FOGSI - ICOG

Good Clinical Practice Recommendations

GCPR on

Update in Managing PCOS in Women

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From the Desk of Prof. Hrishikesh D Pai

Trustee FIGO Asia-Oceania (2023-25)
President Federation of Obstetric and Gynecological Societies of India (FOGSI) (2023)

It is with great pride and enthusiasm that I present to you this well researched and scholarly Good Clinical Practice Recommendations (GCPR) on "Update in Managing PCOS in Women" developed under my leadership as President of FOGSI (2023). This endeavor represents a significant milestone in our ongoing commitment to improving women's healthcare across the nation.

The formulation of this GCPR has been a collaborative effort, bringing together the collective wisdom and expertise of some of the brightest minds in our field. As President of FOGSI, I had the honor of overseeing this ambitious project, and I am deeply grateful for the dedication and hard work of everyone involved.

Our Advisors, past presidents of FOGSI, Dr. Sanjay Gupte and Dr. Hema Diwakar, provided invaluable guidance and support throughout the process. The National Coordinators- Dr. CN Purandare, Dr. Rishma Pai, Dr. Nandita Palshetkar, and Dr. Jaydeep Tank, played a crucial role in coordinating efforts and ensuring the smooth progress of this project.

A pivotal role was played by Dr. Surekha Tayade, Chairperson of the Clinical Research Committee of FOGSI. As the Coordinator of the GCPR, she ensured that each step of the development process was meticulously followed. Her tireless dedication and attention to detail have been truly commendable.

I thank the Convenor, Dr Rakhi Singh, Chairperson of Endocrinology Committee, FOGSI, and the Co-convenor Dr Parag Biniwale, Vice President, ICOG who toiled for the development of this GCPR.

This GCPR was developed through a rigorous process. A drafting committee comprising 6-7 renowned experts in the field reviewed all existing literature and evidence to formulate the initial draft, which was presented to a team of 10-12 experts who reviewed it and provided feedback. Multiple meetings were organized to review and incorporate these suggestions, ensuring the latest evidence and best practices were incorporated.

We believe this good practice recommendation will be an invaluable resource for healthcare practitioners, enabling them to provide the highest standard of care to women across India and beyond.

Warm regards,

Hrishikesh D Pai
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Fogsi Good Clinical Practice Recommendations

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OVERVIEW

Purpose of Good Clinical Practice Recommendation

"The purpose of having a Good Clinical Practice Recommendation (GCPR) is to provide a uniform, national, evidence-based guideline with clear information for the assessment and management of polycystic ovary syndrome (PCOS). Its purpose is not only to aid healthcare professionals in clinical decisions and providing optimal patient care but also to help avoid missing diagnoses, delays, under- or over diagnosis, recognize complications, and prompt referral to specialist care, as well as to frame evidence-based management."

Context and Background

Polycystic ovary syndrome (PCOS) is a common endocrinological problem that affects the women of all reproductive ages. The prevalence of PCOS in premenopausal reproductive-aged women can be up to 18%, and it is a complex metabolic issue in this age group, depending on the population studied and diagnostic criteria used.[1] PCOS is often associated with metabolic derangements, cosmetic issues, and altered reproductive, psychological, and sexual functions. It is a multifactorial disorder characterized by a disproportionate increase in intraovarian androgens, leading to menstrual irregularity, polycystic ovaries, subfertility, and biochemical/clinical hyperandrogenism.[2] Studies in India have reported a prevalence of PCOS in young women to be around 3.7–22.5%.[3] The prevalence of PCOS in Indian adolescents ranges from 9.13% to 36%.[4] The pooled prevalence of PCOS in India, according to the Rotterdam's diagnostic criteria, is estimated to be 11.34% **(Table 1)**.[5]

Compared to the women with PCOS of the Caucasian ethnicity, the Indian women with PCOS have a higher degree of hirsutism, infertility, and acne, and experience lower live birth rates following in vitro fertilization. Similarly, the South Asians with PCOS have a higher prevalence of insulin resistance and metabolic syndrome compared to body mass index (BMI)-matched PCOS patients from other ethnic groups.[6] Different phenotypes are defined in PCOS women,[7] and with ethnic variation and presentation, differences within the diagnostic criteria and care provided lead to many challenges. Hence, there is a need for a consistent, national, evidence-based guideline for the assessment and management of PCOS, addressing concerns across all reproductive ages.

Table 1 Diagnostic criteria

Parameter	*Phenotype A*	*Phenotype B*	*Phenotype C*	*Phenotype D*
Polycystic ovary syndrome (PCOS) features	HA/OD/PCOM	HA/OD	HA/PCOM	OD/PCOM
Hyperandrogenism (HA)	✓	✓	✓	
Ovulatory dysfunction (OD)	✓	✓		✓
Polycystic ovarian morphology (PCOM) features	✓		✓	✓
Rotterdam 2003 criteria	✓	✓	✓	✓
AE-PCOS 2006 criteria	✓	✓	✓	-

METHODOLOGY

A systematic review of the literature was conducted to provide the best possible evidence-base for the GCPR. Existing guidelines, meta-analyses, systematic reviews, and key cited articles relating to PCOS were reviewed by a group of doctors, and recommendations relevant to the Indian scenario were framed. The GCPR is developed in accordance with the American Association of Clinical Endocrinologists (AACE) protocol for the standardized production of clinical practice guidelines **(Table 2)**. Recommendations are based on their clinical importance.

Table 2 Recommendation

GRADING	*Recommendation*	
A	Strongly Recommended	At least one randomized controlled trial (RCT) as part of a body of literature of overall good quality and consistency that addresses the specific recommendation.
B	Suggested	Availability of well-controlled clinical studies, but no RCTs are available on the topics of recommendation.
C	Unresolved	Evidence obtained from the expert committee reports of opinions and/or clinical experiences of respected authorities, which indicates an absence of directly applicable clinical studies of good quality.
CPP	Clinical Practice Points	Evidence not sought. A practice point has been made by the guideline development group where important issues arose from discussion of evidence-based or clinical consensus recommendations.

1. HISTORY AND CLINICAL ASSESSMENT[8,9]

1.1	Ovulatory dysfunction is assessed by the menstrual history of oligo/anovulation with bleeding intervals outside the normal interval (21–35 days), happening frequently at ≤21 days and/or infrequently at ≥35 days.	Grade A
1.2	A comprehensive history and physical examination should be completed to assess for the symptoms and signs of clinical hyperandrogenism, which may include hirsutism, acne, and alopecia. In adolescents, it is important to pay special attention to severe acne and hirsutism as these may indicate an underlying endocrine disorder such as PCOS.	Grade A
1.3	Unwanted excess hair growth and/or alopecia as reported by the patient should be considered important, regardless of apparent clinical severity.	Grade A
1.4	Health professionals should be aware of the potential negative psychosocial impact of clinical hyperandrogenism.	Grade A
1.5	Detailed history of previous treatments, including lifestyle modifications and their outsomes, has to be noted.	Grade A

2. RISK FACTOR ASSESSMENT[9] (TABLE 3)

Table 3 Risk factor assessment

Clinical symptoms	*Clinical characteristics*
• Pubertal deviations (early or late) • Disturbances in periodicity/timing of menstrual cycle • Early acne or hirsutism, persistent severe acne, frequent relapse in acne, acne in facial 'V' area, persistent acne and hirsutism for more than 2 years • Recent weight gain (particularly around abdomen) • Sedentary lifestyle • Family history of diabetes or PCOS	• Dyslipidemia (elevated serum total cholesterol, triglyceride and LDL-C levels) • Presence of PCOM on USG • High BMI for overweight/ obesity >23 kg/m^2 for adults and > 97.5th percentile for age in adolescents) • Features of insulin resistance like acanthosis nigricans, abdominal obesity

Abbreviations: BMI, body mass index; LDL-C, low-density lipoprotein-cholesterol; PCOM, polycystic ovarian morphology; PCOS, polycystic ovarian syndrome; USG, ultrasonography

2.1	Indian women who present with any of these symptoms or signs, have to be considered at the risk of developing PCOS.	Grade A
2.2	The women with the above risk factors have to be monitored at regular intervals to look for other symptoms and signs of PCOS.	Grade A
2.3	More than 2 risk factors have to be tested further by gynecologist to rule out PCOS.	CPP

3. DIAGNOSTIC CRITERIA FOR PCOS[8-12]

3.1	In adult Indian women, it is recommended that the diagnosis of PCOS be made using the Rotterdam criteria, meeting two of the following three conditions: If 2 criteria are evident, then there is no need to confirm the 3rd criterion.	Grade A

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3.2 Irregular cycle and ovulatory dysfunction 3.2a. 1 to <3 years post menarche: <21 or >45 days. 3.2b. 3 years post menarche to perimenopause: <21 or >35 days or <8 cycles per year. 3.2c. 1 year post menarche >90 days for any one cycle. 3.2d. Primary amenorrhea by age 15 or >3 years post thelarche (breast development). 3.2e. Normal in the first year postmenarche, due to puberty changes	Grade A
3.3 Clinical hyperandrogenism (refer annexure) 3.3a. Adults with PCOS should undergo a thorough history and physical examination to evaluate for clinical signs of hyperandrogenism, with hirsutism being a strong predictor, and acne and alopecia being weaker predictors 3.3b. Hirsutism and severe acne should be assessed in adolescents. 3.3c. Hirsutism – Standardized visual scales are preferred when assessing hirsutism, such as the modified Ferriman–Gallwey score (mFG). 3.3d. Scores <4 indicate mild hirsutism, 4–7 indicate moderate hirsutism, ≥8 indicate severe hirsutism. 3.3e. Acne – The Indian Acne Association (IAA) criteria is used for assessing severity acne. 3.3f. Inquire about the history of treatment for these cosmetic issues, as it may highlight the severity of these features.	 Grade A Grade A Grade A Grade A CPP
3.4 Biochemical hyperandrogenism 3.4a. Serum total testosterone levels, free testosterone and calculated free androgen index should be used to assess biochemical hyperandrogenemia in the diagnosis of PCOS. 3.4b. When androgen levels are significantly elevated, with or without signs of rapid virilization, it becomes necessary to consider other conditions of hyperandrogenemia.	 Grade A CPP
3.5 ULTRASOUND AND PCOM 3.5a. Ultrasound is used only in adults. Should not be used for women with gynecological age <8 years. 3.5b. The transvaginal ultrasound approach is preferred in the diagnosis of PCOS, if sexually active and if acceptable to the individual being assessed. 3.5c. Using endovaginal ultrasound transducers with a frequency bandwidth that includes 8 MHz, the threshold for PCOM should be a follicle number per ovary of ≥20 and/or an ovarian volume ≥10 mL on either ovary, ensuring no corpora lutea, cysts, or dominant follicles are present. 3.5d. Transabdominal ultrasound the threshold for PCOM could be an ovarian volume ≥10 mL on either ovary	 Grade A Grade A Grade A CPP
3.6 MENOPAUSE LIFE STAGE 3.6a. Postmenopausal women with a history of PCOS during their reproductive years or with a long-term history of irregular menstrual cycles and hyperandrogenemia, with or without polycystic ovary morphology (PCOM) on ultrasound, may be considered to have postmenopausal PCOS.	 Grade B
3.7 Anti-mullerian hormone AMH 3.7a. If there is clinical or biochemical hyperandrogenemia along with irregular menstruation, there is no need for AMH assessment. 3.7b. However, if one of these features is absent, serum AMH levels could be utilized for diagnosing PCOS in adults. 3.7c. The serum AMH level cutoff of 3.2 ng/mL (23 pmol/L) with the Elecsys AMH Plus immunoassay exhibits high sensitivity and specificity in identifying PCOM, regardless of age or PCOS phenotype.	 Grade A CPP CPP
3.8 Acanthosis nigricans with or without obesity is an additional diagnostic criterion for PCOS in adults and adolescents in India.	Grade B

4. ASSESSMENT OF ALL WOMEN WITH PCOS[8,9]

4.1 Clinical assessment has to be done in first visit, irrespective of their presenting complaint Follow-up visits (6 months in high risk and 1 year in low-risk patients).	Grade A
4.2 a. Weight/BMI b. Waist circumference/waist to hip ratio c. Blood pressure.	Grade A
4.3 a. Hirsutism: mFg score b. Acne: IAI score c. Alopecia: Ludwig's scale. d. During each visit, it is important to monitor clinical signs of hyperandrogenism, such as hirsutism, acne and female pattern hair loss, to assess improvement and make any necessary adjustments to the treatment plan	Grade A CPP
4.4 Acanthosis nigricans –Burks scale is preferred to grade acanthosis nigricans (refer annexure).	Grade A
4.5 Cardiovascular risk factors to be assessed in all.	Grade A
4.6 Mental health assessment in all PCOS patients Patient Health Questionnaire-9 (PHQ-9) for depression (refer annexure).	Grade A

Differential Diagnosis of PCOS and Investigations in PCOS (Table 4)[8,9,13-16]

Table 4 Differential diagnosis of PCOS and investigations in PCOS

Clinical features	*Condition*	*Tests*
Anovulation (irregular menstruation, amenorrhea)		
Amenorrhea, nausea, vomiting	Pregnancy	Pregnancy test/Serum B hCG Pelvic ultrasound
Amenorrhea, clinical h/o low body weight/BMI, excessive exercise. No androgen excess	Hypothalamic	FSH, LH, ESTRADIOL LEVELS GnRH stimulation test
Irregular menstruation/amenorrhea	Pituitary (Sheehan's syndrome, traumatic brain injury, granulomatous brain disease, brain surgery)	FSH, LH levels Imaging studies
Irregular menstruation, galactorrhea, headache, visual defects	Hyperprolactinemia	Serum prolactin levels MRI brain – pituitary adenoma
Amenorrhea + Symptoms of estrogen deficiency	Ovarian 1. Primary ovarian failure 2. Premature ovarian failure	LH, FSH, AMH, Estradiol Ultrasound – ovary size and volume
Asymptomatic/goiter/irregular menstruation	Thyroid disorders	Thyroid function tests/Thyroid scan
Features suggestive of Hyperandrogenemia		
Precocious puberty, hirsutism, baldness, menstrual irregularities, infertility	Nonclassical adrenal hyperplasia	17 OH progesterone (before 8 am)
Hirsutism, striae, myopathy, obesity, dorsocervical fat (buffalo hump), glucose intolerance	Cushing's syndrome	24-hr urinary collection for urinary free cortisol (elevated) Overnight dexamethasone suppression test
Rapid onset of virilizing symptoms (clitoromegaly, extreme hirsutism, male-pattern alopecia)	Androgen-secreting tumors—ovarian/adrenal	Serum testosterone and DHEAS levels (markedly elevated), Ultrasound imaging and MRI of ovaries and adrenals (mass/tumor)
Acanthosis nigricans, skin tags, hirsutism, polycystic ovaries, menstrual irregularities, or oligomenorrhea	Severe insulin resistance syndrome	Fasting and 2 hour OGTT (Glucose and Insulin Levels)
Hirsutism, regular menstruation	Idiopathic hirsutism Drug-induced – anabolic steroids, antiepileptics	Total testosterone level, pelvic USG

Abbreviations: AMH, anti-müllerian hormone; BMI, body mass index; DHEAS, dehydroepiandrosterone sulfate; FSH, follicle-stimulating hormone; GnRH, gonadotropin hormone-releasing hormone; hCG, human chorionic gonadotropin; LH, luteinizing hormone; MRI, magnetic resonance imaging; USG, ultrasonography

The above clinical conditions can be classified as secondary causes mimicking PCOS, and have to be sought for as they are completely curable.[13]

5. INVESTIGATIONS TO BE DONE IN PCOS (TABLE 5)

Table 5 Investigations to be done in PCOS

To confirm diagnosis and to rule out common differential diagnosis	*To assess complications of PCOS*
• Serum TSH, T3, T4 (thyroid disorders) • Serum prolactin (hyperprolactinemia) • Serum FSH, serum LH • Serum AMH (optional)	In all patients of PCOS • OGTT (75 gm glucose, single test 2-hour test, fasting) • FBS, HbA1C (if OGTT test is not feasible) • Fasting serum lipid profile

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To confirm diagnosis and to rule out common differential diagnosis	*To assess complications of PCOS*
• Total testosterone/free androgen index (if clinical hyperandrogenism signs are absent) • USG for PCOM (TVS is preferred) If clinically indicated • Androgen profile (if rapid virilization) rule out androgen secreting tumors – Testosterone – Androstenedione – Dehydroepiandrosterone sulfate (DHEAS) – Imaging studies • Dexamethasone suppression test (Cushing's syndrome)	If required based on clinical assessment • LFT • USG abdomen to assess fatty liver • Sleep study (if symptoms of OSA) • TVS to assess endometrial thickness in women with abnormal uterine bleeding

Abbreviations: AMH, anti-müllerian hormone; FSH, follicle-stimulating hormone; LFT, liver function test; LH, luteinizing hormone; OGTT, oral glucose tolerance test; OSA, obstructive sleep apnea; PCOM, polycystic ovarian morphology; PCOS, polycystic ovarian syndrome; T3, triiodothyronine; T4, thyroxine; TSH, thyroid-stimulating hormone; TVS, transvaginal ultrasound; USG, ultrasonography

Principles of Management of PCOS

A holistic approach is required for the management of PCOS and pharmacological therapy should be considered alongside education, lifestyle changes, and other options, including cosmetic therapy and counseling. It is important to provide patients with comprehensive care that addresses their physical, emotional, and psychological needs to improve their quality of life and achieve optimal health outcomes.

Desired results are:
- Menstrual regularity
- 5–10% weight loss
- Improvement in their presenting complaint
- Improvement in metabolic parameters
- Psychological well-being
- Pregnancy (in women seeking fertility).

Adolescent PCOS[8,9,17,18]

The World Health Organization (WHO) defines an adolescent as any person between 10 years and 19 years of age. The diagnosis of PCOS in this age group is challenging as the features of PCOS overlap with the transitional characteristics from puberty to adulthood. Additionally, it is important to expand on approaches to identify girls 'at risk' of PCOS who have not yet been diagnosed. Future follow-up is needed to ensure that associated future complications can be prevented. The pooled prevalence of PCOS among Indian adolescent girls is high, approximately one in five.

Evaluation for Adolescent PCOS

Adolescents with one or more of the following characteristics but do not fit into the criteria, could be at risk of developing PCOS:
- Hirsutism or inflammatory acne vulgaris, that is poorly responsive to topical therapies or oral antibiotics
- Focal hirsutism, which refers to localized areas of excessive sexual hair growth, should be taken seriously if it is accompanied by menstrual abnormalities
- Menstrual abnormalities include persistent amenorrhea (absence of menstrual periods), oligomenorrhea (infrequent menstrual periods), or excessive uterine bleeding.
- Significant weight gain

These adolescents "at risk "should be reassessed at 8 years postmenarche	(CPP)

6. LIFE-STYLE MODIFICATION[8,9,19-21]

6.1 a. Healthy lifestyle behaviors, including healthy eating and regular physical activity, should be recommended to all individuals with PCOS to achieve and/or maintain a healthy weight and optimize hormonal outcomes, general health, and quality of life throughout the lifespan.	Grade A
6.1 b. Lifestyle modification (preferably multicomponent including diet, exercise, and behavioral strategies) should be recommended in all those with PCOS and excess weight, for reductions in weight, central obesity, and insulin resistance.	Grade A
6.1 c. In overweight women, 5–10% weight loss is known to yield significant clinical improvements and should be recommended.	CPP
6.2 Behavioral modifications in individuals with PCOS can include the use of SMART (Specific, Measurable, Achievable, Realistic, and Time-bound) goal-setting, self-stimulus control, problem-solving, assertiveness training, slower eating, reinforcing changes, and relapse prevention strategies.	Grade A
6.3 Diet: General healthy eating principles, including a balanced and varied diet, should be recommended to all women with PCOS throughout their life course. There is limited evidence that any specific energy-equivalent diet type is superior to another. However, an energy deficit of 30% or 500–750 kcal/day in overweight women may be beneficial.	Grade A
6.4 Exercise:	
6.4 a. Physical activity should be encouraged in all women with PCOS and may include leisure time activities, active transportation such as walking or cycling, occupational work, household chores, games, sports or planned exercise, in the context of daily, family, and community activities. Daily accumulation of 10,000 steps is an ideal goal.	Grade A
6.4 b. Adults: A minimum of 150 min/week of moderate intensity physical activity and muscle strengthening activities on 2 non-consecutive days/week for weight maintenance; for weight loss the duration and the intensity of physical activity has to increase >150 min/week.	Grade A Grade A
6.4 c. Adolescents should engage in at least 60 minutes of moderate to vigorous intensity physical activity daily, which should include activities that strengthen muscle and bone at least three times per week.	CPP
6.4 d. Reducing sedentary behavior is recommended for individuals with PCOS, including minimizing sitting or screen time.	

7. PHARMACOTHERAPY AND BARIATRIC SURGERY[8,9,22-30]

7.1 COMBINED ORAL CONTRACEPTIVE PILLS (COCPs)	7.1 a. Principles of prescribing COCPs in PCOS: i. All preparations of COCPs are equally effective in PCOS. ii. Use the lowest effective dose such as 20–30 micrograms of ethinyloestradiol or equivalent iii. Relative and absolute contraindications to be noted. iv. Consider obesity, hypertension, and dyslipidemia which are common in PCOS.	Grade A
	7.1 b. COCPs alone in the management of irregular cycles and/or hyperandrogenemia: i. Should be recommended in all adults. ii. Should be recommended in adolescents and could be considered in adolescents at the risk of developing PCOS. iii. Between 12-16 years of age, low-dose COCs only to be used, for short period (up to 7 days). iv. After 16 years, low-dose COCs to be used.	Grade A Grade A Grade C Grade C
	7.1 c. COCPs with metformin: Should be recommended in adults and adolescents with obesity/ metabolic complications when lifestyle modification (LSM) and COCP is not effective.	Grade A
7.2 Metformin	7.2 a. In adult women with PCOS with BMI ≥ 25 kg/m^2 for management of weight and metabolic outcomes. Metformin alone should be considered along with LSM	Grade A
	7.2 b. Could be given to adolescents with BMI ≥25 kg/m^2 for the management of weight and metabolic outcomes if LSM is not effective.	Grade B
	7.2 c. Metformin offers greater benefit in high metabolic risk groups including those with diabetes risk factors, impaired glucose tolerance.	Grade B
7.3 Antiandrogens (Spironolactone, CPA, finasteride)	7.3 Antiandrogens could be considered to treat hirsutism and androgen-related alopecia when COCs are contraindicated or not tolerated or not effective after 6 months of therapy (in concurrence with Endocrinologist).	Grade B
7.4 Antiobesity pharmacological agents	7.4 a. Antiobesity medications liraglutide, semaglutide and orlistat could be considered in management of higher weight in adults with PCOS, in addition lifestyle modification (in concurrence with Endocrinologist).	Grade B
	7.4 b. Additional contraception should be advised to patients taking these medicines.	CPP
7.5 Inositols	7.5 a. Inositols could be beneficial for improving metabolic parameters, hyperandrogenemia, and menstrual irregularity in women with PCOS.	Grade B
	7.5 b. Inositols may be used, when metformin is causing severe gastric side effects.	CPP
7.6 Bariatric surgery	7.6 a. Women with PCOS may consider bariatric/metabolic surgery as an option to enhance weight loss, address metabolic complications, improve irregular menstrual cycles, and increase ovulation and pregnancy rates.	Grade B

Metformin: Principles of Therapy[27-30]

Metformin is an antidiabetic agent used in type 2 diabetes mellitus (T2DM) and prediabetes (insulin resistance). It acts as an insulin sensitizer and is effective in weight loss and improving metabolic parameters. Metformin is of greater benefit in high metabolic risk groups including those with diabetes risk factors, impaired glucose tolerance, or high-risk ethnic groups like Indians. Currently, metformin is the only ADA-recommended antidiabetic for prediabetes.

In the management of PCOS in overweight, obese women and women with impaired glucose tolerance (IGT), diabetes, metformin therapy can be started with an initial dose of 500 mg once or twice a day for immediate release oral formulation. The daily dose is often titrated weekly in the increments of 500 mg to minimize gastrointestinal (GI) adverse effects.

Metformin is generally regarded as safe and well tolerated. Gastrointestinal side effects, including diarrhea, nausea, and vomiting, are very common and typically occur in up to 30% of patients taking metformin. Less frequent side effects are chest discomfort, headache, diaphoresis, hypoglycemia, weakness, and rhinitis. Decreased vitamin B12 levels are associated with long-term metformin and should be monitored, particularly in anemic or peripheral neuropathy patients. The supplementation of vitamin B12 may be necessary.

Metformin is contraindicated in patients with severe renal dysfunction, hypersensitivity to metformin, and metabolic acidosis.

8. RECOMMENDATIONS FOR MANAGEMENT OF PCOS[8,9, 31-34]

8.1 All patients (adults and adolescents) with PCOS-	Lifestyle modification for 6 months.	Grade A
8.2 Menstrual irregularity	8.2. a. Lifestyle modification for 6 months. 8.2. b. Lifestyle modification + low-dose COCP. 8.2. c. Lifestyle modification + progesterone withdrawal. 8.2. d. Lifestyle modification + Metformin, if COCP is not tolerated.	Grade A
8.3 For PCOS with hyperandrogen features like hirsutism and acne a. Hirsutism	8.3 a. i. It is recommended to refer patients with hirsutism to a dermatologist for a comprehensive evaluation and management plan that may include direct hair removal methods such as electrolysis, laser therapy, plucking, waxing, shaving, and bleaching. The choice of treatment depends on individual patient characteristics, including skin type, hair type and color, and treatment cost and availability. 8.3 a. ii. Lifestyle modification + low-dose COCP with antiandrogen progestin (cyproterone acetate, drospirenone, or desogestrel), duration of therapy minimum of 6 months. 8.3 a. iiii. Direct hair removal methods (Laser) are recommended along with COCs as first-line therapy. 8.3 a. iv. Antiandrogens used only if COCP are not tolerated or are causing side effects and also if COCP therapy is not effective in reducing hirsutism after 6 months. Spironolactone or finasteride are the antiandrogens recommended (in concurrence with endocrinologist); while on antiandrogen therapy, pregnancy is to be avoided.	Grade A Grade A Grade A Grade B
8.3 b. Acne	8.3 b. i. It is recommended to refer women with PCOS who have moderate-to-severe acne to a dermatologist for further evaluation and management. Topical medication and pharmacological interventions can be used based on the clinical presentation of acne. 8.3 b. ii. For severe acne: In consultation with a dermatologist, COCP (cyproterone acetate, drospirenone, or desogestrel as progestin component) is the first-line therapy.	Grade A Grade A
8.3 c. Alopecia	8.3 c. i. COCP or antiandrogens (such as spironolactone) are recommended as the first-line therapy (in concurrence with an endocrinologist). 8.3 c. ii. Referral to a dermatologist is recommended for the management of alopecia in PCOS. The dermatologist can provide appropriate local therapy options such as topical minoxidil and hair transplantation in severe alopecia.	Grade B Grade A

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8.4 PCOS with obesity and/or metabolic risk	8.4 a. Refer to a physician/endocrinologist. 8.4 b. Lifestyle modification. 8.4 c. Lifestyle modification + Metformin. 8.4 d. Lifestyle modification + Antihypertensive, statins, heptoprotective medications if required are prescribed by the physician.	Grade A Grade A Grade A Grade B
8.5 PCOS women with mental health complications	8.5 a. Lifestyle Modification. 8.5 b. Refer to psychologist for counseling, behavioral therapy. 8.5 c. Refer to psychiatrist for evaluation and pharmacotherapy as required.	Grade A Grade A Grade A
8.6 PCOS women with pregnancy	8.6 a. Women with PCOS experience more complications during pregnancy. 8.6 b. Women with PCOS have increased risk of developing gestational diabetes, miscarriage, hypertension during pregnancy, small for gestational age and preterm babies and should be tested for the same 8.6 c. Life style modification is recommended in all women with PCOS who are planning for pregnancy; and OGTT and regular blood pressure monitoring should be recommended before pregnancy.	Grade A Grade A CPP

9. MANAGEMENT OF INFERTILITY[8,9,35-43]

9.1 Patient counseling	9.1 a. Women with PCOS should be counseled regarding the identification and treatment of risk factors that may have long-term effects on their fertility potential such as smoking and alcohol consumption.	Grade A
	9.1 b. Women with PCOS should be counseled regarding the importance of behavioral strategies such as goal setting, self-monitoring, assertiveness, slow eating to optimize weight, healthy lifestyle, and emotional well-being.	Grade A
	9.1 c. Pretreatment counseling on weight reduction using lifestyle modification should be recommended.	Grade A
	9.1 d. Role of the husband in the emotional well-being of subfertile women with PCOS during the course of treatment, should be emphasized.	Grade B
	9.1 e. Counseling should be done on type of treatment, time needed for the treatment, side effects, success rate and cost of the treatment.	Grade A
9.2 Lifestyle modifications	9.2 a. Physical activity of 60 min/day up to 3 months along with the restriction of other risk factors (excessive caffeine intake, alcohol consumption, and smoking) should be recommended in all women trying for pregnancy.	Grade A
	9.2 b. The age-related decline in fertility should be given appropriate consideration when prescribing the duration of lifestyle management interventions.	Grade B
	9.2 c. In PCOS patients who are morbidly obese, weight reduction should be done before starting pharmacological methods for ovulation induction.	Grade A
	9.2 d. Yoga could be recommended as an aid for the treatment of subfertile PCOS.	Grade B
	9.2 e. In an event of unsuccessful weight reduction with diet and exercise alone for 2–3 months in morbidly obese patients, treatment with orlistat recommended in concurrence with endocrinologist.	Grade B
9.3 Pharmacological intervention	9.3 a. Pretreatment with COCs: Women with PCOS (with or without lifestyle modification), having the high levels of LH (three times the basal levels) need to be pretreated with low-dose COCPs for at least 2 months to normalize the LH levels.	Grade B
	9.3 b. Aromatase Inhibitors: i. Letrozole is recommended to be the first-line pharmacological agent for ovulation induction in women with PCOS who have anovulatory infertility and with no other fertility factors to improve ovulation. Letrozole should not be used for more than six cycles. ii. If letrozole is not available, health professionals should use other ovulation induction agents.	 Grade A CPP
	9.3 c. Clomiphene Citrate: i. CC is recommended as second line pharmacological agent for a maximum of six cycles. ii. Ultrasound monitoring should be offered to infertile PCOS women who are on CC for the monitoring of ovulatory response and to minimize the risk of multiple pregnancy. In an event of unavailability of ultrasound, monitoring of LH levels can be another alternative.	 Grade A CPP

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	9.3 d. Insulin-sensitizing agent: Metformin is recommended along with fertility treatment in:	
	i. PCOS women with impaired glucose intolerance (disturbed oral glucose tolerance test).	Grade A
	ii. Obese PCOS women along with clomiphene citrate.	Grade A
	iii. Clomiphene citrate-resistant women.	Grade A
	iv. PCOS women who are at a high risk of hyperstimulation.	Grade A
	9.3 e. Gonadotropins and GnRH analogues:	
	i. In women with letrozole failure/clomiphene citrate failure or resistance and with anovulatory infertility with no other fertility factors. Gonadotropins are recommended as the second-line treatment.	Grade A
	ii. Patients should be counseled regarding the need for strict monitoring of cycle, the risk of ovarian hyperstimulation syndrome (OHSS) and multiple pregnancy, the cost of treatment, and cycle cancellation criteria before treatment initiation.	CPP
9.4 Surgical interventions	9.4 a. LAPAROSCOPIC SURGERY:	
	i. Laparoscopic ovarian surgery is recommended as the second-line therapy over gonadotropin therapy in anovulatory PCOS women who have failed the first-line oral ovulation induction therapy or who are clomiphene citrate resistance and have hypersecretion of LH levels with no other fertility factors.	Grade A
	ii. It is suggested that laparoscopic ovarian drilling (LOD) be used in anovulatory PCOS women with clomiphene citrate resistance and no other fertility factors, who cannot access hospital facilities for intensive monitoring required with gonadotropin therapy and in women requiring the laparoscopic assessment of the pelvis.	Grade C
	iii. The number of punctures should depend on the size of ovary, but it should be limited to a maximum of 4.	Grade B
	9.4 b. BARIATRIC SURGERY:	
	i. Bariatric surgery is recommended as a second-line treatment in morbidly obese (BMI >27.5 kg/m^2) subfertile PCOS patients who are unsuccessful in achieving weight reduction by lifestyle management and metformin and antiobesity drugs.	Grade B
	ii. First-line therapy for weight reduction in PCOS patients with BMI 50 kg/m^2.	Grade B
	iii. Avoid conception for at least 12 months after bariatric surgery in subfertile PCOS women because the effects of these interventions on the evolution of early pregnancy are not yet known.	Grade B
9.5 Assisted reproductive technology	9.5 a. Intrauterine insemination is recommended in:	
	i. Anovulatory subfertile PCOS women with male factor subfertility.	CPP
	ii. In anovulatory subfertile PCOS women with unsuccessful conception despite ovulation induction.	CPP
	9.5 b. IN VITRO FERTILIZATION:	
	i. IVF is recommended as the third-line treatment option in women with PCOS who have not responded to the first-line and second line ovulation induction, in the absence of absolute indication for IVF/intracytoplasmic sperm injection (ICSI).	Grade C
	ii. The GnRH antagonist protocol is preferred over the GnRH agonist long protocol due to a lower incidence of severe OHSS while maintaining similar clinical pregnancy rates.	Grade A
	iii. In women with PCOS undergoing IVF with an antagonist protocol, a GnRH analogue trigger can be used with the option of a "freeze-all" policy to reduce the incidence of OHSS. Additionally, split-cycle IVF involves endometrial preparation followed by the transfer of human frozen-thawed embryos.	CPP
	iv. IN VITRO MATURATION (IVM):	CPP
	a. IVM is a term used to describe the maturation of immature oocytes in vitro, collected from the antral follicles. It could be done in both stimulated or unstimulated cycles without human chorionic gonadotropin trigger.	CPP
	b. In units with sufficient expertise and experience in IVM, it could be offered to achieve pregnancy and live birth rates approaching those with standard IVF treatment without the risk of OHSS in women with PCOS, where embryos are developed through IVM, frozen, and then thawed and transferred in the subsequent cycle.	Grade A
	v. Luteal Phase Support: In subfertile women with PCOS undergoing OI or assisted reproduction, the administration of luteal phase progesterone is recommended.	

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9.6 HCG	9.6 a. In women with PCOS undergoing IVF with an antagonist protocol, a GnRH analogue trigger can be used with the option of a "freeze-all" policy to reduce the incidence of OHSS.	Grade A
	9.6 b. HCG trigger should be avoided to trigger in women with PCOS as it is associated with an increased risk of OHSS.	Grade A
	9.6 c. The frozen embryos are thawed and transferred in the subsequent cycle after preparing the endometrium. This is called segmented IVF.	Grade A

10. METABOLIC COMPLICATIONS OF PCOS[8,9,44-54]

Physicians should be aware of the metabolic complications associated with PCOS. Prompt screening and referral to specialist care can prevent and manage these serious complications **(Table 6)**.

Table 6 Metabolic complications of PCOS

Condition	*Prevalence in Indian women*	*Prevalence in Indian women with PCOS*	*Prevalence in PCOS international*	*Clinical features*	*Diagnosis*	*Complications*
Insulin resistance	15–46%	50–75%	50–75%	Acanthosis, central obesity, skin tags	FBS, fasting insulin PPBS, postprandial insulin	IGT, diabetes, NAFLD, GDM, miscarriage
Impaired glucose tolerance	18%	19.1%	35%		FBS/OGTT	Diabetes
Diabetes	14.4%	5–10-fold increase	4-fold increase	Polyuria, polydypsia, weight loss	FBS/PPBS	Multiorgan disease
Dyslipidemia	14–30%		70%		Fasting lipid profile	CVD, stroke
Metabolic syndrome	35%	46%	43%		AC >32 inches, BP >130/85 FBS >110, HDL<50, TG >150	CVD, stroke, cancer mortality, depression
NAFLD	9–32%	31–67%	27–60%	Nonspecific	LFT- AST/ALT USG/CT	Cirrhosis, hepatocellular carcinoma
Depression/ Anxiety	10–25%	54%	28–60%	Low mood/ depression/loss of interest	PHQ-9	Suicide, CVD
OSA	2.5–7.4%	32%	35%	Disturbed sleep, snoring, apneic spells, daytime sleeping	Nocturnal polysomnography, sleep study	Hypertension, metabolic syndrome, CVD
Endometrial cancers	4.3/1 lakh women	2–6 fold increase	2–6 fold increase	Abnormal bleeding/ discharge	TVS for ET, biopsy	Morbidity, metastasis, mortality

Abbreviations: AC, abdominal circumference; ALT, alanine transaminase; AST, aspartate transaminase; BP, blood pressure; CT, computed tomography; CVD, cardiovascular disease; FBS, fasting blood sugar; GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; IGT, impaired glucose tolerance; LFT, liver function test; NAFLD, nonalcoholic fatty liver disease; OGTT, oral glucose tolerance test; OSA, obstructive sleep apnea; PHQ, patient health questionnaire; PPBS, postprandial blood sugar; TG, triglycerides; USG, ultrasonography

- Insulin Resistance: It is the main association observed in PCOS and plays a significant role in pathophysiology and in the development of complications of PCOS. Insulin resistance is observed 50–75% in PCOS; 70–80% in obese PCOS; 20–25% in lean PCOS. Glucose intolerance in Indian women with PCOS was reported as **16.3%** (adults 19.1% adolescents 9.7%). Regardless of age, the prevalence of gestational diabetes, impaired glucose tolerance, and type 2 diabetes mellitus (T2DM) (5-fold in Asia, 4-fold in the America, and 3-fold in Europe) are significantly increased in PCOS.

- Cardiovascular Disease: Metabolic syndrome and cardiovascular disease (CVD) risk factors are significantly increased in PCOS, highlighting the need to consider overall cardiovascular health. As CVD remains a leading cause of death in women, any condition that further increases CVD risk will have a significant public health impact. ALL WOMEN WITH PCOS SHOULD BE ASSESSED FOR CVD RISK FACTORS.
  The prevalence of hypertension is 10–40% in women with PCOS. Pregnant women with PCOS have a greater risk of pregnancy-induced hypertension and pre-eclampsia. BP measurement in all PCOS patients at every visit. Antihypertensives are indicated when BP is of at least 140 mmHg systolic or 90 mmHg diastolic.
  METABOLIC SYNDROME (MS): It is defined as elevated blood pressure (BP) (>130/85 mmHg), increased waist circumference (>88 cms non-Asian; >80 cms in East/South Asian women), elevated fasting glucose (>100 mg/dL), reduced HDL-C (<50 mg/dL in women), and elevated triglyceride (>150 mg/dL) levels.
- Obstructive sleep apnea (OSA): It is characterized by the recurrent episodes of partial (hypopnea) or complete (apnea) upper airway obstructions that lead to repetitive, futile ventilatory efforts, oxygen desaturations, sleep arousal, and fragmented sleep, causing daytime sleepiness. These episodes are associated with recurrent oxygen desaturations and cyclical changes in heart rate, blood pressure, intrathoracic pressure, and sympathetic activity.
- Women with PCOS have a 2–6 times higher risk of endometrial cancer, with most adenocarcinomas (>95%) including Type I and Type II cancers. Type I cancer is more common in women with PCOS. The increased prevalence of endometrial cancer in PCOS is related to prolonged endometrial exposure to unopposed estrogen in anovulation. Additionally, the endometrium in PCOS may exhibit progesterone resistance. The associations between PCOS and endometrial cancer are complex and comorbid conditions such as obesity, infertility, T2DM, and metabolic syndrome are relevant. PCOS treatment options may also influence cancer risk.
- Nonalcoholic fatty liver disease (NAFLD): It is a chronic disorder characterized by fat accumulation in the liver, which is histologically identical to alcoholic liver disease, in patients with little or no alcohol consumption. Women with PCOS have a reported prevalence of NAFLD ranging from 15% to 60%. A hospital-based study of women with PCOS from India reported a 67% prevalence of nonalcoholicsteatohepatitis (NASH), as well as a 31% prevalence of NAFLD and a 35% prevalence of metabolic syndrome.
  PCOS patients with established NAFLD may progress more rapidly to advanced NAFLD stages such as NASH and cirrhosis. They may also have a higher risk of mortality and poor hepatic and nonhepatic outcomes, even at ages where it is not typically observed. Additionally, NASH is histologically more severe in females with NAFLD when compared to males.

GCPR ON METABOLIC COMPLICATIONS OF PCOS

10.1 Assessment of CVD risk factors	11.1 a. First visit and at every visit (if parameters are normal, follow-up after 1 year. If abnormal profiles, then every 6 months).	Grade A
	11.1 b. All women with PCOS should be assessed for cardiovascular risk factors and global CVD risk.	Grade A
	11.1 c. Overweight and obese women with PCOS, regardless of age, should have a fasting lipid profile	Grade B
	11.1 d. Obtain history of recent smoking habits, if any, or cessation.	Grade A
	11.1 e. Check weight every visit.	Grade A
	11.1 f. Check blood pressure every visit.	Grade A
	11.1 g. Oral glucose tolerance test (75 g) (Empty stomach, 75 mg glucose, sugar tested after 2 hours) - every 2 years.	Grade A
	11.1 h. Specialist cardiovascular (CV) monitoring and care is recommended in all patients showing CV risk factors, irrespective of the severity of their symptoms.	Grade A
10.2 Glucose intolerance and diabetes mellitus	11.2 a. Health professionals and women with PCOS should be aware that, regardless of age, the prevalence of gestational diabetes, impaired glucose tolerance, and T2DM is higher in women with PCOS compared to the general population.	Grade A
	11.2 b. Assessment of glycemic status, including fasting glucose and glucose tolerance tests, should be conducted at baseline in all women with PCOS.	Grade A
	11.2 c. 75 gm OGTT on diagnosis and every 1 year should be done to all adolescent and adult women with PCOS.	Grade A
	11.2 d. HbA1c/FBS should be done, if OGTT is not feasible.	Grade A
	11.2 e. In women with PCOS who have impaired glucose tolerance or T2DM, Metformin is recommended as a first-line treatment either alone or in combination with oral contraceptives.	Grade A

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	11.2 f. Early referral to specialist diabetological care is recommended for women with PCOS who have impaired glucose tolerance or T2DM for management.	Grade A
	11.2 g. When planning pregnancy or seeking fertility treatment, women with PCOS and without diabetes, should be offered 75 gm OGTT.	Grade A
	11.2 h. During pregnancy, OGTT has to be done at first visit, <20 weeks, and repeated at 24–28 weeks.	Grade A
10.3 OSA	11.3 a. All patients with PCOS should undergo assessment for symptoms and signs of obstructive sleep apnea (OSA), including snoring, waking unrefreshed from sleep, and experiencing daytime sleepiness. If these symptoms are present, further evaluation with polysomnography should be considered to confirm the diagnosis of OSA.	Grade A
	11.3 b. Routine screening is not recommended.	Grade B
10.4 NAFLD	11.4 a. Routine screening for NAFLD is not recommended in all PCOS patients.	Grade A
	11.4 b. In women with PCOS who have been diagnosed with insulin resistance and metabolic syndrome, screening for NAFLD is recommended. This can be done by assessing liver function tests (LFTs) for elevated serum aminotransferase levels, as well as using imaging modalities, such as ultrasonography, to look for fatty liver disease.	Grade B
	11.4 c. Patients with NAFLD should be managed by a multidisciplinary team, which may include a hepatologist, endocrinologist, diabetologist, nutritionist, and physical therapist.	Grade B
	11.4 d. The recommended treatment for NASH in PCOS includes lifestyle modifications, such as weight loss, exercise, and a healthy diet.	Grade B
10.5 Endometrial cancer	11.5 a. Gynecologists should understand the increase in risk of endometrial hyperplasia and endometrial carcinoma in premenopausal women with PCOS.	Grade A
	11.5 b. Routine screening for endometrial cancer - Not recommended.	Grade B
	11.5 c. In women with PCOS with unexpected bleeding and spotting, endometrial thickness must be assessed using TVS.	Grade B
	11.5 d. Persistent thickened endometrium and/or risk factors including prolonged amenorrhea, abnormal vaginal bleeding, or excess weight – Endometrial biopsy should be done.	Grade B
	11.5 e. Prevention of endometrial hyperplasia - COCP or progestin therapy medroxy progesterone acetate for 10 days to induce withdrawal bleeding every 2 months.	Grade B

11. MENTAL HEALTH IN PCOS[8,9,55-57]

PCOS has been associated with a reduced health-related quality of life (HRQoL) due to the psychological implications it can have on individuals. These implications include challenges with depression, anxiety, physical appearance and feminine identity, eating habits, and psychosexual dysfunction, which can all have a significant impact on QoL **(Table 7)**.

Depressive symptoms and depression are more common in PCOS, with daily fatigue, sleep disturbances and diminished interest. There is evidence to suggest that hormonal imbalances, insulin resistance, and inflammation associated with PCOS may also contribute to the development of depression and anxiety symptoms.

Women with PCOS judge their appearance and body hair to negatively impact on their sexuality and their ability to engage in relationships.

Body image is defined here as the way a woman may feel, think about, and view their body including their appearance. Relevant physical (excess weight and hirsutism), psychological (self-esteem), and sociocultural factors influence body image.

Diagnosable eating disorders include anorexia nervosa, bulimia nervosa, binge-eating disorder, other specified feeding or eating disorders, and unspecified feeding or eating disorders that do not meet the full criteria for any of the eating disorder diagnoses. Disordered eating refers to a range of eating and weight-related symptoms that do not meet the criteria for a specific eating disorder diagnosis, but can include behavioral patterns (such as bingeing or excessive restriction), cognitive patterns (such as excessive dietary restraint or negative body image), and emotional factors.

Sleep disturbances including difficulty in falling asleep, early morning awakenings, and/or altered sleep duration are increased in PCOS and have profound negative unintended consequences on the cardiovascular system with an increased prevalence of hypertension, coronary heart disease, and stroke.

Table 7 Mental health in PCOS[7]

Mental health condition	*Prevalence in general population*	*Prevalence in PCOS*
HRQoL - Health-related quality of life is reduced in PCOS.		Reduced in PCOS
Depression	2–6%	44%
Anxiety	2.5–7 %	42%
Body image issues	37% adolescents/34% adults	35–46%
Psychosexual problems	14.3%	13–62%
Eating disorders-/bulemia -12%	0.1–1%	21%
Sleep disorders	10–30% of adults	16%/6.2-fold increase

12. GCPR ON MENTAL HEALTH ASSESSMENT IN PCOS

12.1 Quality of life	Health professionals and women should be aware of the adverse impact of PCOS on the quality of life and should enquire into the same.	Grade A
12.2 Anxiety depression	Anxiety and depressive symptoms should be routinely screened in all adolescents and women with PCOS at diagnosis using PHQ-9 questionnaire. Patients with depression should be referred to specialist for psychological counseling and further pharmacogical treatment.	Grade A
12.3 a. Psychosexual function b. Body image c. Eating disorders d. Sleep disorders	Healthcare professionals should be aware of negative impact of PCOS on psychosexual function, body image. Healthcare professionals should be aware of increased eating disorders in women with PCOS. In those suspected with any psychosocial dysfunction, appropriate referral to specialist for further evaluation and management is suggested.	Grade B

ABBREVIATIONS

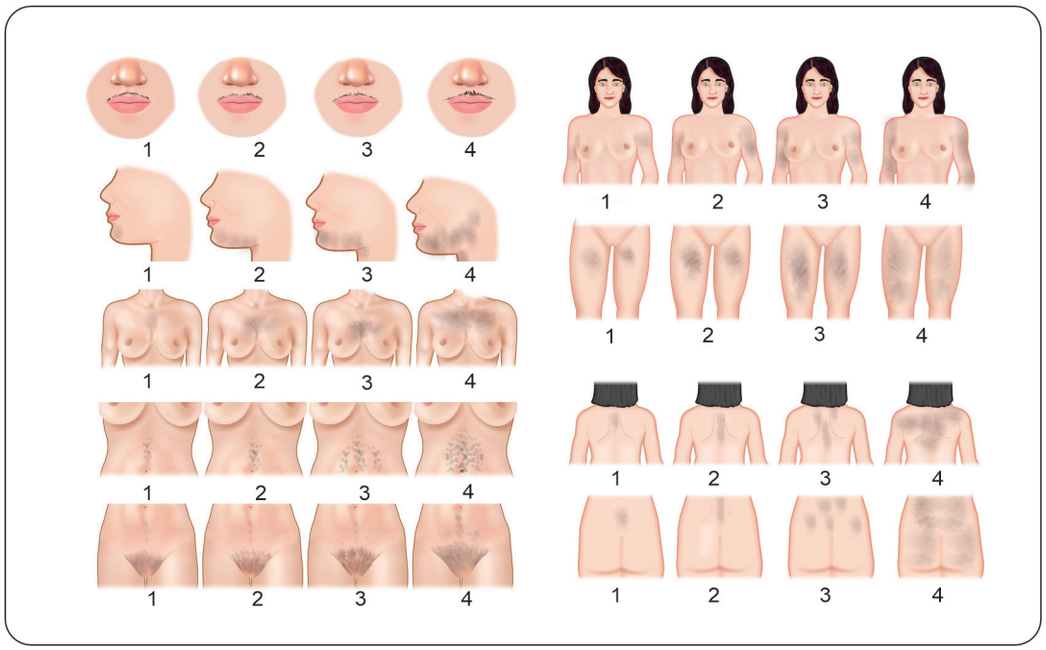
PCOS	Polycystic ovarian syndrome	COCP	Combined oral contraceptive pill
BMI	Body mass index	LSM	Lifestyle modification
HA	Hyperandrogenism	CPA	Cyperoterone acetate
OD	Ovulatory dysfunction	GnRH	Gonadotropin-releasing hormone
PCOM	Polycystic ovarian morphology	LOD	Laparoscopic ovarian drilling
AACE	American Association of Clinical Endocrinologists	IVF	In vitro fertilization
RCT	Randomized controlled trial	ICSI	Intracytoplasmic sperm injection
CPP	Clinical practice point	OHSS	Ovarian Hyperstimulation syndrome
LDL	Low-density lipoprotein	HCG	Human chorionic gonadotropin
mFG	Modified Ferriman-Galleway score	NAFLD	Non-alcoholic fatty liver disease
IAA	Indian Acne Association	GDM	Gestational diabetes mellitus
PHQ -9	Patient Health Questionnaire	PPBS	Postprandial blood sugar
TVS	Transvaginal scan	AC	Abdominal circumference
TSH	Thyroid stimulating hormone	BP	Blood pressure
OGTT	Oral glucose tolerance test	FBS	Fasting blood sugar
OSA	Obstructive sleep apnea	HDL	High density lipoprotein
FSH	Follicle-stimulating hormone	TG	Triglycerides
LH	Luteinizing hormone	CVD	Cardiovascular disease
WHO	World Health Organization	NASH	Nonalcoholic steatohepatitis
SMART	Specific, Measurable, Achievable, Realistic, Time-bound	HRQoL	Health-related quality of life

REFERENCES

1. March WA, Moore VM, Willson KJ, et al. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. Hum Reprod. 2010;25(2):544-55.
2. Nasr A. Effect of N-acetyl-cysteine after ovarian drilling in clomiphene citrate-resistant PCOS women: a pilot study. Reproductive Biomed Online. 2010;20(3):403-9.
3. Gill H, Tiwari P, Dabadghao P. Prevalence of polycystic ovary syndrome in young women from North India: A Community-based study. Indian J Endocrinol Metab. 2012;16(Suppl 2):S389-92.
4. Nidhi R, Padmalatha V, Nagarathna R, et al. Prevalence of polycystic ovarian syndrome in Indian adolescents. J Pediatr Adolesc Gynecol. 2011; 24(4):223-7.
5. Bharali MD, Rajendran R, Goswami J, et al. Prevalence of polycystic ovarian syndrome in India: A systematic review and meta analysis. Cureus. 2022;14(12):e32351.
6. Mehta J, Kamdar V, Dumesic D. Phenotypic expression of polycystic ovary syndrome in South Asian women. Obstet Gynecol Surv. 2013;68(3):228-34.
7. Lizneva D, Suturina L, Walker W, et al. Criteria, prevalence, and phenotypes of polycystic ovary syndrome. Fertil Steril. 2016;106(1):6-15.
8. International evidence-based guideline for the assessment and management of polycystic ovary syndrome. 2018. Available from: https://www.monash.edu/__data/assets/pdf_file/0004/1412644/PCOS_Evidence-Based-Guidelines_20181009.pdf.
9. Malik S, Jain K, Talwar P, et al. Management of polycystic ovary syndrome in India. Fertil Sci Res. 2014;1(1):23-43.
10. Al-Jefout M, Alnawaiseh C, Saleh M, et al. Anti-Müllerian Hormone (AMH) new cutoff as a possible tool for the Diagnosis of Polycystic Ovary Syndrome (PCOS). J Biomed Sci Res. 2021. Available from: https://www.pubtexto.com/journals/journal-of-biomedical-science-and-research/abstracts/antimllerian-hormone-amh-new-cutoff-as-a-possible-tool-for-the-diagnosis-of-polycystic-ovary-syndrome-pcos.
11. Yue CY, Lu LK, Li M, et al. Threshold value of anti-Mullerian hormone for the diagnosis of polycystic ovary syndrome in Chinese women. PLoS One. 2018;13(8):e0203129.
12. Ran Y, Yi Q, Li C. The relationship of Anti-Mullerian hormone in polycystic ovary syndrome patients with different subgroups. Diabetes Metab Syndr Obes. 2021;14:1419-24.
13. Mani H, Davies MJ, Bodicoat DH, et al. Clinical characteristics of polycystic ovary syndrome: investigating differences in White and South Asian women. Clin Endocrinol (Oxf). 2015;83(4):542-9.
14. Jamil AS, Alalaf SK, Al-Tawil NG, et al. Comparison of clinical and hormonal characteristics among four phenotypes of polycystic ovary syndrome based on the Rotterdam criteria. Arch Gynecol Obstet. 2016;293(2):447-56.
15. Panidis D, Tziomalos K, Papadakis E, et al. Associations of menstrual cycle irregularities with age, obesity and phenotype in patients with polycystic ovary syndrome. Hormones (Athens). 2015;14(3):431-7.
16. Khadilkar SS. Can Polycystic Ovarian Syndrome be cured? Unfolding the Concept of Secondary Polycystic Ovarian Syndrome! J Obstet Gynae India. 2019;69(4):297-302.
17. Sharma M, Khapre M, Saxena V, et al. Polycystic ovary syndrome among Indian adolescent girls - A systematic review and metanalysis. Nepal J Epidemiol. 2021;11(3):1063-75.
18. Rosenfield RL, Ehrmann DA, Littlejohn EE. Adolescent polycystic ovary syndrome due to functional ovarian hyperandrogenism persists into adulthood. J Clin Endocrinol Metab 2015;100(4):1537-43.
19. Moreira S, Soares E, Tomaz G, et al. Polycystic ovary syndrome: a psychosocial approach. Acta Med Port. 2010;23(2):237-42.
20. Misra A, Chowbey P, Makkar BM, et al. Consensus statement for diagnosis of obesity, abdominal obesity and the metabolic syndrome for Asian Indians and recommendations for physical activity, medical and surgical management. J Assoc Physicians India. 2009;57:163-70.
21. Hoeger KM. Obesity and lifestyle management in polycystic ovary syndrome. Clin Obstet Gynecol. 2007;50(1):277-94.
22. Bhattacharya SM, Jha A. Comparative study of the therapeutic effects of oral contraceptive pills containing desogestrel, cyproterone acetate, and drospirenone in patients with polycystic ovary syndrome. Fertil Steril. 2012;98(4):1053-9.
23. Badawy A, Elnashar A. Treatment options for polycystic ovary syndrome. Int J Womens Health. 2011;25-35.
24. Al-Nozha O, Habib F, Mojaddidi M, et al. Body weight reduction and metformin: roles in polycystic ovary syndrome. Pathophysiology. 2013;20(2):131-7.
25. Greff Dorina G, Juhasz Anna AE, Váncsa, et al. Inositol is an effective and safe treatment in polycystic ovary syndrome: a systematic review and meta-analysis of randomized controlled trials. Reprod Biol Endocrinol. 2023;21(1):10.
26. Pizzo A, Laganà AS, Barbaro L. Comparison between effects of myo-inositol and D-chiro-inositol on ovarian function and metabolic factors in women with PCOS. Gynecol Endocrinol. 2014;30(3):205-8.
27. Ravn P, Gram F, Andersen MS, et al. Myoinositol vs. metformin in women with polycystic OVARY Syndrome: A randomized controlled clinical trial. Metabolites. 2022;12(12):1183.
28. Costello M, Shrestha B, Eden J, et al. Insulin-sensitising drugs versus the combined oral contraceptive pill for hirsutism, acne and risk of diabetes, cardiovascular disease, and endometrial cancer in polycystic ovary syndrome. Cochrane Database Syst Rev. 2007;(1):CD005552..

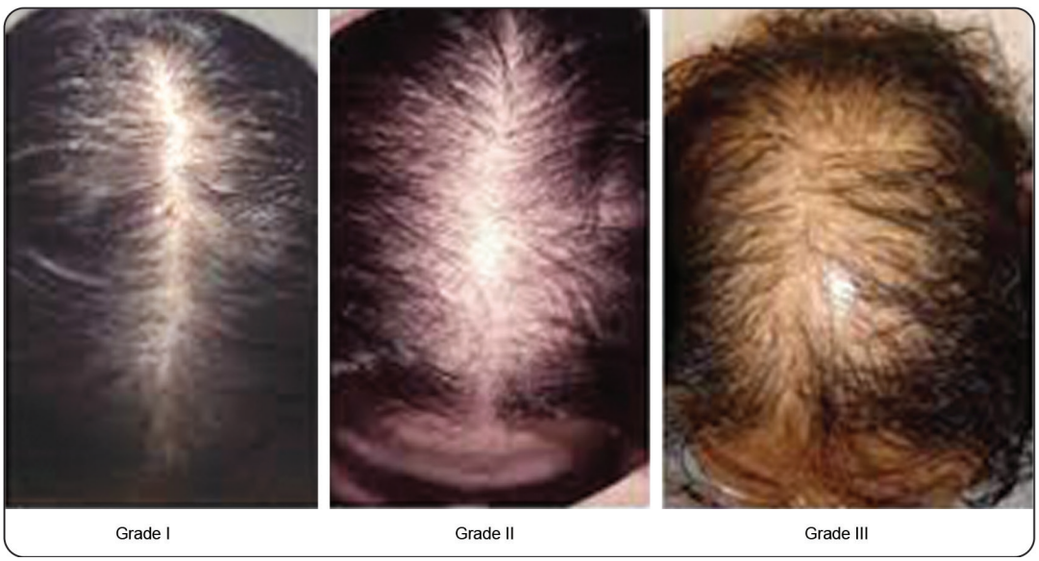
29. Foretz M, Guigas B, Bertrand L, et al. Metformin: from mechanisms of action to therapies. Cell Metab. 2014;20(6):953-66.
30. Corcoran C, Jacobs TF. Metformin. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2023. Available from: https://www.ncbi.nlm.nih.gov/books/NBK518983.
31. Rathi SK. Acne vulgaris treatment: the current scenario. Indian J Dermatol. 2011;56(1):7-13
32. Agrawal NK. Management of hirsutism. Indian J Endocr Metab. 2013;17(Suppl 1):S77-82.
33. Macut D, Pfeifer M, Yildiz BO, et al (Eds). Polycystic Ovary Syndrome. Novel Insights into Causes and Therapy. Basel; Karger Publisher; 2013.
34. Hart R, Doherty DA. The potential implications of a PCOS diagnosis on a woman's long-term health using data linkage. J Clin Endocrinol Metab. 2015;100(3):911-9.
35. Malik S, Verma S, Jain K, et al. Good clinical practice recommendations on management of infertility in patients from India with polycystic ovary syndrome. 2015;2(2):107-32.
36. Kamath MS, Aleyamma TK, Chandy A, et al. Aromatase inhibitors in women with clomiphene citrate resistance: A randomized, double-blind, placebo-controlled trial. Fertil Steril. 2010;94:2857-9.
37. Ray PB, Ray A, Chakraborti PS. Comparison of efficacy of letrozole and clomiphene citrate in ovulation induction in Indian women with polycystic ovarian syndrome. Arch Gynecol Obstet. 2012;285(3):873-7.
38. Abu Hashim H, Shokeir T, Badawy A. Retracted: Letrozole versus combined metformin and clomiphene citrate for ovulation induction in clomiphene-resistant women with polycystic ovary syndrome: a randomized controlled trial. Fertil Steril. 2010;94(4):1405-9.
39. Homburg R, Hendriks ML, König TE, et al. Clomifene citrate or low-dose FSH for the first-line treatment of infertile women with anovulation associated with polycystic ovary syndrome: A prospective randomized multinational study. Hum Reprod. 2012;27(2):468-73.
40. Mukharjee S, Sharma S, Chakravarty BN. Comparative evaluation of pregnancy outcome in gonadotrophin-clomiphene combination vs clomiphene alone in polycystic ovarian syndrome and unexplained infertility – A prospective clinical trial. J Hum Reprod Sci. 2010;3(2):80-4.
41. Tehraninejad ES, Nasiri R, Rashidi B, et al. Comparison of GnRh antagonist with long GnRh agonist protocol after OCP pretreatment in pcos patients. Arch Gynecol Obstet. 2010;282(3):319-25.
42. Haydardedeoglu B, Kilicdag EB, Parlakgumus AH, et al. IVF/ICSI outcomes of the OCP plus GnRH agonist protocol versus the OCP plus GnRH antagonist fixed protocol in women with PCOS: A randomized trial. Arch Gynecol Obstet. 2012;286(3):763-9.
43. Walls ML, Hunter T, Ryan JP, et al. In vitro maturation as an alternative to standard in vitro fertilization for patients diagnosed with polycystic ovaries: A comparative analysis of fresh, frozen and cumulative cycle outcomes. Human Reproduction. 2014;30(1):88-96.
44. Kahal H, Kyrou I, Uthman OA, et al. The prevalence of obstructive sleep apnoea in women with polycystic ovary syndrome: a systematic review and meta-analysis. Sleep Breath. 2020;24(1):339-50.
45. Wild RA, Carmina E, Diamanti-Kandarakis E, et al. Assessment of cardiovascular risk and prevention of cardiovascular disease in women with the polycystic ovary syndrome: a consensus statement by the Androgen Excess and Polycystic Ovary Syndrome (AE-PCOS) Society. J Clin Endocrinol Metab. 2010;95(5):2038-49.
46. Bentley-Lewis R, Koruda K, Seely EW. The metabolic syndrome in women. Nat Clin Pract Endocrinol Metab. 2007;3(10):696-704.
47. Toulis KA, Goulis DG, Kolibianakis EM, et al. Risk of gestational diabetes mellitus in women with polycystic ovary syndrome: a systematic review and a meta-analysis. Fertil Steril. 2009;92(2):667-77.
48. Deswal R, Narwal V, Dang A, et al. The prevalence of polycystic ovary syndrome: a brief systematic review. J Hum Reprod Sci. 2020;13(4):261-71.
49. Kumar K, Misra S. Sex differences in prevalence and risk factors of hypertension in India: Evidence from the National Family Health Survey-4. PLoS One. 2021;16(4):e0247956.
50. Gupta A, Gupta R, Sharma KK, et al. Prevalence of diabetes and cardiovascular risk factors in middle-class urban participants in India. BMJ Open Diabetes Res Care. 2014;2(1):e000048.
51. Pattanaik S, Rajagopal R, Mohanty N, et al. Prevalence of obstructive sleep apnea in an Indian population: using STOPBANG questionnaire. Asian J Pharm Clin Res. 2018;11(11):100-3.
52. Mitra S, De A, Chowdhury A. Epidemiology of non-alcoholic and alcoholic fatty liver diseases. Transl Gastroenterol Hepatol. 2020;5:16.
53. Krishnamoorthy Y, Rajaa S, Murali S, et al. Prevalence of metabolic syndrome among adult population in India: a systematic review and meta-analysis. PLoS One. 2020;15(10):e0240971.
54. Bhattacharya SM. Metabolic syndrome in females with polycystic ovary syndrome and International Diabetes Federation criteria. J Obstet Gynaecol Res. 2008;34(1):62-6.
55. Dattani S, Rodés-Guirao L, Ritchie H, et al. Mental Health. 2023. Available from: https://ourworldindata.org/mental-health#introduction
56. Bhaskar S, Hemavathy D, Prasad S. Prevalence of chronic insomnia in adult patients and its correlation with medical comorbidities. J Family Med Prim Care. 2016;5(4):780-4.
57. Zhang J, Ye J, Tao X, et al. Sleep disturbances, sleep quality, and cardiovascular risk factors in women with polycystic ovary syndrome: systematic review and meta-analysis. Front Endocrinol (Lausanne). 2022;13:971604.

ANNEXURES



Nine body areas (upper lip, chin, chest, arm, upper abdomen, lower abdomen, upper back, lower back, and thighs) are scored from 1 (minimal terminal hairs present) to 4 (equivalent to a hairy man). If no terminal hairs are observed in the body area being examined, the score is zero (left blank). Clinically terminal hairs can be distinguished from vellus hairs primarily by their length (i.e. greater than 0.5 cm) and the fact that they are usually pigmented (reprinted with permission of R. Azziz, copyright 1997).

Fig. 1: Modified Ferriman-Gallway scoring for hirsutism



a. Grade I: Perceptible thinning of the hair on the crown, limited in the front by a line situated 1-3 cm behind the frontal hairline
b. Grade II: Pronounced rarefaction of the hair on the crown within the area seen in Grade I.
c. Grade III: Full baldness (total denudation) within the area seen in Grades I and II

Fig. 2: Ludwig's visual scoring for alopecia

Table 8 Grading of acne Indian Acne Association

Mild acne (Grade I)	Comedones <30
Predominance of comedones	Papules <10
	No scarring
Moderate acne (Grade II)	Comedones any number
Predominance of papules	Papules >10
	Nodules <3
	Scarring ±
Severe acne (Grade III)	Comedones any number
Many nodules	Papules any number
	Nodules/cysts > 3
	Scarring +

Grading of acne is a complex issues. Many grading systems have been devised and deployed over the years to meet different clinical and research requirements. The above grading system is proposed, to pair with algorithms developed by the IAA, to facilitate uniformity and consistency in application of the latter

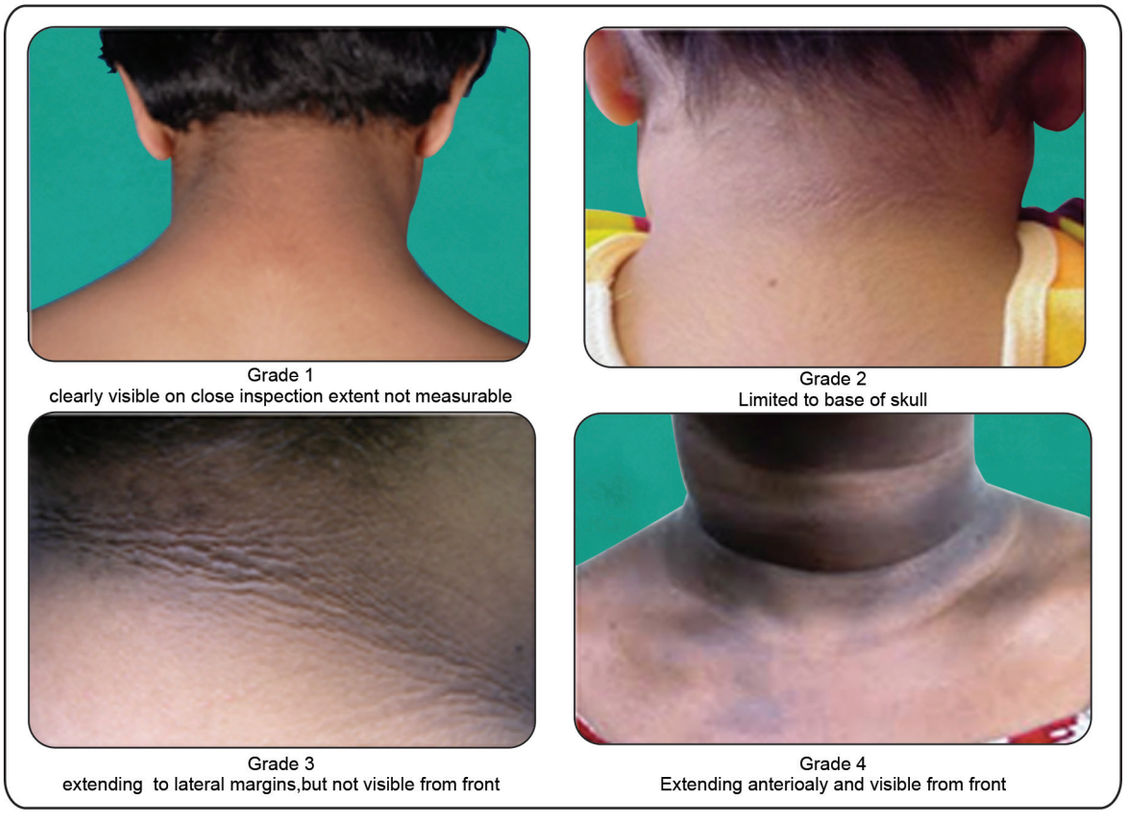


Fig. 3: Burke's grading of acanthosis nigricans

Table 9 PHQ-9 questionnaire for screening depression

Name: _____ ***Date:*** _____

Over the last 2 weeks, how often have you been bothered by any of the following problems? (use "✓" to indicate your answer)

	Not at all	***Several days***	***More than half the days***	***Nearly every day***
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3
	Add colums:	+		+
	Total:			
10. If you checked off *any* problems, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?	Not difficult at all _____ Somewhat difficult _____ Very difficult _____ Extremely difficult _____			

PHQ-9 scores and proposed treatment actions*

PHQ-9 score	***Depression severity***	***Proposed treatment actions***
0–4	None-mimimal	None
5–9	Mild	Watchful waiting: repeat PHQ-9 at follow-up
10–14	Moderate	Treatment plan, considering counseling, follow-up and/or pharmacotherapy
15–19	Moderately severe	Active treatment with pharmacotherapy and/or psychotherapy
20–27	Severe	Immediate initiation of pharmacotherapy and, if severe impairment or poor respone to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management

*Source: Kroenke K, Spitzer RL, Psychiatric Annals. 2002;32:509-521.

Disclaimer - These recommendations for "UPDATE IN MANAGING PCOS IN WOMEN" have been developed, to be of assistance to obstetricians, gynecologists, consulting physicians and general practitioners by providing guidance and recommendations for managing women with anemia and suffering from hemorrhagic conditions. The recommendations included here shouldn't be viewed as being exclusive of other concepts or as covering all legitimate strategies. The suggestions made here are not meant to dictate how a particular patient should be treated because they neither set a standard of care nor do they guarantee a particular result. To diagnose patients, choose dosages, and provide the best care possible while also taking the necessary safety precautions, clinicians must rely on their own experience and knowledge. The writers or contributors disclaim all responsibility for any harm and/or damage to people or property resulting from the use or operation of any techniques, goods, guidelines, or ideas presented in this content.