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REVIEW

PCOS and Obesity: Contraception Challenges

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Abstract: Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders affecting women of reproductive age, with an estimated prevalence of 5–10%. Women with PCOS are at increased risk for metabolic disturbances. A significant proportion of women with PCOS, ranging from 40 to 85%, are either overweight or obese. Oral contraception is the standard first line treatment for PCOS. However, certain conditions associated with PCOS, such as obesity, must be considered when deciding to prescribe combined oral contraception. It seems that there is no clinical advantage in using high-dose ethinyl estradiol over low-dose formulations. Lower-dose EE formulations may be considered a safer option for obese PCOS patients. Combined oral contraception containing natural estrogens, which have a beneficial effect on metabolic parameters, could also be a viable option for this group. Progestin-only (POPs) formulations have minimal metabolic effects, making them a safe contraceptive choice for patients with obesity and a high risk of coronary artery disease, cerebrovascular disease, venous thromboembolism, or hypertension. Non-oral contraceptive methods, such as transdermal patches and vaginal rings, offer a valuable alternative for women with PCOS who prefer not to use daily oral contraceptives. However, the absence of anti-androgenic progestins in these contraceptive methods may limit their effectiveness, especially for women with moderate to severe clinical signs of androgen excess. The use of LNG-IUDs in women with PCOS may be beneficial in several ways. First, in cases where other contraceptive methods are contraindicated, the LNG-IUD provides effective contraception while also regulating abnormal uterine bleeding. Additionally, the relative hyperestrogenism associated with anovulation in PCOS can lead to endometrial hyperplasia with atypia and, in severe cases, endometrial cancer. Therefore, in women with both PCOS and obesity, the LNG-IUD may be preferred over oral megestrol acetate for endometrial protection.

Keywords: PCOS, polycystic ovary syndrome, oral contraception, obesity, IUD

Introduction

Polycystic ovary syndrome (PCOS) is one of the most prevalent endocrine disorders affecting women of reproductive age, with an estimated prevalence of 5–10%, depending on the diagnostic criteria used and the ethnic population studied.[1] This condition is characterized by menstrual irregularities, anovulation, clinical manifestation of androgen excess (such as acne, hirsutism, alopecia), and metabolic dysfunctions such as insulin resistance or dyslipidemia.[2]

Over the past two decades, the diagnostic criteria for PCOS have undergone multiple revisions. Currently, diagnosis is usually based upon the 2023 International Evidence-based Recommendations, which adhere to the criteria outlined in the 2018 guidelines, themselves derived from the earlier 2003 Rotterdam Consensus.[3–5] To confirm a diagnosis of PCOS, at least two of the following criteria must be present: menstrual irregularities or anovulation, clinical or biochemical evidence of hyperandrogenism, or polycystic ovarian morphology (PCOM).[4,5] Furthermore, conditions such as thyroid disorders, non-classical congenital adrenal hyperplasia (NCCAH), or hyperprolactinemia must be ruled out to avoid misdiagnosis.[5]

Four phenotypes of PCOS have been described, labelled alphabetically from A to D, based on the combination of the diagnostic criteria.[6] Phenotype A, regarded as the "complete" form of PCOS, includes all diagnostic criteria, while phenotype B lacks PCOM but retains hyperandrogenism and menstrual irregularities.[7] Both phenotypes A and B are often referred to as "classic" PCOS and are associated with a higher risk of metabolic disorders such as insulin resistance and dyslipidemia.[8]

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Phenotype C, or "ovulatory" PCOS, involves hyperandrogenism and PCOM without ovulatory issues, whereas phenotype D, or "non-hyperandrogenic" PCOS, presents milder symptoms with only PCOM and menstrual cycle irregularities.

PCOS often manifests at puberty, typically with menstrual irregularities such as oligomenorrhea (fewer than nine cycles per year) or amenorrhea (absence of menstruation for more than three consecutive months).[9] Fortunately, these patients tend to experience more regular menstrual cycles after the age of 40, likely due physiological reduction in ovarian reserve.[9]

Hyperandrogenism manifests clinically as hirsutism, acne, and male-pattern hair loss. Acne alone, however, is not a definitive sign of hyperandrogenism, as it is a common feature in adolescence. Severe acne during the perimenarcheal years or moderate inflammatory acne with more than 10 concurrent facial lesions may suggest at a hyperandrogenic etiology.[10] The Ferriman-Gallwey scale is often employed to assess hirsutism, though the threshold values can vary by ethnicity.[11] Hair loss, though less common in adolescents, is typically assessed using the Ludwig visual scale and may present in either male or female pattern distribution.[12] Male pattern alopecia affects the fronto-temporo-occipital regions of the scalp while female pattern alopecia typically begins at the crown of the head.[13] Biochemical evaluation for hyperandrogenism in PCOS patients include measurements of total and free testosterone, as well as other androgens such as androstenedione dehydroepiandrosterone sulfate (DHEA-S).[5]

Polycystic ovarian morphology (PCOM), identified through ultrasound, is characterized by numerous preantral or early antral follicles. It is usually detected via transvaginal or transabdominal ultrasound. The diagnostic criteria for PCOM have evolved alongside advancements in ultrasound technology. The most recent 2023 recommendations define PCOM as the presence of at least one of the following: a follicle count ≥20 in at least one ovary, ovarian volume ≥10 mL, or ≥10 follicles per section.[5] These criteria only apply only to adult patients, as there is no established consensus for assessing PCOM in adolescents.[5] Interestingly, the 2023 guidelines propose anti-Müllerian hormone (AMH) as an alternative to ultrasound in diagnosing PCOM, as AMH levels tend to be elevated in PCOS patients.[5] However, no universally accepted threshold for AMH has been established, though some meta-analyses recommend using a cut-off value of 4.7 ng/mL.[5,14]

PCOS can adversely affect physical, emotional, reproductive, and psychological health.[15] Women with PCOS are at increased risk of developing obesity, metabolic dysfunction, insulin resistance, dyslipidemia, diabetes, infertility, thromboembolic events, and cardiovascular disease.[16,17] The presence and severity of these complications depend on several factors, including age, family history, genetic predisposition, PCOS phenotype, comorbidities, and treatment received.[15] Therefore, early diagnosis and targeted medical management are crucial.

Given the metabolic risks and signs of hyperandrogenism associated with PCOS, therapeutic interventions should be adequately tailored to individual patient needs. Treatment strategies typically include both lifestyle modifications and pharmacological approaches.[5] For patients not seeking immediate pregnancy, hormonal contraceptives are the first-line treatment, addressing both menstrual irregularities and androgen excess.[5] Additional pharmacological options may include insulin sensitizers (such as metformin), anti-androgens (eg, spironolactone, flutamide), and ovulation induction agents (eg, clomiphene citrate, letrozole).[5,18]

The purpose of the review below is to summarize knowledge about the use of hormonal contraception to treat patients with polycystic ovary syndrome, with particular emphasis on patients suffering from metabolic disorders, above all obesity.

Methods

A systematic literature search for relevant English language publications published until January 2025 was conducted in several major databases, including PubMed and ScienceDirect. Authors investigated the available data from clinical studies, review articles, and meta-analyses following Medical Subject Headings (MeSH) terms, alone or in combination: PCOS, Polycystic ovary syndrome, oral contraception, obesity, vaginal ring, contraceptive patch, long-acting reversible contraception, LARC, mini-pill, progestin-only pill, combined contraception. Moreover, reference lists of included articles were manually screened to identify additional studies.

Obesity in PCOS Patients

Women with PCOS are at increased risk for metabolic disturbances, particularly in the presence of obesity. A significant proportion of women with PCOS, ranging from 40 to 85%, are either overweight or obese.[17] While both lean and obese PCOS patients often exhibit reduced insulin sensitivity, although this condition is not included in the diagnostic criteria

for PCOS. Nonetheless, they frequently present with clinical manifestations of insulin resistance, such as acanthosis nigricans or hepatic steatosis.[9]

Globally, the incidence of obesity - defined as a body mass index (BMI) greater than 30 kg/m² - has increased dramatically,[19] particularly in the United States, where over two-thirds of adults and approximately one-third of children and adolescents are classified as overweight or obese.[20] The association between obesity and PCOS was first identified by Stein and Leventhal, who noted it's links with anovulation, hirsutism, and polycystic ovaries.[21] However, many uncertainties remain about the exact nature of this relationship.[22]

Obesity is linked to insulin resistance and compensatory hyperinsulinemia, conditions that overlap with the common features of metabolic syndrome (MetS), which include abdominal obesity, hypertension, dyslipidemia, and glucose intolerance.[23] MetS is highly prevalent among PCOS patients, affecting 33.4% to 47% of this population, significantly higher than the 24% prevalence seen in the general European population.[24] This overlap raises questions about whether obesity and MetS are causes, consequences, or merely coexisting conditions in PCOS.[25] Although not all women with PCOS are obese, as indicated in Stein and Leventhal's initial observations of women with normal or only slightly elevated weight,[26,27] PCOS patients generally tend to exhibit visceral adiposity, which is associated with insulin resistance and exacerbates the metabolic and hormonal imbalances characteristic of the syndrome.[28]

Furthermore, obesity and hyperinsulinemic states in PCOS are strongly associated with hyperandrogenism. Insulin acts as a co-gonadotropin, stimulating ovarian androgen production.[29] Elevated levels of inflammatory molecules and growth factors in obese individuals further contributes to ovarian androgen production while inhibit the aromatization of androgens into estrogens, promoting the development of the PCOS phenotype.[30] Additionally, the aromatization of androgens to estrone in adipose tissue may contribute to anovulation and menstrual irregularities, hallmark features of PCOS.[31]

Insulin resistance and hyperinsulinemia also directly affect the hypothalamus, disrupting gonadotropin secretion and increasing luteinizing hormone (LH) levels, which in turn amplifies androgen production.[32] Insulin resistance further reduces hepatic production of sex hormone-binding globulin (SHBG), leading to increased androgen bioavailability, exacerbating the clinical symptoms of hyperandrogenism in PCOS.[33,34]

Although obesity significantly affects the hypothalamic-pituitary-ovarian (HPO) axis in PCOS, it does not always result in the syndrome. Obesity alone minimally increases the risk of developing PCOS, and despite the dramatic rise in global obesity rates, the prevalence of PCOS has only slightly increased.[22] Research by Dunaif et al demonstrated that obesity and PCOS independently and additively contribute to the development of insulin resistance.[35] Moreover, obesity worsens other metabolic parameters in PCOS, such as the lipid profile,[36] and is implicated in the onset of MetS features.[24]

A meta-analysis by Lim et al found that overweight and obese women with PCOS experienced more severe clinical and metabolic disturbances than non-overweight counterparts. These patients exhibit lower SHBG, increased testosterone levels, a higher free androgen index (FAI), more pronounced hirsutism, elevated fasting glucose, and greater insulin resistance.[37] It is therefore obvious why a more severe PCOS phenotype is typically observed in obese women, as are the findings of greater menstrual irregularity, infertility, miscarriage, gestational diabetes, pregnancy-induced hypertension, clinical and biochemical hyperandrogenism, glucose intolerance, type 2 diabetes mellitus (T2DM), and MetS.[38]

PCOS patients are also at increased risk of cardiovascular disease (CVD), a risk exacerbated by obesity.[39] In this context, the concepts of "metabolically healthy obese" (MHO) and "metabolically unhealthy obese" (MUO) have emerged to differentiate between individuals with and without cardiometabolic risk factors despite obesity.[40] MHO is generally defined by the presence of two of fewer of the four MetS diagnostic criteria, according to the NCEP ATP III definition.[41] MUO-PCOS patients tend to have worse metabolic profiles, including higher testosterone levels, more severe hyperandrogenism (as indicated by Ferriman-Gallwey scores), and poorer outcomes on insulin resistance markers such as the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), Visceral Adiposity Index (VAI), and Fatty Liver Index (FLI).[42]

Given these metabolic and hormonal challenges, managing PCOS in the context of obesity requires a multifaceted approach. Treatment typically includes lifestyle modifications such as dietary changes, increased physical activity, and psychological support, combined with pharmacological interventions.[5] Combined hormonal contraceptives (CHCs), which contain both estrogen and progestin, are considered first-line treatments for the clinical manifestations of PCOS.[16] However, when choosing a contraceptive for women with PCOS, factors such as body weight, menstrual patterns, hyperandrogenism,

and the presence of hyperinsulinemia or MetS must be carefully considered.[43] CHCs must be tailored to the specific needs of the patient, especially in the presence of metabolic and cardiovascular risks associated with obesity.[43]

CHCs containing natural estrogens such as estradiol (E2), estradiol valerate (E2V), or estetrol (E4) are preferred due to their lower impact on hepatic protein production and minimal effects on hemostasis markers and angiotensinogen production,[44] making them a safer choice for women with PCOS and additional cardiovascular risk factors.[44] Furthermore, antiandrogenic progestins, are particularly useful for managing PCOS patients with metabolic disorders, as they have a neutral impact on carbohydrate and lipid metabolism, thereby reducing metabolic complications.

The relationship between obesity and metabolic syndrome in PCOS is complex, with insulin resistance serving as a critical link between the two conditions. Effective management of PCOS in the context of obesity requires addressing both the hormonal and metabolic aspects of the syndrome, with treatment strategies tailored to individual needs of patients.[45,46]

Combined Oral Contraceptives in Obese Patients with PCOS

History of combined oral contraceptives (COC) began in the 1960s in the in the United States, where they were first approved for contraceptive use.[4] Combined oral contraception are defined as contraceptive methods that contain two hormones: an estrogen (usually ethinyl estradiol, 17 beta-estradiol, or estetrol) and a progestin (a synthetic form of progesterone).[47] In addition to their contraceptive effects (primarily through the inhibition of ovulation) COCs also exhibit non-contraceptive benefits. These include the suppression of hyperandrogenemia and hyperandrogenism by inhibiting luteinizing hormone (LH) (via the progestin component), increasing levels of sex hormone-binding globulin (SHBG) (via the estrogen component), and blocking testosterone receptors.[45] These properties make COCs an effective treatment for menstrual disorders and hyperandrogenism.

As previously described, PCOS is the most common endocrine disorder in women of reproductive age. COCs are the standard first line treatment for PCOS, specifically for managing irregular menstrual cycles and symptoms of hyperandrogenism such as hirsutism, acne vulgaris.[5]

However, certain conditions associated with PCOS, such as obesity, must be considered when deciding to prescribe COCs. Obesity exacerbates many PCOS symptoms. COCs containing cyproterone acetate in combination with ethinyl estradiol (EE) can offer benefits for obese PCOS patients, particularly in reducing hyperandrogenism. Nevertheless, EE/CPA COCs are not recommended as first line treatment due to the significantly increased risk thromboembolism.[47]

Teede et al[4] have indicated that there is no clinical advantage in using high-dose ethinyl estradiol (>30 microgram) over low-dose formulations (< 30 microgram). General population guidelines should be followed when prescribing COCs in adults and adolescents with PCOS, as specific types and dose of progestins and estrogens or combinations of COCs cannot be recommended based on available evidence (Summary in Table 1).

Table 1 Combined Hormonal Contraception in Obese Patients With PCOS – Summary Table

Reference	Study Type	Population	Intervention / Focus	Key Findings
Teede et al, 2018[4]	Guideline (Evidence-based)	Women with PCOS (including obese)	Comprehensive PCOS management recommendations	CHCs recommended as first-line therapy for cycle regulation and hyperandrogenism. It is indicated that there is no clinical advantage in using high-dose ethinyl estradiol (>30µcg) over low-dose formulations (< 30 µcg).
Teede et al, 2023[5]	Updated Guideline	Women with PCOS	Updated evidence-based PCOS guideline	Highlights cardiovascular risks with CHC in obese women, advises individualized assessment. Natural estrogen preparation and the lowest effective estrogen doses (20–30 µcg) should be considered

(*Continued*)

Table 1 (Continued).

Reference	Study Type	Population	Intervention / Focus	Key Findings
Forslund et al, 2024[47]	Guideline Perspective	Nordic population with PCOS	Regional application of international guideline	Reinforces Teede et al's recommendations for obese women
De Medeiros et al, 2024[48]	Meta-analysis (RCTs)	Obese women with PCOS	CHC use and outcomes	CHCs improved cycle regulation and hirsutism; small increased VTE risk in obese subgroup. Certain CHC formulations might increase fat mass deposition and increase in lipid levels in PCOS patients.
Belail Hammad et al, 2023[49]	Narrative Review	Women with obesity	Overview of contraceptive methods	CHCs effective but caution in women with BMI > 35 due to cardiovascular and thromboembolic risk.
Rosano et al, 2022[50]	Review	Obese women	Contraceptive use and CV risk	CHC use associated with increased CV risk in obesity; alternative methods should be considered.
Stein et al, 2005[51]	Observational study	General population	Obesity as VTE risk factor	Obesity independently increases VTE risk, relevant when considering CHC
Horton et al, 2016[52]	Systematic Review	Obese women	CHC and cardiovascular events	CHC use in obese women may increase risk of thromboembolism and stroke

Lower-dose EE formulations may be considered a safer option for obese PCOS patients. COCs containing natural estrogens, which have a beneficial effect on metabolic parameters, could also be a viable option for this group, although further clinical studies are needed to confirm these benefits.

De Medeiros at al.[48] conducted a study to assess whether obesity-related outcomes might be influenced by different COCs formulations in women with PCOS. Their analysis, which included data from 13 randomized clinical trial, suggested that certain COC formulations might increase fat mass accumulation and lipid levels in PCOS patients. However, the authors emphasized caution in drawing definitive conclusions due to concerns about the quality and heterogeneity of the studies included.

In line with the findings of Teede et al[5] there is no clinical advantage in using high doses of ethinyl estradiol versus low doses. General population guidelines should be followed when prescribing COCs in adults and adolescents with PCOS as no specific progestin or estrogen dose can be recommended.

The authors also suggest that natural estrogen preparation and the lowest effective estrogen doses (20–30 micrograms) should be considered, balancing efficacy, metabolic risk profile, side effects, costs, and availability. Special consideration should be given to patients with higher body weight and cardiovascular risk.

Additionally, the relative and absolute contraindications and side effects of COC must be taken into account. While the UK and US medical eligibility criteria do not consider obesity a contraindication for contraception, clinical caution is advised when prescribing COCs to obese women due to the synergistic effect of obesity and COCs on the risk of vein thrombosis (DVT).[49]

According to Rosano et al[50] the use of COCs in obese women warrants careful consideration, particularly due to the heightened risk of venous thromboembolism (VTE). Stein et al[51] found that the relative risk of VTE in obese individuals is 2.5 times higher compared to non-obese individuals. In women over the age of 40, the risk increases to 5.19. Horton et al[52] reported that obese COC users had a 5 to 8 times higher risk of VTE than obese non-users, and approximately 10 times the risk compared to non-obese, non-users.

Another important consideration in the use of COCs for obese PCOS patients is their potential metabolic risk or risk factors for diabetes.[16] In these cases, combining COCs with metformin may be beneficial. COCs can be used over metformin for managing hirsutism and irregular menstrual cycles in PCOS. One of the main goal to use COCSs over metformin is to control metabolic problems, particularly to address metabolic issues. Combining COCs with metformin is

especially effective for PCOS patients diagnosed with obesity, diabetes risk factors, impaired glucose tolerance, or belonging to high-risk ethnic groups. When COCs are contraindicated or poorly tolerated, metformin alone may be used to regulate menstrual cycles in obese PCOS patients.[16]

POPs in PCOS Patients with Obesity

Progestin-only pills (POPs), also known as mini-pills, are a suitable contraceptive option for individuals who cannot or prefer not to use estrogen-containing contraception. POPs work by thickening cervical mucus to inhibit sperm migration, suppressing ovulation, reducing midcycle peaks of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), slowing the movement of an ovum through the fallopian tubes, and thinning the endometrium.[53]

The composition of POPs varies, with the most common formulations containing low daily dose of levonorgestrel (LNG), norethindrone, or desogestrel (DSG). Most of these oral contraceptives are taken continuously, with the exception of preparations containing drospirenone (DRSP) which is taken daily for 24 days followed by a 4-day placebo period. DRSP is frequently used due to its ovulation suppression and anti-mineralocorticoid properties[53] (Summary in Table 2). Norethindrone, on the other hand, primarily acts by thickening cervical mucus to inhibit sperm penetration, suppressing ovulation, reducing midcycle LH and FSH peaks, slowing the ovum's movement through the fallopian tubes, and altering endometrial thickness. Some progestins possess potent anti-androgenic properties, making them more effective in managing polycystic ovary syndrome, hirsutism, and acne.[54,55] Although dienogest has strong anti-androgenic effects, it is not approved for use as oral contraception.

While continuous use of POPs may be easier for some patients, it is associated with a higher incidence of breakthrough bleeding compared to COCs.[43] POPs must be taken daily, ideally at the same time each day, which can be less convenient than other contraceptive methods, such as the patch or vaginal ring.[43]

In patients with amenorrheic PCOS, alternative progestins such as micronized natural progesterone, oral medroxyprogesterone acetate (MPA), or nomegestrol acetate (NOMAC) can be administered in short cycles to protect the endometrium from the hyperplasic effects of unopposed estrogen exposure.[56] Although the only absolute

Table 2 POP in Obese Patients With PCOS – Summary Table

Reference	Study Type	Population	Intervention / Focus	Key Findings (Focused on POP)
Hickey et al, 2012[56]	Cochrane Review	Women with anovulatory bleeding (incl. PCOS)	Progestogens with/ without estrogen for irregular bleeding	Progestins alone are effective in reducing irregular bleeding; evidence limited for obese PCOS subgroup
Cortés & Alfaro, 2014[57]	Review	Women using hormonal contraceptives	Impact on glycemic control	Progestin-only pills have minimal impact on glycemic regulation; may be preferred in case of insulin resistance
Li et al, 2017[58]	Systematic Review	Women with PCOS	Drospirenone vs standard treatments	DRSP compared to CPA and DGS demonstrates comparable or superior efficacy in improving symptoms and protecting the cardiovascular system. For PCOS patients with insulin resistance (IR) or obesity, combining DRSP with metformin may be more effective than using DRSP alone.
Tepper et al, 2016[59]	Systematic Review	Women using POPs	Risk of thromboembolism with progestin-only methods	POP is not associated with increased VTE risk—even in obese women;
Bergendal et al, 2014[60]	Observational study	Women on hormonal contraception	Hormonal contraception and VTE risk stratified by genotype	VTE risk is significantly lower with POPs than with CHCs, even in high-risk populations

contraindication for POP use is current breast cancer, alternative contraceptive methods should be considered in patients with severe cirrhosis, hepatocellular adenoma/carcinoma, or a history of ischemic stroke or coronary events.[56]

POPs are generally considered appropriate in patients where contraindications are found to estrogen-containing contraceptives or in those who prefer to avoid estrogen exposure. However, the efficacy of POPs may be lower in highly fertile individuals compared to other hormonal contraceptive methods. Additionally, menstrual irregularities are common among POP users, leading to a higher rate of discontinuation. Nonetheless, POPs do not appear to be associated with significant weight gain, though they may increase the incidence of follicular cysts.

Progestin-only formulations have minimal metabolic effects,[57] making them a safe contraceptive choice for patients with a high risk of coronary artery disease, cerebrovascular disease, venous thromboembolism, or hypertension - in which use of estrogen-containing contraceptives are contraindicated. However, it is generally recommended to avoid POPs in individuals with obesity due to concerns over potentially reduced efficacy. In cases where patients with obesity have additional comorbidities that increase cardiovascular risks associated with estrogen use, those who want to avoid estrogen, the use of etonogestrel implant, a levonorgestrel intrauterine device (LNG-IUDs), or depot medroxyprogesterone acetate (DMPA), taking two POPs daily may be an alternative. Although data supporting this approach are lacking.

DRSP has been shown to modulating hormones, insulin, and lipid metabolism in women with PCOS. Compared to commonly used drugs for PCOS symptom management, such as cyproterone acetate (CPA) and desogestrel (DSG), DRSP demonstrates comparable or superior efficacy in improving symptoms and protecting the cardiovascular system. For PCOS patients with insulin resistance (IR), obesity, or a high LH/FSH ratio, combining DRSP with metformin maybe more effective than using DRSP alone.[58]

Given that patients with PCOS often suffer from many metabolic consequences such as insulin resistance, progestin-only formulations, which have little impact on carbohydrate metabolism, represent a reasonable option for this group. Regarding venous thromboembolism (VTE), studies analyzing POPs or non-DMPA progestin-only contraceptives (POPs, LNG-IUDs, and implants) have shown no statistically significant increase in the odds of VTE among non-hormonal contraceptive users (OR 1.3, 95% CI 0.5–3.0 and OR 0.6, 95% CI 0.3–1.5).[59] Additionally, there was no significantly elevated risk of VTE among smokers using POPs (OR 2.4, 95% CI 0.7–8.3 and OR 0.95, 95% CI 0.2–6.0 in two studies when compared to nonusers who did not smoke).[59] Even in women with a personal or family history of VTE or hereditary thrombophilia, no association between POP use and VTE was observed (OR 0.8, 95% CI 0.2–3.9).[59]

Except for high-dose progestogen-only contraception, no increased risk of VTE has been associated with progestin-only contraceptive methods (adjusted OR 0.9, 95% CI 0.7–1,2).[60] Given the common metabolic profile of PCOS patients and the minimal impact of progestin-only formulations on carbohydrate metabolism, contraceptives remain a reasonable option for individuals with PCOS.

Monthly Methods: Patches and Rings as Alternatives to COCs - Benefits and Symptom Control in PCOS

As previously noted, despite being the most widely used form of birth control, combined oral contraceptives (COCs) have certain limitations. Daily oral intake requires strict adherence, which can sometimes lead to compliance issues. Furthermore, COCs undergo hepatic first-pass metabolism, which results in increased systemic side effects.[61] To mitigate these issues, non-oral contraceptive methods have been developed.[61]

Currently, two non-oral combined hormonal contraceptives are available: transdermal patches and vaginal rings.[62] These methods allow hormones such as ethinyl estradiol (EE) and synthetic progestins to bypass the gastrointestinal system, ensuring a steady release of hormones into the bloodstream[63].

Among transdermal options, only the patch containing EE and norelgestromin (NGMN) is globally approved for contraceptive use.[62] The patch is applied weekly for three consecutive weeks, followed by a patch-free week, and releases 20 µg of EE and 0.15 mg of NGMN daily.[64] Once applied, both NGMN and EE reach peak plasma levels in 48 hours and maintain steady concentrations throughout the applied timeframe.[65] NGMN, the active form of norgestimate (NGM), targets progesterone receptors and has minimal androgenic activity, making it suitable for women with androgen excess, such as those with PCOS.[66] A study by White et al compared transdermal patches with COCs

containing EE/NGMN or EE/NGM and found that while both reduced androgenic markers such as free testosterone, androstenedione, dihydrotestosterone, and DHEAS, the contraceptive patch induced a higher increase in sex hormone-binding globulin (SHBG) compared to COCs after three cycles[67] (Summary in Table 3).

Table 3 Patches and Rings in PCOS Patients – Summary Table

Reference	Study Type	Population	Intervention / Focus	Key Findings (Focused on Patches and Rings)
White et al, 2005[67]	Comparative Study	Women using hormonal contraceptives	Oral vs transdermal contraceptives containing EE/NGMN and EE/NGM respectively and androgenic markers	Both reduced androgenic markers but transdermal contraceptive induced a higher increase in SHBG after three cycles.
Smallwood et al, 2001[68]	Clinical Trial	General female population	Transdermal contraceptive efficacy and safety	Patch effective and well tolerated;
Audet et al, 2001[69]	RCT	Healthy women	Patch vs oral contraceptive on efficacy and cycle control	Patch showed comparable efficacy and better adherence;
Creasy et al, 2003[70]	Observational	Women on contraceptive patch	Effect of patch on lipid profile	Minimal changes in lipids; potentially useful in PCOS with dyslipidemia
Kluft et al, 2000[71]	Comparative Study	Healthy women	Patch vs COC and coagulation	Changes in coagulation parameters induced by the contraceptive patch were not significantly different from those observed with COCs containing EE and non anti-androgenic progestins
Creasy et al, 2000[72]	Placebo-controlled	General population	Patch vs placebo on lipid profile	Patch had neutral lipid effects
Tuppurainen et al, 2004[73]	Comparative Study	Women using NuvaRing	NuvaRing and lipid metabolism	Minor impact on lipid profile; potential benefit in PCOS with dyslipidemia
Timmer & Mulders, 2000[74]	Pharmacokinetic study	Healthy women	NuvaRing hormone levels	Stable hormone release profile; supports consistent endometrial effect
Roumen et al, 2001[75]	Clinical Trial	Women using NuvaRing	Efficacy and tolerability	Good cycle control, well tolerated; suitable for PCOS patients
Lopez et al, 2013[76]	Cochrane Review	Women using patch/ring vs COC	Comparative effectiveness and safety	Similar efficacy; ring may improve adherence; patch less favorable for VTE risk
Magnusdóttir et al, 2004[77]	Comparative Study	Healthy women	NuvaRing and hemostasis	Minimal impact on hemostasis; potential advantage in high risk patients
Grigoryan et al, 2008[78]	Observational	Women with type 1 diabetes	NuvaRing use	Safe and well tolerated; does not affect insulin sensitivity or glucose metabolism, even in women with type 1 diabetes.
Cagnacci et al, 2009[79]	RCT	Women using desogestrel/ etonorgestrel	Route of administration and insulin sensitivity	Vaginal ring had less adverse effect on insulin sensitivity vs oral route

(*Continued*)

Table 3 (Continued).

Reference	Study Type	Population	Intervention / Focus	Key Findings (Focused on Patches and Rings)
Dieben et al, 2002[80]	RCT	General female population	NuvaRing efficacy and cycle control	Effective with high user satisfaction;
Wieder & Pattimakiel, 2010[81]	Review	Women using NuvaRing	Efficacy and safety	Well tolerated and effective; Suitable for women at higher metabolic risk such as PCOS women
Mosorin et al, 2023[82]	RCT	Women with PCOS	Oral vs vaginal contraceptives and metabolic effects	Both routes showed similar efficacy in reducing androgenic markers in PCOS patients with only mild effects on glucose metabolism, insulin resistance, lipid profiles, blood pressure and anthropometric parameters.

In studies involving over 3300 women of reproductive age, the contraceptive patch has been shown to be a safe and reliable method of birth control,[68] providing cycle control similar to that of COCs containing EE/Levonorgestrel(LNG).[69] Other than mild skin irritation at the application site and a slight increase in the incidence of breast discomfort, side effects of patch contraceptives are comparable to those of COCs.[70]

Kluft et al also demonstrated in a randomized, open-label study that changes in coagulation parameters induced by the contraceptive patch were not significantly different from those observed with COCs containing EE and progestins without anti-androgenic effects, such as desogestrel (DSG) or LNG.[71] A placebo-controlled trial also showed that weight changes were similar between patch users and a placebo group.[72] Furthermore, increases in cholesterol and triglyceride levels with the patch were comparable to those observed with COCs containing EE/NGM.[70,72]

The vaginal ring is another widely-available non-oral contraceptive option. It contains 15 µg of EE and 120 µg of etonogestrel (ETG), the active form of DSG.[61] The ring is used for one cycle, with three weeks of insertion followed by one week without, and delivers hormones directly through the vaginal mucosa, bypassing first-pass liver metabolism.[73] Clinical research shows that serum levels of EE peak within three days of insertion, while etonogestrel levels peak after approximately one week. Hormone concentrations then decline steadily during the ring-free week.[74] This method effectively inhibits ovulation, with clinical trials reporting excellent cycle control and low rates of unscheduled bleeding (2.6–6.4%).[75] Compared to pill users, ring users reported fewer side effects, such as nausea, irritability, depression, bleeding, and estrogen withdrawal headache, but experienced more vaginal irritation and discharge.[76]

The vaginal ring has minimal impact on coagulation and metabolic parameters. In a non-randomized comparative study, Magnusdóttir et al found no significant differences in coagulation factors or fibrin turnover between women using the vaginal ring and those using COCs with EE and LNG, suggesting that the vaginal ring has a low impact on hemostasis.[77] Additionally, the ring does not affect insulin sensitivity or glucose metabolism, even in women with type 1 diabetes.[78,79] It is also associated with no significant changes in cholesterol or lipoprotein levels and has neutral effects on both systolic or diastolic blood pressure.[80] These attributes make the vaginal ring a particularly suitable contraceptive option for women at higher risk of metabolic conditions or cardiovascular disease, such as those with PCOS.[81]

Compared to COCs containing LNG and EE, the vaginal ring has been shown to increase SHBG levels more significantly, reflecting the lower androgenic activity of ETG.[73] In a recent randomized controlled trial by Mosorin et al, both the vaginal ring (EE/ETG) and COCs (EE 20 µg/DSG 150 µg) were found to be equally effective in reducing androgenic markers in PCOS patients, with only mild effects on glucose metabolism, insulin resistance, lipid profiles, blood pressure and anthropometric parameters (BMI, waist circumference).[82]

Overall, non-oral contraceptive methods, such as transdermal patches and vaginal rings, offer a valuable alternative for women with PCOS who prefer not to use daily oral contraceptives. Both these methods are effective at preventing

pregnancy, offer excellent cycle control, and, particularly in the case of the vaginal ring, tend to have fewer metabolic side effects. However, the absence of anti-androgenic progestins in these contraceptive methods may limit their effectiveness, especially for women with moderate to severe clinical signs of androgen excess.

LARCs in Women with PCOS and Obesity

Long-acting reversible contraceptives (LARCs) are highly effective contraceptive methods[83] that are associated with high adherence,[84] as they do not require daily compliance. LARCs include intrauterine devices (IUDs), which may be non-hormonal (Cu-IUD) or hormonal (levonorgestrel-releasing IUDs, LNG-IUD), subdermal implants (progestin-only, with systemic release), and injections, typically with depot-medroxyprogesterone (DMPA).[85] Due to the absence of estrogens in these formulations, LARCs can often be used when other methods are clinically contraindicated.[85]

In women with PCOS, LARCs are less frequently utilized because they do not address the primary features of the condition, such as hyperandrogenism, metabolic dysfunction, or acne.[5] However, when PCOS is associated with obesity, which exacerbates metabolic dysfunction and cardiovascular risk,[86] LARCs may be considered either alone or in combination with anti-androgen therapy. According to current guidelines, LARCs can be used without restriction in women with obesity and are preferred over combined oral contraceptives in cases where there are multiple risk factors for cardiovascular disease.[85]

IUDs are effective for 3 to 8 years, depending on the formulation[87] (Summary in Table 4). The LNG-IUD works through the local release of LNG, with serum levels typically insufficient to suppress ovulation.[88] The use of LNG-IUDs in women with PCOS may be beneficial in several ways. First, in cases where other contraceptive methods are contraindicated, the LNG-IUD provides effective contraception while also regulating abnormal uterine bleeding. Additionally, the relative hyperestrogenism associated with anovulation in PCOS can lead to endometrial hyperplasia

Table 4 LARCs in Women With PCOS and Obesity – Summary Table

Reference	Study Type	Population	Intervention / Focus	Key Findings (Focused on LARCs)
Bounous et al, 2023[87]	Review	Women in various clinical settings included PCOS	Overview of non-daily hormonal contraception	LARCs are effective and safe in PCOS; suitable for women with adherence concerns
Morelli et al, 2013[92]	Retrospective Study	Obese menopausal women	LNG-IUS for endometrial hyperplasia prevention	LNG-IUS reduced risk of endometrial pathology in obese women
Derbyshire et al, 2021[93]	Feasibility Study	Obese women at high endometrial cancer risk	LNG-IUS for cancer prevention	LNG-IUS protective against endometrial cancer
Oliveira et al, 2024[94]	Systematic Review	Women with bleeding disorders	LNG-IUS and heavy menstrual bleeding	LNG-IUS effective in reducing bleeding; relevant for obese PCOS with HMB.
Morrell et al, 2016[95]	Observational	Women using implants >1 year	Etonogestrel levels and BMI	Confirmed efficacy of the ENG implant remains high across all body mass index (BMI) categories
Reed et al, 2019[96]	Observational	Implant users	Safety profile of Nexplanon	Low complication rates; suitable LARC for obese women
Scott et al, 2021[97]	Observational	Adolescents using LARC	BMI changes with LARC	No significant BMI increase; LARC not associated with weight gain
Ramdhan et al, 2018[98]	Review	General users	Complications of subdermal contraception	Generally safe; risk of irregular bleeding and minor complications
Hadji et al, 2019[99]	Review	Women using estrogen-free contraception	Bone health and LARCs	LNG-IUS seems to be less detrimental to bone than injectable progestins like DMPA
Hillman et al, 2011[100]	Observational	Adolescent bariatric patients	IUD use and menstrual patterns	IUD acceptable and effective post-bariatric surgery; relevant for obese PCOS

with atypia and, in severe cases, endometrial cancer.[89] According to guidelines for managing endometrial cancer, the LNG-IUD may be considered a fertility-sparing treatment, particularly in early-stage disease where patients still desire to conceive.[90] Obesity, which worsens estrogen imbalance, further increases the risk of endometrial hyperplasia and cancer.[91] Therefore, in women with both PCOS and obesity, the LNG-IUD may be preferred over oral megestrol acetate for endometrial protection.[92,93] The LNG-IUD may also be a valuable option for women who require hysterectomy due to menometrorrhagia but are at high surgical risk due to comorbidities, as it can improve quality of life.[88,94]

In obese women, regardless of PCOS status, the Cu-IUD also has an important role. When inserted within five days following unprotected intercourse, it is the preferred method for emergency contraception, as its efficacy is higher than that of oral methods, which may be affected by obesity-related changes in pharmacokinetics.[101,102] A significant drawback of IUDs, which may reduce compliance, is the occurrence of unscheduled breakthrough bleeding, though the exact mechanisms for this remain unclear.[103] Another potential issue is IUD expulsion. An observational cohort study found that overweight and obesity women have the highest risk of IUD expulsion.[104] Obesity can also complicate the insertion procedure, as it may make it difficult for the physician to visualize the cervix and insert the device, increasing the risk of IUD malposition.[105]

Subdermal implants containing etonogestrel (ENG) or LNG are effective for up to 3 years.[87] In obese women, the efficacy of the ENG implant remains high across all body mass index (BMI) categories.[95] Studies have not identified significant differences in the rate of complications (such as misplacement, arm numbness, pain, or removal difficulties) between obese and lean women.[96] While LNG and ENG have androgenic activity,[106] which could exacerbate PCOS symptoms or lead to weight gain,[97] these implants may still be a viable option for patients whose only concern is contraception and who are unable or unwilling to use other methods. Side effects such as insertion site pain, paresthesia, and infection are similar across BMI categories. While spontaneous expulsion is generally unlikely[98] obesity can make implant removal more difficult, particularly when weight gain occurs after insertion, causing the implant to migrate deeply.[98] A promising new alternative is segesterone acetate, a fourth-generation progestin with high selectivity for the progesterone receptor, which may have positive effects on skin and hair.[107] However, literature on its use as a subdermal implant is limited.

DMPA injections, administered either intramuscularly or subcutaneously, must be given every three months. Evidence suggests that DMPA use in obese adolescents is associated with weight gain, and in women with multiple cardiovascular risk factors, the risk of thromboembolic events is significantly increased.[85] Long-term use of DMPA is generally not recommended when other options are available, and fertility may be delayed after discontinuation.[108] Additionally, caution is advised in young girls who have not yet reached the peak bone mass, as DMPA can reduce bone mineral density.[99]

Overview of Treatment Approaches in the Context of Key Symptoms and Comorbidities in Obese PCOS Patients

PCOS, with or without obesity, requires a multidisciplinary treatment approach. Hormonal contraception should not be viewed as a standalone treatment, even though it may address some symptoms that typically return on discontinuation.[5] Therefore, physicians should consider contraception as a short-term strategy to alleviate PCOS symptoms while simultaneously working with patients to mitigate the long-term consequences of the condition.[109,110] Obesity further complicates the clinical picture,[111] underscoring the necessity of a comprehensive, multidisciplinary approach to improve overall health outcomes in these women.[5]

With the goal of improving patient quality of life, physicians should first advise on weight loss, though care should be taken to avoid reinforcing body weight stigma. Recent evidence-based guidelines for PCOS emphasize the importance of effective communication to raise awareness about the condition while avoiding stigmatization related to obesity and other clinical features. As a result, promoting a healthy lifestyle is often more beneficial than focusing solely on weight loss,[5] as even a modest reduction of 5–10% in body weight can significantly improve menstrual cycle regularity and clinical hyperandrogenism.[112]

PCOS is also strongly association with psychiatric disorders, including eating disorders (EDs) such as bulimia and binge-eating disorder.[5] It is critical to assess for the presence of EDs, as they can make lifestyle changes more challenging. Interestingly, women with PCOS often exhibit disordered eating behaviours independent of BMI, likely due to metabolic and endocrine dysregulation affecting appetite control in the hypothalamus. This highlights the need for thorough psychological assessments in all PCOS patients.[113] Beyond EDs, women with PCOS are at increased risk for

anxiety and depression, conditions that are frequently underdiagnosed. This further emphasizes the importance of screening for psychological disorders at the time of diagnosis.[5]

A comprehensive treatment plan for PCOS typically includes caloric restriction, physical exercise, and psychological therapy[114]. Cognitive behavioural therapy (CBT) has been shown to enhance weight loss when combined with lifestyle interventions and to improve patient adherence.[115] Mindfulness and mindful eating practices may also be helpful, particularly in those diagnosed with EDs.[112] Psychological therapy is crucial for addressing the low self-esteem and emotional distress often caused by diminished perceptions of femininity, particularly when patients exhibit overt symptoms of PCOS and face fertility issues.[5]

Bariatric surgery may be considered in cases where weight loss and improved health cannot be achieved with lifestyle modifications and pharmacotherapy alone.[5,116] Compared to drug therapies, bariatric surgery appears to result in more significant improvements in anthropometric, hormonal, and metabolic outcomes,[117] although further research is needed in patients with PCOS. Contraception is strongly recommended both before and immediately after bariatric surgery to avoid unplanned pregnancies, as fertility often returns rapidly following weight loss surgery. Even when pregnancy is desired, it is advisable to wait until full recovery to reduce the risk of obstetric and fetal complications.[100] In this context, IUDs may be preferred due to ease of insertion during sedation for bariatric surgery and their avoidance of oral route options.[100]

Obesity and PCOS are frequently associated with insulin resistance and metabolic syndrome, and medications such as inositols, insulin-sensitizing agents like metformin, and anti-obesity drugs may be used to address these metabolic features.[5,34] Additionally, anti-androgen pharmacotherapy can be combined with hormonal contraceptives to manage hyperandrogenism is PCOS patients[5].

When considering pregnancy, physicians should be aware that the characteristic features of PCOS (ie, obesity, insulin resistance, and hyperandrogenism) not only impact the health of the woman but may also have long-term effects on offspring. These features have the potential to cause epigenetic changes in the fetus, which could predispose the child to PCOS and metabolic disorders. Therefore, it is crucial to provide appropriate counselling and information to women with PCOS prior to conception.[118]

Conclusions

PCOS, with or without obesity, requires a multidisciplinary approach to treatment. Hormonal contraception should not be considered as a stand-alone treatment, although it may effectively treat some of the main symptoms of PCOS, which typically return when discontinued. Therefore, from a precision medicine perspective, clinicians should consider all the types of contraception mentioned above (eg COCs and LARCs), tailoring the strategy to each situation by weighing the risks and benefits. In addition to this, the promotion of a healthy lifestyle and mental health care is essential to achieve long-term improvements. Obesity further complicates the clinical picture, highlighting the need for a comprehensive, multidisciplinary approach to improve the overall health outcomes of these women.

Disclosure

The authors report no conflicts of interest in this work.

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