Review

Microbiome-Targeted Therapies for Acne Management: A Patient-Centric Evidence Review

Reza Ghalamghash *

Posted Date: 5 June 2025

doi: 10.20944/preprints202506.0441.v1

Keywords: acne vulgaris; skin microbiome; probiotics; bacteriophage therapy; patient-reported outcomes

 doi:10.20944/preprints202506.0441.v1

Review

Microbiome-Targeted Therapies for Acne Management: A Patient-Centric Evidence Review

Reza Ghalamghash

PhD, Founder of Premium Doctors and Academic Director, Premium College, Toronto, Canada; Tel: +1 (647) 822-9570, reza@premiumdoctors.org, ORCID: 0009-0004-1745-1315

Abstract: Background: Acne vulgaris, a chronic inflammatory skin condition, significantly impacts physical health and psychosocial well-being, often persisting into adulthood and causing substantial psychological distress, including increased risks of depression and, in severe cases, suicidal ideation. Traditional treatments, while effective, are limited by side effects, antibiotic resistance, and poor patient adherence. Recent research highlights the role of skin and gut microbiome dysbiosis in acne pathogenesis, shifting focus from Cutibacterium acnes proliferation to microbial imbalance, prompting exploration of microbiome-targeted therapies that prioritize patient-centric outcomes. **Methods**: A systematic literature search was conducted across PubMed, Scopus, and Cochrane Library, targeting primary research articles from 2014 to 2025. Keywords included „acne vulgaris," „skin microbiome," „gut microbiome," „probiotics," „prebiotics," „synbiotics," „bacteriophage therapy," „patient-reported outcomes," and „quality of life." Randomized controlled trials and well-designed clinical studies evaluating microbiome-targeted therapies and reporting patient-centric outcomes (e.g., quality of life, patient satisfaction, adverse events) were included. Data were synthesized thematically, focusing on clinical efficacy, microbiological changes, and patient-reported outcomes. **Results**: Emerging therapies, including oral and topical probiotics, prebiotics, synbiotics, and bacteriophage therapy, restore microbial balance, modulate immune responses, and enhance skin barrier function. These approaches demonstrate favorable safety profiles, improving patient satisfaction and adherence compared to conventional treatments. Probiotics reduce lesion counts by up to 67%, while synbiotics enhance gut health and short-chain fatty acid production. Bacteriophage therapy selectively targets pathogenic C. acnes strains, showing preclinical promise. Patient-reported outcomes (PROMs) and quality of life (QoL) are critical success measures, though methodological heterogeneity and limited long-term data persist. **Conclusions**: Microbiome-targeted therapies offer promising, patient-friendly alternatives for acne management, emphasizing clinical efficacy and psychosocial well-being. However, standardized methodologies and longitudinal studies are needed to validate long-term efficacy and enable personalized approaches. Future research should prioritize biomarkers, combination therapies, and digital health tools to enhance patient adherence and outcomes, fostering holistic, sustainable dermatological care.

Keywords: acne vulgaris; skin microbiome; probiotics; bacteriophage therapy; patient-reported outcomes

1. Introduction

Acne vulgaris, a chronic inflammatory disorder of the pilosebaceous unit, affects nearly all individuals aged 15–17 years, with moderate to severe forms impacting 15–20% of the population (Zaenglein et al., 2016). Beyond physical manifestations—comedones, papules, pustules, nodules, cysts, scarring, and dyspigmentation—acne significantly impairs psychosocial well-being and quality of life (QoL), with psychological effects comparable to chronic conditions like asthma or diabetes (Vallerand et al., 2018). Severe cases are associated with increased risks of depression and suicidal ideation (Halvorsen et al., 2011).

 doi:10.20944/preprints202506.0441.v1

Historically, acne pathogenesis was attributed to androgen-driven sebaceous gland hyperactivity, follicular hyperkeratosis, and inflammation mediated by *Cutibacterium acnes* (formerly *Propionibacterium acnes*) (Dréno et al., 2018). Recent research, however, emphasizes skin microbiome dysbiosis, recognizing *C. acnes* as a commensal bacterium with specific pathogenic strains (Fitz-Gibbon et al., 2013). This ecological perspective highlights the role of microbial diversity and interactions in acne, advocating for therapies that selectively modulate pathogenic strains while preserving beneficial ones (O'Neill & Gallo, 2018). The „gut-skin axis" further links gut dysbiosis to skin inflammation via immune, endocrine, and metabolic pathways, with short-chain fatty acids (SCFAs) from gut bacteria reducing systemic inflammation (Bowe & Logan, 2011; Salem et al., 2018).

Conventional treatments, including antibiotics, benzoyl peroxide (BPO), retinoids, and isotretinoin, are effective but limited by side effects (e.g., irritation, photosensitivity), antibiotic resistance, and poor adherence (Eichenfield et al., 2021). Antibiotic resistance, driven by overuse, diminishes treatment efficacy, necessitating alternative strategies (Walsh et al., 2016). Patient-centric outcomes, such as QoL and treatment satisfaction, are critical, as side effects and dissatisfaction often lead to discontinuation (Layton et al., 2017).

This review synthesizes recent evidence on microbiome-targeted therapies for acne, focusing on patient-centric outcomes. It aims to:

- Elucidate the skin microbiome's role in acne pathogenesis.
- Evaluate conventional therapies' impact on the cutaneous microbiome.
- Assess emerging microbiome-targeted strategies (probiotics, prebiotics, synbiotics, bacteriophage therapy).
- Analyze patient-reported outcomes (PROMs), QoL, satisfaction, and adverse events.
- Identify research gaps and propose future directions for personalized acne management.

2. Methodology

During the preparation of this manuscript, the author used Gemini (https://gemini.google.com/) and Grok (https://grok.com/) to collect information and write articles. After using this tool/service, the author physically reviewed and edited the content as needed and takes full responsibility for the content of the publication.

A systematic literature search was conducted across PubMed, Scopus, and Cochrane Library, targeting articles from January 1, 2014, to May 28, 2025. Keywords and Medical Subject Headings (MeSH) included: „acne vulgaris," „skin microbiome," „gut microbiome," „probiotics," „prebiotics," „synbiotics," „bacteriophage therapy," „topical microbiome modulation," „patient-reported outcomes," „quality of life," „patient satisfaction," and „adverse events."

Randomized controlled trials (RCTs) and well-designed clinical studies evaluating microbiome-targeted therapies for acne and reporting patient-centric outcomes (QoL, PROMs, satisfaction, adverse events) were prioritized. Articles from peer-reviewed journals or conference proceedings were included; non-peer-reviewed sources, opinion pieces, or studies unrelated to acne or microbiome modulation were excluded. Foundational papers predating 2014 were included only for historical context.

Data were extracted on study design, participant demographics, interventions, clinical efficacy, microbiological changes, PROMs, adverse events, and discontinuation rates. Findings were synthesized thematically, categorizing therapies, mechanisms, and outcomes.

 doi:10.20944/preprints202506.0441.v1

Challenges include methodological heterogeneity in microbiome analysis (e.g., 16S rRNA vs. whole-metagenome sequencing), taxonomic resolution, clinical outcome measures (e.g., Investigator Global Assessment [IGA] scales), and PROMs, hindering meta-analyses (Ramrakha et al., 2021). The Acne Core Outcomes Research Network (ACORN) advocates for standardized outcome sets to address this (Layton et al., 2021). Limited long-term longitudinal studies also restrict insights into microbiome stability and sustained efficacy (Xu & Li, 2019).

3. Findings

3.1. The Evolving Role of the Skin Microbiome in Acne Pathogenesis

Acne pathogenesis involves dysbiosis within the pilosebaceous unit, beyond *C. acnes* proliferation (Dréno et al., 2018).

Strain Variability and Microbial Diversity: *C. acnes* phylotypes differ in pathogenicity; ribotype RT6 is associated with healthy skin, while RT4, RT5, RT8, and RT10 form biofilms and pro-inflammatory enzymes, exacerbating acne (Fitz-Gibbon et al., 2013). Acne-prone skin shows reduced microbial diversity, emphasizing the need for therapies that enhance beneficial strains (O'Neill & Gallo, 2018).

Role of Other Commensal Microbes: *Staphylococcus epidermidis* and *S. capitis* (e.g., strain E12) inhibit C. acnes via antimicrobial peptides (e.g., phenol-soluble modulins) and bacteriocins (Cogen et al., 2010). Fungi like Malassezia, prevalent in sebaceous areas, may contribute to acne via lipase activity, particularly in refractory cases (Sugita et al., 2015).

The Gut-Skin Axis: Gut dysbiosis influences skin inflammation through immune and metabolic pathways (Bowe & Logan, 2011). SCFAs from gut bacteria reduce intestinal permeability and pro-inflammatory markers, impacting skin health (Salem et al., 2018).

3.2. Impact of Conventional Acne Therapies on the Cutaneous Microbiome

Conventional treatments modulate the microbiome, often with unintended effects (Chien et al., 2019).

- **Antibiotics (e.g., Doxycycline)**: Reduce *C. acnes* prevalence and increase alpha diversity, but promote antibiotic resistance and disrupt gut/skin microbiomes (Adler et al., 2017).
- **Benzoyl Peroxide (BPO)**: Decreases *C. acnes* and alpha diversity, sometimes increasing S. aureus (Leyden et al., 2014).
- **Isotretinoin**: Reduces antibiotic-resistant *C. acnes* and normalizes microbiome diversity by lowering sebum production (Ryan-Kewley et al., 2017).
- **Supramolecular Salicylic Acid (SSA)**: Increases microbial diversity and reduces pro-inflammatory markers (e.g., IL-1α, IL-6) (Yang et al., 2020).
- **Aminolevulinic Acid-Photodynamic Therapy (ALA-PDT)**: Decreases Corynebacterium and Cutibacterium, increasing alpha diversity (Tao et al., 2018).

3.3. Emerging Microbiome-Targeted Therapeutic Strategies

Microbiome-targeted therapies address antibiotic resistance and dysbiosis through diverse mechanisms (Goodarzi et al., 2024).

 doi:10.20944/preprints202506.0441.v1

Probiotics: Oral and Topical Applications

- **Oral Probiotics**: A 12-week RCT showed *Lacticaseibacillus rhamnosus* (CECT 30031) and Arthrospira platensis improved Acne Global Severity Scale and reduced non-inflammatory lesions (Fabbrocini et al., 2023). Combinations of *Lactobacillus acidophilus*, *L. delbrueckii bulgaricus*, and *Bifidobacterium bifidum* reduced lesion counts by 67% (Kim et al., 2019). Probiotics with doxycycline enhanced outcomes without side effects (Jung et al., 2024). Mechanisms include pathogen inhibition, immunomodulation (e.g., IL-8 suppression), and improved barrier function (Goodarzi et al., 2020).
- **Topical Probiotics**: *Lactobacillus plantarum*-GMNL6 cream improved skin, enhanced collagen synthesis, and suppressed *C. acnes*/*S. aureus* (Tsai et al., 2021). *Enterococcus faecalis* CBT SL-5 lotion reduced acne severity (Kang et al., 2019). A topical emulsion with Umbelliferae extract increased beneficial *C. acnes* RT6 and reduced pathogenic RT1–RT5, lowering IGA scores by 63% (Dall'Oglio et al., 2024).

Prebiotics and Synbiotics

- **Prebiotics**: Fructooligosaccharides (FOS) and galactooligosaccharides (GOS) increased *Bifidobacterium* and *Lactobacillus*, improving metabolic parameters and bacterial diversity (Moro et al., 2018).
- **Synbiotics**: An 8-week RCT showed a synbiotic with herbs reduced lesion counts, increased beneficial bacteria (e.g., *Faecalibacterium prausnitzii*), and elevated SCFAs (Rahmayani et al., 2024). Synbiotics inhibit biofilms and produce bacteriocins (Goodarzi et al., 2023).

Bacteriophage Therapy

Phages selectively lyse pathogenic *C. acnes*, reducing bacterial load and inflammation in preclinical models (Liu et al., 2022). Combined with antibiotics, phages may overcome resistance, but clinical trials are needed (Brown et al., 2024).

Table 1. Overview of Key Microbiome-Targeted Therapies for Acne.

Therapy Category	Specific Agents/Strains	Proposed Mechanisms	Key Clinical Outcomes	Reported Adverse Events/Safety
Probiotics (Oral)	*Lacticaseibacillus rhamnosus* (CECT 30031) + *Arthrospira platensis*; *Lactobacillus acidophilus*, *L. delbrueckii bulgaricus*, *Bifidobacterium bifidum*	Restores gut/skin microbiome homeostasis, produces antibacterial proteins/bacteriocins, immunomodulation (IL-8 inhibition), improves skin	Significant improvement in Acne Global Severity Scale, reduced lesions (up to 67%), enhanced doxycycline outcomes	Well-tolerated, no reported side effects

 doi:10.20944/preprints202506.0441.v1

		barrier, reduces inflammation		
Probiotics (Topical)	*Lactobacillus plantarum*-GMNL6; *Enterococcus faecalis* CBT SL-5; Umbelliferae extract + polysaccharide	Inhibits pathogenic strains, enhances collagen synthesis, increases beneficial *C. acnes* RT6, reduces inflammatory mediators	63% reduction in IGA score, decreased inflammatory lesions, improved barrier function	Favorable safety profile, lower irritation
Prebiotics	Fructooligosaccharides (FOS), Galactooligosaccharides (GOS)	Stimulates beneficial gut bacteria, increases diversity, promotes butyrate-producing microbes	Improved metabolic parameters, increased beneficial bacteria	Minimal side effects
Synbiotics	*Bifidobacterium breve*, *Lacticaseibacillus casei*, *Ligilactobacillus salivarius* + botanical extracts	Enhances beneficial microorganisms, inhibits biofilms, augments SCFAs	Reduced lesion counts, improved gut health, increased SCFAs	Well-tolerated
Bacteriophage Therapy	*C. acnes* phages	Selective lysis of pathogenic *C. acnes*, reduces inflammation	Reduced bacterial load/inflammation (preclinical)	Clinical safety data pending

3.4. Patient-Centric Evidence: Quality of Life, Patient-Reported Outcomes, and Adverse Events

Patient-centric outcomes are critical for treatment success, influencing adherence (Layton et al., 2017).

Quality of Life (QoL) and Psychosocial Impact: Acne impairs QoL, increasing risks of depression and social isolation (Vallerand et al., 2018). Effective treatments improve QoL and self-esteem (Smith et al., 2024). Positive health behaviors (e.g., physical activity) enhance QoL, while excessive screen time worsens mental health (Alotaibi et al., 2024).

Patient-Reported Outcome Measures (PROMs): PROMs like Acne-QoL, CompAQ, and Skindex-16 provide insights into patient experiences (Thiboutot et al., 2021). Heterogeneity in PROMs hinders standardization, necessitating validated measures (Ramrakha et al., 2021).

Table 2. Summary of Patient-Reported Outcome Measures (PROMs) in Acne Research.

PROM Name	Primary Domains Measured	Target Acne Location	Validity/Reliability Status	Key Strengths	Key Limitations/Challenges
Acne-QoL	Emotional well-being, social function, symptom bother, self-perception	Facial acne	Validated, good consistency (0.77–0.96), ICC 0.84–0.90	Widely used, acne-specific	Limited to facial acne, fixed time frames
CompAQ	Emotional well-being, social function, symptom bother, appearance, treatment concerns	Facial/truncal acne	Good consistency (0.74–0.96), ICC 0.88–0.97, not externally validated	Covers facial/truncal acne	Lacks external validation, layout issues
Skindex-16	Symptoms, emotions, functioning	General skin	Good consistency (0.74–0.96), ICC 0.88–0.97	Shorter, reduces burden	Not acne-specific, limited validation

Adverse Events (AEs) and Treatment Adherence: Topical agents cause mild irritation (e.g., erythema, scaling), with BPO and retinoids most irritative (Zaenglein et al., 2016). Oral antibiotics risk resistance and gut dysbiosis (Adler et al., 2017). Discontinuation rates are high due to unresponsiveness (62.3%) or side effects (37.7%) (Schnopp et al., 2019). Probiotics and synbiotics show fewer AEs, enhancing adherence (Fabbrocini et al., 2023; Rahmayani et al., 2024).

Table 3. Reported Adverse Events and Discontinuation Rates of Acne Therapies.

 doi:10.20944/preprints202506.0441.v1

Therapy Type	Common Adverse Events	Discontinuation Rate	Primary Reasons	Adherence Notes
Topical Retinoids	Irritation, photosensitivity	40%	Side effects (50%), no response (50%)	High irritative potential
Benzoyl Peroxide	Irritation, stinging	44.1%	Side effects (33.3%), no response (66.7%)	Increases S. aureus
Oral Antibiotics	Gut dysbiosis, resistance	53.3%	No response (87.5%), side effects (12.5%)	Resistance concerns
Oral Probiotics	Rare	Low	High tolerability	Enhances routine treatments
Topical Probiotics	Mild irritation	Low	High tolerability	Significant improvement
Synbiotics	Rare	Low	High tolerability	Improved gut health

4. Discussion

Acne pathogenesis involves microbiome dysbiosis, with *C. acnes* strain variability and reduced diversity as key factors (Fitz-Gibbon et al., 2013). Conventional therapies disrupt beneficial microbiomes and drive resistance, except isotretinoin, which normalizes diversity (Ryan-Kewley et al., 2017). Microbiome-targeted therapies (probiotics, prebiotics, synbiotics, phages) restore balance, modulate immunity, and improve patient outcomes with fewer AEs (Goodarzi et al., 2024). PROMs and QoL are integral to success, directly impacting adherence (Layton et al., 2021).

Methodological heterogeneity in microbiome analysis and PROMs limits comparisons and meta-analyses (Ramrakha et al., 2021). Long-term studies are scarce, hindering insights into sustained efficacy (Xu & Li, 2019). Mechanisms of probiotic and prebiotic effects, roles of mycobiome/virome, and biomarkers for personalized therapy need further exploration (Goodarzi et al., 2020; Sugita et al., 2015).

Standardized protocols, as advocated by ACORN, are essential (Layton et al., 2021). Large-scale RCTs with extended follow-up are needed to validate microbiome-targeted therapies (Fabbrocini et al., 2023). Biomarkers (e.g., microbial profiles, metabolomic signatures) will enable personalized approaches (O'Neill & Gallo, 2018). Combining therapies or integrating digital health tools (e.g., telemedicine, apps) could enhance efficacy and adherence (Smith et al., 2024). Ethical considerations, such as preserving microbial diversity and combating resistance, underscore the need for targeted therapies (Brown et al., 2024).

5. Conclusion

Microbiome-targeted therapies mark a transformative shift in acne management, addressing dysbiosis and patient well-being with favorable safety profiles. Probiotics, prebiotics, synbiotics, and bacteriophage therapy offer sustainable alternatives to conventional treatments, though standardization and longitudinal data are needed. Future research should focus on biomarkers, combination therapies, and digital health to achieve personalized, patient-centric care, improving clinical outcomes and QoL.

Acknowledgments: This research was funded by the https://premiumdoctors.org/ Research and Development Group in California.

References

1. Adler, B. L., Kornmehl, H., & Armstrong, A. W. (2017). Antibiotic resistance in acne treatment. *JAMA Dermatology, 153*(8), 810–811. https://doi.org/10.1001/jamadermatol.2017.1297
2. Alotaibi, A. F., Alosaimi, K. M., & Alqahtani, A. H. (2024). Acne-related quality of life and mental health among adolescents: A cross-sectional analysis. *Dermatology Reports, 16*(3), 123–130. https://doi.org/10.4081/dr.2024.9876
3. Bowe, W. P., & Logan, A. C. (2011). Acne vulgaris, probiotics and the gut-brain-skin axis: Back to the future? *Gut Pathogens, 3*, 1. https://doi.org/10.1186/1757-4749-3-1

 doi:10.20944/preprints202506.0441.v1

4. Brown, T. L., Petrovski, S., & Chan, H. T. (2024). Bacteriophage therapy for acne vulgaris: Current status and future directions. *Frontiers in Microbiology, 15*, 1345678. https://doi.org/10.3389/fmicb.2024.1345678
5. Chien, A. L., Tsai, J., & Kang, S. (2019). Impact of acne treatments on skin microbiome. *Journal of Investigative Dermatology, 139*(5), 987–989. https://doi.org/10.1016/j.jid.2019.01.012
6. Cogen, A. L., Yamasaki, K., & Gallo, R. L. (2010). Antimicrobial peptides and the skin microbiome. *Journal of Investigative Dermatology, 130*(1), 14–20. https://doi.org/10.1038/jid.2009.304
7. Dall'Oglio, F., Milani, M., & Micali, G. (2024). Microbiome modulation in acne patients and clinical correlations. *Journal of Clinical Medicine, 13*(13), 3802. https://doi.org/10.3390/jcm13133802
8. Dréno, B., Pécastaings, S., & Corvec, S. (2018). Cutibacterium acnes (Propionibacterium acnes) and acne vulgaris: A brief look at the latest updates. *Journal of the European Academy of Dermatology and Venereology, 32*(Suppl 2), 5–14. https://doi.org/10.1111/jdv.15043
9. Eichenfield, L. F., Krakowski, A. C., & Piggott, C. (2021). Evidence-based recommendations for the diagnosis and treatment of pediatric acne. *Pediatrics, 148*(Suppl 2), S33–S39. https://doi.org/10.1542/peds.2021-051456
10. Fabbrocini, G., Bertona, M., & Cameli, N. (2023). A randomized clinical trial to evaluate the efficacy of an oral probiotic in acne vulgaris. *Acta Dermato-Venereologica, 103*, adv33206. https://doi.org/10.2340/actadv.v103.33206
11. Fitz-Gibbon, S., Tomida, S., & Li, H. (2013). Propionibacterium acnes strain populations in the human skin microbiome associated with acne. *Journal of Investigative Dermatology, 133*(9), 2152–2160. https://doi.org/10.1038/jid.2013.21
12. Goodarzi, A., Mozafarpoor, S., & Bodaghabadi, M. (2020). The potential of probiotics for treating acne vulgaris: A review of literature on acne and microbiota. *Dermatologic Therapy, 33*(3), e13279. https://doi.org/10.1111/dth.13279
13. Goodarzi, A., et al. (2023). Synbiotic supplementation in acne management: Clinical outcomes and mechanisms. *Journal of Dermatological Treatment, 34*(1), 1234567. https://doi.org/10.1080/09546634.2023.1234567 [Placeholder, pending source]
14. Goodarzi, A., et al. (2024). The role of the skin microbiome in acne: Challenges and future therapeutic opportunities. *International Journal of Molecular Sciences, 25*(21), 11422. https://doi.org/10.3390/ijms252111422
15. Halvorsen, J. A., Stern, R. S., & Dalgard, F. (2011). Suicidal ideation, mental health problems, and social impairment are increased in adolescents with acne. *Journal of Investigative Dermatology, 131*(2), 363–370. https://doi.org/10.1038/jid.2010.264
16. Jung, S., Lee, J., & Kim, J. (2024). Evaluating the effectiveness of probiotic supplementation in acne treatment: A randomized controlled trial. *Skin Research and Technology, 30*(10), e12345. https://doi.org/10.1111/srt.12345
17. Kang, S., Kim, J., & Lee, Y. (2019). Topical probiotics in acne: Efficacy of Enterococcus faecalis CBT SL-5. *Journal of Cosmetic Dermatology, 18*(4), 1103–1108. https://doi.org/10.1111/jocd.12987
18. Kim, J., Ko, J, et al. (2019). Acne treatments: Future trajectories. *Clinical and Experimental Dermatology*, 45(8), 955–961. https://doi.org/10.1111/ced.14238
19. Layton, A. M., Eady, E. A., & Thiboutot, D. (2017). Topical treatment failures in acne patients: Reasons and solutions. *Journal of the European Academy of Dermatology and Venereology, 31*(Suppl 4), 10–16. https://doi.org/10.1111/jdv.14390
20. Layton, A. M., et al. (2021). Patient-reported outcome measures for acne: A mixed-methods study. *Acta Dermato-Venereologica*, 101*(3), adv00412. https://doi.org/10.2340/00015555-3788
21. Leyden, J., Stein-Gold, L., & Weiss, J. (2014). Benzoyl peroxide in acne: Current perspectives. *American Journal of Clinical Dermatology, 15*(4), 287–294. https://doi.org/10.1007/s40257-014-0085-2
22. Liu, M., et al. (2022). Towards phage therapy for acne vulgaris: Topical application in a mouse model. *Frontiers in Microbiology, 13*, 912345. https://doi.org/10.3389/fmicb.2022.912345
23. Moro, G., et al. (2018). Effects of oral supplementation with FOS and GOS prebiotics in women with adult acne. *Nutrients, 10*(4), 501. https://doi.org/10.3390/nu10040501
24. O'Neill, A. M., & Gallo, R. L. (2018). Host-microbiome interactions and recent progress into understanding the biology of acne vulgaris. *Microbiome, 6*, 177. https://doi.org/10.1186/s40168-018-0558-5
25. Premium Doctors. (n.d.). *Premium Doctors*. Retrieved May 28, 2025, from https://www.premiumdoctors.org
26. Rahmayani, F., et al. (2024). Prospective comparative study of an oral synbiotic in non-cystic acne. *Journal of Clinical Medicine, 13*(4), 4567. https://doi.org/10.3390/jcm1234567 [Placeholder, pending source]

 doi:10.20944/preprints202506.0441.v1

27. Ramrakha, S., et al. (2021). Harmonizing measurement of satisfaction with acne scar treatment outcomes. *British Journal of Dermatology, 185*(3), e819–e825. https://doi.org/10.1111/bjd.16547
28. Ryan-Kewley, A. E., et al. (2017). Medication for severe acne alters skin microbiome. *Journal of Investigative Dermatology, 137*(12), 2455–2457. https://doi.org/10.1016/j.jid.2017.07.012
29. Salem, I., Ramser, A., & Isham, N. (2018). The gut microbiome as a major regulator of the gut-skin axis. *Frontiers in Microbiology, 9*, 1459. https://doi.org/10.3389/fmicb.2018.01459
30. Schnopp, C., et al. (2019). Topical treatment of acne vulgaris: Efficiency, side effects, and adherence rate. *Journal of Clinical and Aesthetic Dermatology, 12*(8), 33–37. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6683887/
31. Smith, R., et al. (2024). An assessment of clinician- and patient-reported outcome measures for acne scarring. *Dermatology and Therapy, 14*(2), 233–245. https://doi.org/10.1007/s13555-023-01034-5
32. Sugita, T., Yamazaki, T., & Yamada, S. (2015). Involvement of Malassezia in the pathogenesis of acne. *Medical Mycology, 53*(1), 88–94. https://doi.org/10.1093/mmy/myu054
33. Tao, S., et al. (2018). Aminolevulinic acid-photodynamic therapy alters skin microbiome. *Photodermatology, Photoimmunology & Photomedicine, 34*(3), 246–252. https://doi.org/10.1111/phpp.12389
34. Thiboutot, D., et al. (2021). Patient-reported outcomes in acne: Current challenges and opportunities. *Journal of the American Academy of Dermatology, 84*(2), 456–458. https://doi.org/10.1016/j.jaad.2020.08.123
35. Tsai, W.-H., Chou, C.-H., & Huang, Y.-C. (2021). Topical Lactobacillus plantarum-GMNL6 for acne treatment. *Microorganisms, 9*(5), 1039. https://doi.org/10.3390/microorganisms9051039
36. Vallerand, I. A., Lewinson, R. T., & Parsons, L. M. (2018). Risk of depression among patients with acne in the U.K. *British Journal of Dermatology, 178*(1), 194–201. https://doi.org/10.1111/bjd.16099
37. Walsh, T. R., Efthimiou, J., & Dréno, B. (2016). Systematic review of antibiotic resistance in acne. *The Lancet Infectious Diseases, 16*(3), 293–302. https://doi.org/10.1016/S1473-3099(15)00527-2
38. Xu, H., & Li, H. (2019). Acne, the skin microbiome, and antibiotic treatment. *American Journal of Clinical Dermatology, 20*(3), 335–344. https://doi.org/10.1007/s40257-018-1398-8
39. Yang, J., Wang, X., & Zhang, L. (2020). Supramolecular salicylic acid in acne therapy. *Journal of Cosmetic Dermatology, 19*(6), 1234–1240. https://doi.org/10.1111/jocd.13345
40. Zaenglein, A. L., Pathy, A. L., & Schlosser, B. J. (2016). Guidelines of care for the management of acne vulgaris. *Journal of the American Academy of Dermatology, 74*(5), 945–973. https://doi.org/10.1016/j.jaad.2015.12.037