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Modern treatment techniques for hirsutism in women with polycystic ovary syndrome – the role of combination therapies

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ABSTRACT

Introduction and aim. Hirsutism represents a distressing clinical hallmark of hyperandrogenism in females diagnosed with polycystic ovary syndrome (PCOS), profoundly undermining psychological well-being and health-related quality of life. This narrative overview critically appraises the clinical performance, safety profiles, and biological rationale of multimodal combination regimens relative to single-agent therapies.

Literature search. A structured bibliographic exploration was conducted across PubMed, Embase, and Google Scholar spanning January 2018 through May 2026. The search prioritized peer-reviewed clinical trials, meta-analyses, and updated international consensus statements addressing hyperandrogenism and hirsutism in the setting of PCOS.

Analysis of the literature. Combined oral contraceptives (COCs) remain the cornerstone of initial pharmacological management. When hirsutism persists following at least six months of compliant COC monotherapy, the introduction of an antiandrogenic agent provides meaningful therapeutic gains, though robust contraception remains imperative given potential teratogenic risks. Concurrently, while insulin sensitizers such as metformin and off-label GLP-1 receptor agonists primarily ameliorate underlying metabolic perturbations with modest direct cutaneous outcomes, procedural modalities most notably the 1064 nm Nd:YAG laser furnish immediate aesthetic and psychosocial improvement while systemic endocrine suppression gradually takes effect.

Conclusion. Achieving successful control of PCOS-related hirsutism necessitates a personalized, multi-targeted framework uniting ovarian suppression, metabolic remediation, and direct follicular photoepilation. Rigorously designed prospective clinical investigations are warranted to evaluate post-therapeutic stability and sustained remission over extended follow-up intervals.
Keywords. antiandrogens, combined oral contraceptives, hirsutism, laser hair removal, polycystic ovary syndrome

Introduction

Definition and significance

Hirsutism is defined as excessive growth of terminal hair in women, resembling a male-pattern hair distribution.[1] The occurrence of this disorder is determined by local androgen concentrations, interactions between various serum androgens, and the sensitivity of hair follicles to androgens.[2] The Ferriman-Gallwey scale is used to assess the severity of hirsutism.[1] The reviewed literature shows that among women with polycystic ovary syndrome (PCOS) presenting with hirsutism, symptoms of depression occur in approximately 50% of patients. In comparison, anxiety occurs in approximately 45%, and both are associated with psychosocial distress.[3,4]

Association with PCOS

Hirsutism is a relatively common disorder among women, affecting approximately 5–10% of the female population worldwide.[5] It is estimated that over 80% of hirsutism cases are associated with excess androgens, and approximately 70–80% of women with this disorder are diagnosed with PCOS.[6] It is a complex endocrine disorder characterized by hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology.[7,14] This disorder is also frequently accompanied by metabolic abnormalities, such as insulin resistance, obesity, or metabolic syndrome.[6]

The classic approach to treatment

According to the guidelines of the Endocrine Society and international PCOS recommendations, the cornerstone of pharmacotherapy for hirsutism in women not planning a pregnancy is oral contraceptives (COCs); if monotherapy proves ineffective after six months, the addition of antiandrogen medications is recommended. This strategy is supplemented by lifestyle modifications and direct hair removal methods, taking into account the condition's impact on patients' quality of life.[7,8] Methods of temporary, direct hair removal include shaving and chemical depilation. More permanent methods include electrolysis, laser therapy, and photoepilation.[1]

Despite the availability of international guidelines and systematic reviews addressing individual therapeutic modalities, evidence regarding the optimal integration, sequencing, and complementary use of endocrine, metabolic, and hair-targeted interventions remains fragmented. Moreover, improvements in biochemical hyperandrogenism do not necessarily translate directly into clinically meaningful

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reductions in terminal hair growth. A clinically oriented synthesis of multimodal treatment strategies is therefore warranted.

Aim

The aim of this narrative review was to critically evaluate the efficacy, safety, and clinical rationale of combination and multimodal treatment strategies for hirsutism in women with PCOS, with particular emphasis on the integration of endocrine suppression, metabolic interventions, and direct hair-targeted therapies. The review also examines emerging metabolic therapies and pathophysiological concepts that may contribute to a more individualized approach to the management of PCOS-associated hirsutism.

Literature search

Search strategy and data sources

This article was structured as an integrative narrative review synthesizing modern medical and interventional strategies for hair reduction in individuals affected by polycystic ovary syndrome (PCOS). Comprehensive bibliographic queries were executed within three electronic databases PubMed, Embase, and Google Scholar encompassing records indexed between January 2018 and May 2026. Free-text terminology was combined with standardized medical indexing vocabularies (MeSH descriptors in PubMed and Emtree categories in Embase) utilizing Boolean architecture: (PCOS OR "polycystic ovary syndrome") AND (hirsutism OR hyperandrogenism) AND ("combination therapy" OR "oral contraceptives" OR "antiandrogens" OR "laser" OR "metformin" OR "GLP-1").

Study selection and inclusion criteria

Screening of titles and abstracts was carried out autonomously by two independent reviewers (M.R. and P.T.), followed by full-text scrutiny of candidate records. Selection criteria prioritized: (1) peer-reviewed randomized controlled trials, systematic syntheses, meta-analyses, and internationally recognized consensus guidance (including Endocrine Society and 2023 International PCOS recommendations); (2) investigations probing dual-action pharmacological combinations or integrated pharmacological-physical protocols; and (3) mechanistic inquiries delineating steroidogenic dynamics (notably 11-oxygenated adrenal derivatives) and metabolic insulin signaling pathways. Studies not published in English, reports centered exclusively on operative surgical interventions, animal experimental models, and documents without accessible complete texts were excluded. Ultimately, 44 key publications formed the evidence base for this critical synthesis. Given the narrative methodology, systematic appraisal checklists, PRISMA flow diagrams, formal protocol registry, and pooled statistical meta-analyses were omitted. Surgical management, non-PCOS causes of hyperandrogenism, and detailed discussion of standard monotherapies are outside the scope of this review.

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Analysis of the literature

Pathophysiology of hirsutism in PCOS

Excessive androgen production

Hyperandrogenism is one of the main diagnostic criteria for PCOS and often has a mixed origin. The ovaries, adipose tissue, and adrenal glands can all be sources of excess androgens in women with PCOS.[9,10]

Functional adrenal hyperandrogenism (FAH) is recognized in approximately 20–30% of affected patients. Its hallmark circulating marker, dehydroepiandrosterone sulfate (DHEAS), acts as an abundant circulating prohormone that undergoes peripheral bioactivation into downstream potent androgens within target tissues.[10]

The 11-oxygenated androgen cascade, driven by 11-hydroxyandrostenedione (11OHA4) the second principal adrenal androgen product yields 11-ketotestosterone (11KT). This active steroid displays androgen receptor potency comparable to classic testosterone while circulating at markedly higher molar concentrations, establishing it as an exceptionally sensitive marker of biochemical androgen excess.[11,12] In women with PCOS, elevated circulating 11KT closely parallels degree of insulin resistance and dyslipidemia.[10] Contemporary investigative work underscores the diagnostic and therapeutic value of tracking this pathway in PCOS.[12] Taken together, clinical hyperandrogenism in PCOS reflects an intricate interplay among ovarian steroidogenesis, adrenal activation, and peripheral intracrine processing.[10,11,12]

A hallmark of PCOS is tissue-selective insulin resistance (IR).[9,13] Whereas skeletal muscle and adipose depots exhibit marked metabolic unresponsiveness to insulin, ovarian stroma remains selectively sensitive along its mitogenic and steroidogenic cascades.[13] Elevated insulin concentrations disrupt the hypothalamic-pituitary-ovarian (HPO) axis by accelerating pulsatile gonadotropin-releasing hormone (GnRH) release and elevating circulating luteinizing hormone (LH) levels.[9] Through binding directly to theca-cell insulin receptors, hyperinsulinemia synergizes with LH to stimulate de novo androgen biosynthesis within the ovarian compartment.[9] Consequently, higher circulating androgens closely mirror the severity of systemic insulin resistance.[13]

Under physiological conditions, roughly 99% of circulating testosterone remains sequestered by sex hormone-binding globulin (SHBG) and albumin; hence, cutaneous androgenic manifestations depend essentially on the unbound active fraction (~1%) and local conversion to dihydrotestosterone (DHT).[2] Chronic hyperinsulinemia blunts hepatic SHBG transcription,[13] precipitating a steep drop in circulating carrier protein levels and triggering a rise in bioactive free testosterone that exacerbates cutaneous androgenic symptoms.[9] Thus, hyperinsulinemia directly fuels ovarian hyperandrogenism while concomitantly driving down SHBG levels, bridging metabolic dysfunction with peripheral hyperandrogenic pathology in PCOS.[9,13]

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Hair follicle sensitivity

Androgens activate the androgen receptor (AR) in the hair follicle, stimulate follicle growth, and prolong the anagen phase, which results in the formation of thicker and longer (terminal) hair.[2,15] The intensity of hair growth appears to depend more strongly on local androgen production associated with 5-α-reductase activity and AR sensitivity, than on systemic concentrations.[2,5] Consequently, this intracrine susceptibility may help explain how clinical hirsutism can manifest despite normoandrogenic serum androgen levels.[5,13,15] The role of the CAG nucleotide repeat length polymorphism of the androgen receptor gene in hirsutism has not been unequivocally confirmed, indicating the need for further research in this area.[15] In women with increased 5-α-reductase activity, more DHT is produced locally, which strongly stimulates hair growth, despite normal blood androgen levels. This phenomenon (no abnormalities in laboratory tests, regular menstrual cycles, and normal ovarian appearance) is referred to in the literature as idiopathic hirsutism and is a diagnosis of exclusion.[5,15]

Standard pharmacological treatment of hirsutism

The Ferriman–Gallwey Scale and severity assessment

The modified Ferriman–Gallwey scale (mFG) remains the gold standard for the quantitative assessment of hirsutism severity and for monitoring treatment response.[8,16] This scale covers 9 body areas: upper lip, chin, chest, upper/lower back, upper/lower abdomen, arms, and thighs.[17] Due to ethnic differences, local norms for the mFG scale may vary; therefore, it is important to adjust the threshold to the specific population.[17]

For the European population, a score of ≥ 8 on the mFG scale is clinical evidence of hyperandrogenism, even with normal serum androgen levels.[8] However, the 2023 International Guidelines place greater emphasis on patient-reported symptom burden, recommending treatment when a symptom is clinically bothersome, regardless of the mFG score.[8] A detailed description of the scoring system is presented in Table 1.

Table 1. Description of scoring on the modified Ferriman–Gallwey scale (mFG)

Point	Description
0	Absence of terminal hair
1	Minimal terminal hair growth
2	Terminal hair growth greater than minimal but atypical for male-pattern hair distribution
3	Terminal hair typical of moderate male-pattern hair growth
4	Terminal hair with typical male-pattern density

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Combined oral contraceptives (COCs)

COCs constitute the undisputed initial pharmacotherapy for hirsutism in women with PCOS lacking thrombotic or estrogen-related contraindications.[14,18] Their therapeutic mechanism relies on gonadotropin suppression leading to reduced ovarian androgen synthesis, combined with estrogen-induced stimulation of hepatic SHBG production, which sharply diminishes circulating free testosterone fractions.[16,19,20] In a modern randomized, double-blind trial, 9 cycles of a 24/4 regimen demonstrated a mean 3.8-point reduction in mFG score, signifying meaningful clinical hair regression.[21] Progestins possessing inherent antiandrogenic properties (such as drospirenone or cyproterone acetate) offer enhanced clinical potency by antagonizing androgen receptors or inhibiting local 5-α-reductase.[8,16] Beyond hair control, COCs provide indispensable reproductive health benefits, including reliable endometrial protection against anovulatory hyperplasia.[14]

Some progestogens exhibit antiandrogenic properties by blocking androgen receptors or 5-α-reductase, which limits DHT production.[8,16] Formulations containing antiandrogenic progestogens, such as drospirenone or cyproterone acetate, may provide greater clinical efficacy.[16] Beyond their effects on hirsutism, COCs also provide important systemic benefits in PCOS management, including endometrial protection in women with anovulatory cycles.[14]

Antiandrogens

Antiandrogens may be a second-line treatment option for hirsutism in women with PCOS, particularly when COCs are poorly tolerated or fail to produce sufficient improvement after at least 6 months of therapy. In such cases, current guidelines generally support the addition of an antiandrogen to ongoing COC therapy.[22,23]

Most antiandrogens (spironolactone, flutamide, bicalutamide) work by blocking the androgen receptor, whereas finasteride inhibits 5-α-reductase activity, thereby reducing DHT production.[7,14,23] Despite their efficacy, antiandrogens carry a risk of adverse effects, primarily teratogenicity; therefore, effective contraception must be ensured during therapy, most commonly using COCs.[7,8,14,24] Spironolactone is generally preferred due to its more favorable safety profile compared to the hepatotoxic effects of flutamide.[8,23,25] Spironolactone may cause hyperkalemia; however, routine monitoring of potassium levels is not recommended in women without comorbidities.[23,26] Comparative evidence suggests that 5-α-reductase inhibitors, such as finasteride, and androgen receptor antagonists can achieve similar reductions in mFG scores over time; however, differences in study populations, treatment duration, and limited sample sizes make it difficult to establish clear superiority of one antiandrogen over another.[7,23]

Insulin-sensitizing drugs

Metformin

Metformin enhances peripheral insulin sensitivity primarily via hepatic gluconeogenesis suppression and stimulated skeletal glucose uptake; this mitigates hyperinsulinemia-driven ovarian steroidogenesis

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and permits a modest rebound in hepatic SHBG synthesis, dampening free androgen bioactivity.[5,14,22,27] Nonetheless, clinical responses diverge according to patient metabolic phenotype: lean individuals with marked hyperinsulinemia frequently experience tangible hair reductions, whereas in patients with obesity, the response is predominantly biochemical rather than cutaneous.[13] A Cochrane appraisal synthesizing 44 trials (2,253 subjects) emphasized that metformin remains inferior to COCs in reducing hirsutism scores among overweight and obese cohorts.[28] Hence, despite its undeniable metabolic utility, metformin exhibits limited and less predictable efficacy against dermatologic hyperandrogenism compared to estrogen-progestin therapy.[5,8,27,28]

GLP-1 receptor agonists

The limitations of metformin in improving clinical hyperandrogenism, together with the close association between metabolic dysfunction, obesity, and PCOS, have prompted increasing interest in GLP-1 receptor agonists (GLP-1RAs) as an additional therapeutic approach, particularly in women with obesity and treatment-resistant hyperandrogenism.[29] GLP-1RAs, such as liraglutide, have gained attention for their ability to improve glycemic control, reduce body weight, and indirectly alleviate symptoms of PCOS, including hyperandrogenism and hirsutism.[29] A study comparing three treatment options liraglutide combined with a calorie deficit, metformin combined with a calorie deficit, and calorie restriction alone identified liraglutide as the most effective option, significantly improving the mFG score.[29]

It should be emphasized that GLP-1RAs do not have a formal regulatory indication for the treatment of hirsutism; therefore, their use in this context represents off-label prescribing for appropriately selected patients with obesity and severe insulin resistance.[8,29] GLP-1RAs do not exhibit a direct antiandrogenic effect nor do they directly affect hair follicle structures. Their beneficial effect on hirsutism stems from improved metabolic control and a reduction in hyperandrogenemia secondary to insulin resistance, rather than from direct endocrinological treatment of excessive hair growth itself.[8,29]

Direct treatments targeting hair: hair removal and topical therapies

Mechanical methods, such as shaving or thioglycolic acid creams, are used to treat hirsutism; they remove hair only superficially and do not affect the hair growth cycle. Their effectiveness is short-lived, and their use may lead to irritation or contact dermatitis.[1,22,30]

Electrolysis stands as a clinically established, modality-independent technique for permanent hair elimination, proving exceptionally beneficial for individuals with blonde, red, or unpigmented hair follicles that fail to respond adequately to optical photoepilation. Nonetheless, its widespread adoption is frequently constrained by cumulative financial expense, procedural discomfort, and localized folliculitis or tissue inflammation.[7,9,22] Conversely, optical photoepilation (encompassing IPL platforms and targeted lasers) serves as the primary standard for durable hair reduction (averaging 40–80% clearance), with clinical success dictated by the patient's Fitzpatrick phototype (FST) and hair melanin

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density.[8,31,32] For lighter skin types, alexandrite (755 nm) systems are effective, whereas for deeper skin complexions, long-pulsed 1064 nm Nd:YAG and 810 nm diode platforms achieve deeper follicular penetration with substantially higher epidermal safety.[33,34] In particular, Nd:YAG lasers featuring integrated contact cooling minimize thermal adverse events and deliver significant psychosocial improvement sustained up to 30 months.[9]

However, the efficacy of laser therapy is lower in PCOS (an excellent response in 54% of patients compared to 70% in idiopathic hirsutism) due to follicular resistance resulting from excess androgens, obesity, and insulin resistance, which requires a greater number of sessions.[8,31,32,34] Therefore, for optimal results, concurrent pharmacological treatment is recommended for these patients.[32,34]

Topical eflornithine (13.9%) is used as an adjunct to treatment; it inhibits hair growth only in the early phase.[22,30] The combination of eflornithine with laser therapy yields better therapeutic results in facial hair removal after 6 months of use than either approach alone.[7,9] These results provide a rationale for considering direct, hair-targeted methods as a supplement to pharmacological treatment, with the choice of approach depending on its efficacy duration of effect, and suitability for individual hair and skin characteristics; in women with PCOS, combination with treatment of the underlying hormonal and metabolic abnormalities may further improve clinical outcomes.[7,9,32,34]

Combination therapies

Multimodal regimens leverage complementary therapeutic targets to simultaneously tackle endocrine, metabolic, and follicular facets of PCOS-related hirsutism. Nevertheless, observed clinical gains vary depending on the specific pharmacological agents combined and the clinical endpoints assessed.[8] While select regimens yield superior cutaneous hair clearance, others predominantly correct glycemic indices or circulating hormone titers without noticeable improvement in hair distribution.[8]

Dual metabolic and antiandrogen therapy: Antiandrogens (AA) + metformin

Meta-analytic evaluations of controlled trials reveal that coupling antiandrogens (such as spironolactone) with metformin provides negligible incremental benefit in clinical hirsutism scores beyond metformin alone, even though the combination achieves superior reductions in body mass index and circulating androgen levels.[8] Importantly, this co-administration appears well tolerated and does not elevate the incidence of adverse effects.[8,35]

Combined hormonal-metabolic therapy: COCs + metformin

Published clinical data fail to substantiate a statistically significant superiority of COCs plus metformin over COCs monotherapy in terms of mFG score reduction.[19] Rather, the primary value of dual therapy lies in secondary biological endpoints, notably more pronounced reductions in the Free Androgen Index (FAI) and DHEAS, alongside enhanced SHBG restoration.[19] Furthermore, this combined regimen confers definite metabolic benefits by improving glucose tolerance, lipid parameters, and BMI among

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overweight or obese individuals.[28,36,37] In terms of obstetric safety, while COCs are strictly contraindicated during pregnancy, metformin may be cautiously continued for metabolic indications during early conception under close medical supervision.[27]

Combined hormonal-antiandrogenic therapy: COCs + antiandrogens

Current international consensus establishes COCs as primary foundational therapy for women not seeking conception.[37] Supplementing COC monotherapy with an antiandrogen (AA) significantly enhances cutaneous hair clearance.[7] The underlying pharmacological rationale rests on their synergistic biological actions: COCs curb gonadal androgen synthesis and elevate plasma SHBG,[8,16] while antiandrogens block receptor activation and intracrine 5-α-reductase activity within the pilosebaceous unit.[7,23] Clinical evidence indicates that combining COCs with spironolactone yields marked clinical improvements, with mFG reductions reaching up to 59.9% and documented patient improvement in 85.1% of cohorts,[20] accompanied by meaningful drops in total testosterone, free testosterone, and DHEAS.[38] Given slow follicular turnover, substantial mFG improvements typically demand at least 6 months of continuous therapy.[20]

Pharmacological treatment + mechanical methods

Synchronizing systemic medical therapy with physical hair removal addresses the distinct temporal dynamics of hirsutism management: procedural laser destruction delivers immediate elimination of existing coarse terminal hairs, while systemic hormonal suppression prevents the ongoing conversion of vellus hairs into terminal follicles during the protracted therapeutic lag phase.[22,30] In an observational cohort of 138 patients treated with COCs plus spironolactone, where 60% additionally underwent electrolysis, the adjunct procedural group experienced greater mFG regression and higher subjective satisfaction (95% vs. 83%), although statistical significance was not reached emphasizing the need for nuanced patient counseling.[20]

Lifestyle modifications + pharmacotherapy

Lifestyle modification forms the foundation of therapeutic management for hirsutism and PCOS.[6-8] Since obesity and its complications are strongly associated with excessive hair growth, weight loss significantly improves overall treatment outcomes.[6] When lifestyle changes alone are insufficient, pharmacotherapy is initiated.[8] In patients with severe metabolic disorders, bariatric surgery can be an effective adjunct, which additionally reduces the symptoms of hirsutism.[6,14] Combining lifestyle modification with appropriate pharmacological treatment may improve overall clinical outcomes, particularly in women with obesity and metabolic complications.[6,7,8]

The proposed algorithm for managing hirsutism in women with PCOS is presented in Fig. 1.

Table 2. Comparison and summary of monotherapy and combination therapy*

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	COC alone	Antiandrogen monotherapy	COC + antiandrogen	COC + metformin	Pharmacotherapy + laser/IPL
Efficacy (change in mFG)	Efficacy in adults (MD 0.54–0.8)[28]	High efficacy in adults; no data available for adolescents [36]	Additional benefits of combining COC and AA. May provide additional benefit for clinical hirsutism in selected women; certainty varies by antiandrogen and study design [1,39]	Primarily improves metabolic and biochemical outcomes; additional benefit for clinical hirsutism is inconsistent (MD 1.36 higher for metformin and MD 0.54 higher for OC)[28]	Provides direct reduction of existing hair; may complement delayed pharmacological effects; even better results when combined with eflornithine [39]
Time to response	> 6 months [39]	≥ 6 months [23]	> 6 months [1,22]	3–4 months [27]	> 6 months [40]
Adverse event profile	Worsening of insulin resistance, increased risk of blood clotting disorders, cardiovascular diseases, and inflammatory	Irregular menstrual cycles, hyperkalemia, hypotension;[9] hepatotoxicity	Cumulative profile of adverse effects [7,9]	Gastrointestinal symptoms (nausea, diarrhea)[41]	Skin redness, pain, superficial burns, excessive hair growth,[31] perifollicular edema[40]

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	COC alone	Antiandrogen monotherapy	COC + antiandrogen	COC + metformin	Pharmacotherapy + laser/IPL
	diseases. In women with dyslipidemia, triglyceride levels worsened.[7,9,22,24,37]				
Safety in the context of a possible pregnancy	Not used during pregnancy	Teratogenic effect feminization of male fetuses;[42] requires strict contraception[41]	Not used during pregnancy	Metformin used as monotherapy,[10] possible long-term cardiometabolic risk to the child [41]	Generally compatible with pregnancy planning; treatment choice should consider skin type, hair characteristics and local safety guidance
Effects on the metabolic aspects of PCOS	Regulation of the menstrual cycle, improvement of hyperandrogenism [9]	No established direct metabolic benefit [41]	No data available	Improved prognosis for biochemical hyperandrogenism, BMI, insulin resistance, insulin levels, and	Depends on the medication

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	COC alone	Antiandrogen monotherapy	COC + antiandrogen	COC + metformin	Pharmacotherapy + laser/IPL
				menstrual cycle regularity [27]	
Patient acceptance	Most commonly used [18]	Used in cases of resistance to COC monotherapy [41]	Not for women trying to conceive [28]	No data available	Positive psychological impact [8,9]

* Table 2 represents a narrative comparison of available evidence and not a formal quantitative or network comparison of the listed therapeutic strategies, AA – antiandrogen, BMI – body mass index, COC/COCs – combined oral contraceptives, IPL – intense pulsed light, MD – mean difference, mFG – modified Ferriman–Gallwey scale, OC – oral contraceptive, PCOS – polycystic ovary syndrome

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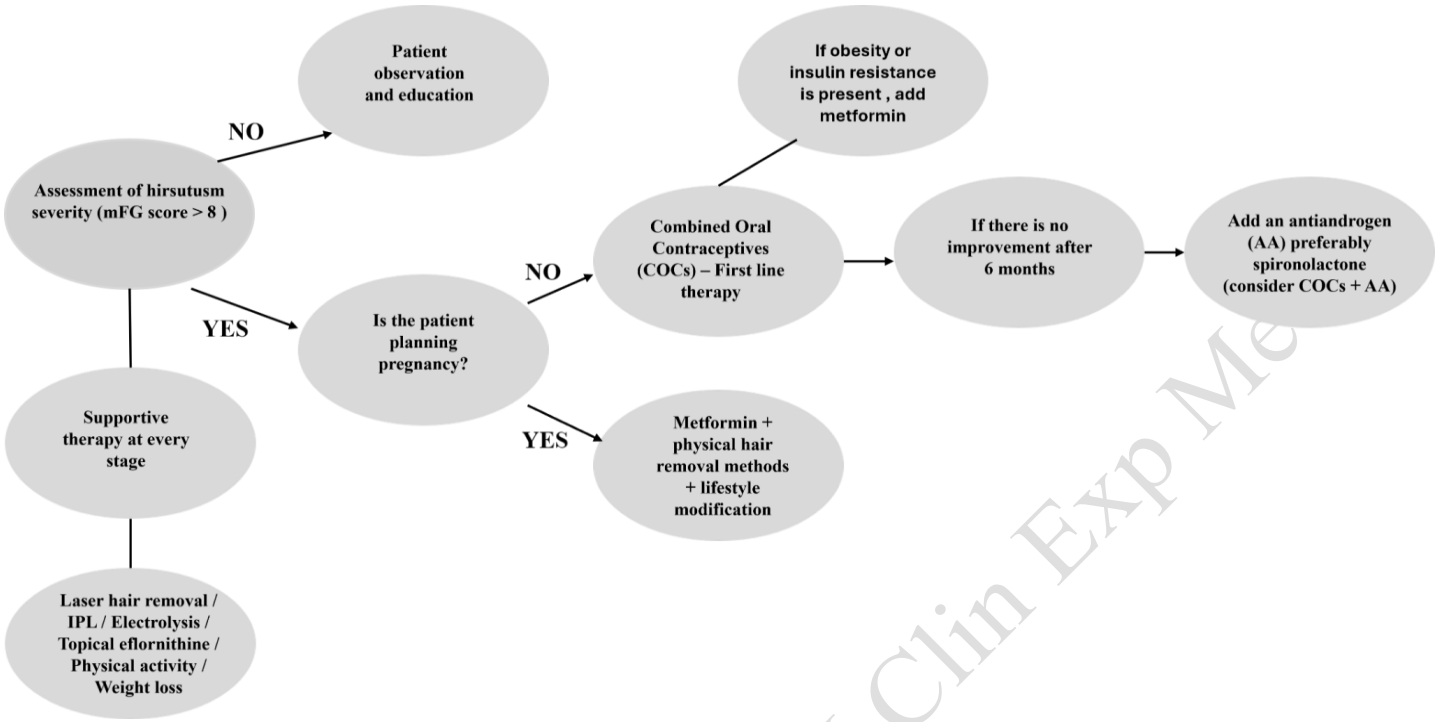

Fig. 1. Proposed management algorithm for the treatment of hirsutism in women with PCOS, the core pathways (first-line COC and subsequent addition of antiandrogens) are derived from the Endocrine Society guidelines,[7,8] whereas the adjunctive mechanical therapies represent consensus from individual clinical studies, to move beyond single-target therapies, this review proposes a tri-axial conceptual framework for PCOS-associated hirsutism management, this model integrates three interdependent domains: first, endocrine suppression by using COCs and antiandrogens; second, modulation of the insulin-adipose tissue pathway using metformin and GLP-1 receptor agonists; and third, direct, local intervention at the hair follicle level using laser photoepilation, topical eflornithine and IPL, targeting these axes simultaneously addresses the multifactorial origin of hirsutism and provides a rationale for multimodal combination therapies, supportive care, lifestyle modifications, and psychological evaluation are maintained across all therapeutic stages, this proposed algorithm represents an author-developed conceptual synthesis of current international guidelines and available clinical evidence, and it has not been prospectively validated in clinical trials

Main findings

The principal contribution of this review is the integration of available therapeutic evidence into a tri-axial framework encompassing endocrine suppression, metabolic modulation, and direct hair-follicle intervention, thereby emphasizing the complementary mechanisms and different time courses of response of these therapeutic domains.

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The synthesis of current evidence confirms that the treatment of hirsutism in women with polycystic ovary syndrome should be multifaceted and tailored to the individual characteristics and needs of the patient. Combination regimens, particularly those integrating COCs with antiandrogens or direct hair-targeted procedures, may provide greater clinical benefit than monotherapy. However, the strength of evidence varies across treatment combinations, patient phenotype, and clinical outcomes. Insulin-sensitizing drugs, such as metformin, improve metabolic parameters and biochemical androgen profiles, whereas their isolated impact on terminal hair growth regression remains modest. GLP-1RAs demonstrate metabolic benefits in women with PCOS and obesity, with potential secondary effects on hyperandrogenic manifestations; however, their application for hirsutism remains off-label and warrants further prospective evaluation.[8,29]

Mechanistic synthesis and clinical-biochemical distinctions

A crucial insight emerging from this critical synthesis is the pronounced clinical-biochemical dissociation characteristic of PCOS management. Laboratory normalization of circulating androgens (such as free testosterone, FAI, and SHBG) routinely precedes visible cosmetic regression of terminal hair by several months.[2,9,13] This lag is attributable to the prolonged duration of the hair follicle growth cycle (anagen-telogen transition), compounded by residual intracrine 5-α-reductase activity and heightened androgen receptor responsiveness at the tissue level.[2,5] This biological discrepancy clarifies why biochemical recovery does not immediately equal cosmetic clearance and reinforces the necessity of incorporating immediate mechanical hair-removal solutions during initial systemic therapy. Furthermore, persistent elevation of 11-ketotestosterone (11KT) and its link to insulin resistance underscore the critical role of adrenal steroidogenesis, helping explain variable clinical responsiveness to ovarian suppression alone and advocating for individualized multi-target regimens.[10-12]

Comparison with previous studies

The conclusions drawn in this review align closely with the current literature advocating an integrated multimodal paradigm for managing PCOS hirsutism. In terms of hormonal therapy, our findings reflect the recent trial by Lobo et al. (2025),[21] demonstrating that 9 cycles of COCs provide clinically meaningful mFG reductions. However, as underscored by Alesi et al. (2023)[23] and the Endocrine Society guidelines,[7] single-agent COC therapy often falls short in moderate-to-severe hirsutism, justifying the structured addition of antiandrogens or physical modalities.

With regard to drugs affecting metabolism, our findings are consistent with the Cochrane review (Fraison et al., 2020)[28] and the meta-analysis by Luque-Ramírez et al. (2018)[37] These studies indicate that, although metformin improves insulin sensitivity and metabolic parameters, its effect on clinical hirsutism is limited. Importantly, improvements in metabolic and biochemical parameters do not necessarily translate into a

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comparable reduction in mFG scores. Similarly, observations reported by Cannarella et al. (2025)[29] support growing interest in GLP-1RAs, such as liraglutide, as metabolic adjuncts. Their potential effects on hirsutism are likely indirect, resulting from weight reduction and improved insulin sensitivity, with consequent changes in SHBG and free androgen levels rather than direct antiandrogenic action at the hair follicle.[9,13,29]

With regard to multimodal therapies combining pharmacotherapy with physical procedures, the results are consistent with the long-term observations by Ezeh et al. (2018),[20] who demonstrated that combining hormonal therapy with hair removal methods may provide greater clinical benefit than pharmacological treatment alone. However, the available evidence is not uniform. For example, although the addition of electrolysis to COC plus spironolactone therapy was associated with a higher proportion of patients reporting improvement (95% vs. 83%), the difference was not statistically significant.[20] This suggests that the apparent benefit of combining systemic and physical treatments should be interpreted in the context of the strength and statistical significance of the available evidence.

With respect to photoepilation, recent findings by Nabi et al. (2022)[34] and Choi et al. (2025)[32] demonstrate that optical clearance rates are noticeably attenuated in PCOS patients relative to idiopathic hirsutism (54% vs. 70% optimal response). This discrepancy is directly attributable to ongoing systemic hyperandrogenemia and hyperinsulinemia continuously restimulating follicular stem cells, necessitating more treatment sessions and solidifying the indispensability of concurrent medical antiandrogenic therapy.[32,34]

A rigorous appraisal reveals notable methodological caveats across the existing literature: many trials are hampered by brief observational windows (6–12 months), limited participant cohorts, and heterogeneous definitions of clinical response. These constraints restrict definitive conclusions regarding the optimal sequential timing and long-term durability of specific combinations once medications are withdrawn. Large prospective investigations utilizing standardized patient-reported and trichoscopic metrics are urgently needed to guide definitive clinical algorithms.

Clinical implications

From a practical standpoint, management must be meticulously customized based on hirsutism severity, metabolic phenotype, teratogenic considerations, and patient psychological priorities. Because pharmacotherapy requires months to exert visible effects, direct hair-elimination technologies serve as crucial immediate interventions during initial therapy. Therapeutic adjustments should therefore be guided not merely by numerical Ferriman-Gallwey scores or laboratory panels, but fundamentally by patient-reported distress and quality-of-life considerations.[8]

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Table 3. Overview of pharmacological interventions, dosages, and clinical notes for the treatment of hirsutism, dosages for COCs, spironolactone, finasteride, flutamide, and metformin reflect current international clinical practice guidelines,[7,8] whereas dosages for liraglutide are based on findings from individual clinical trials[29]*

Drug	Dose	Notes
COC (Guideline-recommended)	1 tablet/day in a 21+7 or 24+4 regimen (e.g., Ethinyl estradiol (EE) 0.02–0.035 mg/20–35 µg + dienogest 2 mg/drospirenone (DRSP) 2 mg/cyproterone acetate (CPA) 2 mg [21,23]	First-line pharmacological option for women not seeking pregnancy and without contraindications to estrogen. Assess individual venous thromboembolism risk and other estrogen-related contraindications
Spironolactone (Guideline-recommended)	25–100 mg/day*[8] 100–200 mg/day**[22]	*Lower risk of side effects **Recommended to be divided into several doses
Finasteride (Guideline-recommended)	2.5–5 mg/day [22]	Generally well tolerated in clinical studies;[22] effective contraception is mandatory because of the risk of teratogenicity to a male fetus
Flutamide (Not routinely recommended; hepatotoxicity concern)	62.5–500 mg/day [22]	Potentially hepatotoxic. Not routinely recommended when safer antiandrogenic options are available[22]
Metformin (Metabolic indication, limited direct effect on hirsutism)	Monotherapy: 1,500–2,500 mg/day [27] In combination with other medications: 500–2,000 mg/day + COC	Used primarily for metabolic indications in PCOS; not recommended solely for hirsutism when COCs are tolerated.[27] Modest direct

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	1,500 mg/day + EE/DRSP 500–1,700 mg/day + Diane-35 1,000 mg/day + pioglitazone 1,000 mg/day + cabergoline[27]	effect on terminal hair regression
Liraglutide (Off-label for hirsutism; metabolic indication in selected patients)	0.6–3.0 mg/day [29]	Minimum dose 0.6 mg/day, increased depending on tolerance.[29] Off-label use; primarily considered for obesity and metabolic indications in PCOS, with secondary indirect effects on hyperandrogenemia

* COC/COCs – combined oral contraceptives, CPA – cyproterone acetate, DRSP – drospirenone, EE – ethinyl estradiol, GLP-1RA – glucagon-like peptide-1 receptor agonist, PCOS – polycystic ovary syndrome, VTE – venous thromboembolism

Review strengths and limitations

A major strength of this review is the integration of the pathophysiological mechanisms underlying hirsutism in PCOS, including the 11-oxyandrogen pathway, insulin resistance, and androgen receptor activity, with current therapeutic evidence. This review prioritizes recent evidence published between 2018 and 2026, while incorporating key seminal studies, considering the recommendations of the Endocrine Society, the 2023 PCOS Guidelines, emerging therapies such as GLP-1 receptor agonists, and contemporary hair-targeted approaches including 1064-nm Nd:YAG laser therapy. Importantly, the review not only summarizes individual treatment modalities but compares their clinical efficacy, limitations, and potential complementary roles within multimodal treatment strategies. Particular attention is also given to the clinical burden of hirsutism and its impact on quality of life and psychological well-being. The high practical value of this work is ensured by a proprietary algorithm and detailed tables that help physicians select therapies, assess safety and efficacy, and provide a tabular summary of drug dosages to support daily therapeutic decisions.

This study is based on a narrative review methodology using the PubMed, Google Scholar, and Embase databases, rather than a systematic review with meta-analysis, which carries a risk of selection bias and

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does not allow for a quantitative synthesis of effect sizes. Heterogeneity in patient characteristics, treatment protocols, follow-up duration, and outcome measures limits direct comparison between studies and prevents firm conclusions regarding the superiority of specific treatment combinations. Another limitation is the subjectivity of the mFG scale and differences in proposed cut-off values across ethnic groups. Most of the analyzed studies had relatively short follow-up periods of 6–12 months and varying methodological quality, making it difficult to assess long-term outcomes and recurrence after treatment discontinuation. Despite the potential benefits of combination therapies, the literature still lacks precise evidence regarding the optimal timing and sequencing during pharmacotherapy. Additional challenges include the off-label use of GLP-1 receptor agonists for the treatment of hirsutism. Furthermore, no formal risk-of-bias assessment or systematic methodological quality appraisal of the included studies was performed, which represents an inherent limitation when evaluating comparative treatment effectiveness.

Unresolved questions and future research priorities

Despite the growing number of studies on the treatment of hirsutism in women with PCOS, there are still significant gaps in the available scientific evidence. Most studies cover a relatively short follow-up period (6-12 months), resulting in a lack of reliable data on the long-term efficacy and safety of combination therapies, as well as on the risk of symptom recurrence after treatment ends. Evidence also remains limited regarding optimal preconception management in women planning pregnancy, particularly with regard to treatment transitions when systemic antiandrogens are contraindicated. Although metformin is considered relatively safe during this period, its long-term effects on the neurological and metabolic development of offspring require further evaluation. Future prospective studies should directly compare multimodal treatment strategies to determine the optimal combination, sequencing, and duration of pharmacological and hair-targeted interventions. These studies should also clarify the potential role of GLP-1 receptor agonists as metabolic adjuncts and evaluate comprehensive approaches incorporating lifestyle modification and bariatric surgery in women with severe obesity and PCOS. Standardized clinical and patient-reported outcomes are needed to enable meaningful comparisons between studies and assess long-term effects on quality of life, psychological well-being, fertility, and pregnancy outcomes.

To summarize, the key literature gaps and priorities for future research include:

- long-term durability: Evaluating hair regrowth (rebound effect) > 12 months post-treatment,
- 11KT as a biomarker: Clarifying its potential role in assessing hyperandrogenism and treatment response in PCOS,
- GLP-1RA optimization: Standardizing off-label protocols and metabolic vs. antiandrogenic pathways,
- multimodal timing: Determining the optimal timing and sequence for combining laser therapy with systemic pharmacological therapies.

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Conclusion

Hirsutism in women with PCOS requires an individualized, multifaceted management strategy. While combined oral contraceptives remain the guideline-recommended first-line pharmacological option and the addition of antiandrogens provides incremental benefit for persistent symptoms, a phenotype-oriented multimodal approach integrating endocrine suppression, metabolic modulation, and direct hair-targeted procedures appears clinically rational. However, the optimal combination, sequencing, and long-term post-discontinuation durability of these multimodal interventions remain insufficiently established. Adequately powered prospective trials utilizing standardized clinical and patient-reported outcomes are needed to refine clinical decision-making.

Declarations

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Author contributions

Conceptualization, M.R., P.T. and A.Z.; Methodology, M.R., P.T. and K.D.; Software, M.W. and M.Ż.; Validation, K.D., M.W., M.Ż. and N.W.; Formal Analysis, M.R., P.T. and A.Z.; Investigation, M.R., P.T., K.D., M.W., M.Ż. and N.W.; Resources, M.W., M.Ż. and N.W.; Data Curation, K.D., M.W. and N.W.; Writing – Original Draft Preparation, M.R., P.T., K.D. and A.Z.; Writing – Review & Editing, M.R., P.T. and A.Z.; Visualization, M.R., P.T. and A.Z.; Supervision, A.Z.; Project Administration, A.Z.

Conflicts of interest

The authors declare no conflict of interest.

Data availability

Data sharing is not applicable to this article as no new datasets were generated or analyzed during the current study.

Ethics approval

Not applicable. This study is a narrative review of previously published literature and did not involve human participants or animal subjects.

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Use of AI and AI-assisted technologies in the writing process

During the preparation of this work, the authors used AI-assisted language tools solely to improve the readability, syntax, and language clarity of the text. The authors reviewed and edited the content and take full responsibility for the content of the published article.

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