

# Diagnosis and Management of Polycystic Ovary Syndrome in Adolescents

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**abstract** Polycystic ovary syndrome (PCOS) is a common female reproductive disorder that often manifests during adolescence and is associated with disruptions in health-related quality of life. Prompt evaluation and clinical support after diagnosis may prevent associated complications and optimize overall health management. This article incorporates the most recent evidence and consensus guidelines to provide an updated review of the pathogenesis, clinical presentation, diagnostic evaluation, and management strategies for adolescents with this complex condition. We will review the recent international guidelines on PCOS; because the diagnosis of PCOS remains controversial, management of this condition is inconsistent. In 2019, PCOS remains a common, yet neglected, condition, in part, because of the lack of agreement around both diagnosis and management.

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Polycystic ovary syndrome (PCOS) is a common, complex, and heterogeneous familial disorder that affects 5% to 10% of females of reproductive age and is seen across race and ethnicity, country of origin, and other sociodemographic backgrounds.<sup>1</sup> PCOS has become an increasingly important adolescent reproductive health diagnosis, given the significant reductions in health-related quality of life observed among affected patients<sup>2,3</sup>; potential long-term cardiovascular, metabolic, and reproductive health outcomes<sup>4</sup>; and annual clinical management costs that exceed \$4 billion annually.<sup>5</sup> In this article, we will highlight current evidence, consensus, and controversy among clinicians regarding the pathogenesis, clinical presentation, diagnostic evaluation, and management of adolescents with PCOS.

Although the etiology of PCOS remains unclear despite decades of both basic science and clinical research, multiple systems and factors including ovarian function, steroidogenesis, metabolism, neuroendocrinology, genetic, and environmental issues have been identified as contributing to the pathophysiology.<sup>6</sup> Normally, there is a highly functional and coordinated process through which follicular development occurs with each menstrual cycle. In adolescents with PCOS, there is an imbalance, resulting from an exaggerated luteinizing hormone (LH) response driving androgen production<sup>7</sup> and inadequate follicle-stimulating hormone (FSH), resulting in inadequate conversion of androgens to estradiol, with follicular arrest.<sup>8</sup> Anti-Müllerian hormone (AMH) plays a key role in regulating the transitional development of follicles, leading to a dominant follicle. However, in adolescents with PCOS, follicular growth is arrested, leading to the many small follicles stemming from anovulation.<sup>9</sup> The phenotypic

expression of this aberration is revealed in ovarian theca cells through increased expression of cytochrome P450 enzymatic activity (through the gene CYP17A1 or p450c17).<sup>10</sup>

Adolescents with PCOS often demonstrate both insulin resistance (IR) and hyperandrogenism. Associated manifestations may be exacerbated in adolescents who are overweight or obese, which can complicate management of PCOS.<sup>11,12</sup> The temporary decline in insulin sensitivity observed during puberty may be a critical moment in the development of IR and hyperinsulinemia in patients predisposed to developing PCOS. The changes in insulin and androgen metabolism appear to be interrelated, as increases in androgens reduce insulin sensitivity and insulin elevations may potentiate androgen secretion in fat tissue.<sup>13-15</sup> Insulin also augments the ovarian response to LH and enhances dysregulated LH secretion from the pituitary gland.

## DIAGNOSIS

### Clinical Presentation

Patients seek evaluation when the absence of or irregularity of menses becomes worrisome and they develop physical findings, such as acne or hirsutism. These physical manifestations, for which home treatments are no longer effective, are typically of great concern to the adolescent patient who is in a period of life when a semblance of normalcy with peers is critically important. They may also have significant concerns about sexual health and their future fertility.<sup>14</sup> Attention to the details of their sexual and reproductive health histories and liberal use of office-based testing to assess for pregnancy in the absence of menses can prevent the need for a costly and unnecessary diagnostic workup. Nonetheless, the PCOS evaluation becomes an important

touch point with these patients who must be carefully managed with thoughtfulness and closely followed to ensure the patient is successful with its clinical management.

The associated clinical findings of PCOS usually begin to manifest during adolescence with the presentation evolving into a clinical picture that can vary considerably. The reproductive dysfunction presents with a range of menstrual disorders, including amenorrhea, oligomenorrhea, and abnormal uterine bleeding associated with anovulation or oligoovulation. Patients may also present with ovarian enlargement, endometrial hyperplasia, and infertility.

Research has demonstrated that up to 80% of patients with PCOS will exhibit clinical or laboratory evidence of androgen excess. Manifestations include hirsutism, acne, male-pattern baldness or alopecia, and elevated androgens (eg, total testosterone, free testosterone, dehydroepiandrosterone sulfate, or androstenedione).<sup>15,16</sup> Hirsutism is common among affected adolescents and women, but often patients have been using home remedies or professional services that range from temporary (eg, tweezing, chemical depilatory agents, waxing) to permanent (eg, electrolysis, thermolysis, laser) hair removal techniques. Although acne is a common presentation during adolescence, in combination with an evolving menstrual disorder, it may be a manifestation of androgen excess.<sup>17</sup> Clinical tools, such as the Ferriman-Gallwey scoring system,<sup>18</sup> have been used to document hirsutism for clinical management. However, in more recent work, authors suggest that patient-, nurse-, and pediatrician-rated hirsutism are highly variable.<sup>19</sup> Temporal recession and/or alopecia as a sign of hyperandrogenism is also important to document with tools such as the Ludwig visual score.<sup>20</sup> In an era of

electronic medical record documentation, use of images at baseline and during follow-up visits may be an objective way to assess the clinical impact of hyperandrogenism and the effectiveness of interim treatment over time. It is critically important to assess preconsultation hair removal or acne treatment being employed by the patient to thoroughly assess the impacts of hyperandrogenism when making the diagnosis and at each follow-up visit to ascertain the effectiveness of combined therapy, minimize side effects, and examine the burden of treatment on health-related quality of life.

### Clinical Guidelines

Given the heterogeneity of clinical findings observed in patients with PCOS, demonstrating engagement of multiple endocrine signaling networks as a manifestation of systems-level disease is critical. Several expert consensus meetings have been convened to generate evidence-based diagnostic criteria to facilitate a uniform approach to identifying and managing this disorder, which is characterized by both disordered menstrual cycles and the clinical symptoms of androgen excess. The multiple clinical guidelines that have been published over the years have led to confusion among clinicians who seek to care for these patients who present in a variety of ways. Most recently, a collaborative group under the International Consortium of Pediatric Endocrinology provided an update to the pathophysiology, diagnosis, and treatment of PCOS care specific to the management of adolescents with the disorder.<sup>6</sup> These recommendations outline the required clinical features and appear to follow most closely the 1990 National Institutes of Health guidelines,<sup>21</sup> which include irregular menses and/or oligomenorrhea and biochemical or clinical evidence of hyperandrogenism.<sup>6</sup> Optional factors include polycystic ovaries on

ultrasound and severe cystic acne. The consortium did not recommend obesity or biochemical (eg, IR or hyperinsulinemia) or clinical evidence (eg, acanthosis nigricans) of aberrant insulin metabolism; these clinical factors may be associated but are not sufficiently specific to PCOS to make the diagnosis.<sup>6</sup> AMH and testosterone-to-dihydrotestosterone ratios have emerged as potential diagnostic biomarkers for clinical use, given their association with follicular development and adverse phenotypes, respectively.<sup>22–25</sup> However, additional research is warranted to define their diagnostic potential in adolescents; therefore, they are not recommended in laboratory evaluation for these patients. The new guideline also stressed the point that a definitive diagnosis of PCOS cannot be made until 2 years postmenarche and, echoing earlier guidelines, other causes of hyperandrogenism are first ruled out (eg, nonclassic congenital adrenal hyperplasia, Cushing's syndrome, etc).<sup>7</sup>

Another recent international guideline on PCOS from the International PCOS Network is also worth consideration, which reviews the available evidence to support both diagnosis and management in both adolescents and women.<sup>20</sup> This guideline notes the evidence for both assessment and management of PCOS to be of low-to-moderate quality. They also recommend an increased focus on patient education, lifestyle modifications, emotional well-being, and quality of life as critical components of intervention. The guideline also asserts that the evidence supports allowing for only 1 year of menstrual irregularity postmenarche before becoming concerned about oligo- or anovulation. Importantly, this guideline allows for a patient to be "at risk for PCOS" with longitudinal follow-up as an acceptable alternative to making an early diagnosis.

However, clinicians can intervene medically with an oral contraceptive as first-line management after observance of hirsutism or alopecia, given the known impacts of each on health-related quality of life. Early intervention can serve as a preventive measure to avoid more severe cosmetic problems. For non-sexually active patients, a 3-month hormonal washout period can be undertaken to reassess hormonal status in patients who are uncertain about their diagnosis and want to determine if their menses will resume on their own.

## CLINICAL ASSESSMENT

### History and Physical Examination

As with all adolescent visits, a detailed, patient-centered interview is critical; this includes an assessment of present illness(es) focused on the patient's clinical symptoms, past medical history, reproductive health history (including details of puberty), menstrual history, social history (including sexual behaviors and pregnancy history), and contraceptive use.<sup>15</sup> The review of systems can be useful in determining the presence of symptoms that are consistent with PCOS (eg, weight, hair, or skin changes) and assessing for other disorders that may impact menstrual function (neck enlargement [thyromegaly], headaches, galactorrhea, weight changes, skin and/or nail changes). Use of prescription and over-the-counter medications and cosmetic procedures to reduce symptoms can also be assessed. Adolescents may not be as aware of family history; therefore, collection of key historical data from parents before engaging in alone time with the patient may be useful for completing the clinical story of a patient.

A comprehensive physical examination can be done that includes vital signs, anthropometric assessment, general appearance, skin

survey to detect alopecia, male-pattern baldness, acanthosis nigricans (Fig 1), acne, hirsutism (Fig 2), Tanner staging, examination of the external genitalia to assess for virilization (indicated by a clitoris glans width >5 mm), and bimanual examination, if tolerated, to assess for an ovarian mass.<sup>15,16</sup>

### Laboratory Evaluation

The goals of laboratory assessment are to support the diagnosis of PCOS to exclude other causes of menstrual irregularity and clinical hyperandrogenism and assess for associated clinical issues, such as diabetes and hyperlipidemia. Free and total testosterone (employing high-quality assays, such as liquid chromatography tandem mass spectrometry and extraction or chromatography)<sup>26</sup> and dehydroepiandrosterone sulfate are routinely measured to assess for the contribution of ovarian and adrenal androgens and consider the possibility of an adrenal or ovarian tumor. If late-onset congenital adrenal hyperplasia is suspected, a morning serum 17-hydroxyprogesterone can be obtained. A serum FSH can be measured to ensure that the ovary is functioning and assess for ovarian insufficiency. Given the aberrant changes in LH, this is often ordered to assess the ratio of LH to FSH. Although the LH-to-FSH ratio is often elevated in patients with PCOS, this



**FIGURE 1**  
Acanthosis nigricans in an adolescent with PCOS. (DermAtlas: Online Dermatology Image Library, with permission [Cohen, B (ed)], All rights reserved).



**FIGURE 2**  
Hirsutism in an adolescent with PCOS. (DermAtlas: Online Dermatology Image Library, with permission [Cohen, B (ed)], All rights reserved).

calculation cannot be used to make the diagnosis in isolation; many patients with the disorder will not have elevations, and the elevated ratio can be seen both in patients with PCOS and in those who are ovulating. As previously noted, AMH levels are associated with the anovulation and fertility issues observed in adult women with PCOS, but this promising biomarker is currently not recommended for diagnostic decision-making because guidelines for use have not been established for adolescents.<sup>24,26</sup>

Patients suspected of having PCOS can also be screened for thyroid disease (thyroxine and thyroid-stimulating hormone), hyperprolactinemia (prolactin), and metabolic abnormalities, such as type 2 diabetes mellitus (fasting glucose or hemoglobin A1c) and hyperlipidemia (fasting lipid profile). Patients with PCOS who are significantly obese and have profound chemical metabolic abnormalities may present with nonalcoholic fatty liver disease; therefore, liver function (aspartate aminotransferase, alanine aminotransferase) testing is warranted in this subgroup.<sup>6,15,16</sup>

Radiologic procedures, such as pelvic sonograms, to determine the presence of the classic ovarian morphology (increased ovarian volume with a thickened white capsule and multiple small 2–8-mm

follicles) are not recommended to diagnose PCOS in adolescents.<sup>26</sup> Although ultrasound findings have been shown to be supportive of the diagnosis in women, these findings are not specific to the disorder and the diagnosis can often be made without an ultrasound.<sup>25</sup> There is also significant overlap between normal adolescent and PCOS morphology. A liver ultrasound is warranted for the patient who is obese with evidence of nonalcoholic fatty liver disease.

### TREATMENT

Because PCOS in adolescence can have lifelong implications for metabolic and reproductive health, early treatment is critical, and the goals of therapy should be discussed with each patient.<sup>6,15,16</sup> These goals include decreasing the risk of endometrial cancer (for unopposed estrogen stimulation, which can lead to endometrial hyperplasia), managing irregular menses (oligomenorrhea and abnormal uterine bleeding), reducing hirsutism and acne, decreasing the risk for development of type 2 diabetes, reducing cardiovascular risks, improving quality of life, and preserving fertility. Affected adolescents have an increased prevalence of multiple metabolic derangements, each of which can present a target condition that merits treatment. Examples include markers for obesity, IR, dyslipidemia, and hypertension. Obesity is one of the most common findings in patients, with 40% to 80% of women with PCOS meeting criteria for being overweight or obese.<sup>26</sup> Obesity can lead to ovarian inflammation, reduced oocyte quality, and abnormal ovulatory patterns that can manifest as infertility. Although both metabolic and reproductive abnormalities are well characterized, there remain many questions regarding the best long-term management strategies for adolescents or women with this diagnosis.<sup>27,28</sup>

Lifestyle modifications, such as dietary changes, exercise, and weight loss, are first-line interventions for adolescents with PCOS<sup>27</sup> and are endorsed by the Endocrine Society's clinical practice guideline<sup>28</sup> as well as the recent international evidence-based guideline on PCOS.<sup>20</sup> This nonpharmacologic therapy is a critical first step for patients who are overweight or obese, which exacerbates the PCOS phenotype.<sup>29</sup> Weight loss as a sole maneuver can decrease androgen production,<sup>30</sup> improving insulin sensitivity and reducing cardiovascular risk. Lifestyle modifications, including a calorie-restricted diet and/or physical activity, has proven effective in altering the disease course of PCOS.<sup>26</sup> One small study of women with PCOS revealed that exercise markedly improved hyperlipidemia.<sup>31</sup> In another study, the authors examined the effectiveness of exercise and/or dietary interventions for affected adolescents and found beneficial effects of exercise for a range of metabolic, anthropometric, and cardiorespiratory fitness-related outcomes.<sup>32</sup> Subgroup analyses revealed the greatest improvements in participants who were overweight or obese, and more outcomes improved when interventions were supervised, aerobic in nature, or shorter in duration.

Estrogen and progestin combination therapy represent the first-line pharmacologic therapy for adolescents with PCOS, most commonly as a combined oral contraceptive (COC), with 20 to 35 µg of ethinyl estradiol.<sup>20,33</sup> This therapy has the potential to mitigate both hirsutism and acne. A combined transdermal patch and the vaginal ring are other options, but there is no evidence to suggest one delivery method to be superior to the others.<sup>31</sup> However, the transdermal patch is not recommended for girls or women whose weight is >90 kg. There have been some concerns raised about an

increased thrombotic risk with a combined patch, but these have not been substantiated across reports.<sup>34</sup> The combined preparations suppress the hypothalamic-pituitary ovarian axis and decrease ovarian and adrenal androgen production. As a result, unwanted hair growth improves in 50% to 70% of hirsute women treated with an oral COC, which represents the most effective therapy for management of hirsutism.<sup>14,28</sup> However, insulin sensitivity does not change.<sup>35</sup> Because there is often the common goal of treating hyperandrogenism and providing contraception for an adolescent, a COC can address both issues.

Antiandrogens can be helpful for severe cases of hirsutism, as an adjunct to a COC, especially when alopecia is present and if hirsutism has not improved after 6 months of a COC as monotherapy.<sup>20</sup> Many young women seek pharmacologic treatment because of the stigma associated with the male-pattern hair growth, even before a diagnosis of PCOS is made. Pediatricians can consider cultural and societal factors around the hirsutism and take into account not only the severity of the hirsutism but also the patient's perception of the severity when determining appropriate treatment.<sup>36</sup> Spironolactone is the most commonly prescribed androgen receptor blocker and can be used in combination with oral contraceptives because this agent can lead to irregular menses and potential teratogenicity (feminization of a male fetus).<sup>14</sup> The recommended dose is 50 to 200 mg/day in 1 to 2 divided doses.<sup>37</sup> Other options include cyproterone acetate, flutamide, and finasteride, but hepatotoxicity has emerged as a concern, and not all medications are available in the United States.

Systemic therapy can be augmented by topical and mechanical treatments for hirsutism (eg, electrolysis, laser

therapy, plucking, waxing, shaving, and bleaching to achieve the desired cosmetic result)<sup>1,15,38,39</sup> and topical therapies for acne. Eflornithine hydrochloride (13.9%) cream (which blocks the enzyme ornithine decarboxylase, needed for hair growth) is another option to lessen facial hirsutism and can augment the effects of laser therapy.<sup>15</sup> However, the benefits of this cream and other topical strategies can be outweighed by their side effects (eg, burning, folliculitis, etc).<sup>15,36</sup> For acne, topical retinoic acid and antibiotics can be helpful adjuncts to oral antibiotics, hormonal therapy, or antiandrogens.

Because IR is common in PCOS, insulin-sensitizing agents are among the most frequently studied agents. Metformin is a biguanide that acts to decrease hepatic glucose production and increase peripheral insulin sensitivity.<sup>28,40</sup> IR, important within the pathophysiology of PCOS, predisposes patients to metabolic dysfunction and increases the risk of type 2 diabetes mellitus. As an insulin-sensitizing agent, metformin has the potential to improve glycemic control and prevent or improve type 2 diabetes, as well as address problems, such as dyslipidemia, that stem from the IR; it has been endorsed by recent clinical guidelines.<sup>6,20</sup>

In a recent study, the authors compared metformin and N-acetylcysteine on clinical, metabolic, and hormonal parameters in women with PCOS.<sup>41</sup> Researchers studied 100 patients with PCOS who received metformin (1500 mg/day) or N-acetylcysteine (1800 mg/day) for 24 weeks. There was significant improvement in BMI, waist circumference, and waist-to-hip ratio in the N-acetylcysteine group, but no significant difference was found in weight reduction among the 2 groups. Markers of IR, including fasting insulin and the fasting glucose-to-insulin ratio, improved significantly after N-acetylcysteine, and a greater

reduction of total testosterone was seen. Enhanced improvement of the metabolic and hormonal profile was observed in the N-acetylcysteine group. Further study is needed, but because of potentially fewer side effects compared to metformin, this therapy may arise as a new option to consider over metformin in the treatment of PCOS.

Adolescents with PCOS often seek care regarding irregular menses, infertility, hirsutism, and acne. For hirsutism, viewed by many adolescents as a “cosmetic emergency,” COCs are a first-line therapy, as endorsed by recent guidelines.<sup>6,20</sup> More than 2 decades ago, we examined whether quality of life was compromised in young adolescents with PCOS.<sup>3</sup> We observed that scores on assessments of health-related quality of life were lower than healthy control subjects, and the issue that generated the most concern was infertility. Although adolescent specialists typically try to prevent pregnancy, it is important to acknowledge that concerns about infertility may be seen even in the young adolescent patient. The effect of this diagnosis on quality of life continues to be mentioned, including in recent clinical guidelines.<sup>6,20</sup>

Mood disturbances are common among adolescent girls with PCOS and have been the subject of recent research. The propensity for obesity and cosmetic concerns (eg, hirsutism, acne, etc) may lead to poor self-esteem and depression. In a recent pilot study, the authors examined mood disturbances as well as IR in adolescents and adult women with PCOS at baseline and after metformin therapy (1500 mg/day).<sup>42</sup> Nineteen adolescents ( $\leq 18$  years old) and 25 women ( $\geq 18$  years old) were enrolled and had their baseline and 90-day anthropometric data tracked as well as measurements of glucose, androgens, and lipids; IR was calculated by using the homeostasis

model assessment for IR. Anxiety and depression were measured by the Beck Anxiety Inventory and the Beck Depression Inventory-II (BDI-II). After 90 days of metformin treatment, both Beck Anxiety Inventory and BDI-II scores decreased, and indicators of IR and obesity were improved. The findings suggest that metformin can decrease IR and improve mood, both in adolescents and adults with PCOS. In another recent study, researchers explored the use of a psychological approach in caring for adolescents with this diagnosis.<sup>43</sup> The researchers examined the prevalence of coping and depression in adolescent girls with PCOS. Adolescent girls 13 to 18 years of age with this diagnosis completed questionnaires and answered interview questions regarding how they coped with their disease and depression. Adolescents perceived little control over many aspects of PCOS, with menstrual irregularities and the threat of infertility reported as the most stressful and least controllable aspects of PCOS. Lower control was a predictor of more significant depression among the participants. These results remind pediatricians to be aware of and screen for depression in this population.

Authors of a few recent studies have explored whether vitamins and supplements are of benefit to adolescents and/or women with PCOS; one study was used to examine vitamin D and probiotic cosupplementation.<sup>44</sup> In a randomized, double-blind, placebo-controlled trial in 60 adult women (18–40 years of age) with PCOS, the effect of vitamin D and probiotic coadministration on mental health, hormonal, and inflammatory and oxidative stress parameters was examined. The intervention was oral 50 000-IU vitamin D<sub>3</sub> every 2 weeks plus  $8 \times 10^9$  colony-forming units per day of the probiotic ( $n = 30$ ) or placebo ( $n = 30$ ) for 12 weeks. Vitamin D and probiotic

cosupplementation, compared to a placebo, significantly improved BDI-II scores, general health questionnaire scores, as well as depression, anxiety, and stress scale scores. Vitamin D and probiotic cosupplementation were associated with a significant reduction in total testosterone, hirsutism, and high-sensitivity C-reactive protein and an increase in total antioxidant capacity compared to the placebo. In a systematic review and meta-analysis, authors similarly concluded that vitamin D supplementation may be beneficial for follicular development and menstrual regulation in patients with PCOS<sup>45</sup>; however, confirmatory trials are needed. Omega-3 fatty acid supplementation has been shown to have short-term (ie, 12 weeks) beneficial effects for mental health parameters, IR, androgens, and inflammatory markers.<sup>28</sup> However, a meta-analysis<sup>46</sup> suggests that IR was not beneficially impacted by omega-3 fatty acids.

In a recent review, authors examined the cardiovascular profile of pharmacologic agents that have been used for the management of PCOS.<sup>47</sup> It has been unclear whether PCOS is associated with increased cardiovascular events in later years, independent of the presence of type 2 diabetes. The medications reviewed included COCs, antiandrogens, clomiphene, and drugs specifically used in diabetes therapy, including metformin. In the review, the authors concluded that therapies used to treat these patients do not confer an increased cardiovascular risk and that there is no evidence that any interventional medical therapy may prevent the onset of diabetes in patients with PCOS. However, in the case of metformin, this agent was suggested to be beneficial in preventing the development of gestational diabetes. Lastly, orlistat is a noteworthy medication that reduces weight and, therefore, might lead to decreased cardiovascular risk.

Considering agents that a clinician might prescribe for the long-term management of PCOS, orlistat is one that has been suggested to have the potential to help achieve weight loss and improve lipid and glucose metabolism.<sup>27</sup> In a recent systematic review, the authors suggested orlistat to be more effective in improving ovulation rate, weight loss, and lipid profiles in women with PCOS.<sup>48</sup> Lastly, a 2018 study revealed that orlistat is more effective and has fewer side effects than metformin.<sup>49</sup>

## CONCLUSIONS

Long-term individualized management that integrates evidence-based practice using a combination of pharmacologic interventions, topical dermatologic treatments, lifestyle intervention, and social support for patients with PCOS is needed to normalize menses, effectively treat associated dermatologic issues (eg, hirsutism and acne), achieve fertility, reduce the burden of obesity and risk of metabolic related diseases, and address health-related quality of life issues associated with the disorder. Surprisingly, the PCOS field is advancing slowly to attain new evidence that would change practice. PCOS is a common diagnosis but is far from “one size fits all” with respect to treatment. Optimal treatment uses a multimodal approach, including nutrition and exercise interventions in adolescents. Pharmacologic therapies can address a variety of symptoms and clinical findings associated with PCOS. COCs address menstrual irregularity, protect the endometrium, and protect against unwanted pregnancy. COCs are also the most effective strategy for the management of hirsutism and acne in both adolescents and women with PCOS. Metabolic dysfunction can be mitigated by using insulin-sensitizing agents, such as metformin, which also have shown to induce some weight

loss and improve glucose tolerance in many patients in randomized controlled clinical trials. Additionally, androgen receptor blockers, such as spironolactone, can aid in the treatment of hirsutism, acne, and alopecia, which are the issues of most concern to adolescents. Patients with PCOS may also benefit from an adolescent medicine or pediatric endocrinology referral for diagnostic evaluation and dermatology services for optimal management of hirsutism and acne. As an adjunct to treatment by subspecialty clinicians, local listings for adolescent-friendly cosmetology services are important for access to temporary and permanent hair removal methods because medical treatments such as laser therapy are expensive and may not be covered by insurance despite the potential positive impact on health-related quality of life. Finally, attention to social, emotional, and vocational development is critically important, given the observed quality of life issues observed in this population, as well as the potential need for alternative financial resources to enable access to assisted reproductive technologies to address potential fertility issues in adulthood. Attention to both the physical and emotional health of affected adolescents is paramount as part of a personalized management strategy designed to improve the overall longitudinal health outcomes for affected adolescents and emerging adults.

## ABBREVIATIONS

AMH: anti-Müllerian hormone  
BDI-II: Beck Depression Inventory-II  
COC: combined oral contraceptive  
FSH: follicle-stimulating hormone  
IR: insulin resistance  
LH: luteinizing hormone  
PCOS: polycystic ovary syndrome

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