

# Algorithm 1: Screening, diagnostic assessment, risk assessment and life-stage

## Step 1: Irregular cycles + clinical hyperandrogenism

(exclude other causes)\* = diagnosis

## Step 2: If no clinical hyperandrogenism

Test for biochemical hyperandrogenism (exclude other causes)\* = diagnosis

## Step 3: If ONLY irregular cycles OR hyperandrogenism

Adolescents ultrasound is not indicated = consider at risk of PCOS and reassess later  
Adults - request ultrasound for PCOM, if positive (exclude other causes)\* = diagnosis

\* Exclusion of other causes requires TSH, Prolactin levels, FSH and if clinical status indicates other causes need to be excluded (e.g. CAH, Cushings, adrenal tumours etc)

## Diagnostic Criteria

### Irregular menstrual cycles

- normal in the first year post menarche = pubertal transition.
- > 1 to < 3 years post menarche: < 21 or > 45 days.
- > 3 years post menarche to perimenopause: < 21 or > 35 days or < 8 cycles per year.
- > 1 year post menarche > 90 days for any one cycle.
- Primary amenorrhoea by age 15 or > 3 years post thelarche (breast development).

With irregular cycles, PCOS should be considered and assessed according to the guidelines.

Ovulatory dysfunction can still occur with regular cycles. If anovulation suspected test progesterone levels.

### Clinical hyperandrogenism

Comprehensive history and physical examination for clinical hyperandrogenism. Adults: acne, alopecia and hirsutism and in adolescents severe acne and hirsutism.

Be aware of potential negative psychosocial impact of clinical hyperandrogenism. Perception of unwanted face and body hair and/or alopecia are important, regardless of apparent clinical severity.

Standardised visual scales are preferred when assessing hirsutism such as the modified Ferriman Gallway score (mFG). A cut-off score of  $\geq 4$ -6 indicates hirsutism, depending on ethnicity. It is acknowledged that self-treatment is common and can limit clinical assessment.

The Ludwig visual score is preferred for assessing the degree and distribution of alopecia.

Hirsutism prevalence is same across ethnicities. mFG cut-offs for hirsutism and severity, vary by ethnicity.

Only terminal hairs relevant in pathological hirsutism (untreated > 5 mm long, variable shape and pigmented).

### Biochemical hyperandrogenism

Use calculated free testosterone, free androgen index or calculated bioavailable testosterone in diagnosis.

Androstenedione and dehydroepiandrosterone sulfate (DHEAS) have limited role in PCOS diagnosis.

High quality assays needed for most accurate assessment. Direct free testosterone assays not preferred. Interpretation of androgen levels should be guided by the reference ranges of the laboratory used.

Reliable assessment of biochemical hyperandrogenism not possible on hormonal contraception. Consider withdrawal for  $\geq 3$  months before testing, advising non-hormonal contraception during this time.

In diagnosis, biochemical hyperandrogenism most useful when clinical hyperandrogenism is unclear.

Where levels are well above laboratory reference ranges, other causes should be considered. History of symptom onset and progression is critical in assessing for neoplasia, however, some androgen-secreting neoplasms may only induce mild to moderate increases in biochemical hyperandrogenism.

### Ultrasound and polycystic ovarian morphology (PCOM)

Ultrasound should not be used for the diagnosis of PCOS in those with a gynaecological age of < 8 years (< 8 years after menarche), due to the high incidence of multi-follicular ovaries in this life stage.

The transvaginal ultrasound approach is preferred in the diagnosis of PCOS, if sexually active and if acceptable to the individual being assessed.

Using endovaginal ultrasound transducers with a frequency bandwidth that includes 8MHz, the threshold for PCOM should be a follicle number per ovary of  $\geq 20$  and/or an ovarian volume  $\geq 10$ ml on either ovary, ensuring no corpora lutea, cysts or dominant follicles are present.

If using older technology, the threshold for PCOM could be an ovarian volume  $\geq 10$ ml on either ovary.

In patients with irregular menstrual cycles and hyperandrogenism, an ovarian ultrasound is not necessary for PCOS diagnosis; however ultrasound will identify the complete PCOS phenotype.

Transabdominal ultrasound should primarily report ovarian volume with a threshold of  $\geq 10$ ml, given the difficulty of reliably assessing follicle number with this approach.

## Ethnic variation

Consider ethnic variation in PCOS including:

- relatively mild phenotypes in Caucasians.
- higher BMI in Caucasians, especially North America and Australia.
- more severe hirsutism in Middle Eastern, Hispanic and Mediterranean women.
- increased central adiposity, insulin resistance, diabetes, metabolic risks and acanthosis nigricans in South East Asians and Indigenous Australians.
- lower BMI and milder hirsutism in East Asians.
- higher BMI and metabolic features in Africans.

## Anti-müllerian hormone (AMH)

Serum AMH levels should not yet be used as an alternative for the detection of PCOM or to diagnose PCOS.

## Cardiovascular disease risk and weight management

All with PCOS should be offered regular monitoring for weight change and excess weight, in consultation with and where acceptable to the individual. Monitoring could be at each visit or at a minimum 6-12 monthly, with frequency planned and agreed between the health professional and the individual.

Weight, height and ideally waist circumference should be measured and BMI calculated.

- BMI categories and waist circumference should follow World Health Organisation guidelines also noting ethnic and adolescent ranges.
- Consideration for Asian and high risk ethnic groups including monitoring waist circumference.

All with PCOS should be assessed for individual cardiovascular risk factors and global CVD risk.

If screening reveals CVD risk factors including obesity, cigarette smoking, dyslipidemia, hypertension, impaired glucose tolerance and lack of physical activity, women with PCOS should be considered at increased risk of CVD.

Overweight and obese women with PCOS, regardless of age, should have a fasting lipid profile (total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglyceride level at diagnosis). Thereafter, measurement should be guided by the results and the global CVD risk.

All women with PCOS should have blood pressure measured annually.

CVD risk in women with PCOS remains unclear pending high quality studies, however prevalence of CVD risk factors is increased, warranting awareness and consideration of screening.

## Gestational diabetes, impaired glucose tolerance and type 2 diabetes

Regardless of age, gestational diabetes, impaired glucose tolerance and type 2 diabetes (5 fold in Asia, 4 fold in the Americas and 3 fold in Europe) are increased in PCOS, with risk independent of, yet exacerbated by obesity.

Glycaemic status should be assessed at baseline in all with PCOS and thereafter, every one to three years, based on presence of other diabetes risk factors.

In high risk women with PCOS (including a BMI > 25kg/m<sup>2</sup> or in Asians > 23kg/m<sup>2</sup>, history of abnormal glucose tolerance or family history of diabetes, hypertension or high risk ethnicity) an oral glucose tolerance test (OGTT) is recommended. Otherwise a fasting glucose or HbA1c should be performed.

An OGTT should be offered in all with PCOS when planning pregnancy or seeking fertility treatment, given increased hyperglycaemia and comorbidities in pregnancy.

If not performed preconception, an OGTT should be offered at < 20 weeks gestation, and all women with PCOS should be offered the test at 24-28 weeks gestation

## Obstructive sleep apnea (OSA)

Screening should only be considered for OSA in PCOS to identify and alleviate related symptoms, such as snoring, waking unrefreshed from sleep, daytime sleepiness, and the potential for fatigue to contribute to mood disorders. Screening should not be considered with the intention of improving cardiometabolic risk, with inadequate evidence for metabolic benefits of OSA treatment in PCOS and in general populations.

A simple screening questionnaire, preferably the Berlin tool, could be applied and if positive, referral.

A positive screen raises the likelihood of OSA, however it does not quantify symptom burden and alone does not justify treatment. If women with PCOS have OSA symptoms and a positive screen, they should ideally be referred to a specialist centre for further evaluation.

## Endometrial cancer

Health professionals and women with PCOS should be aware of a two to six fold increased risk of endometrial cancer, which often presents before menopause; however absolute risk remains relatively low.

Health professionals should have a low threshold for investigation of endometrial cancer in PCOS, with transvaginal ultrasound and/or endometrial biopsy recommended with persistent thickened endometrium and/or risk factors including prolonged amenorrhea, abnormal vaginal bleeding or excess weight. Routine ultrasound screening of endometrial thickness in PCOS is not recommended.

Optimal prevention for endometrial hyperplasia and endometrial cancer is not known. A pragmatic approach could include COCP or progestin therapy in those with cycles longer than 90 days.