



# A Comprehensive Review of Treatment Options for Polycystic Ovary Syndrome (PCOS)

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## KEYWORDS

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## ABSTRACT:

Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder that affects approximately 6% to 20% of women of reproductive age, depending on the diagnostic criteria used—namely, the National Institutes of Health (NIH), Rotterdam, and Androgen Excess and PCOS Society (AE-PCOS) definitions (Teede et al., 2018). It is characterized by a triad of hyperandrogenism, chronic anovulation, and polycystic ovarian morphology. Beyond reproductive complications, PCOS is closely associated with metabolic disturbances including insulin resistance, type 2 diabetes mellitus, dyslipidemia, obesity, and increased cardiovascular morbidity (Legro et al., 2013; Azziz et al., 2016). These diverse manifestations highlight the need for individualized, multidisciplinary treatment strategies.

Currently, the therapeutic landscape of PCOS includes lifestyle modification, pharmacologic interventions, surgical procedures, and a growing body of evidence supporting integrative and emerging therapies. Lifestyle changes, particularly involving diet and exercise, remain the first-line intervention for overweight and obese women with PCOS, demonstrating benefits across reproductive and metabolic domains (Moran et al., 2011). Pharmacologic options range from hormonal contraceptives to insulin sensitizers and ovulation induction agents such as letrozole, which has emerged as a first-line therapy for infertility in PCOS (Legro et al., 2014). For clomiphene-resistant cases, laparoscopic ovarian drilling remains a surgical alternative. Moreover, novel therapies including glucagon-like peptide-1 (GLP-1) receptor agonists, myo-inositol, and N-acetylcysteine are being explored for their dual reproductive and metabolic benefits (Genazzani et al., 2018).

This review synthesizes current evidence on the treatment modalities for PCOS, providing clinicians with a comprehensive understanding of therapeutic approaches tailored to specific clinical goals—whether targeting ovulatory function, hyperandrogenic symptoms, or metabolic risks. A nuanced approach to PCOS management is critical for optimizing both short-term outcomes and long-term health in affected women.

## 1. Introduction

Polycystic Ovary Syndrome (PCOS) is recognized as one of the most prevalent endocrine disorders affecting women of reproductive age, with an estimated global prevalence ranging from 6% to 20% based on the diagnostic criteria used—namely, the National Institutes of Health (NIH) 1990 criteria, the Rotterdam 2003 criteria, and the Androgen Excess and PCOS Society (AE-PCOS) 2006 criteria (Teede et al., 2018). The Rotterdam criteria, which are the most widely used, require the presence of at least two of the following three features for diagnosis: oligo- or anovulation, clinical or biochemical signs of hyperandrogenism, and polycystic ovaries on ultrasound (Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group, 2004).

PCOS is a heterogeneous and multifactorial condition encompassing reproductive, metabolic, dermatologic, and psychological disturbances. The most common clinical manifestations include menstrual irregularities, hirsutism, acne, alopecia, and subfertility. Biochemically, elevated serum androgen levels and insulin resistance are frequently observed. Additionally, polycystic ovarian morphology is evident in many cases on ultrasonographic evaluation (Azziz et al., 2016). Importantly, insulin resistance is estimated to affect up to 70% of women with PCOS, contributing to a heightened risk for type 2 diabetes mellitus, dyslipidemia, non-alcoholic fatty liver disease, and cardiovascular disease (Moran et al., 2010; Dunaif, 2012).



The psychosocial burden of PCOS is equally significant. Studies have documented a higher prevalence of anxiety, depression, body image dissatisfaction, and reduced quality of life among affected individuals, indicating the need for integrated mental health support in management plans (Cooney et al., 2017). Furthermore, the syndrome can present differently across racial, ethnic, and geographic populations, complicating both diagnosis and treatment (Lizneva et al., 2016). This variability, combined with a lack of universal diagnostic consensus, contributes to the continued underdiagnosis and undertreatment of PCOS, particularly in resource-limited healthcare settings.

Despite advances in research, the etiology of PCOS remains incompletely understood. It is believed to involve complex interactions between genetic, environmental, and intrauterine factors, leading to disruptions in the hypothalamic-pituitary-ovarian (HPO) axis, insulin signaling pathways, and androgen biosynthesis (Goodarzi et al., 2011). These diverse pathophysiological mechanisms underscore the importance of personalized and multifactorial treatment approaches.

This review aims to synthesize the current landscape of treatment modalities for PCOS, including lifestyle interventions, pharmacologic therapies, surgical options, and emerging alternatives. By examining the latest clinical evidence and therapeutic strategies, this paper seeks to guide healthcare providers in optimizing care for the various PCOS phenotypes and to highlight gaps requiring further investigation.

## 2. Literature Review

### 2.1. Individualised Treatment Approaches Based on PCOS Phenotypes

Recent literature underscores the importance of personalising treatment due to the heterogeneous nature of PCOS. Different phenotypes—ranging from hyperandrogenic to reproductive and metabolic variants—exhibit distinct clinical and biochemical profiles that influence treatment response (Teede et al., 2018). Letrozole and clomiphene citrate remain mainstays in ovulation induction for anovulatory infertility, while insulin sensitizers such as metformin are preferred for metabolic phenotypes (Legro et al., 2014; Palomba et al., 2021).

### 2.2. Lifestyle Modifications as First-Line Therapy

Lifestyle modification, including dietary changes, regular exercise, and behavioural interventions, is universally recommended as first-line therapy for women with PCOS, especially those who are overweight or obese. A meta-analysis by Moran et al. (2011) demonstrated that lifestyle interventions improve reproductive outcomes, insulin sensitivity, and lipid profiles. A recent systematic review by Behboudi-Gandevani et al. (2023) also affirmed that lifestyle-based strategies are superior to placebo in restoring menstrual cyclicity and reducing androgen levels.

Additionally, novel non-pharmacological interventions like electroacupuncture combined with physical activity and calorie control have shown promising effects in reducing serum testosterone levels and improving insulin resistance (Ma et al., 2024).

### 2.3. Pharmacological Advances: Insulin Sensitizers and Ovulation Induction

Pharmacological treatment of PCOS has evolved significantly over the past decade. Metformin, a well-established insulin sensitizer, has shown efficacy in improving menstrual regularity, reducing androgen levels, and enhancing the effects of ovulation induction agents (Lord et al., 2003; Tso et al., 2021). Letrozole has now surpassed clomiphene citrate as the first-line ovulation induction agent due to its higher rates of ovulation and live births, as demonstrated in a pivotal multicentre trial (Legro et al., 2014).

Emerging evidence also supports the role of glucagon-like peptide-1 (GLP-1) receptor agonists, such as liraglutide, in achieving significant weight loss and improving insulin sensitivity in obese women with PCOS (Elkind-Hirsch et al., 2022). These agents also contribute to the reduction of serum androgen levels, suggesting a dual benefit in PCOS management.

### 2.4. Novel and Complementary Therapies: Inositols, Anti-Androgens, and GLP-1 Agonists

The use of inositol isomers—particularly myo-inositol and D-chiro-inositol—has gained traction as a safe and effective treatment for improving ovulatory function and metabolic outcomes in women with PCOS. A meta-analysis by Unfer et al. (2021) concluded that inositols



are effective in improving ovulation, reducing serum insulin, and restoring menstrual cycles.

Anti-androgens such as spironolactone and finasteride are employed to treat hirsutism and acne; however, these are typically used alongside oral contraceptives to mitigate teratogenic risk (Futterweit and Shapiro, 2023).

### 2.5. Persistent Gaps in PCOS Treatment Research

Despite advancements, there are significant gaps in the literature regarding lean PCOS, adolescent management, and long-term cardiovascular risk. Lean women with PCOS are frequently underdiagnosed, despite having comparable risks of insulin resistance and cardiovascular complications (Diamanti-Kandarakis et al., 2007; Lim et al., 2019). Adolescents with PCOS often experience diagnostic delays, and there is limited consensus on appropriate long-term treatment protocols for this group (Ibáñez et al., 2020).

Furthermore, long-term safety and comparative efficacy data across different pharmacologic treatments remain limited, especially with regard to cardiovascular outcomes, cancer risks, and quality-of-life metrics.

### 2.6. Integrative and Complementary Medicine

Integrative medicine approaches, including acupuncture, herbal remedies, and mind-body interventions (MBIs) such as yoga and meditation, are gaining interest for symptom relief in PCOS. A recent meta-analysis found that acupuncture can enhance ovulation and reduce hyperandrogenism (Lim et al., 2021). Mind-body practices have also been linked to improvements in anxiety, depression, and self-esteem among PCOS patients (Zheng et al., 2024). However, the quality of evidence remains variable, necessitating further high-quality randomised controlled trials.

## 3. Treatment Options for PCOS

### 3.1. Lifestyle Interventions

#### Dietary Management

Lifestyle modification is considered the first-line treatment, particularly for overweight or obese individuals with PCOS (Teede et al., 2018). Low glycaemic index (GI) diets, calorie-restricted plans, and Mediterranean dietary patterns have been shown to improve insulin sensitivity and reduce serum androgen levels. The Mediterranean diet, rich in monounsaturated

fats, fibre, and antioxidants, is associated with reductions in inflammation and improved endocrine profiles in women with PCOS (Barrea et al., 2020).

#### Exercise

Regular aerobic and resistance exercise, typically at least 150 minutes per week, enhances insulin sensitivity and supports weight reduction. Exercise alone or combined with dietary changes can improve ovulation, reduce hyperandrogenism, and enhance psychological well-being (Harrison et al., 2012; Patel et al., 2021).

#### Behavioural Therapy

Cognitive-behavioural therapy (CBT) has shown effectiveness in addressing psychological comorbidities common in PCOS, such as depression, anxiety, and body image concerns. Interventions that combine CBT with lifestyle counselling have been associated with improved adherence and quality of life outcomes (Dokras et al., 2018; Bazarganipour et al., 2020).

### 3.2. Pharmacological Treatments

#### Hormonal Therapies

Combined oral contraceptives (COCs), typically containing ethinyl estradiol and a progestin (e.g., drospirenone), are recommended for the management of menstrual irregularities, acne, and hirsutism. COCs suppress luteinizing hormone (LH) and decrease ovarian androgen production (Azziz et al., 2016). Progestins, when used cyclically or continuously, protect against endometrial hyperplasia in anovulatory women who are not actively pursuing pregnancy (ACOG, 2018).

#### Insulin Sensitisers

Metformin is widely used to improve insulin resistance, lower serum insulin and androgen levels, and promote menstrual regularity in women with PCOS, especially those with impaired glucose tolerance (Morley et al., 2017). Inositols, particularly myo-inositol and D-chiro-inositol, are emerging as effective agents in improving insulin sensitivity and restoring ovulation, with a favourable safety profile (Unfer et al., 2021).

#### Ovulation Induction

Letrozole, an aromatase inhibitor, is now the first-line pharmacological treatment for ovulation induction in women with PCOS due to higher live birth rates and



improved endometrial receptivity compared to clomiphene citrate (Legro et al., 2014). Clomiphene citrate remains effective in approximately 75–80% of cases, though some women are resistant to its effects. Gonadotropins are used as second-line agents in women who do not respond to oral ovulation inducers but require close monitoring to reduce the risk of ovarian hyperstimulation syndrome (Brown et al., 2016).

### Anti-Androgens

Agents such as spironolactone, flutamide, and finasteride are used to manage clinical hyperandrogenism (e.g., hirsutism). These treatments should be combined with reliable contraception due to their teratogenic potential (Carmina et al., 2020).

### 3.3. Surgical Options

Laparoscopic ovarian drilling (LOD) is a minimally invasive surgical procedure indicated for clomiphene-resistant PCOS. It works by reducing ovarian androgen production and may restore spontaneous ovulation (Amer et al., 2017). However, LOD carries risks such as pelvic adhesions and possible reduction in ovarian reserve.

### 3.4. Emerging Therapies

#### GLP-1 Receptor Agonists

Glucagon-like peptide-1 (GLP-1) receptor agonists such as liraglutide and semaglutide have shown benefits in promoting weight loss, improving insulin sensitivity, and potentially restoring ovulation in obese women with PCOS (Elkind-Hirsch et al., 2022). These agents are increasingly being studied for dual metabolic and reproductive benefits.

#### Herbal Medicine and Supplements

Herbal supplements such as cinnamon, berberine, and N-acetylcysteine (NAC) have demonstrated potential for improving insulin resistance and menstrual regularity. Berberine, in particular, may improve glucose metabolism and androgen levels comparable to metformin in some studies (Wei et al., 2012; Oulad Saheb Madarek et al., 2020). However, high-quality trials are needed to confirm efficacy and safety.

### Bariatric Surgery

Bariatric surgery is reserved for morbidly obese women with PCOS who have not responded to conventional therapies. It leads to significant improvements in weight, ovulatory function, insulin sensitivity, and even pregnancy rates (Skubleny et al., 2016).

### 4. Conclusion

Polycystic Ovary Syndrome (PCOS) presents a significant clinical and public health challenge due to its complex pathophysiology, wide-ranging clinical manifestations, and lifelong health implications. Its multifactorial nature—encompassing reproductive, metabolic, dermatological, and psychological domains—necessitates a multifaceted and patient-centered management approach. No single treatment fits all individuals with PCOS; therefore, clinical decision-making must be guided by the patient's phenotype, symptom profile, reproductive intentions, and cardiometabolic risk factors.

Lifestyle modification, including dietary changes, physical activity, and behavioural interventions, remains the cornerstone of PCOS management, particularly for overweight and obese women. Even modest weight loss has been associated with improved ovulatory function, reduced hyperandrogenism, and enhanced insulin sensitivity. These interventions also offer the added benefit of addressing psychological comorbidities, which are frequently under-recognized in PCOS care.

Pharmacologic therapies play a crucial role in symptom control and fertility restoration. Combined oral contraceptives are effective in managing menstrual dysfunction and hyperandrogenic symptoms, while insulin sensitizers such as metformin and inositols target underlying metabolic dysfunction. For women seeking fertility, letrozole has emerged as the preferred first-line agent for ovulation induction due to its superior efficacy over clomiphene citrate. In resistant cases, second-line agents such as gonadotropins or laparoscopic ovarian drilling may be considered.

Emerging therapies, including GLP-1 receptor agonists and certain nutraceuticals like berberine and N-acetylcysteine, hold promise for integrated reproductive and metabolic benefits. However, these agents require further validation through high-quality randomized



controlled trials to determine their long-term safety and efficacy.

Despite the expanding treatment arsenal, there remain significant gaps in the literature. Long-term outcome data—particularly regarding cardiovascular risk reduction, cancer risk, and quality of life—are lacking. Lean PCOS and adolescent populations are often underrepresented in clinical trials, despite facing unique diagnostic and therapeutic challenges. Moreover, there is a pressing need to integrate precision medicine into PCOS management, using biomarkers, genomics, and phenotype-driven models to tailor interventions.

In conclusion, the optimal management of PCOS should be holistic, evidence-based, and individualized. Clinicians must adopt an interdisciplinary approach, combining lifestyle, pharmacological, surgical, and emerging therapies to address the multifaceted needs of women with PCOS. Future research should prioritize long-term outcomes, adolescent care, and personalized treatment pathways to improve clinical efficacy and patient satisfaction.

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