Algorithm 1: Screening, diagnostic assessment, risk assessment and life stage*

Step 1: Irregular cycles + clinical hyperandrogenism

(exclude other causes)* = diagnosis

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Step 2: If no clinical hyperandrogenism

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

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Step 3: If ONLY irregular cycles OR hyperandrogenism

Adolescents: Ultrasound or AMH is not indicated = consider at risk of PCOS and reassess later
Adults: Ultrasound for PCOM* OR Anti-Mullerian Hormone (AMH) level, if positive (exclude other causes)* = diagnosis

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***Exclusion of other causes =s TSH, prolactin, 17-OH progesterone, FSH or if clinically indicated exclude other causes** (e.g. Cushing's syndrome, adrenal tumours etc) Hypogonadotrophic hypogonadism, usually due to low body fat or intensive exercise, should also be excluded clinically and with LH and FSH levels

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 amenorrhea 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 occur with regular cycles. If anovulation suspected, check progesterone levels.

Biochemical hyperandrogenism

Use total testosterone and free testosterone for diagnosis. If not elevated, then androstenedione and dehydroepiandrosterone sulfate could be measured, but are less specific with a limited role in PCOS diagnosis.

Highly accurate tandem mass spectrometry (LC-MS/MS) assays recommended. Direct free testosterone assays not preferred. Use lab reference ranges.

Reliable assessment of biochemical hyperandrogenism not possible on hormonal contraception.
Consider withdrawal for ≥ 3 months with alternative contraception

Biochemical hyperandrogenism role is 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 key in assessing for neoplasia, however, some androgen-secreting neoplasms may only induce mild to moderate increases in hyperandrogenism.

Clinical hyperandrogenism

Comprehensive history and physical examination needed. Adults: acne, female pattern hair loss and hirsutism. Adolescents: severe acne and hirsutism.

Note negative psychosocial impact of clinical hyperandrogenism. Patient perception is important, regardless of apparent clinical severity.

Standardised visual scales are preferred including modified Ferriman Gallway score (mFG), a score of ≥ 4-6 = hirsutism, noting self-treatment impacts assessment.

Ludwig visual score preferred for assessing female pattern hair loss.

Ultrasound and polycystic ovary morphology

With irregular menstrual cycles and hyperandrogenism, an ovarian ultrasound is not necessary for diagnosis.

In diagnosis, follicle number per ovary is most effective, followed by follicle number per cross-section and ovarian volume as ultrasound markers in adults.

Ultrasound should not be used for PCOS diagnosis in adolescents, due to the high incidence of multi-follicular ovaries in this life stage.

Transvaginal ultrasound approach is preferred in diagnosis of PCOS, if sexually active or if acceptable to the individual

Using ultrasound transducers with a frequency bandwidth including 8 MHz, the PCOM threshold is a follicle number per ovary of ≥ 20 and/or an ovarian volume ≥ 10 ml on either ovary, avoiding corpora lutea, cysts or dominant follicles

Serum AMH could be used for defining PCOM in adults as an alternative to pelvic ultrasound. Either serum AMH OR ultrasound may be used but not both to avoid overdiagnosis*

Anti-mullerian hormone (AMH) *

Serum AMH could be used for defining PCOM in adults as an alternative to pelvic ultrasound. Either serum AMH OR ultrasound may be used but not both to avoid overdiagnosis*

Ethnic variation and prevalence

PCOS prevalence appears similar across ethnicities and is 10-13% globally by International guideline/Rotterdam criteria*

Menopause life stage

A diagnosis of PCOS is considered enduring. Postmenopausal women presenting with new-onset, severe or worsening hyperandrogenism including hirsutism, require further investigation to rule out androgen-secreting tumours and ovarian hyperthecosis.

Cardiovascular disease risk*

Women with PCOS have an increased risk of cardiovascular disease and potentially of cardiovascular mortality, but overall risk premenopause is low.*

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

All women with PCOS, regardless of age and BMI, 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 and when planning pregnancy or fertility treatment.

Impaired glucose tolerance and type 2 diabetes

Regardless of age and BMI, impaired glucose tolerance and type 2 diabetes are increased in PCOS, with risk independent of, yet exacerbated by BMI 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 (including a BMI > 25 kg/m² or in Asians > 23 kg/m², history of abnormal glucose tolerance or family history of diabetes, hypertension or high-risk ethnicity.

In high risk women an oral glucose tolerance test (OGTT is the most accurate test for dysglycaemia with fasting glucose or HbA1c second-line due to lower accuracyOGTT 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 the first prenatal visit, and all women with PCOS should be offered the test at 24-28 weeks gestation.

Obstructive sleep apnea

Women with PCOS have a significantly higher prevalence of obstructive sleep apnea.*

If symptoms of PCOS are present, then screen with validated tools or refer for assessment and goals of treatment should target related symptom burden.

Endometrial cancer

Health professionals and women with PCOS should be aware of a two to six fold increased risk of endometrial cancer in premenopausal women with PCOS; however absolute risk remains 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.

Long-standing untreated amenorrhea, higher weight and persistent thickened endometrium are additional to PCOS, are risk factors for endometrial hyperplasia and endometrial cancer. 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.

Risk of PCOS and cardiometabolic risk in first-degree relatives*

Fathers and brothers of women with PCOS may have an increased prevalence of metabolic syndrome, type 2 diabetes, and hypertension, with inadequate data in female relatives.*