Diagnosis of adolescent Polycystic Ovary Syndrome (PCOS) according to the 2018 International Evidence-Based Guidelines for the Assessment and Management of PCOS

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Background

Polycystic ovary syndrome (PCOS) is the most common endocrine condition affecting reproductive aged women. The diagnosis of PCOS during adolescence is controversial as adult diagnostic features overlap with normal physiological events that occur during puberty [1-3]. Previous guidelines for assessment and management of PCOS have not followed rigorous best practice in development, failed to engage consumers and international multidisciplinary perspectives or were outdated [1-3] resulting in inconsistent guidelines for clinicians. The aim of international evidence-based PCOS guidelines was to promote accurate diagnosis, optimal consistent care, prevention of complications and improve patient experiences and health outcomes.

Methods

Extensive international health professional and patient engagement informed the priorities and core outcomes for the guidelines.
International nominated panels including women with PCOS, multidisciplinary teams of health care professionals (paediatrics, endocrinology, gynaecology, primary care, reproductive endocrinology, obstetrics, psychiatry, psychology, dietetics, exercise physiology, public health and other experts across 44 societies and 71 countries), researchers and an evidence synthesis and translation team developed the guidelines that were funded and led by Australia*. The evidence-based guideline development followed international best practice involving 60 systematic and narrative reviews and applying full Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework to reflect quality of the evidence, and consider feasibility, acceptability, cost, implementation and the strength of recommendations.
There were 3 categories of the PCOS guideline recommendations: 1) Evidence based recommendation (EBR) when evidence was sufficient to inform a recommendation made by the guideline development group; 2) Clinical consensus recommendation (CCR) in the absence of evidence a CCR was made by the guideline development group; and 3) Clinical practice point (CPP): Evidence was not sought. A CPP was made by the guideline development group where important issues arose from discussion of EBR or CCR.

Summary of the recommendations

Adolescent recommendations for PCOS diagnosis aimed to avoid over diagnosis, misdiagnosis and delay and under diagnosis include:

1) Irregular menstrual cycles (CCR) and clinical hyperandrogenism (CCR) or biochemical hyperandrogenism (EBR) [See Tables and Figure below].
2) Exclusion of other disorders that mimic PCOS is required in all women but particularly in those with amenorrhea and severe phenotypes.
3) Pelvic ultrasound should not be used for the diagnosis of PCOS in adolescents or 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 (CCR).
4) Serum anti-mullerian hormone levels are not recommended for PCOS diagnosis during adolescence (EBR).

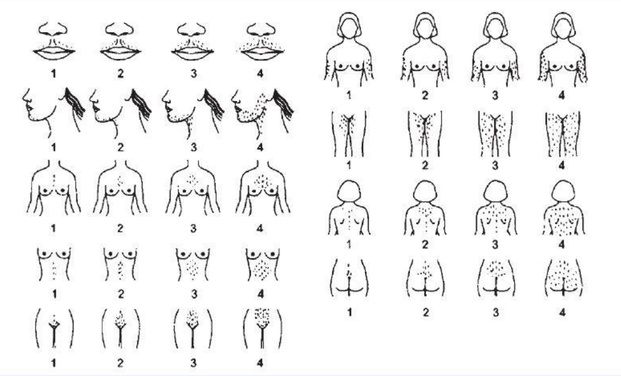
The value and optimal timing of assessment and diagnosis of PCOS should be discussed with the individual patient, taking into account diagnostic challenges at this life stage and psychosocial and cultural factors.
For adolescents who have features of PCOS but do not meet diagnostic criteria, an “increased risk” could be considered and reassessment advised at or before full reproductive maturity, 8 years post menarche. This includes those with features of PCOS before contraceptive pill commencement, those with persisting features and those with significant weight gain.

Irregular menstrual cycles - CCR
• 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 still occur with regular cycles. If anovulation suspected test progesterone levels.

Biochemical hyperandrogenism	
Use calculated free testosterone, free androgen index or calculated bioavailable testosterone in diagnosis.	EBR
Androstenedione and dehydroepiandrosterone sulfate (DHEAS) have limited role in PCOS diagnosis.	EBR
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.	EBR
Reliable assessment of biochemical hyperandrogenism not possible on hormonal contraception. Consider withdrawal for ≥ 3 months before testing, advising non-hormonal contraception during this time.	CPP
In diagnosis, biochemical hyperandrogenism most useful when clinical hyperandrogenism is unclear.	CPP
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.	

Clinical hyperandrogenism	
Comprehensive history and physical examination for clinical hyperandrogenism. Adults: acne, alopecia and hirsutism and in adolescents severe acne and hirsutism.	CCR
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.	CCR
Standardised visual scales are preferred when assessing hirsutism such as the modified Ferriman Gallway score (mFG). A cut-off score of ≥ 4-6 indicates hirsutism, depending on ethnicity. It is acknowledged that self-treatment is common and can limit clinical assessment.	CCR
The Ludwig visual score is preferred for assessing the degree and distribution of alopecia.	CCR
Hirsutism prevalence is same across ethnicities. mFG cut-offs for hirsutism and severity, vary by ethnicity.	CPP
Only terminal hairs relevant in pathological hirsutism (untreated > 5 mm long, variable shape and pigmented).	CPP

Modified Ferriman Gallwey score (mFG) [4]



References: 1. Teede HJ et al, Med J Aust 2011. 2. Legro RS et al, J Clin Endocrinol Metab 2013. 3. Witchel SF et al, Horm Res Paediatr 2015. 4. Yildiz, BO et al, Hum Rep Update 2010.

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Free guidelines availability and resources: https://www.monash.edu/medicine/sphpm/mchri/pcos