

GUIDELINE AND CONSENSUS

Interpretation of the 2026 clinical practice guideline on polycystic ovary syndrome and the gut microbiota: From evidence to clinical translation

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a heterogeneous reproductive, endocrine, and metabolic disorder, and the gut microbiota has emerged as an important focus of mechanistic and translational research. The 2026 clinical practice guideline on PCOS and the gut microbiota was developed to bridge the gap between rapidly evolving microbiome research and uncertainty regarding its clinical application. It addresses nine core questions and provides 15 recommendations covering disease association, microbiome testing, probiotics and prebiotics, dietary interventions, fecal microbiota transplantation, interactions with pharmacologic therapy, metabolic surgery, and the gut-brain axis. This article provides a focused interpretation of these recommendations, emphasizing the clinical implications of recommendation strength, the distinction between research-oriented microbiome analyses and routine diagnostic testing, the adjunctive role of microbiota-targeted interventions, and the need to distinguish mechanistic plausibility from demonstrated clinical benefit. Implementation should remain embedded within established PCOS management, with lifestyle modification, evidence-based pharmacotherapy, reproductive care, and mental health support as the foundation. Microbiota-targeted strategies should be individualized according to evidence maturity, strain or product specificity, patient phenotype, safety, and feasibility. Future priorities include standardized microbiome methodologies, multicenter prospective studies, adequately powered randomized trials, clinically meaningful reproductive outcomes, and long-term safety assessment. This interpretation aims to support appropriate clinical application while avoiding premature translation of preliminary microbiome findings into routine practice.

Keywords: polycystic ovary syndrome, gut microbiota, guideline interpretation, probiotics, dietary intervention, clinical translation

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is among the most prevalent endocrine-metabolic disorders in reproductive-aged women and is characterized by substantial phenotypic heterogeneity. Hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology represent its core reproductive features, whereas insulin resistance, obesity, dyslipidemia, and other metabolic disturbances contribute importantly to long-term morbidity.^[1-3] This heterogeneity also complicates efforts to identify a single pathogenic pathway or a universal therapeutic strategy.

The gut microbiota has emerged as one potential interface linking diet, metabolism, inflammation, endocrine signaling, and host susceptibility. Studies in PCOS have reported differences in microbial diversity and community composition, depletion of several short-chain fatty acid (SCFA)-producing taxa, changes in bile-acid-related microbial functions, and impaired intestinal barrier integrity.^[4-9] Experimental work, particularly microbiota-transfer studies, has strengthened biological plausibility by showing that microbiota-derived signals can influence metabolic and reproductive phenotypes.^[7] Nevertheless, the field remains characterized by substantial between-study heterogeneity, incomplete causal inference in humans, variable laboratory methods, and a predominance of surrogate rather than definitive clinical outcomes.

These features create a translational problem. Clinicians increasingly encounter commercial microbiome reports, probiotic products, dietary claims, and patient interest in fecal microbiota transplantation (FMT), yet the degree of evidence supporting each application differs markedly. The purpose of the 2026 guideline was therefore not simply to summarize associations between PCOS and the gut microbiota, but to define where microbiome-related approaches can reasonably enter clinical or research pathways and where they should remain investigational. The present article interprets the nine clinical questions and 15 recommendations from that perspective, with emphasis on implementation, evidence boundaries, and areas in which mechanistic promise should not be equated with established clinical effectiveness.

The organization of this interpretation was informed by the Reporting Items for Practice Guidelines in Healthcare (RIGHT) for INTroductions and INTerpretations of Clinical Practice Guidelines (RIGHT for INT) framework, which recommends that guideline interpretation articles address the background and development of the source guideline, explain recommendations in context, discuss strengths and limitations, and clarify implications for implementation and future research.^[10] No new

recommendation or re-grading of evidence is introduced here; the original questions and recommendation statements are retained, while the accompanying discussion is reframed to support clinical understanding and translation.

OVERVIEW OF THE GUIDELINE AND HOW TO READ THE RECOMMENDATIONS

Scope, users, and development process

The guideline applies to females with PCOS and is intended for clinicians and researchers in reproductive medicine, obstetrics and gynecology, endocrinology, clinical nutrition, microbiome science, and related disciplines. The working group used a structured process to identify clinically relevant questions, incorporating literature review, Delphi consultation, and the Population, Intervention, Comparator, and Outcome (PICO) framework. Evidence searches covered major international and Chinese databases and were updated through October 2025. Systematic reviews, meta-analyses, and randomized controlled trials (RCTs) were prioritized when available, whereas observational studies and basic experimental evidence were considered when higher-level evidence was insufficient.

Evidence quality and recommendation strength were assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework. The guideline also incorporated good practice statements (GPSs) for clinically important issues for which direct evidence was limited but practical guidance was considered necessary. The development process further included external review, methodological quality assessment using the Appraisal of Guidelines for Research and Evaluation II (AGREE II) instrument, reporting in accordance with RIGHT, and plans for periodic updating. These methodological features are important for interpreting the recommendations because the guideline addresses a field in which the evidence base ranges from relatively mature clinical intervention studies to preliminary mechanistic observations.

How recommendation grades should be interpreted?

A strong recommendation should be understood as a recommendation for which the expected benefits, harms, feasibility, and available evidence support a relatively consistent course of action for most appropriate patients. A conditional or weak recommendation indicates that patient phenotype, preferences, feasibility, uncertainty, or indirectness of evidence may materially affect the decision. Likewise, a moderate or low certainty rating does not mean that an intervention is ineffective; it indicates uncertainty about the magnitude, consistency, or directness of the estimated effect. In this

guideline, this distinction is especially relevant for microbiome-directed interventions because statistically significant changes in metabolic biomarkers do not automatically establish durable reproductive benefit or justify the replacement of standard PCOS treatment.

A second interpretive principle is that the guideline separates three levels of translation: microbiome measurements used for research, microbiota-directed measures used as adjuncts to standard care, and highly selected or investigational interventions. Confusing these levels can lead to overdiagnosis of vaguely defined "dysbiosis," indiscriminate probiotic use, or premature use of invasive microbiome interventions. Table 1 summarizes the GRADE system, and Table 2 reproduces the recommendations for rapid reference.

INTERPRETATION OF THE CORE QUESTIONS AND RECOMMENDATIONS

Question 1: What is the association between PCOS and the gut microbiota?

Recommendation 1: Patients with PCOS generally exhibit gut dysbiosis, characterized mainly by alterations in gut microbial composition and diversity, reduced abundance of SCFA-producing genera, and disruption of the microbial community involved in bile acid metabolism. However, large-scale, multicenter cohort studies are currently lacking to screen and validate specific gut microbial markers for clinical diagnosis and phenotypic subtyping of PCOS. (2B)

Interpretation: A reproducible group-level signal does not yet constitute an individual diagnostic signature. Across observational studies, women with PCOS frequently show altered microbial composition or diversity, reduced abundance of selected SCFA-producing organisms, and differences in microbial functions related to bile-acid and inflammatory pathways.^[4-9] However, the direction and magnitude of these findings are influenced by geography, habitual diet, adiposity, metabolic status, ethnicity, medications, sequencing platforms, and analytical pipelines.^[11-14] The practical implication is that the concept of PCOS-associated dysbiosis is biologically meaningful at the population level, but no single taxon, diversity index, or commercial "dysbiosis score" can currently diagnose PCOS or define a validated PCOS subtype.

Recommendation 2: Mouse experiments have demonstrated that FMT can induce PCOS-related phenotypes, revealing the significant role of the gut microbiota in the development and progression of PCOS. Given the complex bidirectional interactions between endocrine metabolism and the gut microbiota, gut dysbiosis and metabolic disorders may be mutually reinforcing in a vicious

cycle during PCOS progression. (2B)

Interpretation: Causal evidence is suggestive but must be separated by model system. Human-to-mouse FMT and related experiments have shown that transfer of PCOS-associated microbial communities can reproduce metabolic and reproductive abnormalities and have identified mechanistic pathways such as the gut microbiota-bile acid-interleukin-22 (IL-22) axis.^[7] These experiments strengthen the argument that the microbiota can contribute to disease biology rather than merely reflect it. They do not, however, prove that the same causal sequence accounts for the full clinical syndrome in humans. Bidirectional Mendelian randomization analyses and other causal-inference approaches provide additional support for selected associations but remain dependent on instrument validity and available microbial datasets.^[15,16]

Clinical implication. The principal value of Recommendation 1 and Recommendation 2 is therefore conceptual and research-oriented: the gut microbiota should be considered a relevant component of PCOS pathophysiology, while conventional diagnostic criteria and phenotype assessment remain the basis of clinical diagnosis. Future studies should distinguish microbiome effects from confounding by obesity, diet, insulin resistance, and medication exposure rather than assuming that all observed microbial differences are intrinsic to PCOS.

Question 2: What detection methods are recommended for gut microbiota analysis in PCOS?

Recommendation 3: Gut microbiota testing is currently used primarily in case-control studies to provide data supporting clinical translation. For research on PCOS and gut microbiota, methods capable of resolving microbial composition or characterizing functional genes, such as 16S ribosomal RNA (rRNA) gene sequencing and metagenomic sequencing, are recommended, with consideration of sample availability and experimental reproducibility. (2B)

Interpretation: Method selection should follow the research question. 16S rRNA gene sequencing is suitable for broad characterization of bacterial community structure and remains useful when cost, sample number, or comparability with legacy cohorts is important. Shotgun metagenomic sequencing offers greater taxonomic resolution and permits direct analysis of microbial genes and functional potential, but it requires greater sequencing depth, computational capacity, and attention to host DNA and database-dependent annotation.^[17-19] Neither approach, by itself, converts a microbiome profile into a clinically validated diagnostic test. Additionally, pre-analytical and analytical standardization may be more

Table 1: GRADE classification of certainty of evidence and strength of recommendations

Category	Grade	Description
Certainty of evidence	High (A)	We are very confident that the true effect lies close to the estimate of the effect.
	Moderate (B)	We are moderately confident in the estimate of the effect. The true effect is likely to be close to the estimate, but there is a possibility that it is substantially different.
	Low (C)	Our confidence in the estimate of the effect is limited. The true effect may be substantially different from the estimate.
	Very Low (D)	We have very little confidence in the estimate of the effect. The true effect is likely to be substantially different from the estimate.
Strength of recommendation	Strong (1)	The desirable consequences of an intervention clearly outweigh the undesirable consequences, or <i>vice versa</i> .
	Conditional/weak (2)	The balance between desirable and undesirable consequences is uncertain or closely balanced.

GRADE, Grading of Recommendations Assessment, Development, and Evaluation.

important than the choice between two sequencing technologies. Stool collection timing, storage, transport, DNA extraction, batch effects, sequencing depth, negative controls, bioinformatic pipelines, and reference databases can all alter the apparent microbiome signal.^[17–21] Therefore, longitudinal or multicenter studies should pre-specify these variables and incorporate quality-control procedures before seeking disease-specific microbial markers.

Clinical implication. The recommendation supports microbiome profiling principally as a research and translational tool. This boundary is consistent with the 2025 international consensus on microbiome testing, which concluded that evidence remains insufficient for widespread routine clinical use and emphasized standardized testing and cautious interpretation.^[20] A clinician should therefore avoid making treatment decisions solely from a commercial microbiome report unless the measured feature has an independently validated clinical meaning.

Question 3: Are probiotics or prebiotics beneficial for patients with PCOS? How should they be precisely selected, and what are the recommended duration and supplementation method?

Recommendation 4: Supplementation with specific probiotic strains validated in PCOS clinical studies (*e.g.*, certain *Lactobacillus* and *Bifidobacterium* strains) can be used as an adjunct to lifestyle interventions for PCOS and may help improve metabolic and hormonal profiles. (2B)

Recommendation 5: The indiscriminate use of probiotic strains not validated in PCOS populations or broad-spectrum probiotic preparations is not recommended for patients with PCOS. Probiotic interventions should not replace first-line therapies such as lifestyle interventions and metformin. (1B)

Interpretation: The current signal for probiotics is strongest for adjunctive improvement in metabolic and

inflammatory measures, not for replacement of established PCOS therapy. Meta-analyses and RCTs suggest that selected probiotic or synbiotic interventions can improve fasting glucose, insulin resistance, lipid parameters, inflammatory markers, and in some studies body weight or androgen-related biochemical outcomes.^[22–30] The evidence base is nevertheless heterogeneous because products differ in strain composition, viable dose, co-interventions, baseline phenotype, and treatment duration. A statistically favorable pooled effect for "probiotics" should not be interpreted as evidence that all commercially available preparations are interchangeable. Moreover, reproductive benefits remain less certain than metabolic benefits. Several trials report changes in testosterone or other hormonal measures, but robust evidence for sustained ovulation, menstrual regularity, clinical hyperandrogenism, pregnancy, or live birth is limited.^[28,29,31] This distinction matters in counseling patients who may expect a probiotic supplement to directly restore fertility. The guideline therefore positions probiotics as an adjunct to lifestyle and standard pharmacologic treatment rather than as a primary reproductive therapy.

Recommendation 6: When prebiotics are used in patients with PCOS, inulin-type dietary fibers (*e.g.*, inulin) may be prioritized at a recommended dose of 5–10 g/day, for 8–12 weeks. Treatment should begin at a low dose and be gradually adjusted according to individual tolerance. (2B)

Interpretation: Prebiotics are similarly phenotype- and tolerance-dependent. Inulin-type fibers can increase substrates available to beneficial bacteria and have shown favorable metabolic or inflammatory effects in PCOS studies.^[32–35] The suggested 5–10 g/day range over 8–12 weeks should be applied gradually because bloating, abdominal discomfort, and altered bowel habits may limit adherence. The practical objective is not merely to reach a nominal dose but to achieve a sustained, tolerated intervention that complements an overall high-quality diet.

Table 2: Summary of the 2026 guideline recommendations interpreted in this article

Clinical question	Recommendations and classification
Question 1: What is the association between PCOS and the gut microbiota?	Recommendation 1: Patients with PCOS generally exhibit gut dysbiosis, characterized mainly by alterations in gut microbial composition and diversity, reduced abundance of SCFA-producing genera, and disruption of the microbial community involved in bile acid metabolism. However, large-scale, multicenter cohort studies are currently lacking to screen and validate specific gut microbial markers for clinical diagnosis and phenotypic subtyping of PCOS. (2B) Recommendation 2: Mouse experiments have demonstrated that FMT can induce PCOS-related phenotypes, revealing the significant role of the gut microbiota in the development and progression of PCOS. Given the complex bidirectional interactions between endocrine metabolism and the gut microbiota, gut dysbiosis and metabolic disorders may be mutually reinforcing in a vicious cycle during PCOS progression. (2B)
Question 2: What detection methods are recommended for gut microbiota analysis in PCOS?	Recommendation 3: Gut microbiota testing is currently used primarily in case-control studies to provide data supporting clinical translation. For research on PCOS and gut microbiota, methods capable of resolving microbial composition or characterizing functional genes, such as 16S rRNA gene sequencing and metagenomic sequencing, are recommended, with consideration of sample availability and experimental reproducibility. (2B)
Question 3: Are probiotics or prebiotics beneficial for patients with PCOS? How should they be precisely selected, and what are the recommended duration and supplementation method?	Recommendation 4: Supplementation with specific probiotic strains validated in PCOS clinical studies (<i>e.g.</i> , certain <i>Lactobacillus</i> and <i>Bifidobacterium</i> strains) can be used as an adjunct to lifestyle interventions for PCOS and may help improve metabolic and hormonal profiles. (2B) Recommendation 5: The indiscriminate use of probiotic strains not validated in PCOS populations or broad-spectrum probiotic preparations is not recommended for patients with PCOS. Probiotic interventions should not replace first-line therapies such as lifestyle interventions and metformin. (1B) Recommendation 6: When prebiotics are used in patients with PCOS, inulin-type dietary fibers (<i>e.g.</i> , inulin) may be prioritized at a recommended dose of 5–10 g/day, for 8–12 weeks. Treatment should begin at a low dose and be gradually adjusted according to individual tolerance. (2B)
Question 4: How should specific probiotic strains and intervention duration be precisely selected for patients with PCOS?	Recommendation 7: Priority should be given to specific probiotic strains that have improved core PCOS phenotypes, including insulin resistance and hyperandrogenemia, in RCTs involving patients with PCOS. Treatment should continue for at least 8 weeks, with monitoring of metabolic parameters and adverse events. (1B)
Question 5: Which dietary patterns are most beneficial for improving PCOS through gut microbiota modulation?	Recommendation 8: A fiber-rich dietary pattern, such as the Mediterranean diet, is strongly recommended for all patients with PCOS as a core strategy for PCOS management and optimization of the gut microbiota. (1B)
Question 6: Is FMT applicable to the treatment of PCOS?	Recommendation 9: Currently, no direct research evidence exists on the efficacy of FMT in patients with PCOS. However, clinical application of FMT in other metabolic diseases such as obesity and type 2 diabetes has gradually advanced, accumulating practical experience. Therefore, for patients with PCOS and comorbid obesity or diabetes who have suboptimal responses to lifestyle intervention and standard pharmacotherapy and who explicitly express a willingness to undergo FMT, individualized treatment plans may be developed following existing FMT expert consensus and clinical guidelines. (GPS)
Question 7: How does the gut microbiota influence treatment outcomes of PCOS?	Recommendation 10: Preliminary studies suggest that the gut microbiota may influence the clinical efficacy of PCOS treatments, such as metformin, by affecting drug metabolism. Awareness of this potential interaction is advised in clinical practice, but routine adjustment of treatment plans or microbiota testing to predict drug efficacy is not currently required. (2C)
Question 8: Does metabolic surgery improve the gut microbiota in patients with PCOS and comorbid obesity?	Recommendation 11: For patients with PCOS and comorbid obesity ($\text{BMI} \geq 32.5 \text{ kg/m}^2$) who have suboptimal responses to lifestyle and pharmacologic interventions, metabolic surgery (<i>e.g.</i> , gastric bypass, sleeve gastrectomy) may be cautiously considered after multidisciplinary team evaluation and informed consent. Surgery significantly improves PCOS symptoms and metabolic parameters, with benefits partially attributed to postoperative gut microbiota remodeling. However, surgical risks must be thoroughly evaluated and communicated. (1B) Recommendation 12: Metabolic surgery effectively remodels the gut microbiota and rapidly improves the reproductive, endocrine, and metabolic phenotypes of patients with PCOS and comorbid obesity. Indications must be applied strictly, and surgical risks must be fully disclosed. (1B)
Question 9: In patients with PCOS and anxiety/depression, should the "gut-brain axis" be considered? What is the clinical significance of such interventions?	Recommendation 13: Integration of mental health screening and management into the routine clinical pathway for PCOS, as a core component of the overall treatment plan, is strongly recommended. In comprehensive management, improving the gut microbiota may be explored as an adjunctive intervention, and its effect on mood symptoms should be systematically evaluated in future clinical studies. (GPS) Recommendation 14: For mental health screening in patients with PCOS, standardized tools such as the Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS), Patient Health Questionnaire (PHQ-9), or Generalized Anxiety Disorder-7 (GAD-7) can be routinely used. Patients with positive screening results should be promptly referred to a psychology or psychiatry department for specialized evaluation and intervention, and their psychological status should undergo ongoing monitoring throughout the PCOS treatment. (1B) Recommendation 15: It should be recognized that the disruption of the "gut-brain axis" is an important mechanism for the occurrence of anxiety/depression in patients with PCOS. However, there is currently a lack of high-quality evidence to support the use of regulating the gut microbiota (such as probiotics) as a first-line treatment independently of conventional psychological and lifestyle interventions. (2C)

BMI, body mass index; FMT, fecal microbiota transplantation; GPS, good practice statement; RCT, randomized controlled trial; SCFA, short-chain fatty acid; PCOS, polycystic ovary syndrome.

Clinical implication. Recommendations 4–6 should be read as an argument for product specificity and treatment integration. The most defensible choice is a strain or prebiotic formulation supported by PCOS-specific

clinical data, used for a defined period and monitored for tolerability and relevant outcomes. Broad-spectrum products with unverified strain identity or unsubstantiated disease claims should not be preferred simply

because they contain a larger number of organisms.

Question 4: How should specific probiotic strains and intervention duration be precisely selected for patients with PCOS?

Recommendation 7: Priority should be given to specific probiotic strains that have improved core PCOS phenotypes, including insulin resistance and hyperandrogenemia, in RCTs involving patients with PCOS. Treatment should continue for at least eight weeks, with monitoring of metabolic parameters and adverse events. (1B)

Interpretation: Probiotic efficacy is strain-specific, whereas clinical marketing is often genus-level. A result obtained with a defined *Lactobacillus* or *Bifidobacterium* strain, dose, and formulation cannot automatically be extrapolated to another strain from the same genus.^[25,28,35] For this reason, selection should be based on the exact intervention tested in PCOS RCTs whenever possible, with the product label allowing verification of strain identity, dose, storage requirements, and expiration.

Duration and outcome monitoring should be planned before treatment. Most positive PCOS trials have evaluated interventions for approximately 8–12 weeks, and evidence for clinically meaningful effects over shorter periods is limited.^[22,29] Monitoring should therefore focus on pre-specified targets such as fasting insulin, homeostatic model assessment of insulin resistance (HOMA-IR), lipid profile, androgen-related biochemical indices, body weight where relevant, and adverse gastrointestinal effects.^[31] Repeating an intervention indefinitely without evidence of benefit is not supported by the guideline.

Clinical implication. Future probiotic trials should report complete strain nomenclature, viable dose at the end of shelf life, formulation, adherence, background diet, concomitant metformin or other medications, and clinically meaningful reproductive outcomes. These details are necessary if the field is to move from broad class effects to precision microbiome intervention.

Question 5: Which dietary patterns are most beneficial for improving PCOS through gut microbiota modulation?

Recommendation 8: A fiber-rich dietary pattern, such as the Mediterranean diet, is strongly recommended for all patients with PCOS as a core strategy for PCOS management and optimization of the gut microbiota. (1B)

Interpretation: The recommendation favors a dietary pattern rather than a single microbiota-targeting nutrient. Mediterranean-style diets combine higher intake of vegetables, fruits, legumes, whole grains, nuts, and unsaturated fats with lower exposure to refined carbohydrates

and highly processed foods. Studies in PCOS suggest benefits for insulin resistance, body composition, and cardiometabolic risk, while mechanistic studies support increased fermentable substrate availability, SCFA production, improved barrier function, and reduced inflammatory signaling.^[36–44] These pathways are plausible contributors, but the clinical effects of the diet should not be attributed exclusively to microbiome remodeling.

This dietary pattern should be adapted to local food cultures and dietary habits. In the Chinese context, its core principles can be implemented by increasing the intake of whole grains, legumes, and soy products, vegetables, fruits, fish, poultry, and nuts where feasible, while reducing excessive consumption of refined carbohydrates, highly processed foods, and red meat. The goal is to preserve the key nutritional characteristics of the Mediterranean dietary pattern, including high fiber intake, diverse plant-based foods, and high-quality fats, rather than to replicate a Mediterranean menu literally.

Clinical implication. Diet remains a foundational PCOS intervention irrespective of whether microbiome testing is performed. This is consistent with the broader 2023 International Evidence-based PCOS Guideline, in which healthy lifestyle and individualized dietary strategies are central components of care.^[45] In practice, the microbiome provides an additional mechanistic rationale for a fiber-rich dietary pattern, but not a justification to delay evidence-based weight, metabolic, fertility, or pharmacologic management.

Question 6: Is FMT applicable to the treatment of PCOS?

Recommendation 9: Currently, no direct research evidence exists on the efficacy of FMT in patients with PCOS. However, clinical application of FMT in other metabolic diseases such as obesity and type 2 diabetes has gradually advanced, accumulating practical experience. Therefore, for patients with PCOS and comorbid obesity or diabetes who have suboptimal responses to lifestyle intervention and standard pharmacotherapy and who explicitly express a willingness to undergo FMT, individualized treatment plans may be developed following existing FMT expert consensus and clinical guidelines. (GPS)

Interpretation: The key consideration in Recommendation 9 is the absence of direct clinical evidence supporting FMT for PCOS. Current evidence is derived largely from experimental PCOS models, whereas clinical data suggesting metabolic benefits come primarily from populations with obesity, metabolic syndrome, or type 2 diabetes.^[7,46–48] FMT should therefore not be regarded as an established treatment for PCOS. Any consideration of its use should instead be guided by clear indications,

rigorous governance, and safety requirements rather than by a nonspecific diagnosis of dysbiosis. Donor screening, assessment of pathogens and antimicrobial resistance, standardized preparation, traceability, informed consent, and long-term follow-up are essential because transmission of infectious agents and other unintended biological traits remain possible.^[49–59] In addition to short-term gastrointestinal adverse effects, uncertainties regarding long-term engraftment, metabolic consequences, and rare adverse events further support restricting FMT to appropriately regulated research settings.

Clinical implication. In patients with PCOS who also have obesity or diabetes, the presence of the comorbidity does not automatically create a PCOS-specific indication for FMT. If FMT is considered, the rationale should derive from applicable evidence or consensus for the comorbid condition, be undertaken in qualified institutions, and preferably occur in a research protocol when the intended goal is improvement of PCOS outcomes. This interpretation preserves the GPS while preventing it from being read as a routine treatment recommendation.

Question 7: How does the gut microbiota influence treatment outcomes in PCOS?

Recommendation 10: Preliminary studies suggest that the gut microbiota may influence the clinical efficacy of PCOS treatments, such as metformin, by affecting drug metabolism. Awareness of this potential interaction is advised in clinical practice, but routine adjustment of treatment plans or microbiota testing to predict drug efficacy is not currently required. (2C)

Interpretation: The relationship between metformin and the gut microbiota appears to be bidirectional. Metformin can modify microbial composition and short-chain fatty acid-related functions, whereas baseline microbiota characteristics may in turn influence gastrointestinal tolerance or metabolic response.^[60–65] These findings are relevant to mechanistic research and may ultimately contribute to treatment stratification. However, a potential microbial mediator or biomarker should not yet be interpreted as a clinically actionable decision rule. Current human evidence is insufficient to define a reproducible baseline microbiome profile that predicts metformin response with adequate accuracy for routine clinical use, and differences in sequencing platforms, background diet, treatment adherence, PCOS phenotype, and concomitant therapies further limit the generalizability of proposed microbial signatures.

Clinical implication. Metformin should continue to be prescribed according to established PCOS indications, metabolic phenotype, contraindications, and tolerability

rather than according to microbiome results. Routine pre-treatment microbiome testing, probiotic co-prescription solely to improve metformin response, or modification of dose on the basis of an unvalidated microbial signature is premature. Recommendation 10 is therefore primarily a call for clinical awareness and future biomarker research.

Question 8: Does metabolic surgery improve the gut microbiota in patients with PCOS and comorbid obesity?

Recommendation 11: For patients with PCOS and comorbid obesity (body mass index, BMI ≥ 32.5 kg/m²) who have suboptimal responses to lifestyle and pharmacologic interventions, metabolic surgery (*e.g.*, gastric bypass, sleeve gastrectomy) may be cautiously considered after multidisciplinary team evaluation and informed consent. Surgery significantly improves PCOS symptoms and metabolic parameters, with benefits partially attributed to postoperative gut microbiota remodeling. However, surgical risks must be thoroughly evaluated and communicated. (1B)

Interpretation: Metabolic surgery should be selected because a patient meets accepted obesity/metabolic criteria, not because surgery changes the gut microbiota. In appropriately selected women with PCOS and obesity, bariatric or metabolic surgery can produce substantial weight loss and improvement in insulin resistance, menstrual cyclicality, ovulation, and hyperandrogenic features.^[66–70] The decision nevertheless requires multidisciplinary assessment of operative risk, nutritional status, reproductive plans, and long-term follow-up.

Recommendation 12: Metabolic surgery effectively remodels the gut microbiota and rapidly improves the reproductive, endocrine, and metabolic phenotypes of patients with PCOS and comorbid obesity. Indications must be applied strictly, and surgical risks must be fully disclosed. (1B)

Interpretation: Microbiome remodeling is best viewed as one component of a multi-system postoperative response. Surgery changes nutrient flow, caloric intake, bile-acid signaling, gut hormones, weight, insulin sensitivity, and microbial ecology simultaneously.^[71,72] Observed increases in microbial diversity or shifts in beneficial taxa may contribute to metabolic improvement, but these changes should not be presented as the sole mechanism or as a stand-alone indication for surgery.

Clinical implication. Recommendations 11 and 12 reinforce established surgical principles: careful patient selection, informed consent, standardized perioperative management, prevention and treatment of nutritional defi-

ciencies, and lifelong follow-up.^[73–75] Reproductive counseling is essential, including the recommendation to postpone conception during the period of rapid post-operative weight loss and nutritional stabilization. Microbiome research around surgery is valuable, but it should not obscure these conventional safety priorities.

Question 9: In patients with PCOS and anxiety/depression, should the “gut-brain axis” be considered? What is the clinical significance of such interventions?

Recommendation 13: Integration of mental health screening and management into the routine clinical pathway for PCOS, as a core component of the overall treatment plan, is strongly recommended. In comprehensive management, improving the gut microbiota may be explored as an adjunctive intervention, and its effect on mood symptoms should be systematically evaluated in future clinical studies. (GPS)

Recommendation 14: For mental health screening in patients with PCOS, standardized tools such as the Self-Rating Depression Scale (SDS), Self-Rating Anxiety Scale (SAS), Patient Health Questionnaire (PHQ-9), or Generalized Anxiety Disorder-7 (GAD-7) can be routinely used. Patients with positive screening results should be promptly referred to a psychology or psychiatry department for specialized evaluation and intervention, and their psychological status should undergo ongoing monitoring throughout the PCOS treatment. (1B)

Interpretation: Mental-health screening is a mature clinical priority, whereas microbiome-based treatment of psychiatric symptoms remains exploratory. Depression and anxiety occur more frequently in PCOS and can worsen quality of life, treatment adherence, weight management, and reproductive care.^[76] Routine use of validated instruments such as PHQ-9 or GAD-7, followed by appropriate referral when screening is positive, is therefore clinically actionable independent of any microbiome hypothesis.

Recommendation 15: It should be recognized that the disruption of the “gut-brain axis” is an important mechanism for the occurrence of anxiety/depression in patients with PCOS. However, there is currently a lack of high-quality evidence to support the use of regulating the gut microbiota (such as probiotics) as a first-line treatment independently of conventional psychological and lifestyle interventions. (2C)

Interpretation: The gut-brain axis offers a plausible mechanistic framework but not a substitute for psychiatric care. Stress can influence intestinal permeability, immune activity, and microbial composition, whereas

microbial metabolites and inflammatory signaling can in turn affect neural and neuroendocrine pathways.^[77–80] Experimental and pilot studies of psychobiotics or probiotics are of interest,^[77,81,82] but PCOS-specific evidence is not sufficiently mature to support microbiota modulation as first-line treatment for anxiety or depression.

Clinical implication. Recommendations 13–15 should be implemented in two layers: first, systematic identification and evidence-based management of mental-health problems; second, research into whether microbiome-targeted approaches provide incremental benefit. Clinicians should avoid framing probiotics or gut-directed interventions as alternatives to psychological therapy, psychiatric assessment, or indicated pharmacotherapy.

USING THE CLINICAL INTERVENTION FLOWCHART

Figure 1 is best understood as a hierarchy of clinical decisions rather than a sequence requiring microbiome testing for every patient. Initial assessment should characterize the PCOS phenotype, metabolic risk, diet, gastrointestinal symptoms, current treatment, and mental-health status. Core management remains lifestyle-based and should be integrated with established pharmacologic or reproductive treatment according to the patient's indication. Microbiota-related measures such as a fiber-rich diet or selected probiotic/prebiotic products can then be considered as adjuncts when supported by the patient's goals and the available evidence. Highly specialized measures such as FMT or metabolic surgery belong in distinct pathways governed by their own indications, safety requirements, and multidisciplinary oversight.

The flowchart should also be used to avoid therapeutic escalation based solely on an abnormal commercial microbiome report. A change in microbial composition is not itself a treatment target unless the intervention has demonstrated clinically meaningful benefit in an appropriate population. Follow-up should therefore prioritize outcomes that matter to the patient, including metabolic control, menstrual function, ovulation or fertility when relevant, weight-related outcomes, adverse effects, and psychological well-being, rather than normalization of a microbial metric without established clinical significance.

DISCUSSION

What this guideline adds?

The principal contribution of the guideline is to place microbiome science within a graded clinical framework for PCOS. It recognizes that the microbiota is relevant to disease biology while resisting the assumption that every mechanistic association is ready for clinical use.

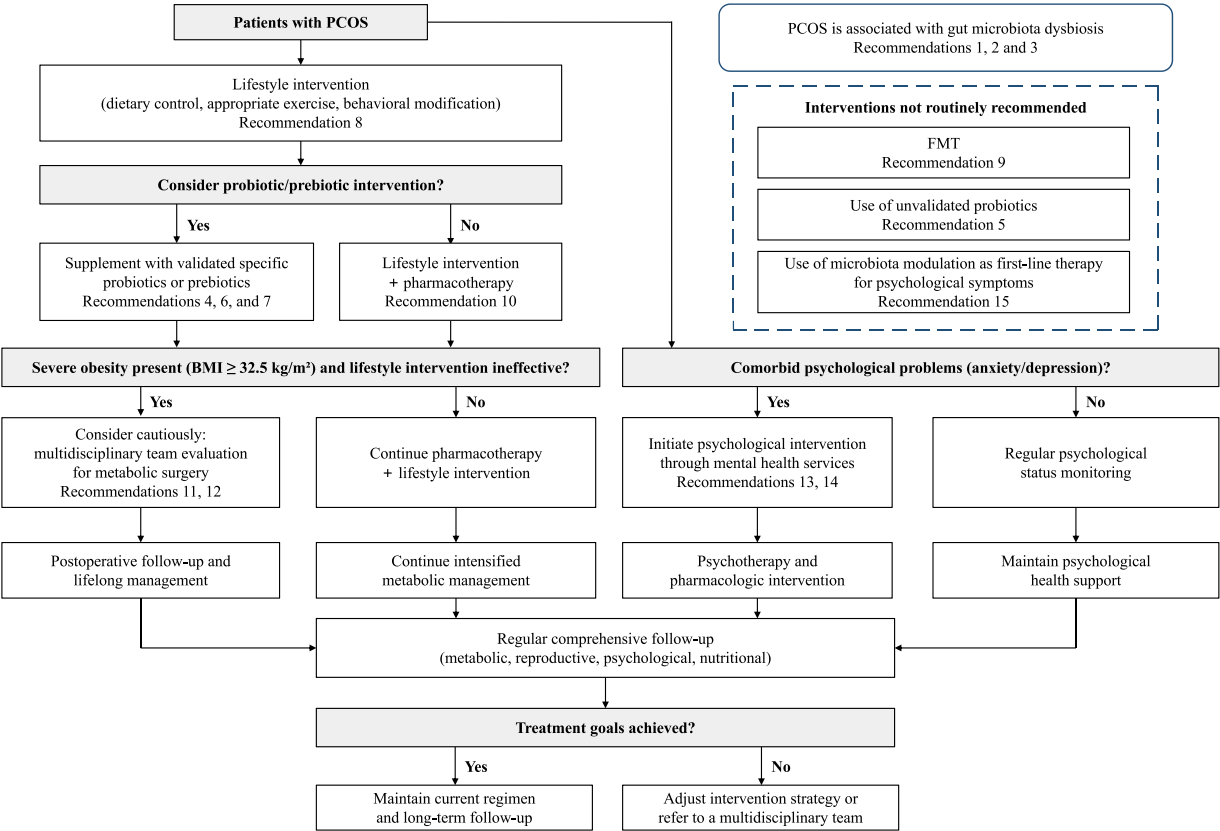


Figure 1. Clinical implementation framework for gut microbiota-related management in polycystic ovary syndrome

Across the 15 recommendations, a coherent translational hierarchy emerges: established PCOS care remains the foundation; diet and selected probiotic or prebiotic interventions may be integrated as adjuncts; microbiome profiling is primarily a research tool; and FMT or other invasive microbiome-directed interventions require much stronger indication and governance. This hierarchy is particularly important in a field where commercial availability has advanced more rapidly than clinical validation.

Relationship to existing PCOS and microbiome guidance

This guideline should be viewed as complementary to, rather than a replacement for, the 2023 International Evidence-based Guideline for PCOS.^[45] The international guideline addresses the full spectrum of diagnosis, lifestyle management, cardiometabolic risk, psychological health, pharmacologic treatment, infertility, and reproductive care. The present microbiome-focused guideline adds a specialized translational layer to that framework. Areas of convergence include the central role of lifestyle intervention, the need to address psychological health, and careful selection of metabolic surgery. The key difference is that the microbiome-focused

guideline explicitly evaluates interventions and tests whose role in routine PCOS care remains less mature.

The recommendations on microbiome testing also align with the 2025 international consensus statement on microbiome testing in clinical practice.^[20] Both documents emphasize methodological standardization, cautious interpretation, and the current lack of evidence for widespread routine clinical testing. This convergence is clinically useful because it provides a safeguard against interpreting taxonomic variation as a validated diagnosis or using unstandardized reports to direct supplements, medications, or restrictive diets.

Strengths of the guideline

Several features strengthen the guideline. First, it focuses on questions that clinicians are already encountering, including probiotic selection, testing methods, FMT, metabolic surgery, and the gut-brain axis. Second, it uses GRADE to make uncertainty visible rather than hiding it behind mechanistic enthusiasm. Third, it integrates evidence from Chinese and international populations and explicitly considers the feasibility of translation. Finally, by combining clinical and mechanistic questions, it creates a bridge between reproductive medicine and

microbiome science that may help standardize future research and reduce fragmented study design.

Limitations and interpretive cautions

The same breadth that makes the guideline useful also creates limitations. Much of the PCOS microbiome literature is cross-sectional, and many intervention studies are small, short, or heterogeneous in product composition and background treatment. Several recommendations therefore rely on moderate or low-certainty evidence, indirect evidence from other metabolic diseases, or GPS-level expert judgment. Surrogate outcomes such as HOMA-IR, inflammatory markers, or hormone concentrations are more frequently reported than sustained ovulation, menstrual regularity, pregnancy, live birth, or long-term cardiometabolic events. Consequently, a biological effect on the microbiota should not be equated with a clinically important effect unless patient-centered outcomes have also been demonstrated.

A second limitation is the instability of taxonomic findings across cohorts. Stool microbiota composition is shaped by diet, geography, obesity, medication exposure, ethnicity, sequencing methods, and other environmental variables.^[11–14,17–19] A future PCOS "microbial signature" will therefore require external validation across populations and should ideally incorporate function, metabolites, and host phenotype rather than rely on relative abundance of a small number of taxa. The guideline appropriately stops short of defining such a signature for current clinical use.

Priorities for future research

Future studies should move from descriptive microbiome comparisons toward reproducible, clinically anchored designs. Prospective multicenter cohorts should standardize stool collection, DNA extraction, sequencing, bioinformatics, diet assessment, medication exposure, and metabolic phenotyping. Intervention trials should specify probiotic strains and viable dose, prebiotic formulation, adherence, co-interventions, and pre-specified primary outcomes. For reproductive medicine, trials should extend beyond biochemical surrogates to menstrual regularity, ovulation, oocyte or embryo outcomes where appropriate, pregnancy, and live birth. Long-term follow-up is also needed to determine whether short-term metabolic improvements persist after supplementation is stopped.

Mechanistic studies should additionally test mediation rather than merely report parallel changes in microbiota and phenotype. Integrating metagenomics with microbial metabolites, bile acids, SCFAs, host inflammatory pathways, and endocrine measures may help identify functional pathways that are more reproducible than taxonomic markers alone. For metformin and other

pharmacologic therapies, predictive models should be externally validated before microbiome features are used to alter treatment. For FMT, PCOS-specific trials would require especially rigorous donor screening, safety monitoring, predefined reproductive and metabolic endpoints, and long-term surveillance before any routine indication could be justified.

Implementation and dissemination

Implementation should emphasize clinical education and shared decision-making. Clinicians need to explain to patients that "microbiome-related" does not necessarily mean "microbiome-tested" and that an intervention can be reasonable because of its overall nutritional or metabolic benefit even when a personalized microbiome test is unnecessary. Dietitians, endocrinologists, reproductive specialists, mental-health professionals, and microbiome researchers should use common terminology and distinguish established care, adjunctive options, and investigational procedures. Local audit of probiotic prescribing, commercial microbiome testing, and referral for invasive microbiota interventions may help identify areas in which practice has moved ahead of evidence.

Periodic updating will be particularly important because the evidence base is rapidly evolving. New strain-specific RCTs, standardized metagenomic cohorts, microbiome-derived biomarkers, and intervention studies may alter the strength or scope of current recommendations. Until such evidence emerges, implementation should favor interventions with independent general health benefits and low risk, preserve established PCOS management, and avoid irreversible or invasive steps on the basis of preliminary microbial associations.

CONCLUSION

The 2026 PCOS and gut microbiota guideline provides a structured framework for translating a rapidly developing research field into clinical practice. Its central message is not that microbiome-directed care should replace established PCOS management, but that microbiome evidence should be used at a level proportionate to its maturity. Microbiome profiling is currently most appropriate for research; selected probiotic, prebiotic, and dietary strategies may be used as adjuncts; treatment decisions for metformin, mental-health care, and metabolic surgery should remain anchored in established clinical indications; and FMT should not be regarded as routine PCOS therapy in the absence of direct clinical evidence. Standardized methods, phenotype-aware study design, patient-centered outcomes, and long-term safety data will determine whether microbiome science can progress from association and mechanistic plausibility to precise and durable benefit for patients with PCOS.

DECLARATIONS

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Author contributions

Dai FF: Investigation, Methodology, Writing—Original draft preparation. Li R: Conceptualization, Methodology, Supervision, Project administration. Mu LS: Conceptualization, Supervision, Project administration, Writing—Review and Editing. Yin TL: Conceptualization, Supervision, Project administration, Writing—Review and Editing.

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Not applicable.

Informed consent

Not applicable.

Use of large language models, AI and machine learning tools

A large language model was used to assist with language editing and structural refinement. All scientific content, interpretations, and final wording were critically reviewed and approved by the authors.

Data availability statement

All data generated or analyzed during this study are included in this published article.

Conflict of interest

The authors declare that they have no conflicts of interest.

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