Current Science
CS 5 (6), 5272-5283 (2025)
Received 17 Oct 2025 | **Accepted 30 October** 2025 | **Online Available 05 November** 2025
https://doi.org/10.52845/CS/2025-5-6-3

Current Science

Current Science

OPEN ACCESS

ISSN (O) 2795-8639

Original Article

A Systematic Review of the Effectiveness of Probiotics in the Treatment of Acne Vulgaris since 2020: A Quantitative Study

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Abstract:

Objective: To evaluate studies published after 2020 on the effectiveness of probiotics in treating acne vulgaris, with a focus on clinical trials.

Methods: The review includes randomized controlled trials (RCTs) and quasi-experimental studies (QES) from Pubmed, Medline, and CINAHL (January 2020 - June 2024). Participants were diagnosed with acne vulgaris, and the interventions involved various probiotics. Data extraction and quality assessment were conducted using a pre-designed form and the Cochrane Risk of Bias Tool.

Results: Five studies (four RCTs and one QES) with 310 participants were reviewed. Probiotics significantly reduced acne lesions and improved skin hydration and overall skin health. Adverse effects were low and mild.

Conclusion: Probiotics show promise as a treatment for acne vulgaris, either alone or with other treatments. They help reduce acne lesions and improve skin health. Further high-quality studies are needed to confirm these findings and optimize treatments.

Keywords: acne vulgaris, probiotics, clinical trials, systematic review

1. Introduction

Acne vulgaris is a chronic inflammatory skin disease involving the sebaceous glandular units of hair follicles[Error! Reference source not found.]. The global all-age prevalence of acne is estimated to be 9.38%[1], ranking eighth on the list of prevalent diseases in the world[2]. The prevalence in adolescents ranges from 35% to 90% at some stages and increases with the age of the adolescent[3,4].

Probiotics are active microorganisms that are beneficial to the host and usually exert their health effects by improving the balance of intestinal flora[5]. In recent years, a large number of studies have identified potential benefits of probiotics in the area of skin health as well. Their mechanisms of action may include the following:

a. Regulation of immune response: Probiotics reduce the inflammatory response of the skin by regulating the body's immune response and reducing the release of inflammatory factors[6].

b. Inhibit the growth of pathogenic bacteria: Some probiotics can reduce the growth of Propionibacterium acnes through competitive inhibition and the production of antimicrobial substances[7].

c. Restoration of skin barrier function: Probiotics can enhance the skin barrier function, improve the skin microenvironment and reduce the possibility of acne[9].

Currently, treatments for acne include topical medications (e.g., benzoyl peroxide, retinoids)[Error! Reference source not found.], oral

antibiotics (e.g., tetracyclines)[10], hormone therapy[Error! Reference source not found.] and isotretinoin[12]. Although these treatments are effective to a certain extent, they have some limitations: side effects (prolonged use of antibiotics may lead to drug resistance, and oral isotretinoin may cause serious side effects[13].), erratic efficacy (some patients do not respond well to traditional treatments, with limited improvement in symptoms[14].) and high relapse rate (many patients are prone to relapse after treatment and require long-term maintenance therapy[15].)

Objective

The objective of this systematic review is to update and evaluate studies published after 2020 on the effectiveness of probiotics in the treatment of acne vulgaris. The research questions of this review are clarified through the PICO framework to ensure that the studies are systematic and comprehensive. Particular focus was placed on increasing the focus on clinical trials to be able to provide stronger evidence that probiotics can treat acne vulgaris.

Methods

Study Type

This review will include both randomized controlled trials (RCTs) and quasi-experimental studies (QES). Considered the gold standard of research design, RCTs are the most reliable method of evaluating the effectiveness of interventions by randomly assigning participants to intervention and control groups, thereby reducing the effects of selection bias and confounding variables[16]. However, as it was evident from the initial literature search results that including only RCTs may have overly limited the search results, resulting in the omission of a large number of relevant studies. And although a growing number of studies have evaluated the effectiveness of probiotics in the treatment of acne vulgaris, the number of studies is still limited, especially those published since 2020, so it was decided to include QES. A QES is a research design used to evaluate the effects of an intervention or treatment but, unlike RCTs, is not characterized by random assignment[17]. Although it may not be as rigorous as RCTs in controlling for confounding variables and cannot provide the causality needed to determine whether probiotics are effective in treating acne vulgaris, they can still provide valuable evidence.

Participant Type

Trial participants included in this review must be patients diagnosed with Acne Vulgaris, with diagnosis based on standardized acne diagnostic criteria (e.g., clinical examination, IGA score, ECCA score, etc.). Patients with different types of Acne vulgaris, regardless of severity (mild, moderate or severe) will be included as trial participants in this review. Exclusion criteria include trials involving participants with other skin disorders, or those without acne but with other skin problems, as well as those involving participants with specific medical conditions or receiving other interventions that may affect the outcome of acne treatment.

Intervention Type

The intervention evaluated in this systematic review is the probiotic treatment for Acne Vulgaris, regardless of the specific probiotic strain type, route of administration (oral or topical), dose, frequency and duration of treatment. All types of probiotics (e.g., Lactobacillus, Bifidobacterium, etc.), as well as different forms of routes of administration (e.g., oral capsules, tablets, topical creams, gels, etc.) will be considered to meet the trial's inclusion criteria. Exclusion criteria were interventions that did not involve probiotics or interventions that involved probiotics but were aimed at patients whose tester was not Acne vulgaris.

Comparator

This review will include trials using placebo and self-control as control groups. The placebo control group shall receive the same intervention course as the treatment group, but without the active probiotic component. The self-control control group should undergo only the interventions required by the trial to act on acne vulgaris for the duration of the trial. Specifically, placebo may include capsules, tablets, topical creams or gels without active ingredients.

Outcome Measures

This review will exclude trials that report only secondary outcome indicators and include only trials that report primary outcome indicators. Primary outcome indicators included changes in acne severity (GAGS score), skin hydration, transcutaneous water loss (TEWL score), sebum production (SEBUTAPET score) and skin inflammation levels, number of acne lesions (total lesion count: including number of inflammatory and non-inflammatory lesions), and salivary T-Blue test score. Secondary outcome indicators included patients' skin condition and overall satisfaction (questionnaires and clinical assessments), and the incidence and severity of adverse reactions reported by patients during treatment, including the incidence of nausea, bloating, and diarrhea.

Information sources of studies

The search strategy for the databases is described in Appendix B. I systematically searched Pubmed, Medline and CINAHL for studies published from January 2020 to June 2024 on the effectiveness of probiotics in the treatment of acne vulgaris. These databases cover the three key disciplines of this topic: medicine, dermatology and public health. In addition, these databases were included in previous Cochrane reviews for studies related to the treatment of acne vulgaris. And this review focuses on epidemiologic studies (RCTs and cross-sectional studies) with quantifiable outcome indicators. These studies were conducted to assess the effect of probiotic treatment on acne and were published in English. A reference check of previous literature reviews[7] was also performed to ensure comprehensive coverage of relevant studies.

Data Collection

In order to ensure the accuracy and completeness of data collection, this review used a pre-designed pilot form for data extraction, but as it was a student project, only one person extracted the data independently. In order to minimize the effect of some degree of individual bias, the pilot form was therefore filled out multiple times.

Quality Assessment

This review will use the Cochrane Risk of Bias Tool to assess the quality of the methodology of the included studies. As this review focuses on RCTs, the choice of this tool is appropriate. The tool covers all major types of bias (selection bias, performance bias, detection bias, attrition bias, and reporting bias, among others) and ensures standardization of the assessment process, making quality assessment comparable across studies and providing simple graphical representations that make results easy to understand and interpret[Error! Reference source not found.].

Data Extraction

Data will be extracted using a customized data extraction form, a full example of which is available in the Appendix C. The extracted data include study characteristics, participant characteristics, interventions, comparison measures, and outcome indicators. The benefits of using a form to extract data, in addition to reducing reporting bias, will increase transparency of the results so that inconsistencies or problems in the data extraction process can be identified and resolved[19].

Synthesis of Results

As the five articles varied considerably in terms of study group characteristics and exposure

assessment techniques, this resulted in too few studies for each single endpoint to allow a formal meta-analysis to be conducted. Therefore this study anticipates the use of narrative synthesis to explore the findings of the included studies, as the initial search results suggest that the quality of the studies may be low and the heterogeneity significant, narrative synthesis will allow for an analysis of the impact of similarities[20], differences and contextual factors on the results to provide detailed insights into the treatment of acne vulgaris with probiotics.

Results

Study Selection

The search strategy (see appendix B) identified 32 papers; the small number was anticipated due to limitations of RCTs and QES. Figure 1 demonstrates the stages at which studies were rejected to reach the final five studies.

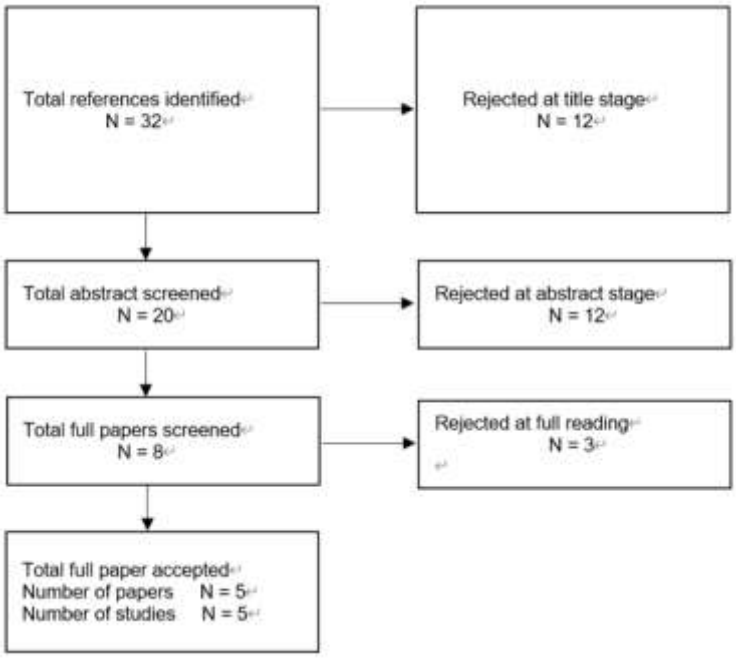

Figure 1. PRISMA diagram

Description of Study

Design

The five trials in the review include four RCTs[21,22,23,24] and a QES[25]. The five trials include data from 310 participants. The number of participants in each trial was small and ranged from 20 to 104 (see Table 1 for details).

Table 1. Study setting, funding and number of participants

Study author and date	Country of origin	Source of funding	Study setting	Number of participants
Ho 2022	Taiwan	This information was not explicitly provided in the extracted text.	A dermatology research center	n(Treatment)=n(Control)=20 (Self-Control)
Eguren 2024	Spain	This information was not explicitly provided in the extracted text.	Not explicitly mentioned	Treatment n=42 Control n=39

Sathikulpakdee 2022	Thailand	This study was funded by the Faculty of Medicine, Srinakharinwirot University	Skin Center, Faculty of Medicine, Srinakharinwirot University, Bangkok, Thailand	Treatment n=52 Control n=52
Marasca 2022	Italy	This information was not explicitly provided in the extracted text.	Not explicitly mentioned	n(Treatment)=n(Control)=30 (Self-Control)
Irshad 2023	Pakistan	This information was not explicitly provided in the extracted text.	Pak Emirates Military Hospital	n(Treatment)=n(Control)=75 (Self-Control)

Population

All participants in the trials (n=310) suffered from acne vulgaris. Participants in two of the trials were over the age of 18[23,24], in two others the age of the participants included minors: 12 to 30 years old[22] and 15 to 35 years old[25], and in the remaining trial, the average age of the participants was 28 years old[21]. In all trials, the duration of the trial varied, ranging from four weeks to three months (see Table 2 for details). Two trials targeted participants for in vitro studies (rubbing gel[21] and lotion[23]); three trials targeted participants for in vivo studies (oral capsules[22,25] and supplements[24]).

Table 2. Study Design

Study name/Setting	Study design	Population	Intervention	Comparator	Outcome
Ho 2022	RCT	Patients with acne vulgaris who met specific inclusion criteria	4-Week A cosmetic gel includes a TAC/Collagen formula	The baseline was 4 weeks ago as the control group (Self-Control)	Antibacterial activity against propionibacterium acnes and anti-inflammatory effect around lesions
Eguren 2024	RCT	Patients diagnosed with acne vulgaris by AGSS	12-week Lyophilized composed of the probiotic Lacticaseibacillus rhamnosus and the cyanobacterium Arthrospira platensis	Containing only maltodextrin as placebo	The difference between the 2 study groups in the number and percentage of patients who improve regarding AGSS category
Sathikulpakdee 2022	RCT	Participants who had active skin lesions on the face	2 and 4 weeks Probiotic-derived lotion	2.5% benzoyl peroxide as placebo	Acne lesion counts, erythema index, and side effects
Marasca 2022	RCT	Patients with acne	60 days Oral probiotic	The baseline was 60 days	Global Acne Grading System

		vulgaris who met specific inclusion criteria (within 60 days)	supplement and topical gel product	ago as the control group (Self-Control)	(GAGS) Score, seborrhea assessment, trans-epidermal water loss (TEWL), inflammatory state via T-Blue test.
Irshad 2023	CT	Patients with mild to moderate acne vulgaris	3 months Azithromycin and probiotics i.e. Hi-Flora sachet	The baseline was 3 months ago as the control group (Self-Control)	Counting the total acne lesions

Intervention

All five studies explored the use of probiotics in the treatment of acne. Although the specific interventions utilized were different. Each required participants to involve the use of probiotics as the primary treatment, different measures of probiotics were utilized to assess their effectiveness in the treatment of common acne. Because of the inconsistency of the interventions, comparisons by number of implementations were not desirable. And the duration of each trial was inconsistent. The specific interventions are shown in Table 2.

Comparator

The control groups for the five studies were not identical. In three of them, the treatment effect was assessed by comparing the skin condition before and after the test[21,24,25], creating self-control and thus eliminating the effect of individual differences on the results. The control groups for the other two were set up as placebo controls[22,23], where the placebo group received a placebo with the same appearance as the test group but without the active probiotic ingredient, and underwent the same experimental procedure for the same amount of time as the test group.

Outcome Measure

The primary outcome measure in three of the trials was a change in the number of acne lesions[22,23,25]. In one trial, the primary outcome measures were changes in skin hydration and skin inflammation levels[21]. The primary outcome measures in the other trial were acne severity[24].

The secondary outcome measure for two of the trial was the incidence of adverse reactions and severity, reported by patients during treatment[24,25]. The secondary outcome indicator for both studies was the change in the skin condition of the patients[22,23]. One trial had no secondary outcomes[21].

In four of the trials, the outcome measure was measured once at the end of the study time[21,22,24,25]. Only one trial had an outcome measure that was measured twice, at the midpoint of the trial and at the end of the trial[23]. See Table 2 for details.

Study Quality

Overall, the quality of these five studies was mixed, reflecting the differences in study design and implementation outlined in Figure 2 and detailed in Table 3. Specifically, only one trial[24] demonstrated a low risk of bias in randomized sequence generation, allocation concealment, blinding of participants and researchers, blinding of outcome assessment, and treatment of incomplete outcome data, demonstrating high study quality. One trial[23] also performed well in randomized sequence generation, allocation concealment, and blinding of outcome assessment, but details were unclear in other

areas. Two trials[21,22] had unclear risk of bias in allocation concealment and blinding and lacked detailed reporting. One trial[25] showed a high risk of bias in random sequence generation and allocation concealment, which may have implications for the reliability of the study results. In addition, all five trials demonstrated an unclear risk of bias in terms of selective reporting that was not explicitly mentioned. Although some of the trials performed well in some areas, as a whole these studies were still deficient in preventing bias and ensuring the reliability of the results.

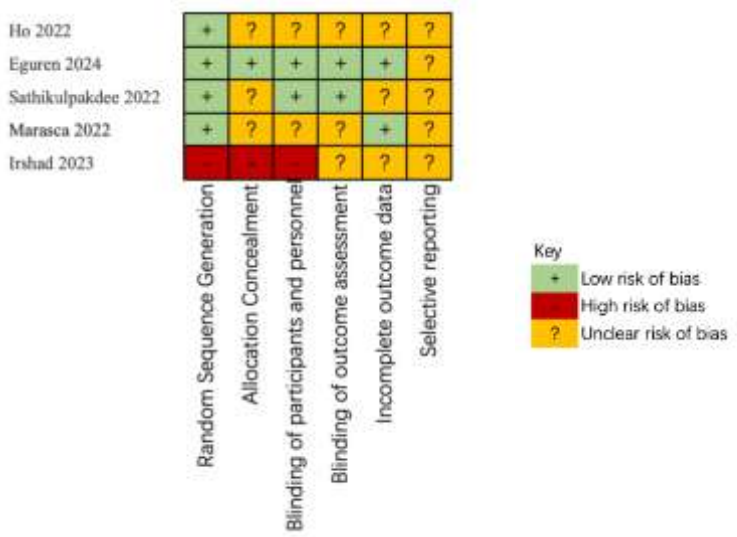

Figure 2. Study Quality: Overview

Table 3. Study Quality: detail (low risk: LR, unclear risk: UR, high risk: HR)

Study name	Random Sequence Generation	Allocation Concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting
Ho 2022	LR: Computer-generated randomization	UR: Not specified	UR: Not specified	UR: Not specified	UR: Not specified	UR: Not specified
Eguren 2024	LR: Closed envelopes or central randomization systems are used	LR: Closed envelopes or central randomization systems are used	LR: Double-blind	LR: Blinded outcome assessment	LR: No withdraws or exclusions	UR: Not specified
Sathikulpakdee 2022	LR: Allocation by computer-generated block randomization method	UR: Not specified	UR: Lack of information about blinding	LR: Blinded outcome assessment	UR: Not specified	UR: Not specified
Marasca 2022	LR: Computer-generated randomization	UR: Not specified	UR: Not specified	UR: Not specified	LR: No withdraws or	UR: Not specified

					exclusions	
Irshad 2023	HR: Lack of information about method of random sequence generation	HR: Due to lack of randomisation	HR: Single blinded	UR: Not specified	UR: Not specified	UR: Not specified

Results

See Table 4, showing the results of each study at the end of treatment. All five trials showed the effectiveness of their respective interventions in improving acne vulgaris symptoms. Combination treatments usually show better results, and probiotics as either stand-alone or adjunctive treatments have shown significant potential and efficacy. Three studies found statistically significant differences in the presence of probiotics on the manifestation of the number of acne lesions[22,23,25]. Three studies found that the presence of probiotics had a significant effect on improving skin hydration and were able to improve the skin aspects of health[21,22,24]. Only one study conducted a follow-up, which took place at one month and two months after the end of the treatment, and showed that the reduction in the number of acne lesions maintained a good effect during the follow-up period. The reduction in the number of lesions was well maintained[25]. In terms of sebum secretion and inflammatory markers, statistical analysis showed a statistically significant difference of $P<0.05$, which can be confidently attributed to the significant effect of probiotics in decreasing sebum secretion and reducing inflammation in the skin[24]. However, there were two trials where there was no significant difference in performance on secondary outcome indicators[21,23]. From Figure 3 it can be seen that the confidence intervals for each study do not cross zero. Therefore, all five trials regarding the therapeutic effect of probiotics on acne vulgaris are statistically significant.

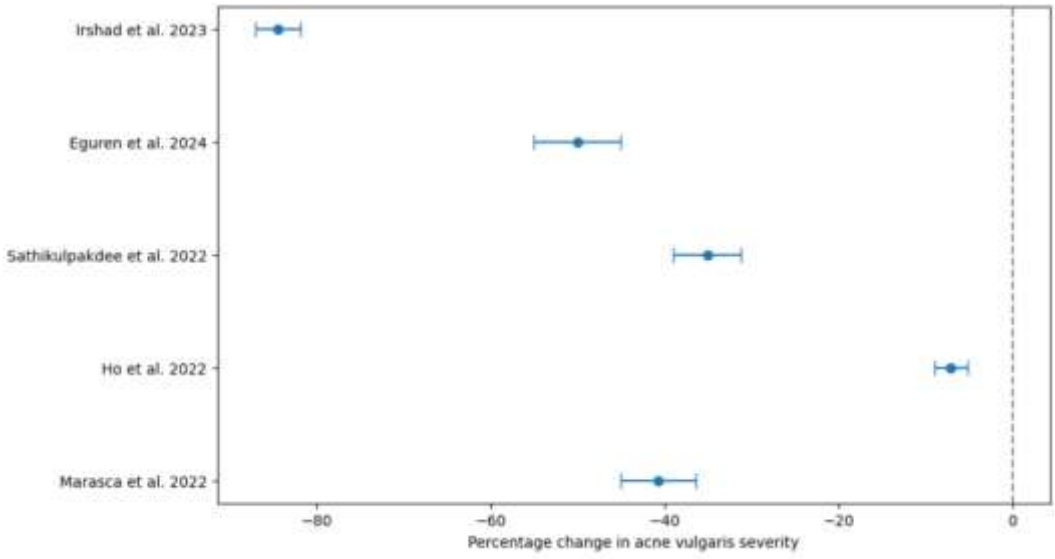

Figure 3. Forest plot of percentage change in acne vulgaris severity across studies

Table 4. Results of studies: post-treatment endpoint

Study name/Setting	Primary outcome measure (mean change scores)	Secondary outcome measure (mean change

		scores)
Ho 2022	Skin Inflammation Index: Placebo = -4.8%, Probiotic = -7.1% *	Porphyrins Index: Placebo = +1.4%, Probiotic = -4.3% *
Eguren 2024	Acne Global Severity Scale: Placebo = 29.41%, Probiotic = 50% *	Global Acne Grading System: Placebo = 20.58%, Probiotic = 42.50% *
Sathikulpakdee 2022	Inflammatory Acne Lesions: Benzoyl Peroxide = -35.1%, Probiotic = -35.1% *	Erythema Index: Benzoyl Peroxide = -5.2%, Probiotic = -6.5%
Marasca 2022	GAGS Score: Placebo = -37.4%, Probiotic = -40.7% *	SEBUTAPETM Score: Placebo = -18%, Probiotic = -44% *
Irshad 2023	Total Lesion Count: Azithromycin = -83.3%, Probiotic = -84.4%, Combination = -90.3% *	Adverse Effects: Probiotic = 4%, Azithromycin = 14%, Combination = 6%

*= significant result ($p < 0.05$)

Discussion

The original review summarized the potential of probiotics in treating acne, noting that probiotics reduce common acne lesions by inhibiting the growth of Propionibacterium acnes, modulating the immune response, and repairing the skin barrier[7]. In my updated review, I analyzed five studies on probiotics for common acne between 2020 and 2024 that included RCTs and the QES trial. The findings suggest that probiotics have significant efficacy in treating acne. Three studies showed that probiotic treatment significantly reduced the number of acne lesions compared to a control group[22,23,25], suggesting the potential of probiotics in reducing acne symptoms. In addition, three studies reported that probiotics significantly improved skin hydration and overall health[21,23,24] while one study found that probiotics significantly reduced sebum secretion and inflammatory markers[21], suggesting that probiotics have additional benefits in maintaining skin health and managing inflammatory processes associated with acne.

From participant questionnaires on adverse effects, it was found that the incidence of adverse effects with probiotics was low and generally mild, and as a result, it can be assumed that probiotics can be used as a therapeutic measure for the safe treatment of acne vulgaris[22]. And it has also been shown that when probiotics are used in conjunction with other treatments (e.g., azithromycin)[25], this therapeutic measure enhances the effectiveness of the treatment and performs better in terms of reducing the number of acne lesions and in terms of sustaining the therapeutic better performance in terms of efficacy.

Although RCTs can provide strong evidence, a number of studies[21,24] were found to be at significant risk of bias through the Cochrane Risk of Bias Tool, and one study was a QES, which on its own is not as good at controlling for bias as RCTs, thus affecting the overall reliability of this paper.

Considering the healthcare delivery side, probiotics can be considered by healthcare providers as adjunctive or alternative treatments for patients who do not respond well to conventional treatments or have significant side effects because of the low incidence of adverse effects. For the patient aspect, the use of probiotics as an alternative or complementary treatment that not only effectively treats acne

vulgaris, but also enhances overall skin health and reduces inflammation, is attractive to patients seeking a comprehensive skin care solution.

This review covers a broader range of study designs and timeframes than the original review[7]. These updated findings support the conclusions of the original review and emphasize the potential for probiotics to be used in combination with other treatments. Overall, the evidence supports probiotics as an effective and safe acne treatment. However, further high-quality studies are needed to confirm these findings and optimize treatment options.

Limitation

This review has some limitations at both the research and review levels. At the study level, limitations were mainly in the risk of bias and the small sample size of each article (underrepresentation), heterogeneity of interventions, and inconsistency in outcome measures. At the review level, limitations were mainly in the fact that the literature search was limited to the English language literature and reporting bias (reliance on published studies only). In addition, as it was a student project, only one person performed the quality assessment and data extraction, which may have been subject to bias and error. This paper used a narrative synthesis and did not use meta-analysis.

Conclusion

Despite some limitations of this review, it still emphasizes that probiotics can be considered bit adjunctive or alternative therapies for the treatment of acne vulgaris, especially for those patients who suffer from side effects from conventional treatments. Future studies should aim to conduct larger, high-quality RCTs, incorporate a wider range of literature, and employ a multi-reviewer approach to strengthen the evidence base.

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