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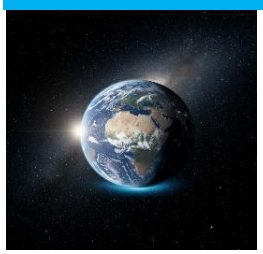

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Lifestyle modification and selected pharmacological therapies in Polycystic Ovary Syndrome: current evidence and emerging approaches

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in women of reproductive age, associated with hyperandrogenism, menstrual irregularities, infertility, insulin resistance, and increased cardiometabolic risk.

Aim: The aim of this narrative review was to summarize current evidence-based therapies for PCOS management, focusing on lifestyle modification and selected pharmacological options.

Materials and Methods: A literature search was conducted in PubMed using the term "Polycystic Ovary Syndrome (PCOS)" combined with the following keywords: "lifestyle", "physical activity", "exercise", "diet", "pharmacotherapy", "treatment", "metformin", "fertility", "GLP-1", "inositol", and "gut microbiota". Articles published from 2019 onwards were included.

Results: Lifestyle modification remains the first-line approach and may improve metabolic, hormonal, and reproductive outcomes. Pharmacotherapy is used as an adjunct when lifestyle measures are insufficient. Established options include metformin, combined oral contraceptives, antiandrogens in selected cases, and ovulation induction agents. Emerging evidence supports GLP-1 receptor agonists for obesity-related PCOS, although long-term data are limited. Inositol and gut microbiota-targeted strategies remain experimental.

Conclusions: PCOS management should be individualized and long-term, combining lifestyle interventions with appropriate pharmacotherapy and patient education to improve adherence and outcomes.

Key words: Polycystic ovary syndrome; PCOS; lifestyle modification; physical activity; diet; insulin resistance; metformin; combined oral contraceptives; GLP-1 receptor agonists; patient education

Introduction

Polycystic ovary syndrome is one of the most common endocrine disorders affecting women of reproductive age worldwide, with a prevalence of approximately 8–13% depending on the population studied and diagnostic criteria used. [1] Although many years have passed since this disorder was first described, it still poses a significant therapeutic challenge in everyday clinical practice. It is primarily characterized by excess androgens, menstrual disorders, and fertility problems accompanied by insulin resistance and often obesity. [2,3] According to the Rotterdam criteria from 2003, which are still in force, the basis for the diagnosis of PCOS is the coexistence of 2 out of 3 criteria, which include 1) rare or absent ovulation, 2) clinical and/or

biochemical features of hyperandrogenism, 3) polycystic ovaries on ultrasound examination. [3,4]

The above disorders mean that this syndrome significantly increases the risk of further diseases and complications, such as cardiovascular disease, type II diabetes (T2DM), and metabolic syndrome. [5,6]. It also contributes to coexisting mental disorders such as depression and anxiety disorders. [5,7] Due to its multifactorial nature and possible long-term effects, PCOS requires a comprehensive and individualized therapeutic approach rather than short-term treatment focused on symptoms.

Lifestyle modification is widely accepted as the first-line therapy for PCOS, especially in overweight or obese women. [1,4] It has been shown that dietary changes, increased physical activity, and behavioral interventions improve tissue sensitivity to insulin, hormonal balance, and menstrual cycle regularity, even with modest weight loss. [2,8]. Most importantly, lifestyle interventions can significantly reduce cardiometabolic risk and improve overall well-being, making them the cornerstone of long-term treatment strategies. [6] However, adherence to these recommendations remains a significant challenge, and the clinical response among patients to lifestyle changes alone is often variable.

Pharmacological treatment is often introduced when lifestyle changes alone do not lead to satisfactory clinical results or when specific symptoms require targeted therapy. [2] One of the most commonly prescribed drugs for women with PCOS, especially those with accompanying insulin resistance, is metformin. [9] It has been shown to improve metabolic parameters in patients and, in some cases, ovulatory function. [10] Other pharmacological options include combined oral contraceptives (COCs), used primarily to reduce symptoms of androgenization and regulate the menstrual cycle, as well as drugs such as letrozole and clomiphene citrate, used mainly in the context of infertility treatment. [1,2,11,12] Although drug therapy can be effective in controlling symptoms, it does not address all aspects of PCOS and is often insufficient as a long-term strategy on its own.

In recent years, new pharmacological therapies that may provide additional benefits in the treatment of PCOS have been attracting increasing attention. Among them, glucagon-like peptide-1 (GLP-1) receptor agonists are of great interest due to their effect on weight reduction, insulin sensitivity, and metabolic parameters. [13] Preliminary studies indicate that these drugs may be used as adjunctive therapy, especially for women with concomitant obesity and

significant metabolic disorders. However, data on their long-term safety and impact on fertility still require caution and further verification.

Due to the highly complex nature of the disease and the limitations of using a single treatment method, patients with PCOS require a comprehensive approach that includes both behavioral and medical interventions.

Patient education is essential for sustained lifestyle implementation and adherence to therapy– it is the basis for following medical recommendations, setting realistic goals, and maintaining healthy habits in the long term. By providing patients with clear information on the pathophysiology and chronic nature of PCOS, clinicians can improve patients' understanding of the condition and motivate them to persevere with the changes introduced in order to improve their quality of life.

The aim of this narrative review is to summarize current evidence-based therapeutic approaches, including lifestyle changes and pharmacological treatment, and evidence of their effectiveness, with a particular focus on new therapies. In addition, the review also addresses the importance of patient education as part of the interventions implemented and long-term treatment strategies.

Pathophysiology of PCOS relevant to lifestyle and pharmacological interventions

Polycystic ovary syndrome (PCOS) is a heterogeneous endocrine and metabolic disorder characterized by complex interactions between insulin resistance, hyperandrogenism, and chronic low-grade inflammation. Insulin resistance, frequently present regardless of body weight, leads to compensatory hyperinsulinemia, which enhances ovarian androgen production and reduces hepatic synthesis of sex hormone-binding globulin (SHBG), thereby increasing circulating free androgen levels. Hyperandrogenism, in turn, disrupts follicular development and ovulatory function, contributing to menstrual irregularities and infertility. In parallel, chronic low-grade inflammation may further aggravate metabolic dysfunction and reproductive impairment. These interrelated mechanisms represent key therapeutic targets for lifestyle modification and pharmacological interventions and justify integrated and individualized management strategies for PCOS. [5,14]

Lifestyle Changes in the Management of PCOS

Role of Diet in Metabolic and Hormonal Regulation

Lifestyle modification is widely recommended as the first-line intervention in the management of polycystic ovary syndrome (PCOS), given its beneficial effects on metabolic, hormonal, and reproductive outcomes. Dietary interventions play a central role in improving insulin sensitivity and overall metabolic health, particularly in women with insulin resistance and obesity. Diets characterized by a low glycemic index, high fiber content, and reduced intake of refined carbohydrates have been shown to improve glucose homeostasis and attenuate hyperinsulinemia, which may indirectly reduce circulating androgen levels. Importantly, the beneficial effects of dietary modification may occur independently of significant weight loss, highlighting the importance of diet quality rather than caloric restriction alone [14,15]

Anti-inflammatory Dietary Patterns and Nutritional Supplementation

Mediterranean and other anti-inflammatory dietary patterns, rich in fruits, vegetables, whole grains, unsaturated fats and omega-3 fatty acids, have gained increasing attention in the management of PCOS. These dietary approaches combine favorable glycemic characteristics with antioxidant and anti-inflammatory properties, which may be particularly relevant in the context of chronic low-grade inflammation associated with PCOS. While ketogenic and other highly restrictive diets may result in short-term improvements in body weight and selected metabolic parameters, concerns remain regarding their long-term sustainability, nutritional adequacy and safety. In addition to dietary patterns, selected nutritional supplements, such as vitamin D, omega-3 fatty acids, and antioxidants, may provide adjunctive benefits in selected patients; however, their use should be individualized and considered as a complement rather than an alternative to comprehensive lifestyle modification. [14–16]

Dietary Interventions and Reproductive Outcomes in PCOS

Increasing evidence indicates that dietary interventions may positively influence reproductive function in women with polycystic ovary syndrome. Serum anti-Müllerian hormone (AMH) levels, which are typically elevated in PCOS and correlate with hyperandrogenism and oligo-anovulation, have been shown to decline more rapidly following dietary modification,

suggesting a potential improvement in ovarian function. Adherence to dietary interventions, particularly low-carbohydrate and calorie-restricted dietary patterns, has been associated with improved menstrual regularity, reduced androgen levels, and increased pregnancy rates. Importantly, reproductive benefits appear to be more pronounced with sustained dietary adherence and longer intervention duration. When combined with physical activity, dietary changes further improve ovulatory function and reproductive outcomes, highlighting the role of integrated lifestyle interventions in improving fertility-related parameters in women with PCOS. [8,17]

Physical Activity as a Core Component of Lifestyle Modification

Regular physical activity is an essential component of lifestyle modification in women with polycystic ovary syndrome and should be routinely integrated into clinical care. Both aerobic and resistance exercise improve insulin sensitivity, reduce body fat and favorably modify cardiometabolic risk, with additional benefits for menstrual regularity, ovulatory function and psychological well-being. Current international guidelines recommend at least 150 minutes per week of moderate-intensity aerobic activity (e.g. brisk walking or cycling) or 75 minutes per week of vigorous-intensity exercise, combined with muscle-strengthening activities on at least two non-consecutive days per week. For modest weight loss and prevention of weight regain, higher activity volumes (up to 250 minutes per week of moderate-intensity exercise or equivalent) are associated with greater metabolic benefit. Importantly, reducing sedentary behavior and adapting physical activity prescriptions to individual capabilities, lifestyle patterns, and cultural context are key determinants of long-term adherence and clinical effectiveness in women with PCOS. [1,8,15]

Pharmacological Treatment of PCOS: Established Options and Emerging Therapies

Role of Pharmacotherapy in PCOS Management

Pharmacological treatment is considered a complementary approach to lifestyle modification and should be selected individually based on the patient's predominant symptoms, reproductive goals and metabolic profile. [1] The primary aims of pharmacotherapy in PCOS include reduction of hyperandrogenism, regulation of the menstrual cycle, restoration of ovulation and fertility, as well as prevention and treatment of metabolic complications. [2]

Established Pharmacological Options

Metformin as an Insulin-Sensitising Agent

Metformin is one of the most commonly used insulin-sensitising drugs in the treatment of polycystic ovary syndrome. Originally introduced as a first-line therapy for type 2 diabetes mellitus, it has been used in PCOS management since the 1990s. Its clinical role derives from its beneficial effects on insulin resistance, hyperandrogenism and ovulatory dysfunction, combined with a well-documented safety profile and low cost. Metformin improves tissue insulin sensitivity primarily by reducing hepatic glucose production and modulating metabolic pathways, which secondarily leads to decreased circulating insulin and androgen concentrations and promotes normalization of ovarian function. Additionally, metformin may support modest weight loss through effects on appetite regulation and lipid metabolism.

Although lifestyle modification remains the recommended first-line intervention in PCOS, its effectiveness may be limited by suboptimal adherence. This provides a rationale for combination therapy with metformin, particularly in women with pronounced insulin resistance or obesity. Available evidence suggests that combined lifestyle and metformin therapy may result in greater improvements in metabolic parameters and menstrual regularity compared with lifestyle modification alone, while effects on clinical manifestations of hyperandrogenism remain moderate. Treatment response appears to depend on PCOS phenotype and the severity of underlying metabolic disturbances. [1,10]

Combined Oral Contraceptives (COCs)

Combined oral contraceptives are generally considered when lifestyle modification alone fails to achieve adequate symptom control in women with PCOS. Among available pharmacological options, COCs have demonstrated efficacy in regulating menstrual cycles and improving clinical features of hyperandrogenism, such as hirsutism and acne, with greater effectiveness than progestogen-only preparations. Their therapeutic effects are mediated through suppression of luteinising hormone secretion, increased hepatic production of sex hormone-binding globulin, and reduced androgen action at both ovarian and peripheral levels.

No specific oestrogen–progestogen combination has been shown to be superior; therefore, contraceptive choice should be guided by patient preferences and minimisation of adverse effects. However, COCs may negatively influence insulin sensitivity and lipid metabolism, and their use is not recommended in women with metabolic syndrome or severe insulin resistance. In accordance with World Health Organization recommendations, formulations containing higher oestrogen doses and cyproterone acetate should be reserved as second-line therapy for severe acne or hirsutism due to an increased risk of thromboembolic events. Careful individual risk–benefit assessment is therefore essential when considering COCs in the management of PCOS. [1,2,11]

Antiandrogen Therapy

In cases of intolerance or contraindications to combined oral contraceptives, and provided that effective contraception is ensured, antiandrogen therapy may be considered for the treatment of hyperandrogenic symptoms in women with PCOS. Antiandrogens act by inhibiting androgen synthesis, metabolism, or activity at the level of target tissues, contributing to improvements in hirsutism and androgenic alopecia. Due to their potential teratogenic effects, these agents should be prescribed exclusively to women who are not planning pregnancy and always in combination with reliable contraception.

According to current recommendations, antiandrogens in combination with COCs should be considered only in women with hirsutism who have not achieved sufficient improvement after at least six months of COC therapy and cosmetic treatments. It should be emphasized that there is currently insufficient evidence to support clear recommendations regarding specific antiandrogen agents or dosing regimens in PCOS, which limits their routine use and necessitates individualized clinical assessment. [1,18]

Pharmacological Ovulation Induction

In women with PCOS and anovulatory infertility, pharmacological ovulation induction represents a key therapeutic strategy. Agents commonly used for this purpose include clomiphene citrate and letrozole. According to current international guidelines, letrozole is recommended as the first-line pharmacological treatment in women with PCOS without additional infertility factors, due to its superior effectiveness in improving ovulation, pregnancy,

and live birth rates. Compared with clomiphene citrate, letrozole is also associated with a lower risk of multiple pregnancy.

In women who fail first-line oral ovulation induction therapy, gonadotrophins may be considered. However, due to the high number of antral follicles in women with PCOS and the associated increased risk of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancy, current recommendations emphasize the use of low-dose step-up regimens. [1,12]

Emerging evidence suggests that adjunctive therapies, such as dexamethasone combined with clomiphene citrate, may further improve ovulation and pregnancy rates by reducing ovarian androgen levels and enhancing follicular responsiveness. Nevertheless, high-quality randomized controlled trials are required to confirm efficacy, establish optimal dosing, and assess long-term safety. [19]

Emerging Therapies in PCOS

GLP-1 Receptor Agonists

Obesity and insulin resistance play a central role in the pathophysiology and clinical expression of polycystic ovary syndrome, with excess body weight being associated with adverse metabolic profiles, hyperandrogenism, menstrual dysfunction and prolonged time to pregnancy. Although lifestyle modification remains the recommended first-line intervention in obese women with PCOS, long-term success is limited, and many patients remain obese despite structured dietary and physical activity programs. Traditional insulin-sensitising agents, such as metformin, induce only modest weight reduction, which has led to increasing interest in incretin-based therapies.

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), originally developed for the treatment of type 2 diabetes mellitus, promote weight loss through appetite suppression, delayed gastric emptying and reduced energy intake. These agents have demonstrated clinically meaningful metabolic benefits in women with overweight or obesity and PCOS. [4,20–22]

Early clinical evidence supporting the use of GLP-1 RAs in PCOS largely originates from studies involving liraglutide, often administered in combination with metformin, showing significant weight loss and improvements in metabolic and androgen parameters, albeit with heterogeneous effects on insulin resistance and menstrual cyclicity. More recently, semaglutide

has emerged as a potentially more potent option. In obese women with classic PCOS phenotypes unresponsive to lifestyle interventions, low-dose semaglutide administered once weekly resulted in substantial and sustained reductions in body weight and BMI, with nearly 80% of patients achieving clinically significant weight loss. These improvements were accompanied by marked reductions in insulin resistance indices and normalization of fasting glucose levels, even among individuals who did not meet predefined weight-loss response thresholds. Extended treatment was also associated with improved menstrual regularity in the majority of responders and a low incidence of adverse effects, suggesting a favourable risk–benefit profile compared with earlier pharmacological strategies. [4,20,21]

Beyond weight reduction, GLP-1 RAs may exert broader endocrine and reproductive effects in PCOS through improvements in insulin sensitivity, attenuation of chronic low-grade inflammation and potentially direct ovarian actions, as GLP-1 receptors are expressed in ovarian tissue. Reductions in visceral adiposity—a key determinant of metabolic risk in PCOS—have also been observed, including in women without overt obesity. Combination therapy with GLP-1 RAs and metformin appears particularly promising, with emerging data indicating superior effects on menstrual regularity, ovulation rates, and hyperandrogenism compared with monotherapy. Nevertheless, weight regain following treatment discontinuation, limited long-term safety data in non-diabetic populations, and substantial interindividual variability in treatment response highlight the need for personalized therapeutic strategies. Future research should aim to identify PCOS phenotypes most likely to benefit from GLP-1 RA therapy, clarify optimal dosing and treatment duration, and explore next-generation incretin-based agents, such as dual GLP-1/GIP receptor agonists, as potential additions to PCOS management algorithms. [13,21–24]

Inositol Supplementation

Inositol, in its various forms (myo-inositol and D-chiro-inositol), is widely used as a dietary supplement in women with PCOS due to its potential insulin-sensitising properties and possible effects on ovarian steroidogenesis. Despite substantial patient interest, current international guidelines classify inositol as an experimental therapy, citing limited and inconsistent evidence regarding its clinical efficacy. A high-quality systematic review and meta-analysis underpinning the 2023 recommendations demonstrated inconclusive results, with metformin remaining superior in improving key clinical parameters such as waist-to-hip ratio and hirsutism. Although some studies suggest potential metabolic or ovulatory benefits in selected PCOS

phenotypes, further well-designed clinical trials, standardized dosing regimens, and clearer identification of responder subgroups are required before inositol can be routinely recommended. [1,25,26]

Modulation of Gut Microbiota: Polyphenols and Probiotics

Growing evidence indicates that gut microbiota dysbiosis constitutes an important component of PCOS pathophysiology, contributing to insulin resistance, chronic low-grade inflammation, and metabolic and hormonal disturbances. Studies in women with PCOS and in animal models have demonstrated significant differences in gut microbial composition compared with healthy populations. In this context, polyphenols—natural plant secondary metabolites such as flavonoids, stilbenes, and phenolic acids found in fruits, vegetables, tea, and grapes—have attracted attention due to their potential prebiotic properties. Polyphenols may modulate gut microbiota composition by promoting the growth of beneficial bacterial strains (e.g. Lactobacillus and Bifidobacterium) and reducing inflammatory activity.

In parallel, probiotics have been investigated for their potential to improve lipid profiles, inflammatory markers, and selected hormonal parameters, including reductions in free androgen index and normalization of sex hormone-binding globulin levels. Some data also suggest effects on the gut–brain–ovary axis through increased production of short-chain fatty acids and modulation of the LH/FSH ratio. Despite promising preliminary findings, both polyphenols and probiotics remain adjunctive, experimental therapies. Considerable heterogeneity in probiotic strains, doses, and treatment protocols underscores the need for further well-designed clinical trials before these approaches can be incorporated into standard PCOS management. [5,27,28]

Discussion

The management of polycystic ovary syndrome requires an integrated, long-term approach that reflects its heterogeneous presentation and multifactorial pathophysiology. Evidence summarized in this review supports lifestyle modification as the cornerstone of PCOS management across phenotypes, with beneficial effects on metabolic health, hormonal balance, and reproductive outcomes. However, variable response and limited adherence in routine practice justify the use of adjunctive pharmacotherapy tailored to individual needs.[6]

Pharmacological treatment should be considered complementary to lifestyle interventions rather than a standalone strategy. Metformin remains a well-established option, particularly in women with insulin resistance or obesity, improving metabolic parameters and menstrual regularity, although its impact on clinical manifestations of hyperandrogenism appears limited. In contrast, combined oral contraceptives are effective for cycle regulation and symptom control of androgen excess, including acne and hirsutism, but require careful risk–benefit assessment in women with increased cardiometabolic risk. [2,10,11]

Emerging therapies, especially GLP-1 receptor agonists, may expand treatment options for women with obesity-related PCOS who do not achieve sufficient results with lifestyle modification alone. Beyond weight reduction, these agents may provide broader metabolic benefits; however, limited long-term data and variability in treatment response highlight the importance of individualized selection and monitoring. [4]

Adjunctive approaches such as inositol supplementation and gut microbiota modulation are of growing interest, but current evidence remains inconsistent and insufficient for routine recommendation. [1,5,25,27,28] Overall, combining lifestyle-based strategies with appropriately selected pharmacotherapy, supported by patient education and long-term follow-up, appears essential to optimize metabolic, reproductive, and quality-of-life outcomes in women with PCOS.

Implications for Patient Education and Long-Term Management

Effective management of polycystic ovary syndrome requires a long-term, individualized approach and active patient engagement in the therapeutic process. As PCOS is a chronic and heterogeneous condition, patient education should emphasize that symptoms and priorities may change across the lifespan, and management often requires ongoing adjustment rather than a single, short-term intervention. Education should focus not only on the reproductive aspects of PCOS, but also on the long-term metabolic and cardiovascular risks, including insulin resistance, dyslipidaemia, weight gain, and potential progression to type 2 diabetes. In this context, lifestyle modification should be presented as the foundation of treatment regardless of pharmacological strategies, with particular attention to sustainable dietary habits, regular physical activity, reduction of sedentary time, sleep quality, and stress management.

Enhancing health literacy and supporting self-management skills may improve adherence and treatment outcomes. This includes setting realistic and achievable therapeutic goals, addressing barriers to lifestyle implementation (e.g. time constraints, low motivation, psychosocial burden), and promoting gradual, measurable changes rather than strict or short-lived regimens. Incorporating patient preferences—including reproductive plans, symptom burden (e.g. acne, hirsutism), and expectations regarding weight management—into shared decision-making may increase satisfaction and long-term engagement. Importantly, effective counselling should also address the role of regular follow-up and monitoring of metabolic and reproductive parameters, enabling early identification of risk factors and timely modification of therapy. Therefore, empowering patients through structured education, behavioural support, and individualized long-term care remains a key determinant of successful PCOS management and improved quality of life.

Conclusions

Polycystic ovary syndrome is a chronic condition requiring individualized, long-term management focused on both reproductive and cardiometabolic health. Lifestyle modification—particularly structured physical activity and dietary strategies—should remain the foundation of care, while pharmacological interventions may be introduced according to symptom profile and patient priorities. Emerging therapies such as GLP-1 receptor agonists show promising metabolic benefits in selected patients, although further research is needed to clarify long-term safety and optimal treatment pathways. Patient education and shared decision-making are essential to support adherence, improve quality of life, and enhance long-term outcomes in women with PCOS.

Disclosure:

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AI

AI was utilized for two specific purposes in this research. Text analysis of clinical reasoning narratives to identify linguistic patterns associated with specific logical fallacies. Assistance in refining the academic English language of the manuscript, ensuring clarity, consistency, and adherence to scientific writing standards. AI were used for additional linguistic refinement of the research manuscript, ensuring proper English grammar, style, and clarity in the presentation of results. It is important to emphasize that all AI tools were used strictly as assistive instruments under human supervision. The final interpretation of results, classification of errors, and conclusions were determined by human experts in clinical medicine and formal logic. The AI tools served primarily to enhance efficiency in data processing, pattern recognition, and linguistic refinement, rather than replacing human judgment in the analytical process.

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