

## ALGORITHM 1:

### DIAGNOSTIC AND METABOLIC RISK ASSESSMENT FOR ALL WOMEN WITH POLYCYSTIC OVARY SYNDROME

The 2003 Rotterdam criteria for diagnosis of Polycystic Ovary Syndrome (PCOS) – requires two of the following three criteria:  
1) Oligo- or anovulation 2) Clinical and/or biochemical signs of hyperandrogenism 3) Polycystic ovaries, exclusion of other aetiologies such as congenital adrenal hyperplasia, androgen-secreting tumours, Cushing's syndrome

#### CHALLENGES IN DIAGNOSTIC ASSESSMENT

HYPERANDROGENISM	Late-onset congenital adrenal hyperplasia, although rare, needs to be considered before the diagnosis of polycystic ovary syndrome is confirmed. In more severe clinical cases of hyperandrogenism, 21-hydroxylase deficiency, the most common form of congenital adrenal hyperplasia, can be excluded by measuring serum 17-hydroxyprogesterone in the follicular phase to explore this diagnosis. <b>[CR]</b>
	Calculated bioavailable testosterone, calculated free testosterone or free androgen index should be first line investigation for biochemical determination of hyperandrogenism in PCOS. The addition of androstenedione and dehydroepiandrosterone sulfate could be second line investigation for biochemical determination of hyperandrogenism in PCOS. <b>[C]</b>
	<b>GOOD PRACTICE POINT</b> It is difficult to assess androgen status in women on the oral contraceptive pill as effects include oestrogen mediated increases in sex hormone-binding globulin and reduction in androgens. Where the oral contraceptive pill has already been commenced, it should be withdrawn for at least three months before appropriate hormonal assessments for diagnosis of polycystic ovary syndrome are undertaken. Contraception should be otherwise managed during this time. <b>[PP]</b>
HYPERANDROGENISM	<b>GOOD PRACTICE POINT</b> If androgen levels are markedly above laboratory reference ranges, secondary causes may be considered. Mild elevations of androstenedione may be seen in polycystic ovary syndrome, whereas marked elevations are more indicative of non-classical adrenal hyperplasia. Reference ranges for different methods and different laboratories vary widely and clinical decisions should be guided by the reference ranges of the laboratory used. <b>[PP]</b>
	<b>GOOD PRACTICE POINT</b> In adolescent women (<18 years), after two years of irregular cycles ( $\geq 35$ or $< 21$ days) following the onset of menarche, PCOS should be considered and appropriate assessment should be undertaken. As polycystic ovary syndrome is a diagnosis of exclusion, other causes of irregular cycles (such as thyroid dysfunction or hyperprolactinaemia) need to be considered and excluded prior to the diagnosis of polycystic ovary syndrome. <b>[CR]</b>
IRREGULAR CYCLES IN ADOLESCENTS	<b>GOOD PRACTICE POINT</b> If oral contraceptive pill therapy is being considered or has commenced in adolescents (<18 years), the following are recommended: *After twelve months of irregular cycles ( $>35$ or $<21$ days) after onset of menarche, PCOS should be considered before commencement of the oral contraceptive pill. * Where the oral contraceptive pill has already been commenced, when girls are not sexually active, if biochemical hyperandrogenism is needed for the diagnosis of PCOS, the oral contraceptive pill could be withdrawn for three months to facilitate appropriate hormonal assessments. Withdrawal of the oral contraceptive pill may facilitate assessment and early diagnosis of PCOS as diagnosis can have important implications including optimisation of healthy lifestyle, regular metabolic screening and proactive fertility planning, with consideration of planning for conception at an earlier age. However, the risk of unplanned pregnancy needs to be considered and weighed up against potential benefits of early diagnosis. Contraception may still need to be otherwise managed during this time.
	<b>GOOD PRACTICE POINT</b> Given the apparent lack of specificity of polycystic ovaries on ultrasound in adolescents, generally, ultrasound should not be recommended first line in this age group for diagnosis of polycystic ovary syndrome pending further research. If pelvic ultrasounds are to be ordered in adolescents, the results should be interpreted with caution. <b>[CR]</b>
POLYCYSTIC OVARIES IN ADOLESCENTS	<b>GOOD PRACTICE POINT</b> Vaginal ultrasound is not appropriate in adolescents who have not been sexually active. <b>[PP]</b>

#### ASSESSMENT OF CARDIOMETABOLIC RISK

RISK OF CARDIOVASCULAR DISEASE	All women with PCOS should be assessed for cardiovascular disease risk by assessing individual cardiovascular disease risk factors. If screening in women with polycystic ovary syndrome shows that any of the following cardiovascular disease risk factors are present, these women with polycystic ovary syndrome should be considered at increased relative risk of cardiovascular disease (obesity, cigarette smoking, dyslipidemia, hypertension, impaired glucose tolerance, lack of physical activity) and those with metabolic syndrome and/or type 2 diabetes, at even greater risk. <b>[CR]</b>
	All women with PCOS should be assessed for excess weight at every visit. In assessing women with PCOS < 8 years, age appropriate and gender appropriate body mass index should be calculated at every visit. All women with polycystic ovary syndrome should be assessed for cigarette smoking. <b>[CR]</b>
	<b>GOOD PRACTICE POINT</b> Body mass index should be assessed in all women with PCOS using the following criteria: BMI $\leq 25\text{kg/m}^2$ = lean, BMI $\geq 25\text{kg/m}^2$ = overweight, BMI $\geq 30\text{kg/m}^2$ = obese, BMI $\geq 35\text{kg/m}^2$ = morbidly obese. Significant benefits have been demonstrated with 5-10% weight loss in overweight women with polycystic ovary syndrome and is a feasible initial target (see 5.4c). BMI doesn't always reflect adverse body fat stores and waist circumference will be useful. Waist circumference should be assessed using the following criteria (NHMRC 2003): Waist circumference $>80\text{cm}$ = increased risk of metabolic complications, Waist circumference $>88\text{cm}$ = substantially increased risk of metabolic complications <b>[PP]</b>
RISK OF CARDIOVASCULAR DISEASE	A complete lipid profile should be measured every two years in women with PCOS who have normal lipid profiles. A complete lipid profile should be measured annually in women with PCOS who have abnormal lipid profiles and/or excess weight. <b>[CR]</b>
	<b>GOOD PRACTICE POINT</b> In women with PCOS, a lipid profile should include: <b>Total cholesterol</b> - total cholesterol should $< 4$ mmol/L. <b>Low density lipoprotein cholesterol (LDL-C)</b> - in women without additional cardiovascular disease risk factors, LDL-C levels should be $< 3.4$ mmol/L. In women with metabolic syndrome or type 2 diabetes, LDL-C levels should be $< 1.8$ – $2.6$ mmol/L or $1.8$ mmol/L, respectively. <b>High density lipoprotein cholesterol (HDL-C)</b> - HDL-C levels should be $> 1.0$ mmol/L. <b>Triglycerides</b> - Triglyceride levels should be $< 1.7$ mmol/L. <b>[PP]</b>
	Prediabetes and/or type 2 diabetes should be assessed in all women with PCOS. (See 3.2a and 3.2b). <b>[CR]</b>
RISK OF DIABETES	Blood pressure should be measured annually in women with PCOS and a Body mass index $\leq 25\text{kg/m}^2$ (lean). Blood pressure should be routinely measured at each visit in women with PCOS and a body mass index $\geq 25\text{kg/m}^2$ (overweight/obese). <b>[CR]</b>
	<b>GOOD PRACTICE POINT</b> In women with PCOS who are at high risk of type 2 diabetes, the ideal day time blood pressure should not exceed 135 mmHg systolic and 85 mmHg diastolic. <b>[PP]</b>
	To assess for risk of type 2 diabetes, in addition to PCOS status, the following diabetes risk factors should be considered: age, gender, ethnicity, parental history of diabetes, history of high blood glucose level, use of antihypertensive medications, smoking, physical inactivity, waist circumference. <b>[CR]</b>
RISK OF DIABETES	An oral glucose tolerance test should be performed every second year in all women with polycystic ovary syndrome and annually in those found to have additional risk factors for developing type 2 diabetes as outlined in 3.2a. <b>[CR]</b>
	<b>GOOD PRACTICE POINT</b> Reference ranges for: <b>Impaired fasting glucose</b> - fasting plasma glucose: 6.1 - 6.9 mmol/L. <b>Impaired glucose tolerance</b> - 2 hour glucose level: 7.8-11 mmol/L. <b>Type 2 diabetes</b> - fasting plasma glucose: $\geq 7.0$ mmol/L or 2 hour oral glucose tolerance test: $\geq 11.1$ mmol/L. Ideally 150 grams of carbohydrate per day should be consumed for three days before, and women should then fast for 8 hours immediately prior to the oral glucose tolerance test since low carbohydrate intake may lead to false positive glucose tolerance tests. <b>[PP]</b>