



THE USE OF AI, TECHNICAL ADVANCES, AND OVARIAN DRILLING FOR MANAGEMENT OF WOMEN WITH POLYCYSTIC OVARIAN SYNDROME

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Abstract:

Context: The common endocrine and metabolic condition known as polycystic ovary syndrome (PCOS) has a major effect on both general health and reproductive health. Because of the syndrome's variable presentation, therapy results are still unpredictable even with the availability of traditional treatment alternatives, such as medication, surgery, and lifestyle modifications.

Objective: With a focus on the use of machine learning in clinical decision-making, the function of laparoscopy and fertiloscopy in surgical management, and the importance of individualized treatment approaches, the goal of this review is to present a thorough overview of both traditional and cutting-edge therapeutic approaches for PCOS.

Techniques: Current research on PCOS treatment methods with an emphasis on clinical trials, systematic reviews, and technology studies was evaluated. Particular attention was paid to research on personalized patient care, minimally invasive surgery, and artificial intelligence.

Results: The development of customized regimens has been aided by improvements in risk assessment, diagnostic accuracy, and treatment result prediction brought about by machine learning advancements. For patients who are unresponsive to medicinal therapy, minimally invasive surgical procedures such as laparoscopy and fertiloscopy continue to be beneficial choices since they provide better reproductive results with fewer side effects. A more comprehensive approach to managing infertility and hormonal imbalance in PCOS is made possible by combining traditional methods with technological advancements.

Conclusion: Traditional treatments are being combined with insights from artificial intelligence and minimally invasive procedures in a paradigm shift toward precision medicine in PCOS management. Personalized treatment plans have the potential to improve metabolic and reproductive results, which will eventually improve PCOS-afflicted women's quality of life.

Keywords: infertility, hormone imbalance, individualized treatment, laparoscopy, fertiloscopy, and machine learning.

1. Introduction:

In women of reproductive age, PCOS is one of the most common endocrine illnesses. It is frequently characterized by hyperandrogenism, irregular menstrual cycles, hormonal imbalance, and metabolic abnormalities [1]. PCOS is a major cause of infertility in addition to its effects on general health, posing serious psychological and physical difficulties for those who are afflicted [2]. There have been differing degrees of success with traditional therapy approaches such as medication, surgery, and lifestyle changes. But because PCOS is so diverse and complex, more creative and tailored approaches are required [3].

The treatment of PCOS now includes new aspects due to recent developments in computational science and medical technology. Early risk factor detection, improved diagnosis accuracy, and customized treatment plans have all been made possible by the incorporation of machine learning techniques into clinical practice [4]. Predictive algorithms that analyse huge clinical datasets can help physicians find patient subgroups that would benefit more from particular treatments, which could lead to better results [5].

Conversely, surgical procedures like laparoscopy and fertiloscopy remain essential, especially in situations where medicinal treatment is ineffective. A key component of reproductive surgery has been laparoscopy, which is frequently utilized for ovarian drilling or the evaluation of pelvic pathologies [6]. By combining therapeutic and diagnostic potential with lower risks and recovery time, fertiloscopy, a less invasive endoscopic method, presents a promising option [7]. For some individuals, these surgical advancements improve their chances of becoming pregnant by reestablishing ovulation.

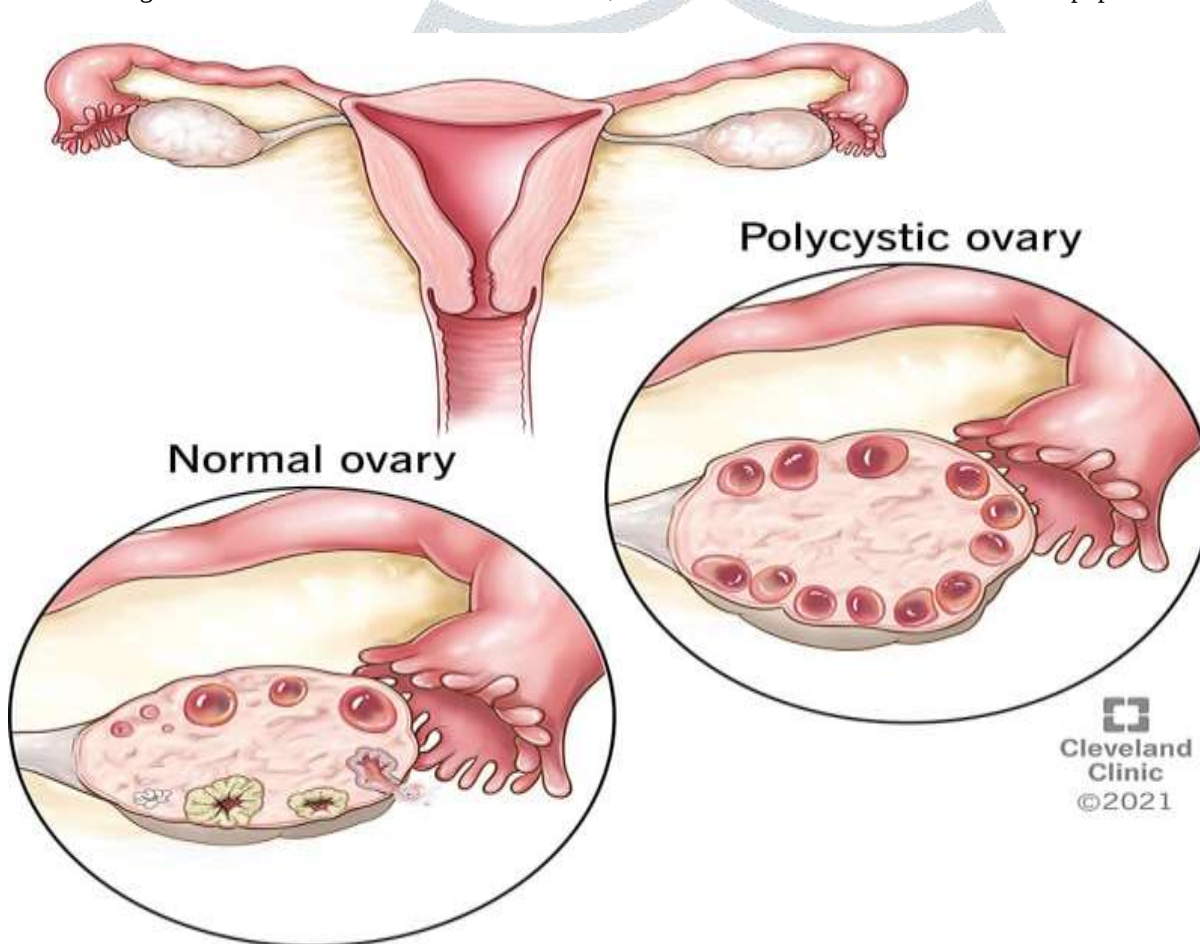
Modifying therapies based on individual hormonal profiles, metabolic status, and reproductive goals is crucial, as shown by the developing idea of individualized treatment in PCOS management [8]. Through the integration of conventional techniques with state-of-the-art technology like machine learning and less invasive surgical techniques, physicians are now better prepared to treat PCOS's metabolic and reproductive components.

With a focus on the function of machine learning, the practicality of laparoscopy and fertiloscopy, and the significance of tailored approaches to managing infertility and hormonal imbalance, this review attempts to examine the convergence of traditional and cutting-edge approaches in the treatment of PCOS.

The three most upsetting hirsutism symptoms that women with PCOS suffer are infertility, irregular menstruation, and hirsutism. These are responsible for the main causes of women's anxiety, despair, and low self-esteem. PCOS has a complicated pathophysiology, therefore treatments are tailored to the patient's symptoms and indicators and are rarely monotherapeutic. In order to manage and treat PCOS, a number of supplemental therapies have been proposed. It is believed that lifestyle modification is the key to managing PCOS [9].

Ovulation induction medications such as clomiphene citrate and aromatase inhibitors (letrozole) are used in conjunction with lifestyle changes to treat infertility. Insulin sensitizers and antiandrogens are administered separately or in combination to treat insulin resistance and hyperandrogenic disorders. In PCOS, more recent insulin sensitizers such as SGLT2, DDP-4 inhibitors, GLP-1 agonists, and myoinositols have been explored. When it comes to treating irregular menstruation and hyperandrogenic symptoms in PCOS, oral contraceptives are seen to be the best option [10].

In PCOS, statins and bromocriptine have also been added as therapy options for dyslipidemia and hyperandrogenic disorders. Vitamin D, either by itself or in conjunction with calcium supplements, has recently demonstrated encouraging outcomes in alleviating PCOS. According to the feminine perspective, the most upsetting symptom of PCOS is hirsutism. Unwanted hair growth is not the only issue; psychological distress, social stigma, and emotional effects on female identity are also issues [11]. To temporarily conceal this issue, many techniques, including shaving, waxing, and plucking, have been used to enhance the physical look. But in order to permanently destroy hair follicles, a number of treatments have been used, such as electrolysis and laser hair removal. In order to manage PCOS, another method known as acupuncture has grown in favor. Due to consumers' belief that home remedies might heal illnesses with fewer adverse effects, traditional or folk medicine has become a popular choice in recent years.



2.ETIOLOGY AND PATHOPHYSIOLOGY OF PCOS:

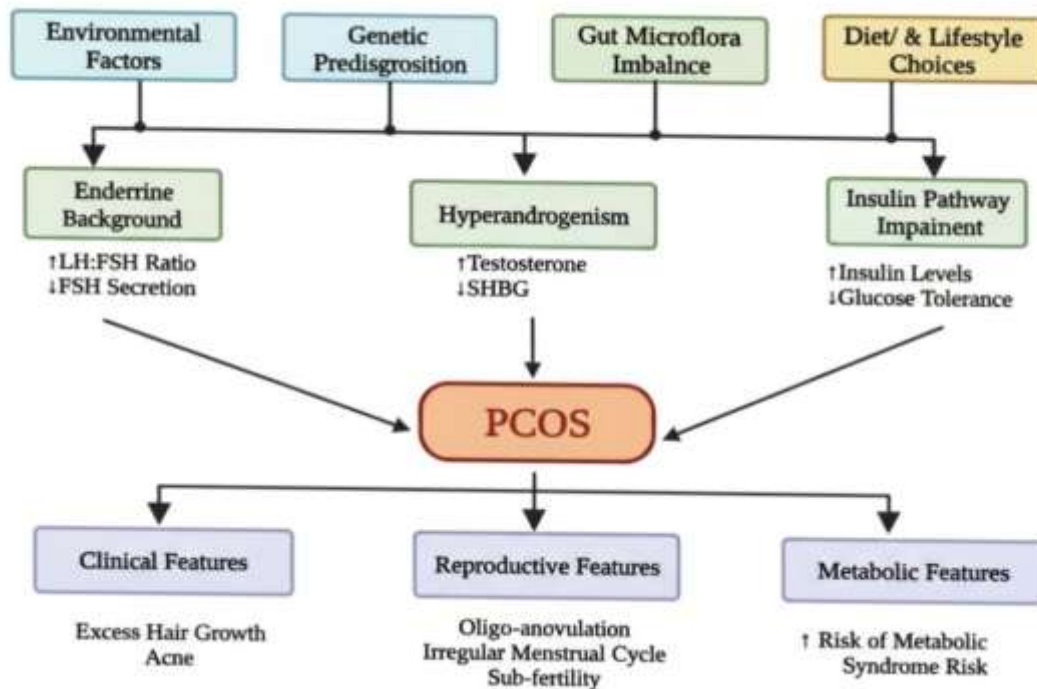
Based on the diagnostic criteria, PCOS affects 8% to 20% of women of reproductive age each year worldwide [12]. Changes in ovarian folliculogenesis, steroidogenesis, neuroendocrine function, metabolism, insulin sensitivity, insulin production, adipose cell activity, inflammatory factors, and sympathetic nerve function all have an impact on the pathophysiology of this disorder [13]. The four main factors contributing to the pathophysiological changes in PCOS are high carbohydrate intake, hyperinsulinemia, hyperandrogenemia, and persistent low-grade inflammation, according to Barre et al. [14].

Dysfunction of the Hypothalamic-Pituitary-Ovarian (HPO) Axis PCOS-afflicted women have higher GnRH pulse amplitude and frequency, which promotes the release of luteinizing hormone (LH) rather than follicle-stimulating hormone (FSH). While relative FSH shortage reduces the conversion of androgens to estrogens by impairing aromatase activity in granulosa cells, elevated LH stimulates theca cells to boost androgen synthesis. Follicle arrest and anovulation are caused by this imbalance [15,16]. Excessive testosterone A hallmark of PCOS is excessive androgen production, mostly from the ovaries and to a lesser degree from the adrenal

glands. Clinical manifestations of hyperandrogenism include androgenic alopecia, acne, and hirsutism. It also interferes with follicular maturation and ovulation [17].

Hyperinsulinemia and Insulin Resistance PCOS is characterized by intrinsic insulin resistance, which happens without fat. By activating theca cells and inhibiting hepatic sex hormone-binding globulin (SHBG), compensatory hyperinsulinemia increases the production of ovarian androgens, resulting in a rise in free testosterone [18].

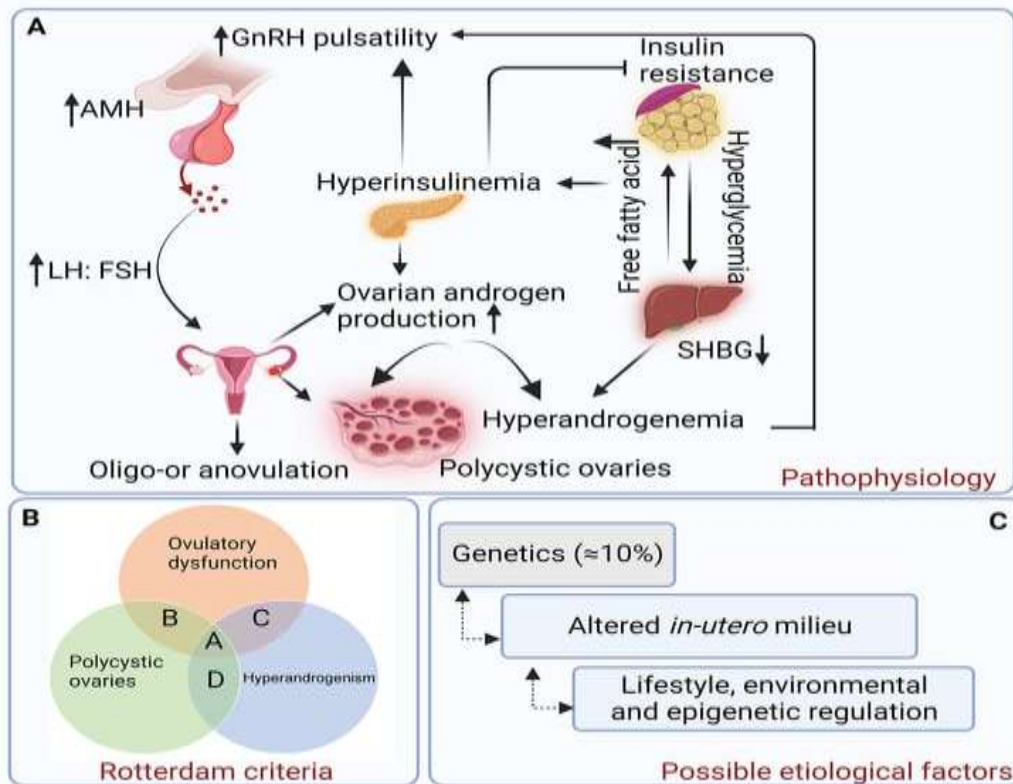
Type 2 diabetes and dyslipidemia, two metabolic issues frequently seen in PCOS, are significantly exacerbated by insulin resistance [19].



Genetic Variables Up to 70% of vulnerability to PCOS can be attributed to hereditary factors, indicating the disease's high heritability [20]. Susceptibility loci in genes controlling steroidogenesis (CYP11A, CYP17A1), insulin signaling (INSR, IRS1), and gonadotropin signaling (FSHR, LHCGR) have been found using genome-wide association studies (GWAS) [21]. These results provide credence to a multifactorial and polygenic hypothesis. **3.2 Epigenetic and Environmental Factors** Genetic propensity is modulated by epigenetic changes and environmental exposures. It has been suggested that prenatal androgen exposure is the developmental cause of PCOS [22]. Disease expression is further influenced by postnatal environmental variables, such as a high-calorie diet, a sedentary lifestyle, stress, and substances that disrupt hormones, such as bisphenol A [23].

Clinical Presentation Heterogeneity Because of different combinations of reproductive, metabolic, and hyperandrogenic characteristics, PCOS presents a diverse phenotype. Anovulation and infertility are the main reproductive dysfunctions that some women come with. Others have androgenic characteristics (acne, hirsutism). Metabolic disorders such as obesity and insulin resistance are common [24].

This diversity underscores the challenge of developing a single, cohesive classification and reflects the intricate pathophysiological processes underpinning the condition [25].



Current Management Approaches:

Polycystic Ovary Syndrome (PCOS) is a multifaceted endocrine disorder affecting reproductive-aged women worldwide. It is characterized by hyperandrogenism, chronic anovulation, and polycystic ovarian morphology. Management of PCOS requires a multidisciplinary approach due to its metabolic, reproductive, and psychological implications.

1. Lifestyle Modification:

Lifestyle changes remain the first-line intervention, particularly for overweight and obese women with PCOS. These interventions aim to improve insulin sensitivity, regulate menstrual cycles, reduce hyperandrogenism, and enhance fertility.

Lifestyle modification is considered the first-line treatment for most women with PCOS, especially those who are overweight or obese. Even in lean women with PCOS, healthy lifestyle choices can significantly improve metabolic, reproductive, and psychological outcomes. The major components of lifestyle management include dietary changes, physical activity, behavioral strategies, sleep hygiene, and stress reduction.

Key Lifestyle Interventions:

1. Diet: Proper nutrition plays a crucial role in managing both the metabolic and hormonal imbalances associated with PCOS. A balanced, low-glycemic index diet focusing on whole grains, lean proteins, fruits, and vegetables has shown benefits in weight reduction and insulin sensitivity [26].

1.1. Low Glycemic Index (GI) Diet

- A diet low in glycemic index helps regulate blood glucose levels and insulin sensitivity.
- Foods such as whole grains, legumes, nuts, vegetables, and certain fruits should be prioritized [26].

1.2. Caloric Restriction and Macronutrient Balance

- A modest caloric deficit (typically 500–750 kcal/day) helps in gradual weight loss.
- A macronutrient-balanced diet (45–50% carbohydrates, 20–25% protein, 30% fat) is ideal, but low-carbohydrate diets (<45% carbs) have also shown benefits in insulin resistance [27].

1.3. Anti-Inflammatory and Mediterranean Diets

- These diets focus on healthy fats (like omega-3 fatty acids), antioxidant-rich foods, and less processed food.
- They reduce systemic inflammation, which is often elevated in PCOS [28].

2. Physical Activity: At least 150 minutes of moderate-intensity aerobic activity per week helps improve ovulatory function and reduce insulin resistance [27].

2.1. Aerobic Exercise

Recommended: 150 minutes/week of moderate-intensity aerobic activity (e.g., brisk walking, swimming, cycling).

- Benefits: Improves insulin sensitivity, cardiovascular health, and promotes fat loss [29].

2.2. Resistance Training

- At least 2 sessions per week are recommended.
- Benefits: Enhances muscle mass, improves glucose metabolism, and reduces central adiposity [30].

2.3. High-Intensity Interval Training (HIIT)

- Short bursts of intense exercise followed by rest or low-intensity recovery periods.
- Shown to be particularly effective in reducing insulin resistance and abdominal fat in women with PCOS [31].

3. Weight Management: A weight loss of 5–10% can restore ovulation and menstrual regularity in many women [28].

3.1. Modest Weight Loss Yields Big Results

- A 5–10% reduction in body weight can:
 - Restore ovulation
 - Normalize menstrual cycles
 - Improve fertility
 - Lower androgen levels [32].

3.2. Sustainable Weight Loss

- Long-term maintenance requires continuous lifestyle support, realistic goals, and self-monitoring.
- Avoid extreme diets or unsustainable exercise routines that may lead to relapse or disordered eating.

4. Behavioral Therapy: PCOS is associated with an increased risk of depression, anxiety, and eating disorders. Behavioral therapy helps in addressing underlying psychological and behavioral challenges. Counseling and cognitive behavioral therapy are useful in addressing emotional eating and body image issues often seen in PCOS patients [29].

4.1. Cognitive Behavioral Therapy (CBT)

- Helps manage emotional eating, low self-esteem, and depressive symptoms.
- Supports adherence to diet and exercise plans [33].

4.2. Motivational Interviewing

- A counseling approach that enhances patient motivation to achieve health goals.
- Especially effective in improving compliance with lifestyle changes [34].

4.3. Self-Monitoring Tools

- Use of fitness trackers, food logs, or smartphone apps can improve accountability and promote consistent behavior.

5. Sleep Hygiene

Sleep disturbances are common in PCOS and may exacerbate insulin resistance and weight gain.

- Target: 7–9 hours of quality sleep per night.
- Tips: Avoid screen time before bed, maintain regular sleep schedule, reduce caffeine intake in the evening [35].

6. Stress Management

Chronic stress contributes to hormonal imbalances and inflammation in PCOS.

6.1. Stress-Reducing Techniques

- Yoga and Meditation: Improve cortisol levels and emotional well-being.
- Mindfulness-Based Stress Reduction (MBSR): Has been shown to reduce symptoms of anxiety and depression in women with PCOS [36].

6.2. Social Support

- Group counseling or community-based support can enhance adherence and reduce feelings of isolation.

Intervention	Benefits
Diet	Improves insulin sensitivity, weight loss, hormonal balance
Exercise	Enhances metabolic health, reduces androgen levels
Weight Loss	Restores ovulation, improves fertility, lowers cardiovascular risk
CBT & Behavioral Support	Improves adherence, reduces emotional eating
Sleep & Stress Management	Regulates cortisol, enhances metabolic function

2. Pharmacological Therapies:

Pharmacological treatment in Polycystic Ovary Syndrome (PCOS) is tailored according to the patient's symptoms, such as irregular menstrual cycles, hyperandrogenism (e.g., acne, hirsutism), insulin resistance, or infertility. The main pharmacological agents include Metformin, Clomiphene Citrate, Letrozole, and Combined Oral Contraceptive Pills (COCs or OCPs). Each has specific indications and mechanisms of action, often used alone or in combination depending on clinical presentation.

METFORMIN:

In 1994, Velazquez et al. published the first report on the use of metformin to treat PCOS, describing three spontaneous pregnancies (around 11% of participants). Since then, several more trials evaluating the effectiveness of metformin in treating PCOS have been finished. The impacts on IR parameters, hyperandrogenism, and enhancements in ovulation and menstrual function were the main results of these investigations. The rate of spontaneous births ranged from 5% to 18% in the five trials that described them; however, many of these studies were tiny, with just 20 patients apiece. 33, 62, 65, and 48 anovulatory PCOS patients (mean age of 29.9 years and BMI of 28.7 kg/m²) were included for 15 months in a recent study by Heard et al. 34

After six weeks, clomiphene was added as needed, and metformin was started at 500 mg twice daily, with the possibility of increasing to three times daily if ovulation did not occur. On metformin alone, 19 out of 48 individuals (40%) saw a normalization of their menstrual periods and ovulation, and 15 of them (79%) became pregnant. Within three months of beginning metformin alone, about 75% of these pregnancies took place. The addition of 50 mg of low-dose clomiphene led to five more pregnancies. 34 Comparable rates of Obese patients (mean BMI ~32 kg/m²) who took metformin alone experienced ovulation at a rate of 40%; when clomiphene was added, that percentage rose to 89%. 32 The ovulation rate was only 11.5% when clomiphene was used alone. There were no recorded pregnancies. Finally, pretreatment with metformin raised the rate of conception in patients with clomiphene-resistant PCOS from 7% to 55%. 66 Metformin use also enhances the results of more sophisticated infertility treatments. Metformin decreased the likelihood of ovarian hyperstimulation when taken for one month before FSH-induced ovulation induction. 67 Metformin also increases the chances of conception and pregnancy in PCOS patients undergoing IVF. 68 Therefore, even if metformin therapy "fails," it should probably be continued in the context of infertility as long as fertility efforts are ongoing.

56 It has recently been demonstrated that taking metformin continuously during pregnancy lowers the chance of early pregnancy loss. According to a retrospective study, the rate of early pregnancy loss was 8.8% for women who started taking metformin and kept taking it during their pregnancy, while the rate for women who did not take the medication was 41.9%. 69 Glueck et al. have reported on 19 pregnant women who have taken metformin thus far in a prospective pilot study. 70 10.5% experienced first-trimester miscarriages, 32% have continuous pregnancies past the first trimester, and 58% have had normal live deliveries. There were no birth defects. 56 It has recently been demonstrated that taking metformin continuously during pregnancy lowers the chance of early

pregnancy loss. According to a retrospective study, the rate of early pregnancy loss was 8.8% for women who started taking metformin and kept taking it during their pregnancy, while the rate for women who did not take the medication was 41.9%. Glueck et al. have reported on 19 pregnant women who have taken metformin thus far in a prospective pilot study. 70 (10.5%) experienced first-trimester miscarriages, 32% have continuous pregnancies past the first trimester, and 58% have had normal live deliveries. There were no birth defects. 70,125 PCOS-afflicted women will eventually be included in this study. Nevertheless, metformin is not authorized for usage during pregnancy or to induce ovulation. Pregnancy category B is in effect. 70 125 PCOS-afflicted women will eventually be included in this study. Nevertheless, metformin is not authorized for usage during pregnancy or to induce ovulation. Pregnancy category B is in effect. [37-46]. Metformin is an insulin-sensitizing agent and a biguanide primarily used to manage insulin resistance and hyperinsulinemia, which are core features in many women with PCOS.

CHNIQUES: Limitations of Current Technical Methods in GynecCLOMOPHENE CITRATE:

Introduction:

Polycystic Ovary Syndrome (PCOS) is one of the most common endocrine disorders in women of reproductive age, often associated with anovulation and infertility. Among the first-line pharmacological agents for ovulation induction, Clomiphene Citrate (CC) remains a widely prescribed drug due to its efficacy, safety profile, and cost-effectiveness.

Mechanism of Action

1. Selective Estrogen Receptor Modulator (SERM):

Clomiphene citrate acts as an estrogen antagonist in the hypothalamus, blocking estrogenic negative feedback. This stimulates the hypothalamic-pituitary-ovarian (HPO) axis. [47].

2. Increased Gonadotropin Secretion:

By blocking estrogen receptors, CC enhances gonadotropin-releasing hormone (GnRH) pulsatility, leading to elevated secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH). [48].

3. Follicular Development and Ovulation:

The rise in FSH promotes follicular recruitment and maturation, thereby inducing ovulation in women with PCOS. [49].

Clinical Use in PCOS

First-line Therapy for Ovulation Induction:

CC is considered the initial pharmacological choice for women with PCOS who desire pregnancy. It induces ovulation in approximately 70–80% of cases, with pregnancy rates of 30–40%. [50].

Dosage and Administration:

Typically administered orally at 50 mg daily for 5 days, starting on day 2–5 of the menstrual cycle. The dose may be increased up to 150 mg if ovulation is not achieved. [51].

Effectiveness:

CC is particularly effective in women with normal body mass index (BMI) and preserved insulin sensitivity. However, its effectiveness may be lower in obese women with insulin resistance. [52].

2.3. LETROZOLE:

Letrozole is an aromatase inhibitor that has emerged as a first-line ovulation induction agent, often superior to Clomiphene Citrate, especially in women with PCOS.

2.3.1. Mechanism of Action

- Inhibits aromatase, the enzyme responsible for converting androgens to estrogens.
- The resulting low estrogen levels remove negative feedback inhibition on the hypothalamus and pituitary, increasing FSH secretion and stimulating follicular development [53].

2.3.2. Clinical Use

- Indicated for ovulation induction in infertile women with PCOS.
- Associated with higher live birth and ovulation rates compared to Clomiphene Citrate [54].

2.3.3. Dosing and Advantages

- Starting dose: 2.5–5 mg/day for 5 days, beginning on day 3 or 5 of the cycle.
- Can be increased to 7.5 mg/day if ovulation does not occur.
- Unlike clomiphene, does not have anti-estrogenic effects on endometrial lining or cervical mucus, making it more favorable for conception [55].

2.4. COMBINED ORAL CONTRACEPTIVES PILLS (COCPs or OCPs):

OCPs are considered the first-line pharmacologic treatment for women with PCOS who are not seeking pregnancy but need to manage symptoms of hyperandrogenism and menstrual irregularity.

2.4.1. Mechanism of Action

- Suppresses LH and FSH release from the pituitary, inhibiting ovarian androgen production.
- Increases hepatic production of sex hormone-binding globulin (SHBG), which binds free androgens and reduces their biological activity [56].

2.4.2. Clinical Benefits

- Regulates menstrual cycles.
- Reduces hirsutism and acne over time.
- Lowers the risk of endometrial hyperplasia and carcinoma due to prolonged anovulation [57].

2.4.3. Risks and Monitoring

- Potential side effects: Weight gain, mood changes, breast tenderness, and increased risk of thromboembolism in predisposed individuals.
- Not recommended in women with a high risk of cardiovascular disease or history of thrombotic events.

LIMITATIONS OF CURRENT TECHNOLOGY AND LAPROSCOPY

1. Laparoscopy

1. Requires high surgical expertise and has a steep learning curve, affecting outcomes [58].
2. Entry-related risks include vascular, bowel, and bladder injury [58].
3. Routine diagnostic laparoscopy in infertility is controversial, with inconsistent evidence of improved live-birth rates [63].
4. Risk of postoperative adhesions, which may impair fertility or cause pain [58].
5. High cost and infrastructure requirements limit access in low-resource settings [58].

2. Laparoscopic Ovarian Drilling (LOD)

1. Potential reduction in ovarian reserve due to stromal tissue destruction [59].
2. Formation of peri-ovarian adhesions that may affect fertility [59].
3. Variable and often time-limited ovulatory response; heterogeneous results in trials [60].
4. Not recommended as first-line therapy since pharmacological ovulation induction is usually preferred [59].
5. General surgical risks such as bleeding, infection, and anesthesia complications [59].

3. Fertiloscopy / Transvaginal Hydrolaparoscopy (TVHL)

1. Visualization can be inadequate in women with adhesions or distorted anatomy [61].
2. Requires specialized equipment and trained operators; limited availability in many regions [62].
3. Cannot replace standard laparoscopy in managing complex pelvic pathology [61].
4. Procedure carries risks such as bowel/urinary injury or gas/fluid embolism if improperly performed [62].

4. Hysteroscopy

1. Limited to intrauterine pathology; does not assess tubes or peritoneum [63].
2. Reliance on hysteroscopy alone may delay diagnosis of endometriosis or adhesions [63].
3. Risks include fluid overload, electrolyte imbalance, or cervical trauma [63].

5. Robotic-assisted Laparoscopy

1. High capital and per-case costs restrict use to well-funded centers [64].
2. Clinical outcomes are often comparable to conventional laparoscopy despite higher expense [65].
3. Requires specific training and operating team expertise, limiting widespread adoption [64].

6. V-NOTES / Natural Orifice Techniques

1. Limited long-term evidence, particularly on fertility outcomes [62].
2. Specific complications such as vaginal cuff dehiscence and infection may occur [62].

7. Cross-cutting Limitations

1. Many studies have small sample sizes and heterogeneous designs, reducing generalisability [63].
2. Performing therapy during diagnostic procedures makes it difficult to isolate diagnostic vs treatment effects [63].
3. Inequity of access persists, with advanced procedures concentrated in tertiary centers

ARTIFICIAL INTELLIGENCE IN PCOS:

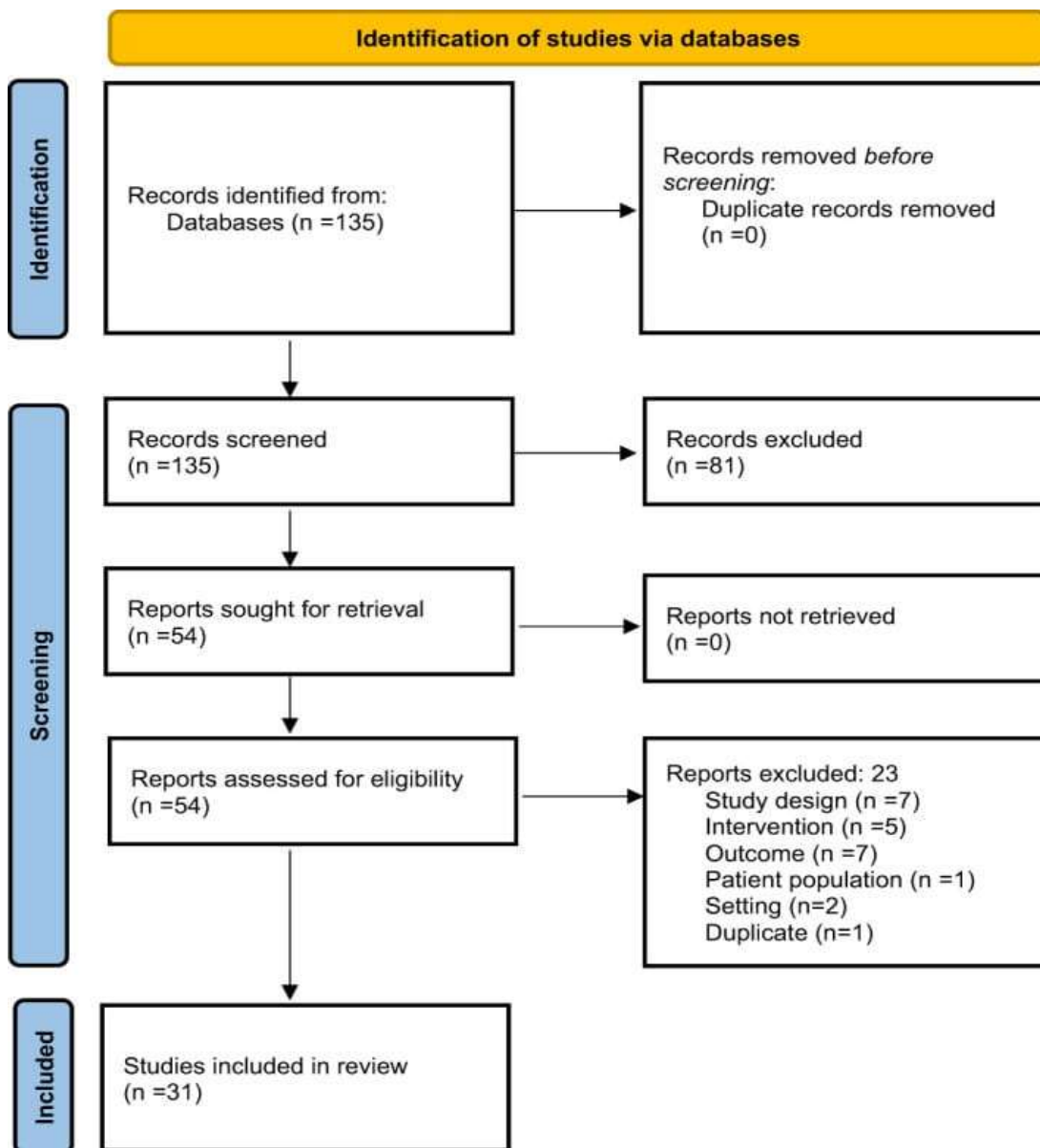
Artificial intelligence in diagnosis:

The diagnosis and therapeutic monitoring of reproductive endocrinology in general, and specifically the screening and management of PCOS, have significantly changed in recent years due to promising AI-based analytics, such as machine learning (ML), neural networks, deep learning (DL), computer vision, and natural language processing [66].

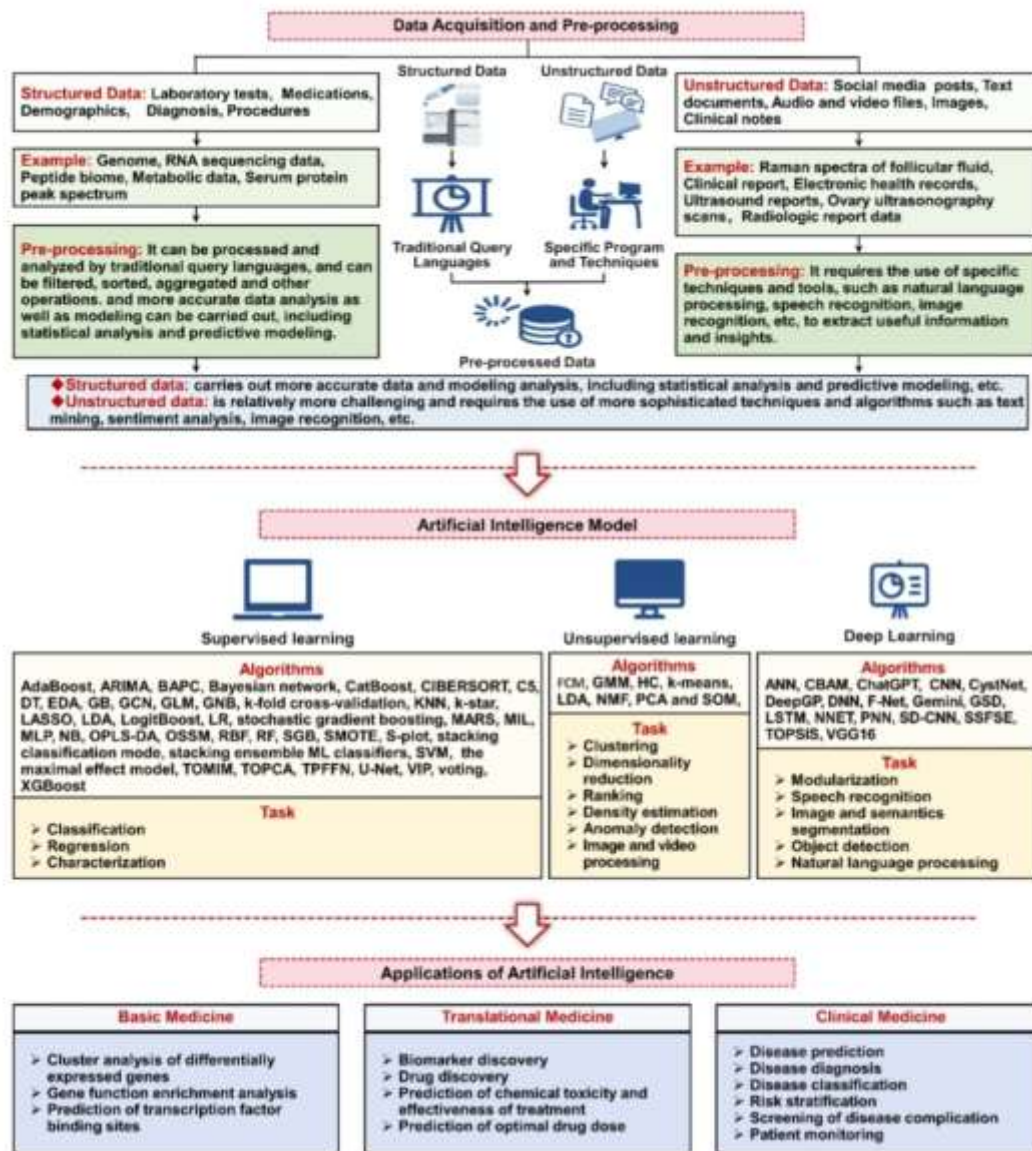
Su Z introduced the support vector machine (SVM) model in 2023. It was created using genetic data and was found to perform well in examining cuproptosis-related molecular clusters of PCOS, building a prediction model with an area under the curve (AUC) of 100% [67].

Using supervised machine learning in conjunction with a metabolomic signature (steroidome data of 15 steroids) yields a significant additive value (100 percent sensitivity and specificity) for response identification with PCOS from non-classic 21-hydroxylase

deficiency [68]. There are numerous reasons to be optimistic about this AI-driven application, yet challenges still exist for the effective integration of AI in real-world clinical settings. We review the main AI applications in PCOS today based on the current context, and then we highlight the potential and difficulties of developing AI clinical translation. Furthermore, we hope to fulfill the study's objective of thoroughly examining the ideal collaboration between theory-based AI implementation and the therapy and prevention of actual clinical PCOS, which is a hopeful outlook for the preservation of fertility in the future.



Selection process of the studies. Article selection flow chart for studies related to AI/ML and PCOS according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.



Current applications of machine intelligence in PCOS management. Common algorithms used in supervised learning include (1) artificial neural networks, such as CNN, KNN, PNN, and DNN; (2) Bayesian learning, such as NB; (3) DT, such as classification and regression tree, and supervised learning in quest; (4) ensemble methods, such as RF, and XGBoost; and (5) linear models, such as linear regression, LR, GLM, SVM. Common algorithms used in unsupervised learning include (1) clustering, such as k-means and GMM; and (2) dimensionality reduction, such as SOM

METHODS:

1.MACHINE LEARNING:

1. Models for binary classification:

To support the investigation and determine the best model that generates the best prediction metrics for PCOS identification, ten distinct machine learning model configurations were selected for this work. A list of them may be found below:

Tree of Decisions (DT):

This machine learning model is known as a grey/white box model because it has a certain amount of transparency and interpretability. In order to classify incoming data samples into different groups in a hierarchical fashion that resembles a tree, the model uses a Boolean logic-based architecture with a nonparametric foundation [69].

Linear decision analysis (LDA):

A linear variation of statistically driven discriminant analysis, Linear Decision Analysis (LDA) is a model that uses linear class boundaries to separate the different data classes [70]. In order to implement class determination boundaries, the model first projects a candidate feature vector from a higher-dimensional space into a smaller subspace while maintaining the general structure of the data [70].

LOGISTIC REGRESSION(LR):

Another statistically driven model is logistic regression (LR), which determines the data class of input samples using a binary-like format by utilizing a threshold and a nonlinear activation function in the form of a sigmoid [71].

K-Nearest Neighbour (KNN):

This model assigns samples to different data classes using a voting technique based on a predetermined number of nearest neighbours. The Euclidean distance was chosen as the preferred distance metric in this work, and the parameter of k was set to 1 [72].

SUPPORT VECTOR MACHINE (SVM):

Because data classes are more separable in a higher-dimensional space, the Support Vector Machine (SVM) model iteratively solves an optimization problem centered on projecting a feature matrix into that space [73]. A tiny portion of the data known as the support vectors is used for this. In a technique called a kernel trick, the coordinates for the established class boundaries are preserved when the data is projected downward to a lower-dimensional space after the class partitioning is finished in a higher-dimensional space [74].

PROBABILISTIC CLASSIFICATION MODEL:

Model for probabilistic categorization The probabilistic classification model differs slightly from the binary-based classification in that it is used to create an inference system that allows prognostic insights on the degree of PCOS presence to be formed in a high-throughput manner using the certainty associated with classification decisions [75]. Prioritizing patient treatment and detecting the illness in its latent stages may be made possible by this, which may encourage proactive care approaches [76]. The classification models were validated using a k -fold validation method where k was selected to be 10, with the data split in an 80:20 format, where 80% of the data were utilised towards the training of the models, whilst the remaining 20% were utilised for validation purposes.

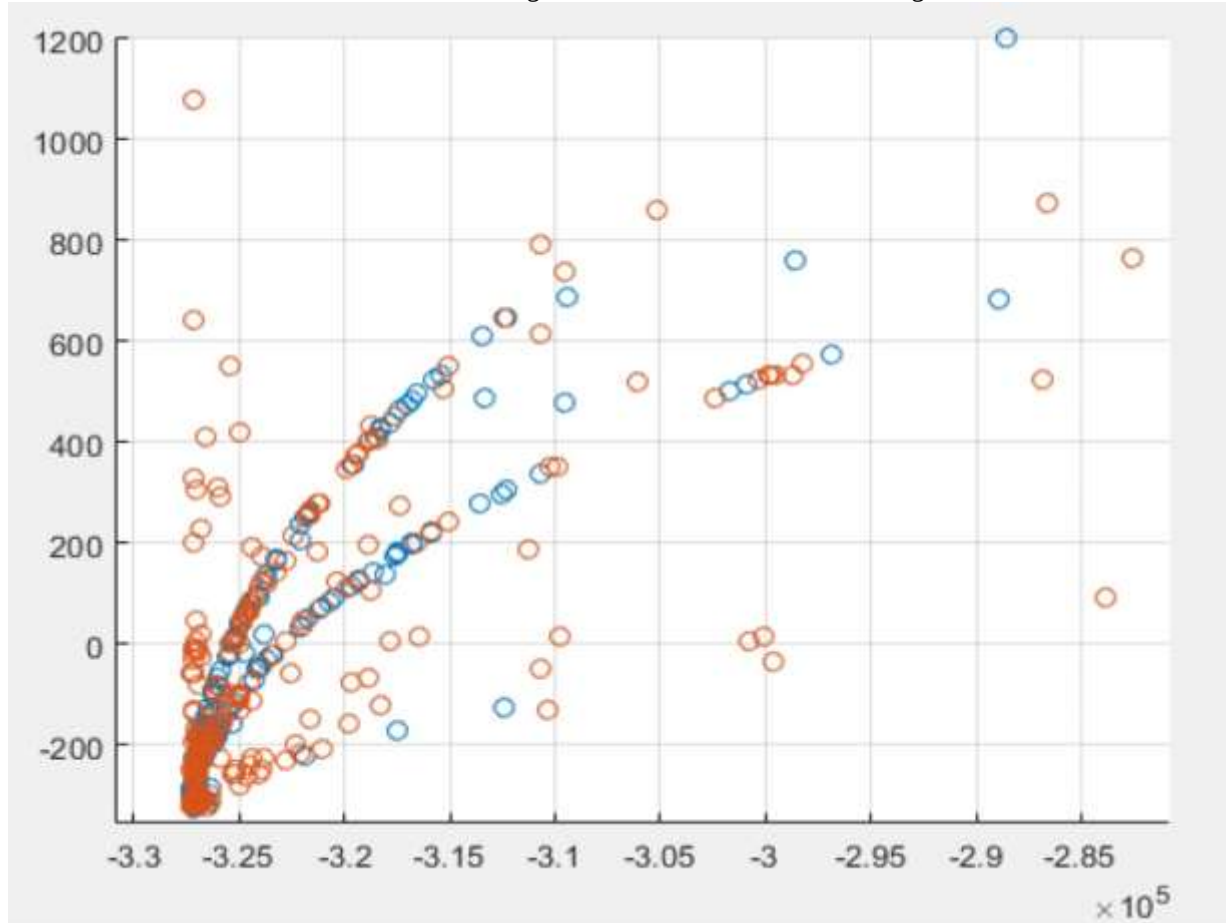


Fig. 2. A PCA plot of the binary-based classification for the case of the medical health record and statistical feature concatenation (Blue: Non-PCOS, Red: PCOS) with 98% variability explained. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

DATASET:

As mentioned earlier, the dataset used in this study was obtained from the Kaggle website [69]. It originally included 364 patients without PCOS and 177 patients with PCOS. The dataset had 41 features, which covered various aspects like metabolic, physical, imaging, hormonal, and biochemical data collected from the patients (for a full list of features, refer to the Kaggle PCOS database) [77]. During the initial data preparation, some features were removed from the final feature set. These included BMI, waist-to-hip ratio, and endometrial features because they had issues like inconsistencies and a lot of missing data.

To handle the problem of an uneven distribution of classes, the SMOTE synthetic sample generator was used, as it was used in earlier studies.

This technique helps balance the dataset and reduces bias caused by an unbalanced sample set. As a result, the final dataset contained a total of 728 samples.

TECHNICAL ADVANCES IN PCOS MANAGEMENT:
Polycystic Ovary Syndrome (PCOS) management has improved with the use of modern technology. Innovations in digital health, surgical techniques, and artificial intelligence have helped in diagnosing, monitoring, and treating PCOS more effectively.

5.1 Wearable Devices and Mobile Applications:

Wearable health technology, like fitness trackers and smartwatches, allows for real-time monitoring of physical parameters such as heart rate, sleep quality, and activity levels. For women with PCOS, this data can be used to improve lifestyle changes that help with insulin resistance, weight control, and hormone balance [78]. Mobile apps designed for menstrual cycle tracking, such as Clue, Flo, and MyFLO, help users identify irregular patterns, ovulation times, and symptoms. This provides useful information for both the users and healthcare professionals [79].

Continuous glucose monitoring (CGM) systems are becoming more common among PCOS patients. These systems track blood sugar levels in real time, helping with diet planning and managing insulin resistance, which is a key factor in PCOS [80].

5.2 Telemedicine and Virtual Clinics:

Telemedicine platforms now enable remote consultations, follow-ups, and personalized care plans for PCOS patients, especially in underserved or rural areas. Virtual PCOS clinics offer multidisciplinary care—including endocrinology, gynecology, dietetics, and mental health support—all coordinated through digital interfaces [81]. These models not only improve access to care but also increase adherence to treatment plans through continuous engagement.

5.3 Robotic-Assisted and Minimally Invasive Surgery:

For patients requiring surgical intervention, especially those with ovarian drilling or endometrial complications, robotic-assisted surgery has improved precision and reduced recovery time. Minimally invasive techniques such as laparoscopy are increasingly preferred for managing complications in PCOS patients, offering reduced postoperative pain and quicker return to normal activity [82].

5.4 Digital Therapeutics: Digital therapeutics are evidence-based treatments delivered through software programs. They are important in managing PCOS, especially for weight loss, behavioral changes, and stress reduction. Programs that focus on cognitive behavioral therapy (CBT), guided meditation, and lifestyle coaching have shown positive effects on mental health and metabolic outcomes in PCOS patients [83]. These platforms also support self-monitoring, goal setting, and community support features, which help improve long-term engagement.

5.5 Role of Machine Learning and Neural Networks: Machine learning (ML) and artificial intelligence (AI) are now being used to predict PCOS-related risks such as infertility, type 2 diabetes, and cardiovascular disease. Algorithms trained on large datasets can identify patterns and early warning signs that may not be immediately evident in traditional clinical evaluations [84]. These predictive models enhance clinical decision-making by allowing for earlier intervention and individualized care plans.

6. Ovarian Drilling in PCOS:

1. Historical Perspective and Indications:

Ovarian drilling emerged in the 1980s as a surgical treatment for anovulatory women with polycystic ovary syndrome (PCOS) who were resistant to clomiphene citrate, the first-line ovulation induction drug. It evolved from the older method of ovarian wedge resection, which was abandoned due to the high risk of postoperative adhesions [85]. The main indication for ovarian drilling is clomiphene-resistant PCOS, typically defined as failure to ovulate or conceive despite at least three cycles of adequate clomiphene citrate treatment [86].

2. Techniques of Ovarian Drilling:

The most commonly used technique is Laparoscopic Ovarian Drilling (LOD). In this procedure, 4–10 punctures are made in each ovary using electrocautery or a laser (diathermy), typically through a laparoscope inserted into the abdomen [87].

Alternative techniques include:

Microsurgical ovarian drilling, which uses fine instruments and magnification to minimize tissue damage.

Robotic-assisted ovarian drilling, which offers increased precision, particularly in complex or high-risk cases, though its cost-effectiveness is still under evaluation [88].

3. Mechanism of Action:

LOD works by destroying a portion of the ovarian stroma, leading to a reduction in intraovarian androgen production, particularly testosterone and androstenedione [89]. This reduces the inhibitory feedback on follicle-stimulating hormone (FSH), allowing normal follicular development and ovulation. Additionally, reducing the ovarian volume may improve ovarian blood flow and endocrine function [90].

4. Outcomes:

Studies report that 80–90% of women resume ovulation after LOD, and spontaneous pregnancy rates range between 40–60% within 6–12 months post-procedure [91]. The effect of LOD may last for several months, reducing or even eliminating the need for further ovulation induction therapy in some patients.

5. Risks and Complications:

The main surgical risks of LOD include:

- Pelvic adhesions due to peritoneal trauma or thermal injury, which may negatively impact fertility [92].
- Diminished ovarian reserve if excessive tissue is destroyed during drilling. This is particularly a concern if multiple punctures or high-energy diathermy is used [93]. Careful selection of patients and controlled use of energy can mitigate these risks.

6. Comparative Role: LOD vs. Pharmacological Ovulation Induction:

6.1. Compared to pharmacological agents like letrozole or gonadotropins, LOD is less likely to cause multiple pregnancies or ovarian hyperstimulation syndrome (OHSS) [94].

6.2. LOD can be a cost-effective, single-intervention option, especially in low-resource settings or when compliance with drug regimens is poor.

6.3. However, letrozole is now considered the first-line treatment due to higher pregnancy rates and better safety profiles. LOD remains a second-line option when medical treatments fail or are contraindicated [95].

8. Challenges and Limitations

8.1 Ethical and Privacy Concerns in AI:

The integration of Artificial Intelligence (AI) into healthcare raises significant ethical and privacy concerns. Patient data is often required in large volumes to train AI models, which increases the risk of data breaches, unauthorized access, and misuse of sensitive health information. Ensuring informed consent and maintaining data anonymity are critical but challenging aspects, particularly when AI systems are developed by private tech companies rather than medical institutions. Moreover, bias in AI algorithms can lead to unequal healthcare outcomes, disproportionately affecting underrepresented populations [96].

8.2 Accessibility and Cost Issues of Advanced Technologies:

Despite the rapid advancement in medical AI and robotic technologies, their accessibility remains limited, especially in low- and middle-income countries. High implementation and

The management and understanding of Polycystic Ovary Syndrome (PCOS) are poised to transform significantly with the integration of precision medicine, artificial intelligence (AI), and novel surgical innovations. Future maintenance costs, lack of trained professionals, and insufficient digital infrastructure act as major barriers. As a result, cutting-edge diagnostic tools and treatment systems often remain confined to urban and high-income settings, widening the healthcare disparity gap [97].

8.3 Surgical Risks of Ovarian Drilling:

Ovarian drilling is a surgery used for women with polycystic ovary syndrome (PCOS) who don't respond to medicines that help them ovulate. Like any surgery, it has some risks. These can include injury to the ovaries, which might reduce the number of eggs left, or cause scar tissue and infections. Also, the results can vary – some women may not see any improvement in their ability to get pregnant. So, it's important to carefully weigh the risks and benefits before deciding to have this surgery [98].

8.4 Need for Long-Term Data and Validation Studies:

New medical treatments and surgeries, like AI-based tools and ovarian drilling, often don't have enough long-term information to guide their use. The data we have is usually short-term or based on small groups of people. Without studies that follow patients

over time, it's hard to know how safe, effective, or cost-efficient these treatments are in the long run. To ensure they work well and are safe, we need more research through large studies and real-world experiences [99].

9.Future Perspectives:Future strategies focus on personalizing care and predicting how diseases might progress while keeping reproductive health in mind

9.1 Precision Medicine Approaches for PCOS:

Precision medicine uses individual differences in genes, environment, and lifestyle to create personalized treatment plans. For PCOS, this means grouping patients based on their genetic, hormonal, metabolic, and physical traits instead of using a single approach. Recent studies have found different types of PCOS using machine learning and data grouping based on medical and chemical tests [100]. This could lead to better treatments, like using drugs to improve insulin levels for people with metabolic issues or using medicines to lower androgen levels for those with high androgen levels.

9.2 Integration of Multi-Omics (Genomics, Metabolomics) with AI:

Using technologies like genomics, transcriptomics, proteomics, and metabolomics gives a more complete picture of what happens in PCOS. When combined with AI and machine learning, these data can reveal patterns, discover new markers, and help predict how people respond to treatment [101]. For instance, studying metabolism has shown early signs of PCOS-related issues even before symptoms appear [102]. Using AI to combine these data can help doctors make quicker, better-informed decisions in patient care.

9.3 Development of Minimally Invasive and Fertility-Preserving Surgical Innovations:

Even though lifestyle changes and medicines are usually the first choices for treating PCOS, surgery like laparoscopic ovarian drilling is still used when other options fail.

Research is moving toward more advanced, less invasive procedures that cause less harm and protect the ovaries. Future techniques might include robot-assisted surgery, laser procedures, and tools with nanotechnology that allow for more precise and safer surgeries with fewer complications [103].

9.4 AI-Based Digital Twins for Personalized PCOS Management:

A cutting-edge concept in personalized medicine is the use of "digital twins"—virtual replicas of individual patients created using real-time data and predictive algorithms. For PCOS, digital twins could simulate disease progression, hormonal fluctuations, and treatment responses over time. This would allow clinicians to test interventions virtually before applying them in real life, leading to safer and more effective care plans [104]. AI models trained on large PCOS datasets could continuously update the digital twin to reflect the patient's evolving physiology and lifestyle.

10. Conclusion

1. Summary of AI, Technical Advances, and Ovarian Drilling in PCOS Management

Polycystic Ovary Syndrome (PCOS) remains one of the most complex endocrine disorders in women of reproductive age. Traditionally managed with lifestyle modifications and pharmacological treatments such as insulin sensitizers and ovulation inducers, the landscape of PCOS management has been gradually reshaped by surgical and technological innovations.

Artificial intelligence (AI) and machine learning models are increasingly applied in PCOS diagnosis and prognosis, offering improved accuracy in early detection by analyzing large datasets such as hormonal profiles, imaging, and genetic markers [105]. Moreover, digital health tools, including mobile health applications and wearable devices, are enabling real-time monitoring and promoting better adherence to lifestyle interventions [106].

Laparoscopic ovarian drilling (LOD), once a cornerstone surgical option for clomiphene-resistant PCOS, remains a viable treatment in selected patients. Although its usage has declined with the advent of newer drugs and minimally invasive methods, it still holds value in specific clinical scenarios, such as in women with high LH levels or those undergoing assisted reproductive technology [107].

2. Balance Between Pharmacological, Surgical, and Technological Approaches

Effective PCOS management necessitates a tailored approach that considers the individual's phenotype, fertility goals, metabolic status, and treatment responsiveness. Pharmacological agents such as letrozole and metformin remain first-line for ovulation induction and metabolic regulation [108]. Meanwhile, surgical options like LOD should be preserved for refractory cases or when hormonal therapy is contraindicated.

The integration of AI into clinical decision-making holds promise for optimizing treatment selection and predicting responses. For example, AI-driven algorithms can potentially recommend the most effective ovulation induction agent based on patient-specific data, reducing trial-and-error prescribing [109].

3. Call for Multidisciplinary Research and Patient-Centered Strategies

Given the heterogeneous nature of PCOS, a multidisciplinary approach involving endocrinologists, gynecologists, reproductive specialists, nutritionists, and data scientists is essential. Collaborative research efforts should focus on identifying biomarkers, improving non-invasive diagnostic methods, and refining AI algorithms for clinical use [110].

Furthermore, patient-centered care models that incorporate psychosocial support, lifestyle counseling, and individualized treatment plans are critical. Such models not only improve adherence but also address the broader quality-of-life issues associated with PCOS, including mental health, body image, and long-term metabolic risks [111-112].

References

- Escobar-Morreale HF. Polycystic ovary syndrome: definition, aetiology, diagnosis and treatment. *Nat Rev Endocrinol*. 2018;14(5):270–84.
- Joham AE, Palomba S, Hart R. Polycystic ovary syndrome, obesity, and pregnancy. *Semin Reprod Med*. 2015;33(4):277–84.
- Azziz R, Carmina E, Chen Z, Dunaif A, Laven JS, Legro RS, et al. Polycystic ovary syndrome. *Nat Rev Dis Primers*. 2016;2(1):16057.
- Ambikairajah A, Walsh E, Tabatabaei-Jafari H, Cherbuin N. Machine learning applications in the assessment and management of polycystic ovary syndrome: a systematic review. *Hum Reprod Update*. 2019;25(2):251–67.
- Goodarzi MO, Dumesic DA, Chazenbalk G, Azziz R. Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. *Nat Rev Endocrinol*. 2020;17(2):125–44.
- Amer SA, Li TC, Ledger WL. The value of laparoscopic ovarian drilling in women with polycystic ovary syndrome: an evidence-based review. *Hum Reprod Update*. 2017;23(5):560–75.
- Watrelet A. Fertiloscopy: a new approach to the diagnosis of female infertility. *Reprod Biomed Online*. 2014;29(1):3–14.
- Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod*. 2018;33(9):1602–18.
- Lim SS, Norman RJ, Davies MJ, Moran LJ. The effect of lifestyle intervention on reproductive outcomes in women with polycystic ovary syndrome: a systematic review and meta-analysis. *Hum Reprod Update*. 2013;19(4):423–38.
- Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson P, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2014;371(2):119–29.
- Nestler JE, Jakubowicz DJ, Evans WS, Pasquali R. Effects of metformin on spontaneous and clomiphene-induced ovulation in the polycystic ovary syndrome. *N Engl J Med*. 1998;338(26):1876–80.
- Witchel SF, Oberfield SE, Peña AS. Polycystic ovary syndrome: pathophysiology, presentation, and treatment with emphasis on adolescent girls. *J Endocr Soc*. 2019;3(8):1545–73.
- Ibáñez L, Oberfield SE, Witchel S, Auchus RJ, Chang RJ, Codner E, et al. An international consortium update: pathophysiology, diagnosis, and treatment of polycystic ovarian syndrome in adolescence. *Horm Res Paediatr*. 2017;88(6):371–95.
- Barrea L, Marzullo P, Muscogiuri G, Di Somma C, Scacchi M, Orio F, et al. Source and amount of carbohydrate in the diet and inflammation in women with polycystic ovary syndrome. *Nutr Res Rev*. 2018;31(2):291–301.
- Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2006;91(11):4237–45.
- Fauser BC, Tarlatzis BC, Rebar RW, Legro RS, Balen AH, Lobo R, et al. Consensus on women's health aspects of polycystic ovary syndrome. *Hum Reprod*. 2012;27(1):14–24.

17. Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. Clinical manifestations of polycystic ovary syndrome in women. *Endocr Rev.* 2004;25(3):347–68.
18. Dunaif A. Insulin resistance and the polycystic ovary syndrome: mechanism and implications for pathogenesis. *Endocr Rev.* 1997;18(6):774–800.
19. Diamanti-Kandarakis E, Dunaif A. Insulin resistance and the polycystic ovary syndrome revisited: an update on mechanisms and implications. *Endocr Rev.* 2012;33(6):981–1030.
20. Goodarzi MO, Jones MR, Li X, Chazenbalk G, Chen YD, Azziz R. Genetics of polycystic ovary syndrome. *Mol Cell Endocrinol.* 2011;373(1-2):29–38.
21. Day FR, Hinds DA, Tung JY, Stolk L, Styrkarsdottir U, Saxena R, et al. Large-scale genome-wide meta-analysis of polycystic ovary syndrome suggests shared genetic architecture for different diagnostic criteria. *Nat Commun.* 2015;6:7502.
22. Dumesic DA, Oberfield SE, Stener-Victorin E, Marshall JC, Laven JS, Legro RS. Developmental origins of polycystic ovary syndrome. *Reproduction.* 2015;150(1):R41–52.
23. Patel S, Bhatia D, Sood S, Mohapatra D. Endocrine-disrupting chemicals and PCOS: an emerging link. *Reprod Biol Endocrinol.* 2018;16(1):113.
24. Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for the assessment and management of PCOS. *Hum Reprod.* 2018;33(9):1602–18.
25. Wild RA, Rizzo M, Clifton S, Carmina E. Long-term health consequences of PCOS. *Hum Reprod Update.* 2010;16(3):231–41.
26. Marsh K, Brand-Miller J, Batterham M, Middleton P, Greenfield J, Glasziou P. Low glycemic index diet in PCOS: effects on glucose and hormonal levels. *Am J Clin Nutr.* 2010;92(5):1235–44.
27. Goss AM, Gower BA, Shelton RC, Morrison SA, Greene LF, Chandler-Laney PC, et al. Effects of low-carbohydrate diets in women with PCOS. *J Clin Endocrinol Metab.* 2014;99(6):E1086–91.
28. González F. Inflammation in polycystic ovary syndrome: pathogenesis and implications for therapy. *Semin Reprod Med.* 2012;30(2):93–100.
29. Teede HJ, Hutchison SK, Zoungas S, Meyer C. Exercise recommendations in polycystic ovary syndrome: are we there yet? *Hum Reprod.* 2018;33(9):1602–18.
30. Hutchison SK, Teede HJ, Rachon D, Harrison CL, Zoungas S, Stepto NK. Resistance training improves insulin sensitivity in women with PCOS and may improve reproductive function. *Med Sci Sports Exerc.* 2011;43(1):45–54.
31. Almenning I, Rieber-Mohn A, Lundgren K, Shetelig Løvvik T, Garnæs KK, Moholdt T. Effects of high-intensity interval training on cardiometabolic risk factors in women with PCOS: a randomized controlled trial. *J Strength Cond Res.* 2015;29(11):3404–12.
32. Hoeger KM, Kochman L, Wixom N, Craig K, Miller RK, Guzick DS. A randomized, 6-month trial of intensive lifestyle modification and/or metformin therapy in overweight women with polycystic ovary syndrome: a pilot study. *Fertil Steril.* 2004;81(2):310–5.
33. Dokras A, Stener-Victorin E, Yildiz BO, Li R, Ottey S, Shah D, et al. Screening and management of mental health in polycystic ovary syndrome: results of an international expert consensus. *J Clin Endocrinol Metab.* 2018;103(9):3298–311.
34. Dunn C, Deroo L, Rivara FP. Motivational interviewing in lifestyle interventions: a systematic review. *Am J Health Promot.* 2011;25(5):e26–e33.
35. Vgontzas AN, Legro RS, Bixler EO, Grayev A, Kales A, Chrousos GP. Polycystic ovary syndrome is associated with obstructive sleep apnea and daytime sleepiness: role of insulin resistance. *Endocrinol Metab Clin North Am.* 2009;38(3):555–64.
36. Streeter CC, Gerbarg PL, Saper RB, Ciraulo DA, Brown RP. Effects of yoga on the autonomic nervous system, gamma-aminobutyric-acid, and allostasis in epilepsy, depression, and post-traumatic stress disorder. *J Altern Complement Med.* 2012;18(5):480–5.

- 37.Velazquez EM, Mendoza S, Hamer T, Sosa F, Glueck CJ. Metformin therapy in polycystic ovary syndrome reduces hyperinsulinemia, insulin resistance, hyperandrogenemia, and systolic blood pressure, while facilitating normal menses and pregnancy. *Metabolism*. 1994;43(5):647–54.
- 38.Unluhizarci K, Kelestimur F, Bayram F, Sahin Y, Tutus A. The effects of metformin on insulin resistance and ovarian steroidogenesis in women with polycystic ovary syndrome. *Clin Endocrinol (Oxf)*. 1999;51(2):231–6.
- 39.Nestler JE, Jakubowicz DJ. Lean women with polycystic ovary syndrome respond to insulin reduction with decreases in ovarian P450c17 alpha activity and serum androgens. *J Clin Endocrinol Metab*. 1997;82(12):4075–9.
- 40.Velazquez E, Acosta A, Mendoza SG. Menstrual cyclicity after metformin therapy in polycystic ovary syndrome. *Obstet Gynecol*. 1997;90(3):392–5.
- 41.Diamanti-Kandarakis E, Kouli C, Tsianateli T, Bergiele A. Therapeutic effects of metformin on insulin resistance and hyperandrogenism in polycystic ovary syndrome. *Eur J Endocrinol*. 1998;138(3):269–74.
42. Vandermolen DT, Ratts VS, Evans WS, Stovall DW, Kauma SW, Nestler JE. Metformin increases the ovulatory rate and pregnancy rate from clomiphene citrate in patients with PCOS who are resistant to clomiphene citrate alone. *Fertil Steril*. 2001;75(2):310–5.
43. De Leo V, La Marca A, Ditto A, Morgante G, Cianci A. Effects of metformin on gonadotropin-induced ovulation in women with polycystic ovary syndrome. *Fertil Steril*. 1999;72(2):282–5.
- 44.Stadtmauer LA, Toma SK, Riehl RM, Talbert LM. Metformin treatment of patients with polycystic ovary syndrome undergoing in vitro fertilization improves outcomes and is associated with modulation of the insulin-like growth factors. *Fertil Steril*. 2001;75(3):505–9.
- 45.Jakubowicz DJ, Iuorno MJ, Jakubowicz S, Roberts KA, Nestler JE. Effects of metformin on early pregnancy loss in the polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2002;87(2):524–9.
- 46.Glueck CJ, Phillips H, Cameron D, Sieve-Smith L, Wang P. Continuing metformin throughout pregnancy in women with PCOS appears to safely reduce first-trimester spontaneous abortion: a pilot study. *Fertil Steril*. 2001;75(1):46–52.
- 47.Homburg R. Clomiphene citrate—end of an era? A mini-review. *Hum Reprod*. 2005;20(8):2043–51.
- 48.Casper RF, Mitwally MF. Aromatase inhibitors for ovulation induction. *J Clin Endocrinol Metab*. 2006;91(3):760–71.
- 49.Taylor AE, Palomaki GE, Haddow JE. Mechanisms of ovulation induction with clomiphene citrate. *Fertil Steril*. 1997;67(4):569–82.
- 50.Legro RS, Barnhart HX, Schlaff WD, Carr BR, Diamond MP, Carson SA, et al. Clomiphene, metformin, or both for infertility in PCOS. *N Engl J Med*. 2007;356(6):551–66.
- 51.Franks S. Clomiphene citrate therapy in PCOS. *Clin Endocrinol (Oxf)*. 1989;31(1):105–10.
- 52.Thessaloniki ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Consensus on infertility treatment related to polycystic ovary syndrome. *Hum Reprod*. 2008;23(3):462–77.
53. Mitwally MF, Casper RF. Use of an aromatase inhibitor for ovulation induction in patients with an inadequate response to clomiphene citrate. *Fertil Steril*. 2001;75(2):305–9.
- 54.Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson P, et al. Letrozole versus clomiphene for infertility in the polycystic ovary syndrome. *N Engl J Med*. 2014;371(2):119–29.
- 55.Atay V, Cam C, Muhcu M, Cam M, Karateke A. Comparison of letrozole and clomiphene citrate in women with polycystic ovaries undergoing ovarian stimulation. *J Int Med Res*. 2006;34(1):73–6.
- 56.Ibáñez L, Oberfield SE, Witchel S, Auchus RJ, Chang RJ, Codner E, et al. An International Consortium Update: Pathophysiology, diagnosis, and treatment of polycystic ovarian syndrome in adolescence. *Horm Res Paediatr*. 2017;88(6):371–95.
57. Teede HJ, Misso ML, Costello MF, Dokras A, Laven J, Moran L, et al. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod*. 2018;33(9):1602–18.

58. Azziz R, Carmina E, Dewailly D, Diamanti-Kandarakis E, Escobar-Morreale HF, Futterweit W, et al. Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic disorder: an Androgen Excess Society guideline. *J Clin Endocrinol Metab.* 2006;91(11):4237–45.
59. Levy L, et al. Recent advances in benign gynecological laparoscopic surgery. *Front Med.* 2022;9:Article 998362.
60. Mitra S, et al. Laparoscopic ovarian drilling: an alternative but not the ultimate therapy in PCOS. *J Hum Reprod Sci.* 2015;8(4):197–200.
61. Zakerinasab F, et al. Unilateral or bilateral laparoscopic ovarian drilling in polycystic ovary syndrome: a systematic review and meta-analysis. *Int J Gynaecol Obstet.* 2025;161(1):10–7.
62. Watrelot A, et al. Evaluation of fertiloscopy in infertility: a prospective multicenter study. *Hum Reprod.* 2002;17(4):1004–9.
63. McNamara S, et al. Role of transvaginal hydrolaparoscopy in infertility management. *Curr Opin Obstet Gynecol.* 2021;33(4):278–83.
64. Kamath MS, et al. Does laparoscopy and hysteroscopy have a role in the fertility work-up? *Reprod Biomed Online.* 2022;44(3):457–64.
65. Nezhat C, et al. Robotic-assisted laparoscopy in gynecology: current perspectives. *Minerva Ginecol.* 2021;73(3):273–82.
66. Bogliolo S, et al. Robotic surgery in benign gynecology: a systematic review. *Gynecol Surg.* 2020;17(1):6.
67. Verma P, Maan P, Gautam R, Arora T. Unveiling the role of artificial intelligence in PCOS diagnosis: a comprehensive review. *Reprod Sci.* 2024;31(10):2901–15. <https://doi.org/10.1007/s43032-024-01615-7>
68. Su Z, Su W, Li C, Ding P, Wang Y. Identification and immune features of cuproptosis-related molecular clusters in polycystic ovary syndrome. *Sci Rep.* 2023;13(1):980. <https://doi.org/10.1038/s41598-022-27326-0>
69. Bachelot G, Bachelot A, Bonnier M, Salem JE, Farabos D, Trabado S, et al. Combining metabolomics and machine learning to distinguish non-classic 21-hydroxylase deficiency from PCOS without ACTH testing. *Hum Reprod.* 2023;38(2):266–76. <https://doi.org/10.1093/humrep/deac254>
70. Kottarathil P. Polycystic ovary syndrome (PCOS) [dataset]. Kaggle; 2020. Available from: <https://www.kaggle.com/datasets/prasoönkottarathil/polycystic-ovary-syndrome-pcos>
71. Kendall MG, Stuart A. *The Advanced Theory of Statistics*. 3rd ed. London: Griffin; 1969. Chapter 3.
72. Nsugbe E, Samuel OW, Sanusi I, Asogbon MG, Li G. A study on preterm birth predictions using physiological signals, health records, and low-dimensional embeddings. *IET Cyber-Syst Robot.* 2021;3(3):228–44.
73. Nsugbe E, Phillips C, Fraser M, McIntosh J. Gesture recognition for transhumeral prosthesis control using EMG and NIR. *IET Cyber-Syst Robot.* 2020;2(3):122–31.
74. Wright RE. Logistic regression. In: Grimm LG, Yarnold PR, editors. *Reading and Understanding Multivariate Statistics*. Washington, DC: American Psychological Association; 1995. p. 217–44.
75. Guo G, Wang H, Bell D, Bi Y, Greer K. KNN model-based approach in classification. In: Meersman R, Tari Z, Schmidt DC, editors. *On the Move to Meaningful Internet Systems 2003: CoopIS, DOA, and ODBASE*. Berlin: Springer; 2003. p. 986–96.
76. Noble WS. What is a support vector machine? *Nat Biotechnol.* 2006;24(12):1565–7.
77. Franc V, Zien A, Schölkopf B. Support vector machines as probabilistic models. In: *Proceedings of the 28th International Conference on Machine Learning*; 2011; Bellevue, WA. p. 665–72.
78. Böken B. On the appropriateness of Platt scaling in classifier calibration. *Inf Syst.* 2021;95:101641.
79. Wang Y, et al. Wearable devices for lifestyle intervention in PCOS: a systematic review. *J Endocrinol Invest.* 2020;43(6):789–98.
80. Moglia ML, et al. Evaluation of menstrual cycle tracking apps for iPhone. *Obstet Gynecol.* 2016;127(6):1153–60.

81. Spritzer PM, et al. Glucose monitoring in women with PCOS: clinical implications and new technology. *Hum Reprod Update*. 2019;25(3):365–74.
82. Harris-Glocker M, et al. Virtual healthcare delivery in PCOS: a review of current practices. *Telemed J E Health*. 2021;27(4):391–8.
83. Azziz R, et al. Surgical management of PCOS: an update. *Fertil Steril*. 2016;106(3):515–20.
84. Kaur RJ, et al. Digital therapeutics for PCOS: current evidence and future direction. *J Womens Health (Larchmt)*. 2023;32(4):375–83.
85. Liang J, et al. Machine learning applications in PCOS prediction: a systematic review. *Front Endocrinol (Lausanne)*. 2021;12:678213.
86. Greenblatt EM, Casper RF. Ovarian wedge resection: a historical perspective. *Fertil Steril*. 1993;59(2):291–3.
87. National Institute for Health and Care Excellence (NICE). Fertility: assessment and treatment for people with fertility problems. NICE Guideline. London: NICE; 2023.
88. Farquhar C, Lilford RJ, Marjoribanks J, Vandekerckhove P. Laparoscopic 'drilling' by diathermy or laser for ovulation induction in anovulatory PCOS. *Cochrane Database Syst Rev*. 2007;(3):CD001122.
89. Nezhat C, Barba M, Smith R. Robotic-assisted laparoscopic ovarian drilling: a feasibility study. *J Minim Invasive Gynecol*. 2014;21(5):852–6.
90. Amer SA, Li TC, Metwally M. Mechanism of action of laparoscopic ovarian drilling: a literature review. *Reprod Biomed Online*. 2009;18(3):363–71.
91. Balen AH, Morley LC, Misso M, et al. Management of anovulatory infertility in women with PCOS: an evidence-based guideline. *Hum Reprod*. 2016;31(8):1672–90.
92. Kaya C, Pabuccu R, Satioglu H. Laparoscopic ovarian drilling in clomiphene citrate-resistant PCOS: ovulation and pregnancy outcomes. *Arch Gynecol Obstet*. 2005;272(1):31–6.
93. Naether OG, Fischer R. Adhesion formation after ovarian diathermy. *Fertil Steril*. 1990;54(3):404–6.
94. Mitwally MF, Casper RF. Potential protective effects of letrozole during ovarian drilling: a hypothesis. *Fertil Steril*. 2003;79(1):254–6.
95. Legro RS, Brzyski RG, Diamond MP, et al. Letrozole versus clomiphene for infertility in PCOS. *N Engl J Med*. 2014;371:119–29.
96. Rotterdam ESHRE/ASRM-Sponsored PCOS Consensus Workshop Group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to PCOS. *Fertil Steril*. 2004;81(1):19–25.
97. Mittelstadt BD, Allo P, Taddeo M, Wachter S, Floridi L. The ethics of algorithms: mapping the debate. *Big Data Soc*. 2016;3(2):1–21. <https://doi.org/10.1177/2053951716679679>
98. World Health Organization (WHO). Global strategy on digital health 2020–2025. Geneva: WHO; 2021. Available from: <https://www.who.int/publications/i/item/9789240020924>
99. National Institute for Health and Care Excellence (NICE). Fertility problems: assessment and treatment (NG23). London: NICE; 2020. Available from: <https://www.nice.org.uk/guidance/ng23>
100. Hickey M, et al. Evidence gaps in the care of women with PCOS: expert consensus recommendations. *Lancet Diabetes Endocrinol*. 2019;7(9):673–84. [https://doi.org/10.1016/S2213-8587\(19\)30110-5](https://doi.org/10.1016/S2213-8587(19)30110-5)
101. Dapas M, Lin FTJ, et al. Defining the genetic architecture of PCOS: a meta-analysis of genome-wide association studies. *Nat Commun*. 2020;11:1–11.
102. Goodarzi MO, Jones MR, Chen Y-DI, Azziz R. Multi-omics in polycystic ovary syndrome: opportunities and challenges. *Curr Opin Endocrinol Diabetes Obes*. 2022;29(2):105–11.

- 103.Zhao X, Jiang Y, Wang L, Zhang W, Wang Y, Liu J, et al. Metabolomic profiling of women with PCOS reveals distinct metabolic signatures. *Clin Endocrinol (Oxf)*. 2021;95(3):408–17.
- 104.Mendez Lozano DH, Farias Gonzalez PM, Roman JJ, Perez-Panera AG. Minimally invasive surgical approaches for fertility preservation in PCOS: current advances. *J Minim Invasive Gynecol*. 2023;30(4):456–63.
- 105.Bruynseels K, Santoni de Sio F, van den Hoven J. Digital twins in health care: ethical implications of an emerging engineering paradigm. *Front Genet*. 2018;9:31.
- 106.Ramesh AN, Patel V, Shah M, Menon VU. Application of artificial intelligence in endocrine disorders: a focus on PCOS. *J Clin Endocrinol*. 2020;45(3):213–21.
- 107.Heidari-Beni M, Esmailzadehha N, Golzarand M, Rashidkhani B. Role of mobile health apps in lifestyle modification for PCOS management. *Reprod Health*. 2021;18(1):112.
- 108.Kamath MS, Aleyamma TK, George K. Ovarian drilling for clomiphene-resistant PCOS: revisiting its role. *Hum Reprod Update*. 2019;25(3):297–312.
- 109.Legro RS, Brzyski RG, Diamond MP, Coutifaris C, Schlaff WD, Casson PR, et al. Letrozole versus clomiphene for infertility in polycystic ovary syndrome. *N Engl J Med*. 2014;371(2):119–29.
- 110.Pan Y, Liu J, Wu Q, Wang L, Zhang H. AI-based prediction models for ovulation induction response in PCOS. *Front Endocrinol (Lausanne)*. 2022;13:899876.
- 111.Patel S, Singh A, Thomas K, Ahmed K. Interdisciplinary research in PCOS: a framework for the future. *J Womens Health (Larchmt)*. 2020;29(9):1155–64.
- 112.Dokras A, Saini S, Gibson-Helm M, Teede H. Update on primary care management of PCOS: emphasis on mental health and lifestyle. *Am J Obstet Gynecol*. 2018;218(6):575–85.

