



# Long term health consequences of PCOS

This statement has been developed and reviewed by the Women's Health Committee and approved by the RANZCOG.

A list of Women's Health Committee Members can be found in [Appendix A](#).

**Disclaimer** This information is intended to provide general advice to practitioners. This information should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient. This document reflects emerging clinical and scientific advances as of the date issued and is subject to change. The document has been prepared having regard to general circumstances.

**First endorsed by RANZCOG: March 2010**

**Current: March 2017**

**Review due: March 2020**

**Objectives:** To provide advice on the diagnosis of PCOS and its long term health consequences.

**Outcomes:** Reducing the risk of long-term health consequences of PCOS.

**Target audience:** All health practitioners providing gynaecological care, and patients. In addition, this may provide useful information for those working in Aboriginal communities.

**Evidence:** Medline was searched for randomised trials, prospective cohort studies, and selected retrospective cohort studies on long-term consequences of PCOS.

**Values:** The evidence was reviewed by the Women's Health Committee (RANZCOG) and local generalisability and applicability factors relating to Australia and New Zealand were taken into account.

**Validation:** This statement was compared with guidance published by RCOG,<sup>4</sup> ACOG<sup>5</sup> and National Institutes of Health.<sup>7</sup>

**Background** This statement was first developed by RANZCOG in March 2010 and was most recently revised in March 2017.

**Funding:** The development and review of this statement was funded by RANZCOG.

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## 1. Patient summary

Polycystic ovarian syndrome (PCOS) is a relatively common condition. Women who have PCOS have an increased risk of diabetes and a range of other significant health problems which can be made worse by being overweight or obese. Because of this, women with PCOS should maintain a healthy lifestyle including managing any mental health problems. Life-long strategies should be in place to detect and manage conditions such as diabetes, hypertension, and high cholesterol.

## 2. Summary of recommendations

<b>Recommendation 1</b>	<b>Grade and reference</b>
The diagnosis of PCOS should be made using current international criteria such as the Rotterdam criteria.	Consensus-based recommendation
<b>Recommendation 2</b>	<b>Grade and reference</b>
Women with PCOS should be screened for metabolic dysfunction. Fasting glucose levels are poor predictors of glucose intolerance risk, therefore screening should be undertaken with a two hour oral glucose tolerance. Repeat screening for diabetes should be based on the key predictors such as BMI and family history. Measurement of insulin levels is not recommended.  Screening for cardiovascular risk is by determination of BMI, fasting lipid and lipoprotein levels, and metabolic syndrome risk factors.	Consensus-based recommendation
<b>Recommendation 3</b>	<b>Grade and reference</b>
Women with PCOS have an increased risk of depression and anxiety, therefore screening for these conditions should be undertaken and management tailored accordingly.	Consensus-based recommendation
<b>Recommendation 4</b>	<b>Grade and reference</b>
In women with PCOS, management of hypertension and dyslipidaemia should be undertaken as indicated.	Consensus-based recommendation
<b>Recommendation 5</b>	<b>Grade and reference</b>
Women with PCOS should have formal questioning about the symptoms of obstructive sleep apnoea, and further investigation and management as indicated.	Consensus-based recommendation
<b>Recommendation 6</b>	<b>Grade and reference</b>
Women with PCOS should be offered support with lifestyle modification regarding healthy diet and exercise.	Consensus-based recommendation
<b>Recommendation 7</b>	<b>Grade and reference</b>
The routine use of insulin sensitising agents is not recommended.	Consensus-based recommendation

Recommendation 8	Grade and reference
The use of bariatric surgery should be considered where obesity is not controlled by lifestyle modifications.	Consensus-based recommendation
Recommendation 9	Grade and reference
Due to the increased risks of pregnancy in women with obesity, the use of ovarian stimulation for women with a BMI of 35 Kg/m <sup>2</sup> is contraindicated.	Consensus-based recommendation

### 3. Introduction

Polycystic ovarian syndrome (PCOS) is the most common endocrine abnormality in women of reproductive age. It may be associated with anovulation, infertility, hyperandrogenism, and long-term metabolic sequelae. Insulin resistance is central to this syndrome, driving increased androgen levels and resulting in impaired glucose tolerance and, potentially, an increase in cardiovascular disease.

The prevalence of PCOS is estimated conservatively at 6-7 per cent of the population (or 400,000 Australian women)<sup>1</sup> but recent studies from the Robinson Institute in Adelaide suggest a much higher prevalence<sup>2</sup> especially in the Aboriginal population.<sup>3</sup> Obesity aggravates insulin resistance, and as obesity in the community increases, the prevalence of, and complications from, PCOS are expected to rise.

Women with PCOS should be fully informed about the long-term health consequences of this condition, and advised about how they may reduce their risk.

## 4. Evidence summary and basis for recommendations

### 4.1 How is PCOS diagnosed?

The diagnostic criteria for PCOS remain unresolved. However, all diagnostic approaches require that secondary causes (adult onset congenital adrenal hyperplasia, hyperprolactinaemia, and androgen secreting neoplasms) should first be excluded.<sup>4</sup>

<sup>5</sup>Currently, the most commonly accepted consensus criteria for diagnosis of PCOS are the "Rotterdam" criteria,<sup>6</sup> agreed by ESHRE and ASRM. The NIH has recently affirmed the paramount value of the Rotterdam criteria.<sup>7</sup>

The Rotterdam criteria require two of the three following for the diagnosis of PCOS:

- Polycystic ovaries (either 12 or more peripheral antral follicles or increased ovarian volume).
- Oligomenorrhea or anovulation.
- Clinical and/or biochemical signs of hyperandrogenism.

The Rotterdam criteria will include a number of phenotypes of PCOS, including mild phenotypes that would be excluded by previous criteria.

PCOS should not be over-diagnosed, and diagnosis should be in strict accordance with current international criteria. It is likely that high values of AMH will become an important diagnostic criterion in place of ultrasound.

<b>Recommendation 1</b>	<b>Grade and reference</b>
The diagnosis of PCOS should be made using current international criteria such as the Rotterdam criteria.	Consensus-based recommendation

#### 4.2 What are the metabolic consequences of PCOS?

Women with PCOS, particularly if they are overweight (BMI > 30 kg/m<sup>2</sup>) are at increased risk of impaired glucose tolerance (IGT), Type 2 Diabetes (T2D) and metabolic syndrome (Table 1). The investigation and management of metabolic dysfunction in PCOS is therefore of prime importance. A study of a large cohort of Australian women with PCOS<sup>1</sup> revealed an incidence of IGT of 15.6% and T2D of 4%. Most women in this study were also obese with a mean BMI of 35 kg/m<sup>2</sup>. Although obesity exacerbates insulin resistance, women with PCOS are insulin resistant independent of obesity. Lean women with PCOS have a 2-fold increase in incidence of T2D compared to controls.<sup>8</sup> Women with PCOS are also at increased risk of gestational diabetes (OR 2.94).<sup>9</sup>

Fasting glucose levels are poor predictors of glucose intolerance risk in women with PCOS and therefore screening for IGT should be by a 2-hour oral glucose tolerance test (OGTT).<sup>10</sup> However, there is no current consensus on who should be screened. Some authorities recommend that all women diagnosed with PCOS should be screened with a 2-hour oral glucose tolerance test.<sup>5</sup> Others recommend that an OGTT should be given to women with a fasting blood sugar of 5.6 mmol/l or greater, BMI greater than 30 kg/m<sup>2</sup>, a strong family history of gestational diabetes<sup>4</sup>, or lean PCOS women of advanced age (>40 years).<sup>11</sup> Currently both strategies appear to be acceptable.

Longitudinal studies have also confirmed an increased incidence of T2D over time,<sup>12</sup> and conversion from IGT to T2D.<sup>13</sup> Consideration should be given to repeat screening<sup>5</sup> based on the key predictors for the development of diabetes: age, BMI, family history. Measurement of insulin levels has little practical utility in PCOS and is not recommended.<sup>4, 5</sup>

There is increasing recognition of the metabolic syndrome as a risk for the development of cardiovascular disease. This syndrome is increasingly common in Western societies, and the prevalence in women with PCOS has been found to be up to 45 per cent.<sup>14</sup> Women with PCOS should be screened for cardiovascular risk by determination of BMI, fasting lipid and lipoprotein levels and metabolic syndrome risk factors.<sup>5</sup>

## **Metabolic Syndrome**

Elevated blood pressure (greater than or equal to 130/85)

Increased waist circumference (greater than or equal to 88cm)

Elevated fasting blood glucose levels

Reduced high density lipoprotein cholesterol levels

Elevated triglyceride levels

<b>Recommendation 2</b>	<b>Grade and reference</b>
Women with PCOS should be screened for metabolic dysfunction. Because fasting glucose levels are poor predictors of glucose intolerance risk, screening should be undertaken with a two hour oral glucose tolerance. Screening for cardiovascular risk is by determination of BMI, lasting lipid and lipoprotein levels, and metabolic syndrome risk factors.	Consensus-based recommendation
<b>Recommendation 3</b>	<b>Grade and reference</b>
Repeat screening should be based on the key predictors for development of diabetes: BMI and family history. Measurement of insulin levels is not recommended.	Consensus-based recommendation

### **4.3 What are other risks associated with PCOS?**

#### **4.3.1 Emotional and quality of life issues**

Almost every study of PCOS has shown a higher risk of depression, anxiety and worsened quality of life in this condition. Practitioners must investigate the presence of mental distress and include treatment of this in the management plan. The impact of impaired quality of life on long-term health can be imputed but has not been measured.<sup>15</sup>

<b>Recommendation 4</b>	<b>Grade and reference</b>
Because women with PCOS have an increased risk of depression and anxiety, screening for these conditions should be undertaken and management tailored accordingly.	Consensus-based recommendation

#### **4.3.2 Cardiovascular risk**

Prospective studies have not as yet identified an increase in cardiac events in women with PCOS.<sup>16</sup> However, there is indirect evidence of increased cardiovascular risk. The Nurses' Health Study has revealed an increasing risk of cardiovascular disease with increasing oligomenorrhea.<sup>17</sup> Studies in premenopausal women with PCOS have also revealed an increase in sub-clinical atherosclerosis compared to controls.<sup>18,19</sup> Hypertension should be

actively treated in women with PCOS, but as yet there is insufficient evidence to recommend routine treatment with lipid lowering drugs such as statins.<sup>4</sup> Women diagnosed with PCOS should be strongly advised to refrain from smoking.

Recommendation 5	Grade and reference
In women with PCOS, management of hypertension and dyslipidaemia should be undertaken as indicated.	Consensus-based recommendation

#### 4.3.3 Obstructive sleep apnoea

Obstructive sleep apnoea (OSA) is an independent risk factor for cardiovascular disease and is more common in PCOS. The difference in prevalence of OSA between PCOS and controls remains significant even when controlling for BMI.<sup>20, 21</sup> Women diagnosed with PCOS should be asked about the symptoms of OSA (snoring, daytime fatigue/somnolence) and offered investigation and treatment if indicated.

Recommendation 6	Grade and reference
Women with PCOS should have formal questioning about the symptoms of obstructive sleep apnoea, and further investigation and management as indicated.	Consensus-based recommendation

#### 4.3.4 Cancer

Obesity, which is common in PCOS, is a recognised risk factor for several different cancers. It is also well recognised that oligomenorrhoea or amenorrhoea in women with PCOS may predispose to endometrial hyperplasia and carcinoma.<sup>22</sup> Women with oligomenorrhoea or irregular bleeding should be investigated according to local protocols. This may involve transvaginal assessment of endometrial thickness, endometrial sampling or hysteroscopy. In women with PCOS and oligomenorrhoea or amenorrhoea, the induction of regular withdrawal bleeds (at least every 3-4 months) is advisable using cyclic progestagens for at least 12 days or the oral contraceptive pill.<sup>23</sup> A levonorgestrel releasing IUCD (Mirena) is also a valid option.

### 4.4 How can PCOS be treated?

#### 4.4.1 Lifestyle modification

Lifestyle intervention through diet and exercise are the key treatments for reducing risk in PCOS. Women with PCOS who are not obese, should be strongly advised to maintain their BMI in the normal range. Modest weight reduction (5-10%) is associated with a significant improvement in metabolic indices.<sup>24</sup> Dietary advice should focus on total calorific intake, and on the balance of evidence, low glycaemic index diets are preferred.<sup>25</sup> Regular exercise (30 minutes of aerobic exercise/day) has been shown to decrease central obesity and increase insulin sensitivity and is therefore strongly recommended.<sup>26</sup> Women diagnosed with PCOS should be advised of the long-term health benefits of maintaining a healthy lifestyle.

Recommendation 7	Grade and reference
Women with PCOS should be offered support with lifestyle modification regarding healthy diet and exercise.	Consensus-based recommendation

#### 4.4.2 Drug therapy

Insulin sensitising agents such as metformin have a role when IGT or T2D has been diagnosed. However, there is no current evidence indicating that these drugs lower cardiovascular risk, and their routine use in PCOS is not recommended.<sup>4, 5, 10</sup> Trials suggest that metformin is not superior to lifestyle intervention in improving cardio-metabolic risk or progression to T2D.<sup>27, 28</sup> Cholesterol lowering drugs should be reserved for women with PCOS proven to have dyslipidaemia. Treatment of elevated blood pressure is important for decreasing the risk of cardiovascular disease and antihypertensive medication should be prescribed if lifestyle modifications are ineffective at controlling blood pressure.<sup>11</sup>

Recommendation 8	Grade and reference
The routine use of insulin sensitising agents is not recommended.	Consensus-based recommendation

#### 4.4.3 Bariatric Surgery

Bariatric surgery has been shown to be effective in women with PCOS and may be an option for severely obese women with PCOS in whom long-term diet-based strategies are seldom successful.<sup>29, 30</sup> Surgical induced weight loss, however must be balanced against the risks of surgery, including a 0.1-1% mortality, risk of bowel obstruction, infection, esophagitis and nutritional abnormalities.<sup>29</sup> Bariatric surgery should be performed only when standard weight loss regimes have failed in PCOS women with a BMI greater than 40kg/m<sup>2</sup> or greater than 35kg/m<sup>2</sup> with a high-risk obesity related condition.<sup>31</sup>

Recommendation 9	Grade and reference
The use of bariatric surgery should be considered where obesity is not controlled by lifestyle modifications.	Consensus-based recommendation

Recommendation 10	Grade and reference
Because of the risks of pregnancy in women with obesity, the use of ovarian stimulation for women with a BMI of 35 Kg/m <sup>2</sup> is contraindicated.	Consensus-based recommendation

#### 4.4.4 Ovulation induction

Randomised trials suggest that clomiphene is the first line treatment and more effective than metformin **alone** for ovulation induction in PCOS.

However, pregnancy when obese is associated with many increased risks therefore it is inappropriate to recommend ovarian stimulation as part of first line therapy in the female with a BMI >35 unless there are exceptional circumstances.<sup>32</sup>

## 5. Links to other College statements

Ovarian stimulation in assisted reproduction (C-Gyn 02)

[http://www.ranzcog.edu.au/component/docman/doc\\_download/911-c-gyn-02-ovarian-stimulation-in-assisted-reproduction-.html](http://www.ranzcog.edu.au/component/docman/doc_download/911-c-gyn-02-ovarian-stimulation-in-assisted-reproduction-.html)

Evidence-based Medicine, Obstetrics and Gynaecology (C-Gen 15)

[http://www.ranzcog.edu.au/component/docman/doc\\_download/894-c-gen-15-evidence-based-medicine-obstetrics-and-gynaecology.html?Itemid=341](http://www.ranzcog.edu.au/component/docman/doc_download/894-c-gen-15-evidence-based-medicine-obstetrics-and-gynaecology.html?Itemid=341)

## 6. Patient information

A range of RANZCOG patient information pamphlets can be ordered via:

<https://www.ranzcog.edu.au/Womens-Health/Patient-Information-Guides/Patient-Information-Pamphlets>

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## Appendices

### Appendix A Women's Health Committee Membership

Name	Position on Committee
Professor Yee Leung	Chair
Dr Joseph Sgroi	Deputy Chair, Gynaecology
Associate Professor Janet Vaughan	Deputy Chair, Obstetrics
Professor Susan Walker	Member
Associate Professor Ian Pettigrew	Member
Dr Tal Jacobson	Member
Dr Ian Page	Member
Dr John Regan	Member
Dr Craig Skidmore	Member
Dr Lisa Hui	Member
Dr Bernadette White	Member
Dr Scott White	Member
Associate Professor Kirsten Black	Member
Dr Greg Fox	College Medical Officer
Dr Marilyn Clarke	Chair of the A&TSI WHC
Dr Martin Byrne	GPOAC Representative
Ms Catherine Whitby	Community Representative
Ms Sherryn Elworthy	Midwifery Representative
Dr Amelia Ryan	Trainee Representative

### Appendix B Overview of the development and review process for this statement

#### *i. Steps in developing and updating this statement*

This statement was originally developed in March 2010 and was most recently reviewed in March 2017. The Women's Health Committee carried out the following steps in reviewing this statement:

- Structured clinical questions were developed and agreed upon.
- An updated literature search to answer the clinical questions was undertaken.
- At the February 2017 teleconference, the existing consensus-based recommendations were reviewed and updated (where appropriate) based on the available body of evidence and clinical expertise. Recommendations were graded as set out below in Appendix B part ii).

#### *ii. Grading of recommendations*

Each recommendation in this College statement is given an overall grade as per the table below, based on the National Health and Medical Research Council (NHMRC) Levels of Evidence and

Grades of Recommendations for Developers of Guidelines. Where no robust evidence was available but there was sufficient consensus within the Women’s Health Committee, consensus-based recommendations were developed or existing ones updated and are identifiable as such. Consensus-based recommendations were agreed to by the entire committee. Good Practice Notes are highlighted throughout and provide practical guidance to facilitate implementation. These were also developed through consensus of the entire committee.

Recommendation category		Description
Evidence-based	A	Body of evidence can be trusted to guide practice
	B	Body of evidence can be trusted to guide practice in most situations
	C	Body of evidence provides some support for recommendation(s) but care should be taken in its application
	D	The body of evidence is weak and the recommendation must be applied with caution
Consensus-based		Recommendation based on clinical opinion and expertise as insufficient evidence available
Good Practice Note		Practical advice and information based on clinical opinion and expertise

### Appendix C Full Disclaimer

This information is intended to provide general advice to practitioners, and should not be relied on as a substitute for proper assessment with respect to the particular circumstances of each case and the needs of any patient.

This information has been prepared having regard to general circumstances. It is the responsibility of each practitioner to have regard to the particular circumstances of each case. Clinical management should be responsive to the needs of the individual patient and the particular circumstances of each case.

This information has been prepared having regard to the information available at the time of its preparation, and each practitioner should have regard to relevant information, research or material which may have been published or become available subsequently.