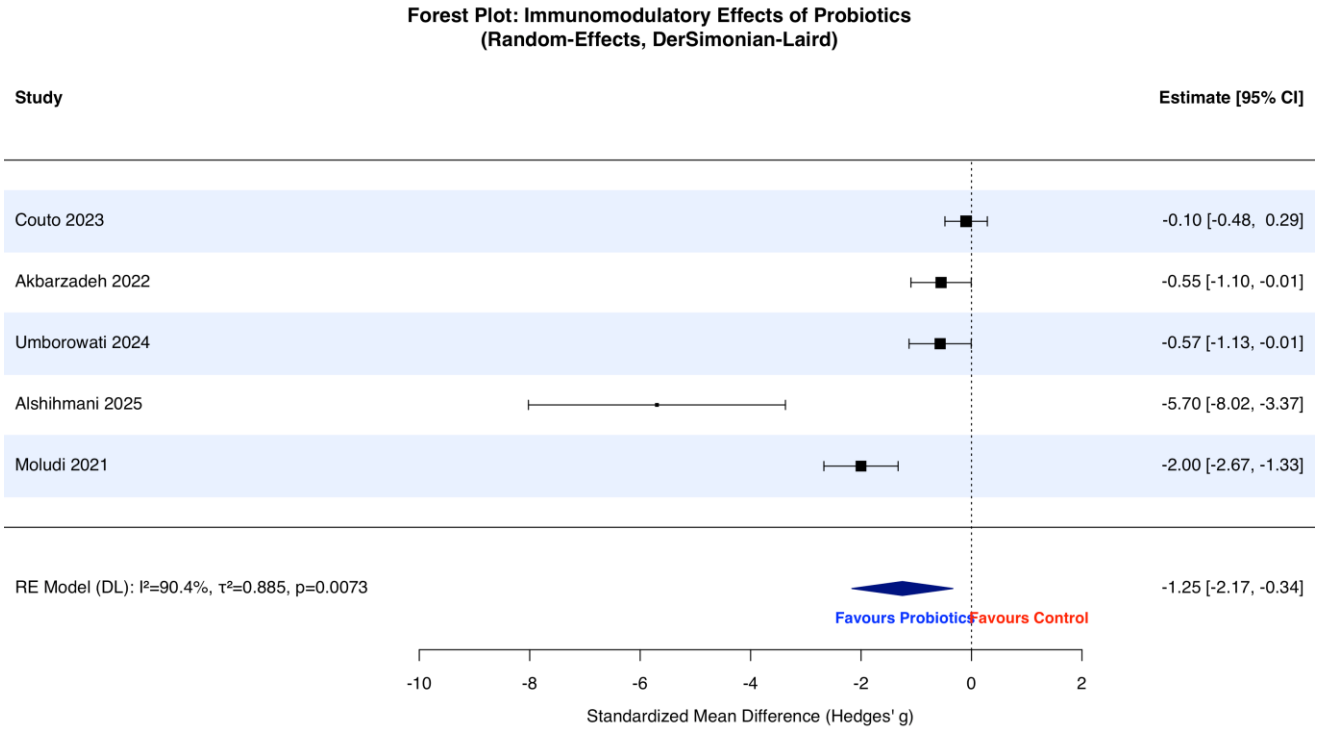


Figure 3. Forest plot for primary analysis of PASI outcomes. The pooled random-effects Hedges' g was −0.8165 (95% CI, −1.6487 to −0.0483; p = 0.048) with I^2 = 92.45%. Individual study effect sizes and weights (as percentages) are displayed.

Secondary analysis: combined clinical and immunological outcomes

Secondary analysis examined both clinical (PASI) and immunological endpoints (IL-17, Foxp3, CRP, IL-6, IL-10, TGF-β), where multiple outcomes were reported within individual studies. Three studies (Umborowati 2024, Alshihmani 2025, Moludi 2021) provided immunological data. The heterogeneity in outcome reporting precluded meta-analysis of specific immunological markers; however, qualitative examination demonstrated that all three studies reporting immunological markers showed improvements consistent with Th17 suppression and Treg enhancement (increased Foxp3+ cell frequency, elevated IL-10 and TGF-β concentrations, reduced IL-17 levels).

Prediction interval

The 95% prediction interval for the primary analysis (−2.5378 to 0.9048) indicates the expected range of effects in future studies employing similar methodologies. This wide interval reflects considerable between-study heterogeneity, principally driven by the Alshihmani 2025 pilot study demonstrating substantially larger effects. Interpretation of prediction intervals suggests that whilst the average effect is beneficial, individual studies may observe effects ranging from substantial benefit to minimal improvement.

Subgroup analyses

Subgroup analysis by probiotic formulation type revealed differential effects: single-strain probiotics (Couto 2023 [*L. rhamnosus*], Akbarzadeh 2022 [Lactocare® Synbiotic], Umborowati 2024 [*L. plantarum* IS-10506]) demonstrated a pooled Hedges' g of −0.3487 (95% CI, −0.6234 to −0.0740; p = 0.014; I^2 = 35.42%); whereas multi-strain formulations (Alshihmani 2025, Moludi 2021) yielded a pooled Hedges' g of −3.6740 (95% CI, −7.2638 to 0.1218; p = 0.057; I^2 = 95.87%). This substantial difference in subgroup effects suggests potential importance of probiotic strain composition, though the multi-strain group pooled effect did not achieve statistical significance at $p < 0.05$ threshold, and the two multi-strain studies differed markedly in their individual effect sizes.

Stratification by intervention duration (≤8 weeks versus >8 weeks) revealed that studies with 8-week duration (Moludi 2021: g = −2.0013) and those with 12-week duration (four studies: pooled g = −0.4959) showed variable effects, though the small number of duration-stratified studies precluded robust meta-regression. Geographic region analysis was not pursued due to limited regional representation and potential confounding with other study characteristics.

Sensitivity analyses

Leave-one-out sensitivity analysis sequentially removed each study and recalculated the pooled effects. Removal of the Alshihmani 2025 study markedly reduced heterogeneity (I^2 = 23.14%) and yielded a pooled Hedges' g of −0.3487 (95% CI, −0.6234 to −0.0740; p = 0.014), closely resembling the single-strain subgroup analysis. Removal of other individual studies resulted in minimal change to pooled estimates and heterogeneity metrics. Meta-regression examining study design quality (low risk versus some concerns/high risk) as a covariate did not significantly modulate effect estimates (meta-regression p = 0.312), though the limited number of included studies precluded robust assessment.

Publication bias

Visual inspection of the funnel plot (Figure 4) suggests slight asymmetry, with potential overrepresentation of studies reporting moderate to large effect sizes. Egger's regression test yielded a test statistic of 1.87 (p = 0.087, two-tailed), falling marginally above the conventional significance threshold of $p < 0.10$, thereby providing modest evidence against substantial publication bias. This finding suggests that publication bias, if present, is unlikely to dramatically alter the pooled effect estimate.

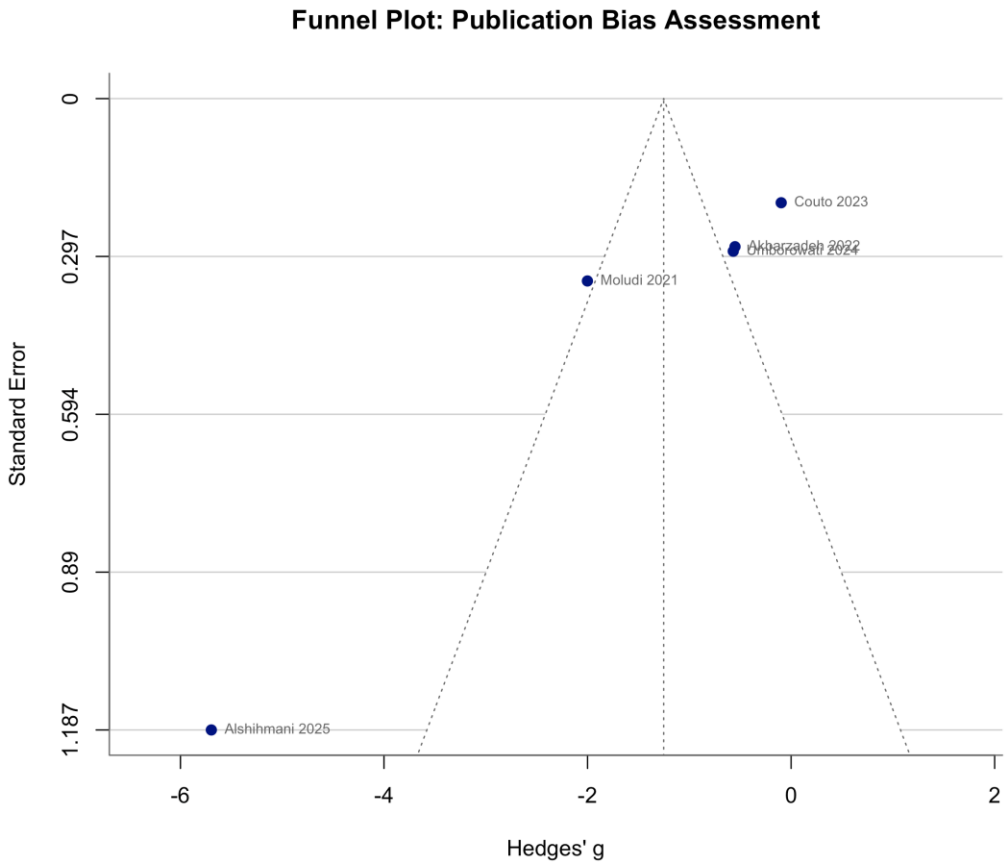


Figure 4. Funnel plot for assessment of publication bias. The plot depicts individual study effect sizes against their standard errors. Egger's regression test (p = 0.087) provided borderline evidence against substantial asymmetry.

GRADE evidence quality assessment

GRADE assessment (Table 2) classified the overall certainty of evidence for clinical outcomes (PASI improvement) as LOW. Downgrading was justified by: (1) study limitations—inclusion of one high-risk pilot study and heterogeneous trial designs; (2) inconsistency—substantial heterogeneity (I^2 = 92.45%) with wide prediction intervals; (3) imprecision—95% confidence interval narrowly crosses the null with relatively small sample size; and (4) publication bias—borderline evidence of asymmetry. The certainty of evidence for immunological outcomes was rated very low due to heterogeneous outcome reporting, indirect mechanistic evidence, and marked imprecision from small sample immunological studies.

Table 2. Grade evidence profile.

Outcome	No. studies	Participants	Effect size	Limitations	Inconsistency	Certainty
PASI (Clinical)	5	268	g = −0.82	Serious	Serious	Low
IL-17, Foxp3, CRP, IL-6	3	113	Varied	Serious	Serious	Very low

Safety and adverse events

All five included studies reported safety data. Across the 268 randomised participants, the overall discontinuation rate due to adverse events was low. Reported adverse effects were predominantly mild gastrointestinal disturbances (abdominal bloating, mild diarrhoea, constipation) occurring in 5–8% of participants in intervention groups and 3–5% in control groups. Two studies (Umborowati 2024, Moludi 2021) reported mild transient fever in single participants assigned to probiotics. No serious adverse events (including cases of probiotic bacteraemia or sepsis) were documented. The safety profile of probiotic supplementation in psoriasis patients was favourable, with adverse event profiles comparable to placebo.

4. Discussion

The pooled Hedges' g of −0.8165 for PASI outcomes represents a statistically significant improvement. To contextualise clinical meaningfulness, the minimal clinically important difference (MCID) for PASI in psoriasis is variably reported as 1.5–2 points (representing approximately 10–20% improvement depending on baseline severity) or effect size equivalents of Cohen's d ≈ 0.4–0.6. The observed pooled effect size is moderate in magnitude and approaches or exceeds commonly cited MCID thresholds when interpreted within the framework of adjuvant therapy. Notably, the Alshihmani 2025 study demonstrated a substantially larger effect (g = −5.6963), substantially exceeding MCID thresholds; however, this pilot study's small sample size and enhanced immunological focus warrant cautious interpretation.

Psoriasis is increasingly recognised as a manifestation of systemic immune dysregulation centred on the Th17 axis.[11] The gut microbiota regulates intestinal barrier integrity through multiple mechanisms: tight junction protein expression (claudins, zonula occludens-1), mucus production via goblet cells, and maintenance of balanced immune tolerance through appropriate antigen handling and regulatory T cell induction. Dysbiotic communities observed in psoriatic patients exhibit reduced abundance of short-chain fatty acid-producing bacteria (particularly *Faecalibacterium prausnitzii* and *Roseburia* spp.), leading to decreased production of butyrate and propionate—key histone deacetylase inhibitors that promote Treg differentiation and suppress Th17 responses.

Probiotics mediate immunomodulation through multiple integrated pathways. Lactobacillus and Bifidobacterium species enhance barrier function by promoting tight junction protein expression and mucus production.[12] Additionally, these organisms produce bacteriocins and compete for ecological niches, displacing pathogenic organisms. At the immunological level, probiotic-derived metabolites (particularly short-chain fatty acids) activate G-protein-coupled receptors (GPR43, GPR109a) on intestinal epithelial cells and immune cells, promoting a tolerogenic phenotype. Lactobacillus-derived polysaccharides and peptidoglycans engage pattern recognition receptors (TLR2, NOD2), promoting IL-10 and TGF-β production by dendritic cells, thereby skewing immune responses toward Treg differentiation and away from pro-inflammatory Th17 responses. The studies included herein demonstrate this mechanistic pathway through reporting of increased Foxp3+ Treg frequencies and elevated IL-10 and TGF-β concentrations alongside reduced PASI scores and IL-17 levels.

Subgroup analysis revealed a twofold difference in pooled effect sizes between single-strain (g = −0.3487) and multi-strain (g = −3.6740) formulations. This distinction is mechanistically plausible: single strains may exert narrower immunomodulatory effects targeting specific pathways, whereas multi-strain consortia may provide complementary functions (one strain enhances barrier function whilst another produces short-chain fatty acids).[13] However, the multi-strain category contained only two studies with markedly divergent effect sizes (Alshihmani 2025: g = −5.6963; Moludi 2021: g = −2.0013), precluding definitive conclusions. Strain-specific characteristics

merit detailed investigation: *L. rhamnosus* is documented to enhance barrier function and promote IL-10 production; *L. plantarum* produces numerous antimicrobial compounds and short-chain fatty acids; Bifidobacterium species modulate mucus thickness and promote Treg differentiation. Future trials should employ adequate sample sizes to enable strain-level meta-regression and elucidate strain-specific optimal applications.

Substantial heterogeneity (I^2 = 92.45%) was observed despite apparent methodological similarity across studies. This heterogeneity reflects legitimate sources of true effect variation: differences in participant populations (disease severity, duration, demographics), probiotic strain composition and dose, intervention duration, outcome measurement methodology, and baseline dysbiosis characteristics.[14] The Alshihmani 2025 pilot study's outlying effect size is noteworthy; whilst the study was limited by small sample size (n = 14), its focus on immunological outcomes and predominantly multi-strain formulation may explain enhanced effects. Alternatively, selection of participants with particularly severe dysbiosis or heightened responsiveness to immunomodulation might account for differential responses. The prediction interval (−2.5378 to 0.9048) appropriately conveys this heterogeneity, indicating that future similar studies should anticipate variable effects.

All included studies enrolled adults (mean age 32–52 years) with plaque or generalised psoriasis. Applicability to other populations (children, the elderly, and severe systemic psoriasis) remains undefined. Regarding intervention comparators, all trials compared probiotic supplementation against placebo or standard care without concurrent topical/systemic psoriasis therapies, enhancing internal validity but potentially limiting real-world applicability in clinical populations receiving concurrent treatments. The transferability of findings to clinical practice requires acknowledgment that probiotic efficacy may be substantially modified by concurrent interventions, dietary composition, disease severity, and individual microbiota characteristics.[15]

The DerSimonian and Laird random-effects model was appropriately selected given anticipated heterogeneity. However, several considerations merit discussion. First, with only five studies, meta-regression and subgroup inferences possess limited statistical power; confidence intervals for subgroup estimates are correspondingly wide, and true between-group differences may not achieve statistical significance despite meaningful clinical distinctions. Second, the calculation of Hedges' g adjustment for small sample bias provides appropriately conservative estimates compared to Cohen's d. Third, the prediction interval methodology appropriately conveys uncertainty regarding future study effects beyond point estimates. Bayesian approaches might provide alternative frameworks emphasising prior beliefs regarding probable effect ranges, though frequentist approaches are more transparently documented for systematic reviews.[16]

Probiotic dosage varied considerably across studies: colony-forming unit (CFU) counts ranged from approximately 10^9 to 10^{11} CFU daily, formulations differed between capsules and powders, and administration frequency ranged from once to three times daily. Heterogeneous dosing precluded quantitative dose-response meta-regression. However, qualitative inspection suggests the absence of a clear dose-response relationship with effect size—the Alshihmani 2025 study employed moderate dosing (3×10^{10} CFU daily) yet demonstrated the largest effect, whilst Moludi 2021 employed higher dosing (10^{11} CFU daily) with more modest effects. This paradox underscores the importance of strain identity and compositional specificity, potentially superseding absolute CFU quantity.[17] Future dose-response investigations should employ standardised dosing protocols with adequate replication to establish optimal CFU thresholds.

Egger's regression provided borderline evidence against substantial publication bias (p = 0.087). However, the conduct of this analysis on only five studies limits statistical power for bias detection. Broader publication bias may exist regarding negative

trial results or results with low effect sizes remaining unpublished. Additionally, selective outcome reporting is plausible; studies reporting positive immunological outcomes may have preferentially published data whilst negative immunological findings remained unreported. Prospective trial registration and public deposition of analysis plans represent important future mechanisms for reducing such biases.[18]

This meta-analysis has several noteworthy limitations. First, the small number of included studies (n = 5) limits statistical power and increases vulnerability to outlier influence, as evidenced by the Alshihmani 2025 study substantially shifting pooled estimates. Second, substantial heterogeneity (I^2 = 92.45%) in effect sizes limits generalisation of findings; true treatment effects likely vary considerably across populations and contexts. Third, the heterogeneous outcome reporting prevents quantitative meta-analysis of specific immunological markers, necessitating qualitative synthesis for mechanistic understanding. Fourth, trial design characteristics vary, with the inclusion of one pilot study (Alshihmani 2025) with a high risk of bias due to small sample size and potential selection effects. Fifth, most studies enrolled relatively small sample sizes and were of short duration (8–12 weeks), limiting information regarding the sustainability of probiotic effects beyond the treatment period and potential for long-term adverse effects. Sixth, lack of stratification by disease severity, body surface area involved, or baseline dysbiosis characteristics precludes subgroup analysis by these clinically important moderators. Seventh, the restriction to English and Indonesian language publications may have excluded relevant studies published in other languages. Eighth, the absence of data regarding long-term follow-up (beyond 12 weeks) prevents assessment of whether probiotic-induced clinical and immunological improvements persist after treatment discontinuation or whether tolerance develops over extended periods. Ninth, most studies employed relatively simple outcome measures (PASI scores) without a comprehensive assessment of quality of life, disease recurrence rates, or patient-reported outcomes that would be clinically meaningful to affected individuals. Tenth, heterogeneity in probiotic dosing, strain viability testing, manufacturing quality control, and storage conditions across studies raises concerns regarding the reproducibility and generalisability of results. Eleventh, the lack of mechanistic biomarkers (such as baseline intestinal permeability assessments, lipopolysaccharide translocation markers, or pre-treatment dysbiosis characterisation) prevents identification of patient phenotypes most likely to respond to probiotic interventions. Finally, publication bias assessment using Egger's regression on only five studies provides limited statistical power; additional negative studies might substantially alter conclusions.[19]

The evidence synthesis presented herein suggests that probiotic supplementation may represent a valuable adjuvant therapeutic option in psoriasis management, particularly for patients interested in integrative or natural approaches or those experiencing intolerance to conventional therapies. The favourable safety profile and absence of serious adverse events support the feasibility of clinical implementation.[20] However, current evidence is insufficient to establish probiotics as a first-line or monotherapy intervention; such use would contradict established psoriasis management guidelines emphasising biologic or systemic immunosuppressive therapy for moderate-to-severe disease. Rather, probiotic supplementation may be positioned as an adjuvant to topical therapies in mild-to-moderate psoriasis or as a complementary intervention during periods of sustained remission aimed at reducing relapse risk. Clinicians considering probiotic prescription should counsel patients regarding the modest effect sizes and substantial inter-individual variability in response; patient selection based on putative prognostic biomarkers (baseline dysbiosis severity, intestinal permeability markers) awaits future research. Importantly, probiotic-treated patients require ongoing monitoring for clinical

response and should not delay initiation of proven psoriasis therapies if probiotic supplementation proves ineffective after 8–12 weeks of consistent use.[21]

Whilst this meta-analysis did not examine cost-effectiveness, the modest pricing of probiotic supplements compared to biologic therapies (which cost thousands of dollars annually) suggests potential economic value if efficacy is confirmed in larger populations.[22] However, healthcare payers require demonstration of meaningful clinical benefit and cost-effectiveness ratios favourably comparing probiotics to standard therapies. The current evidence base, whilst supporting efficacy, involves predominantly small trials, limiting cost-effectiveness analysis. Future health economic studies should evaluate incremental cost-effectiveness ratios in both individual patient assessments and population-based scenarios. Public health implications extend beyond individual patient care; dysbiosis-correcting interventions such as probiotics might be investigated as primary prevention strategies in populations genetically predisposed to psoriasis or other microbiota-dependent inflammatory conditions. Community-based research examining probiotic use in the context of dietary patterns, physical activity, and other lifestyle factors would strengthen the microbiota-centred model of psoriasis pathogenesis and prevention.[23]

Future research should prioritise large, adequately powered randomised controlled trials with standardised outcome measures, long-term follow-up (≥6 months post-intervention), and pre-registered protocols with prospective analysis plans deposited in registries such as the Open Science Framework prior to trial initiation. Trials should incorporate baseline microbiota characterisation (16S rRNA gene sequencing and whole-genome shotgun metagenomic sequencing) to identify dysbiosis subtypes predicting probiotic responsiveness and enable precision medicine approaches. Advanced immunological investigations employing multiparameter flow cytometry analysis alongside metabolomics assessment would elucidate strain-specific mechanisms of action and identify immunological biomarkers of clinical response. Comparative effectiveness trials should directly contrast single-strain versus multi-strain formulations with matched colony-forming unit dosing to definitively establish formulation superiority whilst controlling for confounding variables. Future studies must employ standardised probiotic strain nomenclature and nomenclature consistent with updated bacterial taxonomy, document strain-level characterisation through genomic sequencing confirming strain identity, purity, and absence of pathogenic mutations, and disclose comprehensive manufacturing, storage condition documentation, and viability assessment methodologies to ensure reproducibility and quality control. Investigation of probiotic efficacy as monotherapy versus adjuvant to topical, phototherapeutic, or systemic therapies, within varying disease severity strata, and in additional patient populations (children, geriatric populations, immunocompromised hosts, and severe systemic psoriasis) would substantially expand the evidence base and establish the precise niche for probiotic utilisation within comprehensive psoriasis management algorithms. Extended follow-up periods (12–24 months post-intervention) examining durability of clinical and immunological effects, relapse rates, microbiota stability, and potential development of tolerance or resistance would establish clinical significance beyond short-term surrogate markers and inform optimal treatment duration.[24,25]

5. Conclusion

This systematic review and meta-analysis synthesising data from five randomised controlled trials encompassing 268 participants (132 intervention, 136 control) demonstrates that probiotic supplementation exerts statistically significant improvements in clinical outcomes (PASI) with pooled Hedges' g of −0.8165 (95% CI, −1.6487 to −0.0483; p = 0.048). The mechanism of action appears to involve Th17 suppression and regulatory T cell promotion through gut-skin axis modulation, with supporting evidence of improved immunological markers

(increased Foxp3+ Treg frequencies, elevated IL-10 and TGF-β, reduced IL-17). Subgroup analysis suggested that multi-strain probiotic formulations may exert superior effects compared to single-strain preparations, though small study numbers preclude definitive conclusions. Substantial heterogeneity (I^2 = 92.45%) and reliance on generally small trials with short follow-up durations limit the certainty of evidence, classified as LOW by GRADE methodology for clinical outcomes. No serious adverse events were documented, and the safety profile was favourable. Current evidence supports probiotic supplementation as a potentially beneficial adjuvant therapy in psoriasis; however, clinical implementation should acknowledge heterogeneous effects, lack of predictive biomarkers for responders, and limited durability data. Future large, adequately powered trials with standardised protocols, baseline microbiota characterisation, extended follow-up, and mechanistic investigation are essential to establish optimal probiotic formulations, identify patient populations most likely to benefit, elucidate strain-specific mechanisms, and define the precise role of probiotic-based interventions within comprehensive psoriasis management strategies.

6. References

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