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METFORMIN VERSUS PHARMACOLOGIC AND NON-PHARMACOLOGIC INTERVENTIONS IN PCOS: A REVIEW OF METABOLIC AND ANTHROPOMETRIC OUTCOMES

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a prevalent endocrine and metabolic disorder in reproductive age women, marked by insulin resistance, hyperandrogenism, menstrual irregularities, and increased cardiometabolic risk. This review synthesizes current evidence on the clinical effectiveness of metformin versus alternative strategies across anthropometric, glycemic, and lipid outcomes in women with PCOS.

This narrative review synthesizes secondary data from systematic reviews and meta-analyses retrieved from PubMed and Google Scholar, comparing metformin with other interventions in reproductive-age women with PCOS across anthropometric, glucose, or lipid outcomes.

Metformin showed modest benefits in reducing body mass index, body weight, and waist circumference, with greater effects in overweight and obese individuals. Combined therapies, especially with glucagon-like peptide-1 receptor agonists, were more effective than metformin alone. In glucose metabolism, metformin outperformed placebo and oral contraceptives in reducing fasting glucose, fasting insulin, and homeostatic model assessment of insulin resistance, especially in women with higher insulin resistance. Effects on lipid profiles were moderate; metformin lowered total cholesterol, low-density lipoprotein cholesterol, and triglycerides, particularly when combined with statins. Its effect on high-density lipoprotein cholesterol was limited and sometimes less favorable than that of oral contraceptives.

Metformin remains a core treatment in PCOS, with consistent, modest benefits across metabolic and anthropometric domains. Its effectiveness improves when matched to patient profiles and combined with other agents or lifestyle changes.

KEYWORDS

PCOS, Metformin, BMI, GLP-1

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1. Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine and metabolic disorders affecting women of reproductive age. Characterized by a wide spectrum of clinical features—including menstrual irregularities, hyperandrogenism, infertility, insulin resistance, and cardiometabolic dysfunction—PCOS poses a significant global health challenge. It is estimated to affect between 6% and 13% of women in this age group, with up to 70% of cases remaining undiagnosed [1,2].

In response to the growing need for clarity in diagnosis and care, the International Evidence-Based Guideline for the Assessment and Management of PCOS was published in 2018 and updated in 2023. These comprehensive, multidisciplinary recommendations have redefined diagnostic criteria and therapeutic priorities. PCOS is now diagnosed when two of the following three features are present: clinical or biochemical hyperandrogenism, ovulatory dysfunction, and polycystic ovarian morphology, traditionally assessed via ultrasound. The 2023 update recognizes anti-Müllerian hormone as an alternative diagnostic marker to ultrasound, particularly valuable for its accessibility and cost-effectiveness. The guidelines emphasize individualized care that addresses reproductive, metabolic, psychological, and dermatologic aspects, with lifestyle modification as the foundational treatment strategy. In addition, mental health screening and integrated, patient-centered care models are strongly recommended [3].

From a pathophysiological perspective, insulin resistance is considered a central feature of PCOS and is present in a majority of women with the condition, regardless of body mass index. Insulin resistance not only drives metabolic disturbances but also promotes excess androgen production, thus perpetuating the hormonal imbalance typical of PCOS. Conversely, androgen excess may exacerbate insulin resistance by encouraging visceral fat accumulation and impairing insulin signaling. This bidirectional relationship contributes to a self-reinforcing cycle of endocrine and metabolic dysfunction [2,4]. Moreover, increasing

evidence points to the role of genetic predisposition, epigenetic programming, and environmental exposures, especially during critical developmental windows such as fetal life, in shaping PCOS phenotypes and intergenerational transmission[4].

Lifestyle intervention, particularly weight management through diet and physical activity, is recognized as first-line therapy in overweight and obese individuals. These changes have been shown to improve ovulatory function, reduce insulin resistance, and alleviate some psychological symptoms. However, the degree of benefit varies, and not all women achieve clinically meaningful improvements through non-pharmacological approaches alone [1,3].

Among pharmacologic therapies, metformin has gained prominence due to its multifaceted effects on insulin sensitivity, hepatic glucose production, and intestinal glucose absorption. Its mechanism of action involves inhibition of mitochondrial complex I, activation of AMP-activated protein kinase (AMPK) signaling, and possible modulation of gut microbiotaand glucagon-like peptide-1 (GLP-1) secretion [5]. Beyond glycemic control, metformin has been shown to impact weight, ovulation, and lipid parameters in various PCOS phenotypes, although responses are heterogeneous and may depend on factors such as baseline metabolic profile, degree of insulin resistance, and adiposity [3,5].

Despite its widespread use, the comparative effectiveness of metformin versus other pharmacological agents and non-pharmacological strategies remains incompletely understood. This review aims to evaluate the clinical effectiveness of metformin compared to pharmacological and non-pharmacological interventions across three key outcome domains: anthropometric indices (e.g., body mass index (BMI), body weight, waist circumference (WC) and waist-to-hip ratio (WHR)), glucose metabolism parameters (e.g., fasting glucose, fasting insulin and homeostatic model assessment of insulin resistance (HOMA-IR)) and lipid metabolism parameters (e.g., total cholesterol (TC) high-density lipoprotein (HDL-C), low-density lipoprotein (LDL) and triglycerides (TG)). By synthesizing current evidence across these domains, the review intends to support evidence-informed clinical decision-making and identify directions for future research.

2. Materials and Methods

This narrative review is based on secondary data from published systematic reviews, meta-analyses, and network meta-analyses. The objective was to compare the clinical effectiveness of metformin with pharmacological and non-pharmacological interventions in women with PCOS, focusing on anthropometric, glucose, and lipid metabolism outcomes.

A literature search was conducted from March to May 2025 across PubMed and Google Scholar. Search terms included: polycystic ovary syndrome and metformin. Studies were included if they used a systematic or meta-analytic design, focused on reproductive-age women with PCOS, and reported outcomes for anthropometric indices, glucose metabolism, or lipid parameters. Studies focusing solely on fertility outcomes, pediatric or postmenopausal populations, or lacking relevant outcome data were excluded. Data were extracted manually and synthesized descriptively, with no re-analysis of pooled results. The review highlights findings based on the evidence quality and conclusions reported by original authors.

3. State of knowledge

3.1. Anthropometric Indices

Anthropometric outcomes such as BMI, body weight, WC, and WHR are important markers in evaluating therapeutic effects in women with PCOS. This section presents a structured synthesis of clinical evidence comparing metformin with other pharmacological and non-pharmacological interventions.

Body Mass Index

BMI was the most frequently assessed anthropometric parameter across the studies. Metformin monotherapy showed a modest but consistent reduction in BMI in several comparisons. In large meta-analyses comparing metformin to placebo, metformin was associated with reductions in BMI, although effect sizes varied depending on dose and duration [6,7]. However, some analyses indicated no significant advantage of metformin over placebo in specific contexts [6,8].

A pharmacodynamic modeling study found that metformin's effect on BMI reduction was independent of dosage and exhibited a slow onset of action, requiring over 25 weeks to reach half of the maximal effect in monotherapy. Moreover, combination therapies were predicted to be more effective than metformin alone. These findings suggest that low-dose metformin (e.g., 1000 mg/day) may be sufficient for achieving BMI-related benefits, particularly in long-term treatment [9].

In comparisons with oral contraceptives (OCs), results were mixed. Some subgroup analyses indicated that metformin might be more effective in women with obesity, while in normal-weight and overweight subgroups, the differences were smaller and less consistent [10,11]. In other studies, no differences were detected between metformin and OCs, particularly when used in combination therapies [12].

Combined therapies such as metformin with berberine [13], spironolactone [14], vitamin D [15], sitagliptin [6], and GLP-1 receptor agonists [16,17] showed greater improvements in BMI than metformin alone. In particular, metformin combined with exenatide was also shown to outperform metformin monotherapy [18,19]. Additionally, studies comparing exenatide and metformin as separate monotherapies indicated comparable effects on BMI [20]. In contrast, the combination of metformin with cabergoline did not result in a significant difference in BMI compared to metformin alone [21].

Some agents such as myo-inositol and N-acetylcysteine showed similar effects on BMI compared to metformin, but without a clear advantage [22–24]. On the other hand, thiazolidinediones (TZDs) tended to increase BMI [6,25].

Lifestyle modification was comparable to metformin in reducing BMI. Both interventions led to reductions, and some studies showed that combining lifestyle changes with metformin yielded slightly better results [7,26].

Body Weight

Weight reduction was another outcome frequently evaluated. Metformin consistently showed a positive effect on body weight in comparison to placebo and, in some cases, outperformed other agents such as rosiglitazone [6,27]. However, combining metformin with OCs did not consistently enhance its effect on weight reduction, with several studies showing no additional benefit compared to metformin alone [10–12]. Likewise, the addition of simvastatin to metformin therapy did not result in significant changes in body weight [28].

Combinations of metformin with exenatide were associated with greater reductions in body weight compared to metformin alone [18,19]. Weight loss was observed in both lifestyle modification alone and in combination with metformin, although no significant difference in effectiveness was found between the two approaches [26].

Waist Circumference

The effect of metformin on waist circumference was generally small. Studies showed minimal or inconsistent reductions in WC compared to placebo. No significant differences were observed between metformin and other interventions such as TZDs or liraglutide [6]. However, combinations of metformin with GLP-1 receptor agonists, including exenatide were more effective in reducing WC than metformin monotherapy [16,18,19].

Waist-to-Hip Ratio

WHR was assessed less frequently than other anthropometric outcomes and generally showed minimal or no change across treatment comparisons. Most studies found no significant differences in WHR between metformin and interventions such as OCs, rosiglitazone, pioglitazone, exenatide, spironolactone, myo-inositol, and lifestyle modification [6,11,12,20,22,27,29].

Another analysis reported a small but statistically significant reduction in WHR with metformin compared to placebo, although the effect size was minimal and evidence certainty was low [7]. Some subgroup analyses suggested small improvements with metformin compared to combination therapies, particularly in comparisons with combined oral contraceptive pill (COCP) or COCP plus anti-androgens [11,12], but these findings were limited by small sample sizes and moderate risk of bias. Additionally, one study found that exenatide was more effective than metformin in reducing WHR [19].

3.2 Glucose Metabolism Parameters

PCOS is strongly associated with metabolic dysfunction, particularly insulin resistance and impaired glucose regulation. This section reviews and compares the clinical effectiveness of metformin against a variety of pharmacological and non-pharmacological interventions across three core indicators of glucose metabolism: fasting glucose, fasting insulin, and HOMA-IR.

Fasting Glucose

Metformin has been shown to improve fasting glucose levels compared to placebo, with consistent though modest benefits observed across multiple trials. These improvements are particularly evident in women with higher BMI. While the effect may not always reach high clinical significance, it is consistently favorable in comparison to no treatment or placebo [7,8]. However, some analyses reported heterogeneity in the results, indicating variation in patient response and study design quality [8].

When compared with OCs, metformin tends to perform better in lowering fasting glucose, especially compared to OCs alone [10,30]. However, this effect is not consistently observed when OCs are combined with metformin, as some studies found no significant difference in fasting glucose levels between metformin monotherapy and combination therapy [11,12]. In some BMI-stratified analyses, combination therapy may be more favorable among non-obese women [30]. Notably, some findings lacked statistical significance and were limited by small sample sizes, so should be interpreted with caution [12].

Pharmacological alternatives such as acarbose and simvastatin show mixed results, with some studies reporting a benefit while others show no advantage over metformin [28,31,32]. Similarly, TZDs demonstrate variable performance in lowering fasting glucose, with some studies reporting small benefits over metformin while others show no significant difference [13,27]. Additionally, liraglutide has shown a reduction in fasting glucose, although results across studies are inconsistent and marked by high heterogeneity [25]. A systematic review confirmed metformin's modest superiority over exenatide in lowering fasting glucose, though results varied by study design and sample characteristics [20].

Among non-pharmacological options, lifestyle modification alone generally does not lead to better glucose outcomes compared to metformin. The combination of lifestyle changes with metformin does not appear to significantly outperform metformin alone [26]. A network meta-analysis also supported the effectiveness of metformin over orlistat and some other agents in improving fasting glucose, although the evidence varied across studies and often suffered from inconsistencies and methodological limitations [29]. Moreover, combining metformin with lifestyle or hormonal interventions such as EE/CA (etinylestradiol + cyproteron acetate) or EE/DRSP (etinylestradiol + drospirenon) appears to reduce the negative metabolic effects of OCs and shows particular benefit in improving glucose metabolism in overweight PCOS patients [33].

GLP-1 receptor agonists such as exenatide demonstrate mixed outcomes; while some studies report minor advantages over metformin, the most notable benefits of GLP-1 analogs often lie outside glucose metrics, such as weight loss and ovulation improvement [17–19].

Fasting Insulin

Metformin is generally more effective than placebo and OCs in reducing fasting insulin levels [7,8,10–12]. When compared with agents like myo-inositol, N-acetylcysteine, or combinations of these with metformin, the differences are often minimal or inconsistent [22–24,31]. In some cases, metformin was associated with higher fasting insulin levels compared to N-acetylcysteine, although the quality of evidence was low and results varied with dosage and duration [31].

The combination of metformin with agents like spironolactone or simvastatin may offer greater reductions in fasting insulin than metformin alone, although these effects are not always mirrored in glucose or HOMA-IR outcomes [14,32]. However, one trial reported no notable improvement with the addition of simvastatin to metformin, highlighting the inconsistency of results depending on intervention specifics and study populations [28].

GLP-1 receptor agonists such as exenatide often show stronger reductions in insulin levels compared to metformin alone, particularly in studies with longer interventions [18,19]. Combination therapy with metformin may further enhance this effect, although evidence is limited and mainly supported by single trials [18]. However, not all studies confirm significant differences, and caution is advised due to heterogeneity and low certainty of evidence across studies [17,20].

TZDs, both as monotherapy and in combination with metformin, demonstrate variable efficacy in reducing fasting insulin levels across different populations. In traditional meta-analyses, combinations such as metformin plus TZDs were more effective than metformin alone in lowering fasting insulin. However, network meta-analyses did not confirm consistent superiority, suggesting the effect may depend on patient characteristics or study design [13]. Moreover, comparisons between metformin and either pioglitazone or rosiglitazone showed no overall differences in fasting insulin, although in women with a BMI below 27 kg/m², rosiglitazone alone outperformed the combination with metformin in lowering fasting glucose [27]. Metformin and TZDs were the only insulin sensitizers in the analysis that showed statistically significant reductions in fasting insulin, though direct comparisons of their

relative contributions to the overall effect were not provided [25]. Network meta-analyses indicated that combination regimens including metformin - such as clomiphene citrate plus metformin (CC+MET) or cyproterone acetate plus ethinylestradiol plus metformin (CPA+EE+MET) - were more effective in reducing fasting insulin than the corresponding monotherapies. Still, some comparisons showed inconsistencies, which weakened the reliability of the results in parts of the analysis [29].

Supplementation with vitamin D in combination with metformin has shown to reduce fasting insulin and improve insulin sensitivity parameters compared to metformin alone, though heterogeneity in these studies warrants cautious interpretation [15].

Homeostatic Model Assessment of Insulin Resistance

Metformin is effective in improving insulin resistance, as measured by HOMA-IR, particularly in comparison to placebo [7]. Findings on TZDs, such as pioglitazone and rosiglitazone, are mixed. While some analyses suggest that TZDs or their combination with metformin may reduce HOMA-IR more effectively than metformin alone [13], other studies found no significant difference between these agents and metformin in improving insulin resistance [27].

Several combination therapies and monotherapies involving metformin have demonstrated statistically significant reductions in HOMA-IR compared to other pharmacological interventions. These include metformin plus clomiphene citrate versus clomiphene alone, metformin versus clomiphene, and metformin versus hormonal treatments such as CPA+EE (cyproterone acetate plus ethinylestradiol). In these comparisons, metformin consistently showed superior effectiveness. Although heterogeneity across studies was moderate and not resolved by sensitivity analyses, the overall findings support metformin's advantage over these alternatives [29].

GLP-1 receptor agonists, such as exenatide, have been repeatedly compared with metformin in terms of their effect on insulin resistance measured by HOMA-IR. Some studies suggest that exenatide may offer greater reductions, particularly in longer-duration interventions [17–19]. However, other analyses, including a detailed meta-analysis, found no significant differences between the treatments, and the quality of evidence was rated as very low due to high heterogeneity and small sample sizes [20]. Additionally, one study did not confirm the superiority of exenatide over metformin [31].

Several studies have compared the effect of metformin and OCs on insulin resistance in women with PCOS, with particular focus on HOMA-IR. In direct comparisons women receiving OCs alone had higher HOMA-IR levels compared to those treated with a combination of OCs and metformin, with the effect being more pronounced among women with lower BMI [11]. Another large meta-analysis found no statistically significant difference in HOMA-IR between OCs alone and OCs combined with metformin in the overall population. However, subgroup analyses indicated that the combination was more effective in women using cyproterone acetate-containing OCs and in those receiving short-term treatment (≤3 months), where significant improvements in HOMA-IR were observed [30]. A separate study comparing COCP alone to COCP combined with metformin also found no significant difference in HOMA-IR, but the small sample size limits the reliability of this finding [12].

Metformin combined with spironolactone has demonstrated superior effects on insulin resistance compared to metformin alone, but this benefit appears to depend on the duration of therapy. Significant improvements in HOMA-IR were observed only in studies lasting six months or longer, suggesting that prolonged treatment is necessary to achieve measurable metabolic benefits [14].

Vitamin D supplementation in combination with metformin, when compared to metformin alone, has been associated with modest but significant improvements in HOMA-IR. However, considerable heterogeneity across studies suggests that these findings should be interpreted with caution [15].

Lifestyle modification alone has been shown to improve insulin resistance and, in some studies, may be more effective than metformin. Additionally, limited evidence suggests that combining lifestyle changes with metformin may provide further benefit, although results across studies remain inconsistent [26]. Comparisons between metformin and myo-inositol reveal similar effectiveness on HOMA-IR, without consistent evidence favoring either treatment [22,24].

3.3 Lipid Metabolism Parameters

Dyslipidemia is a frequent metabolic abnormality in women with PCOS, contributing to increased cardiovascular risk. This chapter reviews the comparative effectiveness of metformin versus other pharmacological and non-pharmacological interventions in modifying lipid profiles, specifically total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides (TG).

Total Cholesterol

When compared to COCPs, metformin significantly reduced TC only in women with BMI below 25 kg/m², with no meaningful differences observed in overweight or obese subgroups. Additionally, metformin alone was more effective than the combination of metformin and COCPs in lowering TC, and adding COCPs to metformin did not offer any additional benefit and, in some cases, slightly worsened lipid profiles [10,12,30,33]. This finding was supported by another analysis showing that metformin was superior to COCPs in reducing TC in both adults and adolescents with PCOS [11]. When compared to placebo, metformin provided modest reductions in TC, especially in overweight or obese women [7,12]. Among pharmacological combinations, the addition of simvastatin to metformin consistently produced a greater decrease in TC compared to metformin alone [28,29,32].

No clear superiority was observed when metformin was compared with agents such as pioglitazone or rosiglitazone in terms of TC [27]. In a traditional meta-analysis, TZDs combined with metformin were more effective than metformin alone in reducing TC; however, this superiority was not confirmed in the network meta-analysis [13]. Agonists of the GLP-1 receptor, such as exenatide, did not outperform metformin in improving TC levels [17,19,20]. Inositol-based therapies offered comparable effects to metformin, with no significant differences in TC levels [22]. Adding lifestyle interventions to metformin enhanced its effect on TC, especially in overweight women [33].

High-Density Lipoprotein

Metformin showed no significant effect on HDL-C compared to COCPs in women with BMI below 30 kg/m² and was associated with a slight reduction in HDL-C in those with BMI ≥ 30 kg/m². While metformin alone was more favorable than combination therapy with COCPs for HDL-C in lean women, adding metformin to COCPs resulted in a slight improvement in HDL-C compared to COCPs alone, although the overall effect was minimal [10]. This minimal effect was confirmed in another analysis, which found no significant difference in HDL-C between COCPs alone and in combination with metformin [30]. Other comparisons with COCPs revealed no advantage of metformin, and in women with BMI ≥ 25 kg/m², metformin was associated with lower HDL-C levels compared to COCPs [11,12].

GLP-1 receptor agonists such as exenatide or liraglutyd did not demonstrate a meaningful advantage in raising HDL-C compared to metformin monotherapy [17,19,20]. Comparative studies with inositol, TZDs and simvastatin found no significant difference in HDL-C compared to metformin [22,27,34], while saxagliptin was associated with a greater reduction in HDL-C, suggesting a relative advantage of metformin [34]. Overall, HDL-C appears to be a lipid parameter less responsive to metformin-based interventions [29].

Low-Density Lipoprotein

Compared with placebo, metformin showed modest LDL-C reduction, with better outcomes in women with elevated BMI [7,12,29,35]. In the overall analysis, combining OCs with metformin did not result in a statistically significant difference in LDL-C levels compared to OCs alone; however, a notable reduction in LDL-C was observed when metformin was combined specifically with drospirenone-containing OCs [30]. In women with BMI < 25 kg/m², metformin reduced LDL-C more effectively than COCPs, but this benefit was not observed in overweight or obese subgroups. Notably, in women with BMI ≥ 30 kg/m², metformin was even associated with a slight increase in LDL-C, indicating a potentially unfavorable effect in this population [10]. Compared to metformin alone, the addition of COCPs did not demonstrate a consistent effect on LDL-C levels, and similarly, no significant difference was observed between COCPs alone and in combination with metformin, indicating insufficient evidence to support a benefit or harm of these combinations [10,12].

The combination of metformin with statins, such as simvastatin, resulted in a consistent and clinically relevant reduction in LDL-C, superior to that achieved with metformin alone [28,29,32]. In contrast, combinations with myo-inositol did not yield additional benefit [22].

GLP-1 receptor agonists did not demonstrate better LDL-C outcomes than metformin [17,19,20]. In head-to-head comparisons, rosiglitazone was more effective than metformin in lowering LDL-C, while pioglitazone showed comparable results [27]. Network meta-analysis confirmed that TZDs were more effective than metformin in lowering LDL-C levels [13].

Triglycerides

Compared to placebo, metformin showed modest reductions in TG, particularly in overweight populations [7,12,35]. Metformin reduced TG levels significantly in lean women compared to COCPs, but showed no meaningful benefit in women with BMI $\geq$ 25 kg/m² [10]. The combination of metformin with COCPs was less effective in reducing TG than metformin monotherapy [10,12]. Additionally, when comparing COCPs alone to their combination with metformin, no significant differences in LDL-C levels were observed, despite considerable heterogeneity across studies that could not be attributed to BMI differences [10]. Moreover, in one analysis, COCPs alone were found to reduce TG levels more effectively than when combined with metformin, suggesting a potential adverse interaction between these treatments [12]. Flutamide demonstrated superior efficacy in lowering TG levels compared to both metformin and placebo. According to network meta-analysis results, DPN+EE+MET appeared less effective than placebo in lowering TG, suggesting potential adverse effects on lipid metabolism [29].

GLP-1 receptor agonists, whether used alone or with metformin, did not offer clear advantages in lowering TG over metformin [17,19,20]. Combination therapy with TZDs improved TG levels more than metformin alone and also outperformed TZDs used as monotherapy. Berberine showed a modest but greater effect than metformin in lowering TG [13].

The combination of metformin with simvastatin produced substantial reductions in TG compared to metformin monotherapy [29,32]. Resveratrol combined with metformin demonstrated more favorable effects on metabolic outcomes compared to metformin monotherapy [29]. When compared to myo-inositol, metformin was less effective in TG reduction [22].

4. Conclusions

PCOS presents a multifaceted clinical challenge, with metabolic, reproductive, and endocrine disturbances often intersecting in complex ways. Among the wide array of therapeutic options, metformin remains a cornerstone of pharmacological management due to its insulin-sensitizing effects and broader impact on glucose metabolism, lipid profiles, and anthropometric outcomes.

This review has demonstrated that metformin consistently yields modest but clinically relevant improvements in body weight, BMI, and waist circumference, particularly in overweight and obese populations. While it is not universally superior to other treatments across all anthropometric parameters, its effectiveness increases when used in combination with agents such as GLP-1 receptor agonists or lifestyle interventions.

In terms of glucose metabolism, metformin outperforms placebo and many commonly used agents, including OCs and some insulin-sensitizers, in improving fasting glucose, insulin levels, and insulin resistance (as measured by HOMA-IR). These effects are particularly pronounced in women with higher baseline insulin resistance. However, newer agents such as GLP-1 receptor agonists and certain combination therapies may offer additional benefits, although current evidence is limited and sometimes inconsistent.

With regard to lipid metabolism, metformin provides moderate improvements, particularly in reducing TC, LDL-C, and TG—again most effectively in combination with other agents like statins. Its effect on HDL-C appears limited and is often less favorable than that of OCs in lean women.

Overall, while metformin remains a valuable and widely applicable treatment in PCOS, its clinical benefits are most robust when tailored to patient-specific profiles and used in combination with other pharmacologic or lifestyle strategies. The heterogeneity of PCOS phenotypes underscores the need for individualized care. Future high-quality, long-term comparative studies are essential to refine treatment algorithms and optimize outcomes across metabolic, reproductive, and psychological domains.

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