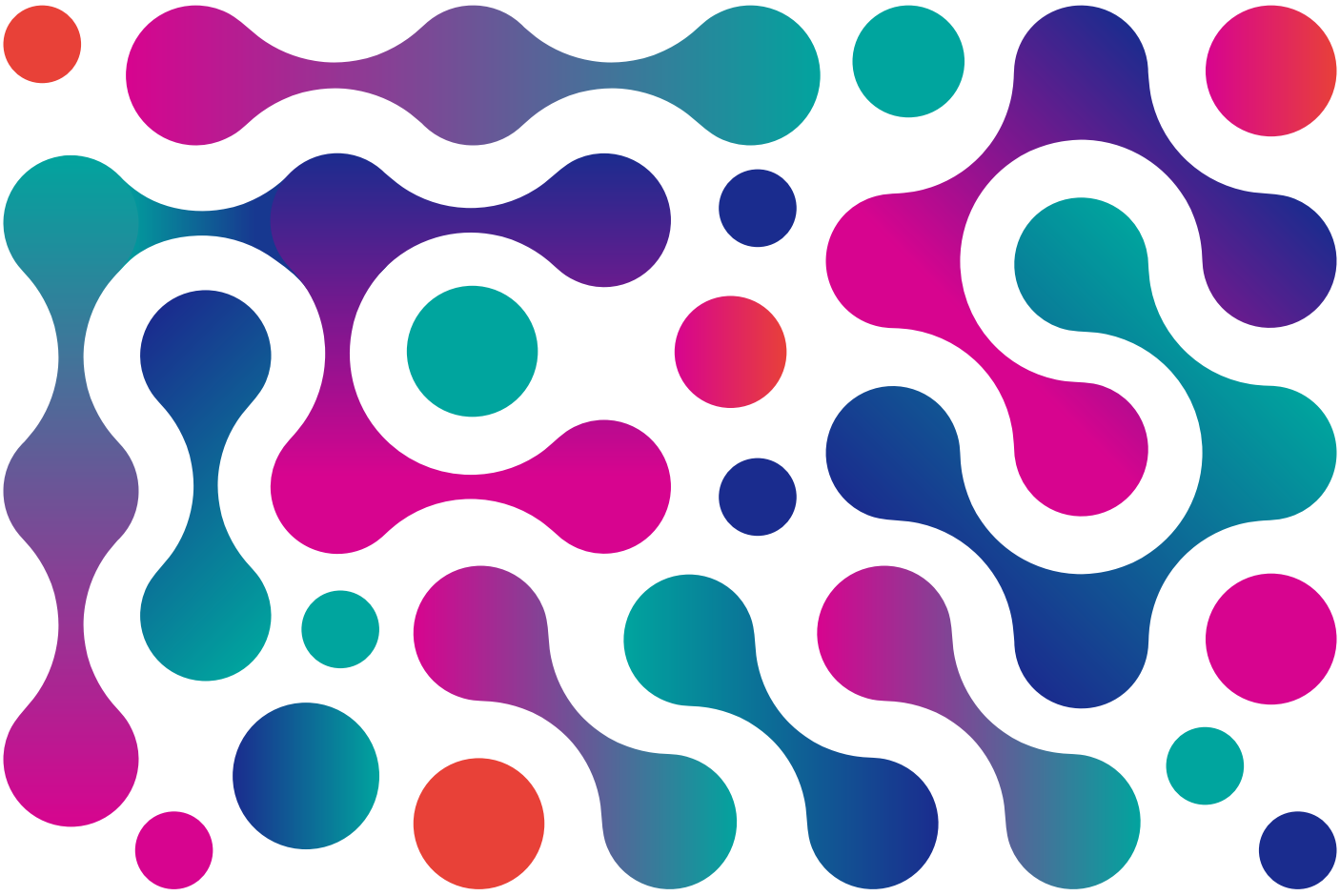
International evidence-based guideline for the assessment and management of **polycystic ovary syndrome 2023** – Summary



MONASH University

CREWHiRL Centre for Research Excellence in Women's Health in Reproductive Life

CREPCOS Centre for Research Excellence in Polycystic Ovary Syndrome

asrm American Society for Reproductive Medicine

ENDOCRINE SOCIETY Hormone Science to Health

eshre SCIENCE MOVING PEOPLE MOVING SCIENCE

European Society of Endocrinology

Abstract

Objective: To develop and translate rigorous, comprehensive evidence-based guidelines for diagnosis, assessment and treatment, to improve the lives of those with polycystic ovary syndrome (PCOS) worldwide.

Participants: Extensive health professional and consumer or patient engagement informed the guideline priority areas. International society-nominated panels included consumers, and experts in paediatrics, endocrinology, gynaecology, primary care, reproductive endocrinology, psychology, dietetics, exercise physiology, sleep, bariatric/metabolic surgery, public health, other co-opted experts, project management, evidence synthesis and translation.

Evidence: Best practice, evidence-based guideline development involved extensive evidence synthesis and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework covered evidence quality, feasibility, acceptability, cost, implementation and ultimately recommendation strength.

Process: Governance included an international advisory panel, management committee and five guideline development groups with 52 members, consumer and translation committees. The Centre for Research Excellence in Women's Health in Reproductive Life, funded by the Australian National Health and Medical Research Council (NHMRC), and led by Monash University, partnered with the American Society for Reproductive Medicine, the Endocrine Society, the European Society of Endocrinology and the European Society of Human Reproduction and Embryology. Thirty-six organisations collaborated with international meetings over nine months. Fifty-five prioritised clinical questions involved 52 systematic and three narrative reviews, generating evidence-based and consensus recommendations with accompanying practice points. Committee members nominated by collaborating organisations provided international peer review, and evidence expert-reviewed methods and outputs were submitted to NHMRC for independent review.

Recommendations: PCOS should be diagnosed using the revised consensus Rotterdam criteria, which are now updated to evidence-based criteria. In adults this requires the presence of two of i) clinical/biochemical hyperandrogenism, ii) ovulatory dysfunction and iii) polycystic ovaries on ultrasound or elevated anti-mullerian hormone (AMH) levels, after other causes of these features are excluded. Where irregular menstrual cycles and hyperandrogenism are present, ultrasound or AMH are not required for diagnosis. In adolescents, both hyperandrogenism and ovulatory dysfunction are required, with ultrasound and AMH not recommended, due to poor specificity. Once diagnosed, assessment and management should address reproductive, metabolic, cardiovascular, dermatologic, sleep and psychological features. A lifelong reproductive health plan is recommended including a focus on preconception risk factors, healthy lifestyle and prevention of weight gain and optimisation of fertility. Metabolic risk factors, diabetes, cardiovascular disease and sleep disorders are all increased in PCOS and screening and management is recommended. PCOS should be considered a high-risk condition in pregnancy with women identified and monitored. An increased premenopausal risk of endometrial cancer should be recognised, whilst absolute risks remain low.

Depressive and anxiety symptoms are significantly increased and should be screened for in all women with PCOS, with psychological assessment and therapy as indicated. Greater awareness of psychological features including eating disorders and impacts on body image and quality of life is needed. Dissatisfaction with PCOS diagnosis and care is high and raised awareness and education is strongly recommended for women and healthcare professionals including high quality, evidence-based resources. Shared decision making and a self-empowerment are fundamental and integrated models of care should be developed, funded and evaluated.

Supported healthy lifestyle remains vital throughout the lifespan in PCOS, with a strong focus on overall health, prevention of weight gain and if required, on weight management. Recognising the benefits if many specific diet and physical activity regimens, there is no one regimen that has benefits over others in PCOS. Weight bias and stigma should be minimised and healthcare professionals should seek permission to weigh women, with explanation of weight-related risks. Combined oral contraceptive pills are first-line pharmacological treatment for menstrual irregularity and hyperandrogenism, with no specific recommended preparation, and a preference for lower dose preparations and those with less side-effects. Metformin is recommended primarily for metabolic features and has greater efficacy than inositol, which offers limited clinical benefits in PCOS. Metformin is not routinely recommended for use in pregnant women with PCOS. Laser therapy is effective for hair reduction in some subgroups, whilst antiandrogens have a limited role, to be used where other therapies are ineffective or are contraindicated. Anti-obesity agents and bariatric/metabolic surgery may be considered based on general population guidelines, balancing potential for benefits and side-effects.

Letrozole is first-line pharmacological infertility therapy, with clomiphene alone or in combination with metformin, gonadotrophins or ovarian surgery having a role as second-line therapy. In the absence of an absolute indication for in vitro fertilisation (IVF), women with PCOS and anovulatory infertility could be offered IVF potentially with in vitro maturation, as third-line therapy where other ovulation induction therapies have failed.

Overall, evidence in PCOS is low to moderate quality. Based on high prevalence and significant health impact, greater priority, funding and research is recommended. Guideline translation will be extensive including multilingual education outputs and evidence-based resources for consumers (the AskPCOS app), healthcare professionals and policy makers.

Context statement on diagnosis: Prelude to the guideline

Here, we build on the 2018 International Evidence-based Guideline for the Assessment, Diagnosis and Management of PCOS, and on the initial consensus-based Rotterdam PCOS diagnostic criteria.[18] Here, we progress evidence-based diagnostic criteria and in adults recommend that this requires two of i) clinical/biochemical hyperandrogenism, ii) ovulatory dysfunction or iii) polycystic ovaries on ultrasound and here add elevated anti-mullerian hormone (AMH) levels. We have included the role of AMH in diagnosis in adults but do not recommend AMH or ultrasound in adolescents, due to overlap with normal reproductive physiology.

Exclusion of thyroid disease (thyroid stimulating hormone), hyperprolactinemia (prolactin), and non-classic congenital adrenal hyperplasia (17-hydroxy progesterone) is recommended with further evaluation recommended in those with amenorrhea and more severe clinical features including consideration of hypogonadotropic hypogonadism, Cushing's disease, or suspected androgen producing tumors, noting that overt virilisation is not consistent with PCOS. Clinicians should refer to other relevant guidelines for these diagnoses.

We acknowledge the challenges in defining specific diagnostic features, including around menarche and menopause, where diagnostic features naturally evolve.

The guideline aims to facilitate timely and appropriate diagnosis for women with PCOS, whilst avoiding over diagnosis, especially in adolescents. Specific recommendations of relevance here include:

- ultrasound and anti-mullerian (AMH) levels are not recommended in diagnosis in those within 8 years of menarche
- young women 'at risk' can be identified, where diagnosis is unclear, with follow-up reassessment
- diagnostic features are refined, focused on specificity, to improve diagnostic accuracy.

Resource use in diagnosis will also be reduced with a focus on clinical features in diagnosis, limited indications for ultrasound and AMH as an alternative and with a focus on clinical overt biochemical hyperandrogenism.

We also endorse the recommendation of the National Institutes of Health (NIH) evidence-based methodology workshop of PCOS 2012 that the name of the condition is a distraction and should be changed. We are building on the evidence and guideline efforts with consumer partnership and processes towards a change in the name.

The value and optimal timing of assessment and diagnosis of PCOS should be discussed with the individual patient, considering psychosocial and cultural factors and preferences. Education is vitally important to women at the time of diagnosis, including reassurance about the potential for prevention of complications and about good general reproductive potential and family size, acknowledging some medical assistance may be required. As a general guiding principal, in partnering with women with PCOS in their diagnosis and care, self-empowerment is a priority and personal characteristics, preferences, culture and values should be considered when undertaking assessment, providing information or recommending intervention or treatments.

Interpreting the recommendations

Detailed methods for stakeholder engagement and guideline development can be found in Chapter six: Guideline development methods. In developing and interpreting the guideline, evidence has been evaluated alongside multidisciplinary health professional expertise and consumer perspectives in all stages from conceptualisation, prioritisation, development, review and translation. Variability in resources, health systems and access to healthcare professionals, investigations and therapies was considered across international settings and consistent with best practice, adaptation may be required in translation. Assistance with adaptation can be obtained by contacting helena.teede@monash.edu.

To assist in interpreting guideline recommendations, these are presented by **category, terms used, GRADE and quality of evidence. The category of the recommendations** includes evidence-based or consensus recommendations and have accompanying relevant practice points as described in Table 1. When sufficient evidence was available in PCOS, an evidence-based recommendation was made, where there was insufficient evidence in PCOS, evidence in general or relevant populations was considered and if appropriate and there was consensus, the GDG made consensus recommendations. Practice points highlight important clinical and implementation issues arising from GDG consideration of evidence-based or consensus recommendations.

Table 1: Categories of the PCOS guideline recommendations

EBR	Evidence-based recommendations: Evidence sufficient to inform a recommendation made by the guideline development group.
CR	Consensus recommendations: In the absence of adequate evidence, a consensus recommendation has been made by the guideline development group, also informed by evidence from the general population.
PP	Practice points: Evidence not sought. A practice point has been made by the guideline development group where important issues arose from discussion of evidence-based or consensus recommendations.

The recommendation terms include 'should', 'could' and 'should not'. These terms are informed by the nature of the recommendation (evidence or consensus), the GRADE framework and evidence quality and are independent descriptors reflecting the judgement of multidisciplinary GDG including consumers. They refer to overall interpretation and practical application of the recommendation, balancing benefits and harms. 'Should' is used where benefits of the recommendation exceed harms, and where the recommendation can be trusted to guide practice. Conditional recommendations are reflected using the terms 'could' or 'should/could consider' which are used where either the quality of evidence was limited or the available studies demonstrate little clear advantage of one approach over another, or the balance of benefits to harm was unclear. 'Should not' is used where there is either a lack of appropriate evidence, or the harms may outweigh the benefits.

The GRADE of the recommendation is determined by the GDG from structured, transparent consideration of the GRADE framework[16] including desirable effects, undesirable effects, balance of effects, resource requirements and cost effectiveness, equity, acceptability and feasibility and includes:

❖	Conditional recommendation against the option
❖❖	Conditional recommendation for either the option or the comparison
❖❖❖	Conditional recommendation for the option
❖❖❖❖	Strong recommendation for the option

Quality of the evidence is categorised (see Table 2) according to:

- information about the number and design of studies addressing the outcome
- judgments about the quality of the included studies and/or synthesised evidence, such as risk of bias, inconsistency, indirectness, imprecision and any other considerations that may influence the quality of the evidence
- key statistical data
- classification of the importance of the outcomes.

The quality of evidence reflects the extent to which our confidence in an estimate of the effect is adequate to support a particular recommendation[16] and was largely determined by the expert evidence synthesis team.

Table 2: Quality (certainty) of evidence categories (adapted from GRADE)[16]

High	⊕⊕⊕⊕	Very confident that the true effect lies close to that of the estimate of the effect.
Moderate	⊕⊕⊕◯	Moderate confidence in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is different.
Low	⊕⊕◯◯	Limited confidence in the effect estimate: The true effect may be substantially different from the estimate of the effect.
Very Low	⊕◯◯◯	Very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

GRADE note that quality of evidence is a continuum; any discrete categorisation involves a degree of arbitrariness. Nevertheless, advantages of simplicity, transparency, and vividness outweigh these limitations.[16]

The recommendations summary in Table 3 below applies the **category, descriptive terms, GRADE of the recommendations and the quality of the evidence**. Within the body of the guideline, we outline the clinical need for the question, the clinical question, the evidence summary, the recommendation and practice points and a summary of the justification developed by the GDG and modified by extensive international peer review. The comprehensive evidence reviews, profiles and GRADE frameworks supporting each recommendation, can be found in the supplementary Technical Report.

Aligned to Cochrane methods, certainty of evidence varies significantly across outcomes for each clinical question. In this guideline, the recorded evidence certainty reflects the lowest certainty for the top three critical outcomes for each question. Here, evidence was often stronger for the most critical outcome and often high quality randomised controlled trials (RCTs) had addressed an individual question, but consideration of multiple outcomes and inclusion of additional low-quality studies may have resulted in low certainty evidence overall. These nuances in the evidence were considered by the GDG for every clinical question and are outlined in the technical report and GRADE tables. Hence, an apparent discrepancy may be observed between the strength of the recommendation and the certainty of the evidence. Where this occurs, a justification is added to the guideline under the relevant clinical question.

This is a living guideline as outlined in Chapter 6. For the most rapidly progressing areas of the guideline where new evidence is anticipated in the shorter term, an annual scoping review will be completed to search for additional evidence and the process followed as per Chapter 6. In the recommendations table and summary, these are denoted by #.

Recommendations summary

Table 3: Recommendations

The recommendation and technical report numbers correspond. Consensus recommendations (CR) and practice points (PP) do not have 'GRADE' ratings, however the evidence summaries outline how they were informed by PCOS and general population evidence. # denoted priority for living guideline updates.

No. Living#	Type	Recommendation	Grade/ Quality
1		**Screening, diagnostic and risk assessment and life stages**	
		General principles	
	PP	All diagnostic assessments are recommended for use in accordance with the diagnostic algorithm one.	
1.1		**Irregular cycles and ovulatory dysfunction**	
1.1.1	**CR**	Irregular menstrual cycles are defined as: • Normal in the first year post menarche as part of the 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) When irregular menstrual cycles are present a diagnosis of PCOS should be considered and assessed according to these PCOS Guidelines.	❖❖❖❖
1.1.2	**PP**	The mean age of menarche may differ across populations.	
1.1.3	**PP**	In adolescents with irregular menstrual cycles, the value and optimal timing of assessment and diagnosis of PCOS should be discussed with the patient and their parent/s or guardian/s, considering diagnostic challenges at this life stage and psychosocial and cultural factors.	
1.1.4	**PP**	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 PCOS features before combined oral contraceptive pill (COCP) commencement, those with persisting features and those with significant weight gain in adolescence.	
1.1.5	**PP**	Ovulatory dysfunction can still occur with regular cycles and if anovulation needs to be confirmed serum progesterone levels can be measured.	

No. Living#	Type	Recommendation	Grade/ Quality
1.2		**Biochemical hyperandrogenism**	
1.2.1	**EBR**	Healthcare professionals should use total and free testosterone to assess biochemical hyperandrogenism in the diagnosis of PCOS; free testosterone can be estimated by the calculated free androgen index.	❖❖❖❖ ⊕◯◯◯
1.2.2	**EBR**	If testosterone or free testosterone is not elevated, healthcare professionals could consider measuring androstenedione and dehydroepiandrosterone sulfate (DHEAS), noting their poorer specificity and greater age associated decrease in DHEAS.	❖❖❖ ⊕◯◯◯
1.2.3	**EBR**	Laboratories should use validated, highly accurate tandem mass spectrometry (LC-MS/MS) assays for measuring total testosterone and if needed, for androstenedione and DHEAS. Free testosterone should be assessed by calculation, equilibrium dialysis or ammonium sulfate precipitation.	❖❖❖❖ ⊕◯◯◯
1.2.4	**EBR**	Laboratories should use LC-MS/MS assays over direct immunoassays (e.g. radiometric, enzyme-linked, etc.) for assessing total or free testosterone, which have limited accuracy and demonstrate poor sensitivity and precision for diagnosing hyperandrogenism in PCOS.	❖❖❖❖ ⊕⊕◯◯
1.2.5	**PP**	For the detection of hyperandrogenism in PCOS, the assessment of biochemical hyperandrogenism is of greatest value in patients with minimal or no clinical signs of hyperandrogenism (i.e. hirsutism).	
1.2.6	**PP**	It is very difficult to reliably assess for biochemical hyperandrogenism in women on the combined oral contraceptive pill (COCP) as the pill increases sex hormone-binding globulin and reduces gonadotrophin-dependent androgen production. If already on the COCP, yet assessment of biochemical androgens is imperative, the pill should be withdrawn for a minimum of three months and contraception should be managed otherwise during this time.	
1.2.7	**PP**	Repeated androgen measures for the ongoing assessment of PCOS in adults have a limited role.	
1.2.8	**PP**	In most adolescents, androgen levels reach adult ranges at 12-15 years of age.	
1.2.9	**PP**	If androgen levels are markedly above laboratory reference ranges, causes of hyperandrogenaemia other than PCOS, including ovarian and adrenal neoplastic growths, congenital adrenal hyperplasia, Cushing's syndrome, ovarian hyperthecosis (after menopause), iatrogenic causes, and syndromes of severe insulin resistance, should be considered. However, some androgen-secreting neoplasms are associated with only mild to moderate increases in androgen levels. The clinical history of time of onset and/or rapid progression of symptoms is critical in assessing for an androgen-secreting tumour.	

No. Living#	Type	Recommendation	Grade/ Quality
1.2.10	**PP**	Reference ranges for different methods and laboratories vary widely, and are often based on an arbitrary percentile or variances of the mean from a population that has not been fully characterised and is highly likely to include women with PCOS. Normal values should be determined either by the range of values in a well characterised healthy control population or by cluster analysis of general population values.	
1.2.11	**PP**	Laboratories involved in androgen measurements in females should consider: • determining laboratory normal values by either the range of values in a well characterised healthy control population or by cluster analysis of the values of a large general population • applying the most accurate methods where available • using extraction/chromatography immunoassays as an alternative to mass spectrometry only where adequate expertise is available • future improvements may arise from measurement of 11-oxygenated androgens, and from establishing cut-off levels or thresholds based on large-scale validation in populations of different ages and ethnicities.	
1.3		**Clinical hyperandrogenism**	
1.3.1	**EBR**	The presence of hirsutism alone should be considered predictive of biochemical hyperandrogenism and PCOS in adults.	❖❖❖ ⊕○○○
1.3.2	**EBR**	Healthcare professionals could recognise that female pattern hair loss and acne in isolation (without hirsutism) are relatively weak predictors of biochemical hyperandrogenism.	❖❖❖❖ ⊕○○○
1.3.3	**CR**	A comprehensive history and physical examination should be completed for symptoms and signs of clinical hyperandrogenism, including acne, female pattern hair loss and hirsutism in adults, and severe acne and hirsutism in adolescents.	❖❖❖❖
1.3.4	**CR**	Healthcare professionals should be aware of the potential negative psychosocial impact of clinical hyperandrogenism and should consider the reporting of unwanted excess hair growth and/or female pattern hair loss as being important, regardless of apparent clinical severity.	❖❖❖

No. Living#	Type	Recommendation	Grade/ Quality
1.3.5	CR	A modified Ferriman Gallwey score (mFG) of 4–6 should be used to detect hirsutism, depending on ethnicity, acknowledging that self-treatment is common and can limit clinical assessment.	❖❖❖❖
1.3.6	CR	Healthcare professionals should consider that the severity of hirsutism may vary by ethnicity but the prevalence of hirsutism appears similar across ethnicities.	❖❖❖
1.3.7	PP	Healthcare professionals should: • be aware that standardised visual scales are preferred when assessing hirsutism, such as the mFG scale in combination with a photographic atlas • consider the Ludwig or Olsen visual scales for assessing female pattern hair loss • note that there are no universally accepted visual instruments for assessing the presence of acne • recognise that women commonly treat clinical hyperandrogenism cosmetically, diminishing their apparent clinical severity • appreciate that self-assessment of unwanted excess hair growth, and possibly acne and female pattern hair loss, has a high degree of validity and merits close evaluation, even if overt clinical signs of hyperandrogenism are not readily evident on examination • be aware that only terminal hairs need to be considered in defining hirsutism, and these can reach > 5 mm if untreated, vary in shape and texture and are generally pigmented • note that new-onset severe or worsening hyperandrogenism, including hirsutism, requires further investigation to rule out androgen-secreting tumours and ovarian hyperthecosis • monitor clinical signs of hyperandrogenism, including hirsutism, acne and female pattern hair loss, for improvement or treatment adjustment during therapy.	
1.4		**Ultrasound and polycystic ovarian morphology**	
1.4.1	EBR	Follicle number per ovary (FNPO) should be considered the most effective ultrasound marker to detect polycystic ovarian morphology (PCOM) in adults.	❖❖❖❖ ⊕⊕○○
1.4.2	EBR	Follicle number per ovary (FNPO), follicle number per cross-section (FNPS) and ovarian volume (OV) should be considered accurate ultrasound markers for PCOM in adults.	❖❖❖❖ ⊕⊕○○
1.4.3	CR	PCOM criteria should be based on follicle excess (FNPO, FNPS) and/or ovarian enlargement (OV).	❖❖❖❖
1.4.4	CR	Follicle number per ovary (FNPO) ≥ 20 in at least one ovary should be considered the threshold for PCOM in adults.	❖❖❖❖
1.4.5	CR	Ovarian volume (OV) ≥ 10 ml or follicle number per section (FNPS) ≥ 10 in at least one ovary in adults should be considered the threshold for PCOM if using older technology or image quality is insufficient to allow for an accurate assessment of follicle counts throughout the entire ovary.	❖❖❖❖

No. Living#	Type	Recommendation	Grade/ Quality
1.4.6	**PP**	There are no definitive criteria to define polycystic ovary morphology (PCOM) on ultrasound in adolescents, hence it is not recommended in adolescents.	
1.4.7	**PP**	When an ultrasound is indicated, if acceptable to the individual, the transvaginal approach is the most accurate for the diagnosis of PCOM.	
1.4.8	**PP**	Transabdominal ultrasound should primarily report ovarian volume (OV) with a threshold of ≥ 10 ml or follicle number per section (FNPS) ≥ 10 in either ovary in adults given the difficulty of assessing follicle counts throughout the entire ovary with this approach.	
1.4.9	**PP**	In patients with irregular menstrual cycles and hyperandrogenism, an ovarian ultrasound is not necessary for PCOS diagnosis.	
1.4.10	**PP**	Thresholds for PCOM should be revised regularly with advancing ultrasound technology, and age-specific cut-off values for PCOM should be defined.	
1.4.11	**PP**	There is a need for training in careful and meticulous follicle counting per ovary and clear standardised protocols are recommended for PCOM reporting on ultrasound including at a minimum: • last menstrual period (or stage of cycle) • transducer bandwidth frequency • approach/route assessed • total number of 2–9 mm follicles per ovary • measurements in three dimensions (in cm) or volume of each ovary • other ovarian features and/or pathology including ovarian cysts, corpus lutea, dominant follicles (≥ 10 mm) (which should not be included in ovarian volume calculations) • reliance on the contralateral ovary FNPO for diagnosis of PCOM, where a dominant follicle is noted • uterine features and/or pathology including endometrial thickness and pattern.	
1.5		**Anti-mullerian hormone in the diagnosis of PCOS**	
1.5.1	**EBR**	Serum anti-mullerian hormone (AMH) could be used for defining PCOM in adults.	❖❖❖ ⊕⊕⊕◯
1.5.2	**EBR**	Serum AMH should only be used in accordance with the diagnostic algorithm, noting that in patients with irregular menstrual cycles and hyperandrogenism, an AMH level is not necessary for PCOS diagnosis.	❖❖❖❖ ⊕⊕⊕◯
1.5.3	**EBR**	We recommend that serum AMH should not be used as a single test for the diagnosis of PCOS.	❖❖❖❖ ⊕⊕⊕◯

No. Living#	Type	Recommendation	Grade/ Quality
1.5.4	EBR	Serum AMH should not yet be used in adolescents.	❖❖❖❖ ⊕⊕⊕◯
1.5.5	PP	Either serum AMH or ultrasound may be used to define PCOM; however, both tests should not be performed to limit overdiagnosis.	
1.5.6	PP	Laboratories and healthcare professionals need to be aware of factors that influence AMH in the general population including: • age: Serum AMH generally peaks between the ages of 20-25 years in the general population • body mass index (BMI): Serum AMH is lower in those with higher BMI in the general population • hormonal contraception and ovarian surgery: Serum AMH may be suppressed by current or recent COCP use • menstrual cycle day: Serum AMH may vary across the menstrual cycle.	
1.5.7	PP	Laboratories involved in AMH measurements in females should use population and assay specific cut-offs.	
1.6		**Ethnic variation**	
1.6.1	EBR	Healthcare professionals should be aware of the high prevalence of PCOS in all ethnicities and across world regions, ranging from 10-13% globally using the Rotterdam criteria.	❖❖❖❖ ⊕⊕◯◯
1.6.2	EBR	Healthcare professionals should be aware that PCOS prevalence is similar across world regions and ethnicities, but may be higher in South East Asian and Eastern Mediterranean regions.	❖❖❖❖ ⊕⊕◯◯
1.6.3	PP	Healthcare professionals should be aware that the presentation of PCOS may vary across ethnic groups.	
1.7		**Menopause life stage**	
1.7.1	CR	A diagnosis of PCOS could be considered as enduring/lifelong.	❖❖❖
1.7.2	CR	Healthcare professionals could consider that both clinical and biochemical hyperandrogenism persist in the postmenopause for women with PCOS.	❖❖❖
1.7.3	CR	PCOS diagnosis could be considered postmenopause, if there is a past diagnosis, or a long-term history of oligo-amenorrhoea with hyperandrogenism and/or PCOM, during the earlier reproductive years (age 20-40).	❖❖❖
1.7.4	CR	Further investigations should be considered to rule out androgen-secreting tumours and ovarian hyperthecosis in postmenopausal women presenting with new-onset, severe or worsening hyperandrogenism including hirsutism.	❖❖❖

No. Living#	Type	Recommendation	Grade/ Quality
1.8		**Cardiovascular disease risk**	
1.8.1	**EBR**	Women with PCOS should be considered at increased risk of cardiovascular disease and potentially of cardiovascular mortality, acknowledging that the overall risk of cardiovascular disease in premenopausal women is low.	❖❖❖ ⊕◯◯◯
1.8.2	**EBR**	All women with PCOS should be assessed for cardiovascular disease risk factors.	❖❖❖❖ ⊕◯◯◯
1.8.3	**CR**	All women with PCOS, regardless of age and BMI, should have a lipid profile (cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglyceride level) at diagnosis. Thereafter, frequency of measurement should be based on the presence of hyperlipidaemia and additional risk factors or global cardiovascular risk.	❖❖❖❖
1.8.4	**CR**	All women with PCOS should have blood pressure measured annually and when planning pregnancy or seeking fertility treatment, given the high risk of hypertensive disorders in pregnancy and the associated comorbidities.	❖❖❖❖
1.8.5	**CR**	Funding bodies should recognise that PCOS is highly prevalent with multisystem effects including cardiometabolic disease, and should diversify and increase research support accordingly.	❖❖❖❖
1.8.6	**CR**	Cardiovascular general population guidelines could consider the inclusion of PCOS as a cardiovascular risk factor.	❖❖❖
1.8.7	**CR**	Healthcare professionals, women with PCOS and other stakeholders should all prioritise preventative strategies to reduce cardiovascular risk.	❖❖❖❖
1.8.8	**PP**	Consideration should be given to the differences in cardiovascular risk factors, and cardiovascular disease, across ethnicities (see 1.6.1) and age, when determining frequency of risk assessment.	
1.9		**Impaired glucose tolerance and type 2 diabetes risk**	
1.9.1	**EBR**	Healthcare professionals and women with PCOS should be aware that, regardless of age and BMI, women with PCOS have an increased risk of impaired fasting glucose, impaired glucose tolerance and type 2 diabetes.	❖❖❖❖ ⊕⊕◯◯
1.9.2	**EBR**	Glycaemic status should be assessed at diagnosis in all adults and adolescents with PCOS.	❖❖❖❖ ⊕⊕◯◯
1.9.3	**CR**	Glycaemic status should be reassessed every one to three years, based on additional individual risk factors for diabetes.	❖❖❖❖
1.9.4	**CR**	Healthcare professionals, women with PCOS and other stakeholders should prioritise preventative strategies to reduce type 2 diabetes risk.	❖❖❖❖

No. Living#	Type	Recommendation	Grade/ Quality
1.9.5	CR	Funding bodies should recognise that PCOS is highly prevalent, has significantly higher risk for diabetes and should be funded accordingly.	❖❖❖❖
1.9.6	CR	Diabetes general population guidelines should consider the inclusion of PCOS as an independent risk factor for diabetes.	❖❖❖❖
1.9.7	PP	Healthcare professionals, adults and adolescents with PCOS and their first-degree relatives, should be aware of the increased risk of diabetes and the need for regular glycaemic assessment.	
1.9.8	PP	Women with type 1 and type 2 diabetes have an increased risk of PCOS and screening should be considered in individuals with diabetes.	
		Glycaemic testing	
1.9.9	EBR	Healthcare professionals and women with PCOS should recommend the 75g oral glucose tolerance test (OGTT) as the most accurate test to assess glycaemic status in PCOS, regardless of BMI.	❖❖❖❖ ⊕◯◯◯
1.9.10	EBR	If an OGTT cannot be performed, fasting plasma glucose and/or glycated haemoglobin (HbA1c) could be considered, noting significantly reduced accuracy.	❖❖❖ ⊕◯◯◯
1.9.11	EBR	An OGTT should be considered in all women with PCOS and without pre-existing diabetes, when planning pregnancy or seeking fertility treatment, given the high risk of hyperglycaemia and the associated comorbidities in pregnancy. If not performed preconception, an OGTT could be offered at the first prenatal visit and all women with PCOS should be offered the test at 24-28 weeks gestation.	❖❖❖ ⊕◯◯◯
1.9.12	PP	Insulin resistance is a pathophysiological factor in PCOS, however, clinically available insulin assays are of limited clinical relevance and are not recommended in routine care (refer to 3.1.10).	
1.10		**Obstructive sleep apnea**	
1.10.1	EBR	Healthcare professionals should be aware that women with PCOS have significantly higher prevalence of obstructive sleep apnea (OSA) compared to women without PCOS, independent of BMI.	❖❖❖❖ ⊕⊕⊕◯
1.10.2	EBR	Women with PCOS should be assessed for symptoms (i.e. snoring in combination with waking unrefreshed from sleep, daytime sleepiness or fatigue) and if present, screen with validated tools or refer for assessment.	❖❖❖❖ ⊕⊕⊕◯
1.10.3	PP	Simple obstructive sleep apnea screening questionnaires (such as the Berlin questionnaire, validated in the general population) can assist in identifying obstructive sleep apnea in women with PCOS, noting that diagnosis requires a formal sleep study.	
1.10.4	PP	Goals of treatment should target obstructive sleep apnea related symptom burden.	

No. Living#	Type	Recommendation	Grade/ Quality
1.11		**Endometrial hyperplasia and cancer**	
1.11.1	**EBR**	Healthcare professionals should be aware that premenopausal women with PCOS have markedly higher risk of developing endometrial hyperplasia and endometrial cancer.	❖❖❖❖ ⊕◯◯◯
1.11.2	**PP**	Women with PCOS should be informed about the increased risk of endometrial hyperplasia and endometrial cancer, acknowledging that the overall chance of developing endometrial cancer is low, therefore routine screening is not recommended.	
1.11.3	**PP**	Long-standing untreated amenorrhea, higher weight, type 2 diabetes and persistent thickened endometrium are additional to PCOS as risk factors for endometrial hyperplasia and endometrial cancer.	
1.11.4	**PP**	Women with PCOS should be informed of preventative strategies including weight management, cycle regulation and regular progestogen therapy.	
1.11.5	**PP**	When excessive endometrial thickness is detected, consideration of a biopsy with histological analysis and withdrawal bleed is indicated.	
1.12		**Risks in relatives**	
1.12.1	**EBR**	Healthcare professionals could consider that fathers and brothers of women with PCOS may have an increased prevalence of metabolic syndrome, type 2 diabetes, and hypertension.	❖❖❖ ⊕◯◯◯
1.12.2	**PP**	The cardiometabolic risk in female first-degree relatives of women with PCOS remains inconclusive.	
2		**Prevalence, screening and management of psychological features and models of care**	
		General principles	
	PP	Psychological features are common and important component of PCOS that all health professionals should be aware of.	
	PP	Funding bodies should recognise that PCOS is highly prevalent, has significantly higher psychological disorders which should be prioritised and funded accordingly.	
2.1		**Quality of life**	
2.1.1	**EBR**	Healthcare professionals and women should recognise the adverse impact of PCOS and/or PCOS features on quality of life in adults.	❖❖❖❖ ⊕⊕◯◯
2.1.2	**PP**	Women with PCOS should be asked about their perception of PCOS related symptoms, impact on quality of life, key concerns and priorities for management.	

No. Living#	Type	Recommendation	Grade/ Quality
2.2		**Depression and anxiety**	
2.2.1	**EBR**	Healthcare professionals should be aware of the high prevalence of moderate to severe depressive symptoms and depression in adults and adolescents with PCOS and should screen for depression in all adults and adolescents with PCOS, using regionally validated screening tools.	❖❖❖❖ ⊕⊕⊕⊕
2.2.2	**EBR**	Healthcare professionals should be aware of the high prevalence of moderate to severe anxiety symptoms and anxiety disorders in adults and should screen for anxiety in all adults with PCOS, using regionally validated screening tools.	❖❖❖❖ ⊕⊕⊕⊕
2.2.3	**CR**	If moderate or severe depressive or anxiety symptoms are detected, practitioners should further assess, refer appropriately or offer treatment.	❖❖❖❖
2.2.4	**PP**	Severity of symptoms and clinical diagnosis of depression or anxiety should guide management. The optimal interval for anxiety and depression screening is not known. A pragmatic approach could include screening at diagnosis with repeat screening based on clinical judgement, risk factors, comorbidities and life events, including the perinatal period. Screening for mental health disorders comprises assessment of risk factors, symptoms, and risk of self-harm and suicidal intent.	
2.3		**Psychosexual function**	
2.3.1	**CR**	Healthcare professionals could consider the multiple factors that can influence psychosexual function in PCOS including higher weight, hirsutism, mood disorders, infertility and PCOS medications.	❖❖❖
2.3.2	**CR**	Permission to discuss psychosexual function should be sought noting that the diagnosis of psychosexual dysfunction requires both low psychosexual function, combined with related distress.	❖❖❖❖
2.4		**Body Image**	
2.4.1	**EBR**	Healthcare professionals should be aware that features of PCOS can have a negative impact on body image.	❖❖❖❖ ⊕⊕○○
2.5		**Eating disorders and disordered eating**	
2.5.1	**EBR**	Eating disorders and disordered eating should be considered in PCOS, regardless of weight, especially in the context of weight management and lifestyle interventions (see sections 2.4 and 3.6).	❖❖❖ ⊕⊕○○
2.5.2	**PP**	If disordered eating or eating disorders are suspected, appropriately qualified practitioners should further assess via a full diagnostic interview. If an eating disorder or disordered eating is detected, appropriate management and support should be offered.	

No. Living#	Type	Recommendation	Grade/ Quality
2.6		**Information resources, models of care, cultural and linguistic considerations**	
2.6.1		**Information needs**	
2.6.1.1	**EBR**	Tailored information, education and resources that are high-quality, culturally appropriate and inclusive should be provided to all with PCOS.	❖❖❖❖ ⊕⊕⊕◯
2.6.1.2	**EBR**	Information, education and resources are a high priority for patients with PCOS and should be provided in a respectful and empathic manner.	❖❖❖❖ ⊕⊕⊕◯
2.6.1.3	**CR**	Entities responsible for health professional education should ensure that information and education on PCOS is systemically embedded at all levels of health professional training to address knowledge gaps.	❖❖❖❖
2.6.1.4	**PP**	The diversity of the population should be considered when adapting practice paradigms. Healthcare professional opportunities should be optimised at all stages of graduate and postgraduate training, continuing professional development and in practice support resources.	
2.6.1.5	**PP**	Women should be counselled on the risk of misinformation and guided to evidence-based resources.	
2.6.2		**Models of care**	
2.6.2.1	**CR**	Models of care should prioritise equitable access to evidence-based primary care with pathways for escalation to integrated specialist and multidisciplinary services as required.	❖❖❖❖
2.6.2.2	**PP**	Strategies to deliver optimal models of care could include health professional education, care pathways, virtual care, broader health professional engagement (e.g. nurse practitioners) and coordination tools.	
2.6.3		**Support to manage PCOS**	
2.6.3.1	**CR**	Public health actors should consider increasing societal awareness and education on PCOS to reduce stigma and marginalisation.	❖❖❖
2.6.3.2	**PP**	Culturally appropriate resources and education on PCOS across the life span for families of those with the condition, should be considered.	

No. Living#	Type	Recommendation	Grade/ Quality
2.6.4		**Patient care**	
2.6.4.1	**EBR**	Healthcare professionals should employ shared decision making and support patient agency or ability to take independent actions to manage their health and care.	❖❖❖❖ ⊕⊕⊕◯
2.6.4.2	**EBR**	The importance of being knowledgeable about PCOS, of applying evidence-based practices when sharing news on diagnosis, treatment and health implications, and of ascertaining and focusing on patient priorities, should be recognised.	❖❖❖❖ ⊕⊕⊕◯
2.6.4.3	**CR**	Healthcare system leaders should enable system wide changes to support health professional training, knowledge and practice in sharing news optimally, shared decision making and patient agency, including ensuring adequate consultation time and accessible resources.	❖❖❖❖
2.6.4.4	**PP**	Evidence-based strategies for shared decision making and for sharing news (such as the SPIKES framework) are readily available and should be used to inform PCOS care. All healthcare professionals partnering with women with PCOS should be knowledgeable in sharing news, in shared decision making and in supporting patient self-management. Evidence-based strategies and resources can be used to support patient activation, which refers to modifiable knowledge, skills, ability, confidence and willingness to self-manage one's own health and care.	
2.7		**Psychological therapy**	
2.7.1	**CR**	Women with PCOS diagnosed with depression, anxiety, and/or eating disorders should be offered psychological therapy guided by regional general population guidelines and the preference of the woman with PCOS.	❖❖❖❖
2.7.2	**CR**	Women with PCOS with disordered eating, body image distress, low self-esteem, problems with feminine identity, or psychosexual dysfunction should be offered evidence-based treatments (e.g. cognitive behaviour therapy) where appropriate.	❖❖❖❖
2.8		**Antidepressant and anxiolytic treatment**	
2.8.1	**CR**	Psychological therapy could be considered first-line management, and antidepressant medications considered in adults where mental health disorders are clearly documented and persistent, or if suicidal symptoms are present, based on general population guidelines.	❖❖❖
2.8.2	**PP**	Lifestyle intervention and other therapies (e.g. COCP, metformin, laser hair removal) that target PCOS features should be considered, given their potential to improve psychological symptoms. Where pharmacological treatment for anxiety and depression is offered in PCOS, healthcare professionals should apply caution: • to avoid inappropriate treatment with antidepressants or anxiolytics • to limit use of agents that exacerbate PCOS symptoms, including weight gain. Healthcare professionals should be aware that not managing anxiety and depression may impact adherence to PCOS treatment/management.	

No. Living#	Type	Recommendation	Grade/ Quality
3		**Lifestyle management**	
3.1		**Effectiveness of lifestyle interventions**	
3.1.1	**EBR**	Lifestyle intervention (exercise alone or multicomponent diet combined with exercise and behavioural strategies) should be recommended for all women with PCOS, for improving metabolic health including central adiposity and lipid profile.	❖❖❖❖ ⊕◯◯◯
3.1.2	**CR**	Healthy lifestyle behaviours encompassing healthy eating and/or physical activity should be recommended in all women with PCOS to optimise general health, quality of life, body composition and weight management (maintaining weight, preventing weight gain and/or modest weight loss).	❖❖❖❖
3.1.3	**PP**	Healthcare professionals should be aware that lifestyle management is a core focus in PCOS management.	
3.1.4	**PP**	Lifestyle management goals and priorities should be co-developed in partnership with women with PCOS, and value women's individualised preferences.	
3.1.5	**PP**	There are benefits to a healthy lifestyle even in the absence of weight loss.	
3.1.6	**PP**	In those with higher weight, weight management can be associated with significant clinical improvements and the following key points need to be considered including: • a lifelong focus on prevention of further weight gain • if the goal is to achieve weight loss, a tailored energy deficit could be prescribed for women, considering individual energy requirements, body weight and physical activity levels • the value of improvement in central adiposity (e.g. waist circumference, waist-hip ratio) or metabolic health • the need for ongoing assessment and support.	
3.1.7	**PP**	Healthcare professionals should be aware of weight stigma when discussing lifestyle management with women with PCOS [see 3.6].	
3.1.8	**PP**	Healthy lifestyle and optimal weight management, in the context of structured, intensive and ongoing clinical support, appears equally effective in PCOS as in the general population.	
3.1.9	**PP**	In those who are not overweight, in the adolescent and at key life points, the focus should be on healthy lifestyle and the prevention of excess weight gain.	
3.1.10	**PP**	Insulin resistance is a pathophysiological factor in PCOS, however, clinically available insulin assays are of limited clinical relevance and should not be used in routine care (refer to 1.9.12).	

No. Living#	Type	Recommendation	Grade/ Quality
3.2		**Behavioural strategies**	
3.2.1	**CR**	Lifestyle interventions could include behavioural strategies such as goal-setting, self-monitoring, problem solving, assertiveness training, reinforcing changes and relapse prevention, to optimise weight management, healthy lifestyle and emotional wellbeing in women with PCOS.	❖❖❖
3.2.2	**PP**	Behavioural support could include: goal-setting, problem solving, self-monitoring and reviewing, or SMART goals (Specific, Measurable, Achievable, Realistic and Timely).	
3.2.3	**PP**	Comprehensive healthy behavioural or cognitive behavioural interventions could be considered to increase support, engagement, retention, adherence and maintenance of healthy lifestyle and improve health outcomes in women with PCOS.	
3.3		**Dietary interventions**	
3.3.1	**EBR**	Healthcare professionals and women should consider that there is no evidence to support any one type of diet composition over another for anthropometric, metabolic, hormonal, reproductive or psychological outcomes.	❖❖❖ ⊕○○○
3.3.2	**CR**	Any diet composition consistent with population guidelines for healthy eating will have health benefits, and within this, healthcare professionals should advise sustainable healthy eating tailored to individual preferences and goals.	❖❖❖❖
3.3.3	**PP**	Tailoring of dietary changes to food preferences, allowing for a flexible, individual and co-developed approach to achieving nutritional goals and avoiding unduly restrictive and nutritionally unbalanced diets, are important, as per general population guidelines.	
3.3.4	**PP**	Barriers and facilitators to optimise engagement and adherence to dietary change should be discussed, including psychological factors, physical limitations, socioeconomic and sociocultural factors, as well as personal motivators for change. The value of broader family engagement should be considered. Referral to suitably trained allied healthcare professionals needs to be considered when women with PCOS need support with optimising their diet.	
3.4		**Exercise interventions**	
3.4.1	**EBR**	Healthcare professionals and women could consider that there is a lack of evidence supporting any one type and intensity of exercise being better than another for anthropometric, metabolic, hormonal, reproductive or psychological outcomes.	❖❖❖ ⊕○○○
3.4.2	**CR**	Any physical activity consistent with population guidelines will have health benefits and within this, healthcare professionals should advise sustainable physical activity based on individual preferences and goals.	❖❖❖❖

No. Living#	Type	Recommendation	Grade/ Quality
3.4.3	CR	Healthcare professionals should encourage and advise the following in concordance with general population physical activity guidelines: • All adults should undertake physical activity as doing some physical activity is better than none. • Adults should limit the amount of time spent being sedentary (e.g. sitting, screen time) as replacing sedentary time with physical activity of any intensity (including light intensity) provides health benefits. For the prevention of weight gain and maintenance of health, adults (18-64 years) should aim for a minimum of 150 to 300 minutes of moderate-intensity activities or 75 to 150 minutes of vigorous-intensity aerobic activity per week or an equivalent combination of both spread throughout the week, plus muscle strengthening activities (e.g. resistance/flexibility) on two non-consecutive days per week. For promotion of greater health benefits including modest weight loss and prevention of weight regain, adults (18-64 years) should aim for a minimum of 250 min/week of moderate-intensity activities or 150 min/week of vigorous intensities or an equivalent combination of both, plus muscle strengthening activities (e.g. resistance/flexibility) ideally on two non-consecutive days per week. Adolescents should aim for at least 60 minutes of moderate- to vigorous-intensity physical activity per day including activities that strengthen muscle and bone, at least three times per week.	❖❖❖❖
3.4.4	PP	Physical activity is any bodily movement produced by skeletal muscles that requires energy expenditure. It includes leisure time physical activity, transportation (e.g. walking or cycling), occupational (i.e. work), household chores, playing games, sports or planned exercise, or activities in the context of daily, family and community activities.	
3.4.5	PP	Aerobic activity is best performed in bouts of at least 10 minutes duration, aiming to achieve at least 30 minutes daily on most days.	
3.4.6	PP	Barriers and facilitators to optimise engagement and adherence to physical activity should be discussed, including psychological factors (e.g. body image concerns, fear of injury, fear of failure, mental health), personal safety concerns, environmental factors, physical limitations, socioeconomic factors, sociocultural factors, and personal motivators for change. The value of broader family engagement should be considered. Referral to suitably trained allied healthcare professionals needs to be considered for optimising physical activity in women with PCOS.	
3.4.7	PP	Self-monitoring including with fitness tracking devices and technologies for step count and exercise intensity, could be considered as an adjunct to support and promote active lifestyles and minimise sedentary behaviours.	

No. Living#	Type	Recommendation	Grade/ Quality
3.5		**Factors affecting weight gain in PCOS**	
3.5.1	**EBR**	Healthcare professionals and women with PCOS could consider that there is a lack of consistent evidence of physiological or behavioural lifestyle differences, related to weight, in women with PCOS compared to women without PCOS.	❖❖❖ ⊕◯◯◯
3.5.2	**PP**	Whilst the specific mechanisms are unclear, it is recognised that many women with PCOS will have underlying mechanisms that drive greater longitudinal weight gain and higher BMI which may: • underpin greater challenges with weight management • highlight the importance of lifelong healthy lifestyle strategies and prevention of excess weight gain • assist women with PCOS and healthcare professionals in forming realistic, tailored lifestyle goals.	
3.6		**Weight stigma**	
3.6.1	**EBR**	Many women with PCOS experience weight stigma in healthcare and other settings and the negative biopsychosocial impacts of this should be recognised.	❖❖❖❖ ⊕⊕◯◯
3.6.2	**CR**	Healthcare professionals should be aware of their weight biases and the impact this has on their professional practice and on women with PCOS.	❖❖❖❖
3.6.3	**CR**	Health policy makers, managers and educators should promote awareness of weight stigma and invest in weight stigma education and minimisation strategies.	❖❖❖❖
3.6.4	**PP**	Healthcare professionals should be aware of weight-inclusive practices which promote acceptance of and respect for body size diversity and focus on improvement of health behaviours and health outcomes for people of all sizes. In PCOS this includes: • acknowledging that whilst higher weight is a risk factor for PCOS and its complications, it is only one indicator of health and broader factors should be assessed • asking permission to discuss and measure weight and using strategies to minimise discomfort (e.g. blind weighing) • recognising that the terms 'overweight' and 'obese/obesity' can be stigmatising with suggested alternatives including 'higher weight' • if weighing, explaining how weight information will be used to inform risks prevention and treatment and how not knowing may impact on recommendations • ensuring appropriate equipment is available for women of all sizes • offering options of weight-centric care (promoting intentional weight loss) or weight-inclusive care (promoting healthy lifestyle change without focusing on intentional weight loss) tailored to individual goals and preferences • offering all women best practice assessment, treatment and support regardless of weight, acknowledging that weight may be a non-modifiable risk factor when using lifestyle modification alone.	
3.6.5	**PP**	Increasing awareness of weight stigma among family members of women and adolescents with PCOS should be considered.	

No. Living#	Type	Recommendation	Grade/ Quality
4		**Management of non-fertility features**	
4.1		**Pharmacology treatment principles in PCOS**	
	PP	Shared decision making between the patient (and parent/s or guardian/s, if the patient is a child) and the healthcare professional is required.	
	PP	An individual's characteristics, preferences and values must be elicited and considered when recommending any intervention alone or in combination.	
	PP	Understanding how individual adults and adolescents value treatment outcomes is essential when prescribing medications.	
	PP	Medical therapy is generally not approved for use specifically in PCOS and recommended use is therefore evidence-based, but off-label. Healthcare professionals need to inform adults, adolescents and their parents/s or guardian/s and discuss the evidence, possible concerns and side-effects. Regulatory agencies should consider approval of evidence-based medications for use in PCOS.	
4.2		**Combined oral contraceptive pills**	
4.2.1	**EBR**	The combined oral contraceptive pill (COCP) could be recommended in reproductive age adults with PCOS for management of hirsutism and/or irregular menstrual cycles.	❖❖❖ ⊕◯◯◯
4.2.2	**EBR**	The COCP could be considered in adolescents at risk or with a clear diagnosis of PCOS for management of hirsutism and/or irregular menstrual cycles.	❖❖❖ ⊕◯◯◯
4.2.3	**EBR**	Health professionals could consider that there is no clinical advantage of using high dose ethinylestradiol (≥ 30 µg) versus low dose ethinylestradiol (< 30 µg) when treating hirsutism in adults with PCOS.	❖❖❖ ⊕◯◯◯
4.2.4	**EBR**	General population guidelines should be considered when prescribing COCP in adults and adolescents with PCOS as specific types or doses of progestins, estrogens or combinations of COCP cannot currently be recommended.	❖❖❖ ⊕◯◯◯
4.2.5	**EBR**	The 35 µg ethinyl estradiol plus cyproterone acetate preparations should be considered as second-line therapy over other COCPs, balancing benefits and adverse effects, including venous thromboembolic risks.	❖❖❖ ⊕◯◯◯

No. Living#	Type	Recommendation	Grade/ Quality
4.2.6	EBR	Progestin only oral contraceptives may be considered for endometrial protection, based on general population guidelines, acknowledging that evidence in women with PCOS is limited.	❖❖❖ ⊕○○○
4.2.7	PP	When prescribing COCPs in adults and adolescents with PCOS, and adolescents at risk of PCOS: • It is important to address main presenting symptoms and consider other treatments such as cosmetic therapies. • Shared decision making (including accurate information and reassurance on the efficacy and safety of COCP) is recommended and likely to improve adherence. • Natural estrogen preparations and the lowest effective estrogen doses (such as 20-30 micrograms of ethinyl estradiol or equivalent), need consideration, balancing efficacy, metabolic risk profile, side-effects, cost and availability. • The relatively limited evidence on COCPs specifically in PCOS needs to be appreciated with practice informed by general population guidelines • The relative and absolute contraindications and side-effects of COCPs need to be considered and be the subject of individualised discussion. • PCOS specific features such as higher weight and cardiovascular risk factors, need to be considered.	
4.3		**Metformin**	
4.3.1	EBR	Metformin alone should be considered in adults with PCOS and a BMI ≥ 25 kg/m² for anthropometric, and metabolic outcomes including insulin resistance, glucose, and lipid profiles.	❖❖❖ ⊕○○○
4.3.2	EBR	Metformin alone could be considered in adolescents at risk of or with PCOS for cycle regulation, acknowledging limited evidence.	❖❖❖ ⊕○○○
4.3.3	CR	Metformin alone may be considered in adults with PCOS and BMI < 25 kg/m², acknowledging limited evidence.	❖❖❖
4.3.4	PP	Where metformin is prescribed the following need to be considered: • Shared decision making needs to consider feasibility and effectiveness of active lifestyle intervention. Women should be informed that metformin and active lifestyle intervention have similar efficacy. • Mild adverse effects, including gastrointestinal side-effects are generally dose dependent and self-limiting. • Starting at a low dose, with 500 mg increments 1-2 weekly and extended-release preparations may minimise side-effects and improve adherence. • Suggested maximum daily dose is 2.5 g in adults and 2 g in adolescents. • Use appears safe long-term, based on use in other populations, however indications for ongoing requirement needs to be considered. • Use may be associated with low vitamin B12 levels, especially in those with risk factors for low vitamin B12 (e.g. diabetes, post bariatric/metabolic surgery, pernicious anaemia, vegan diet etc.), where monitoring should be considered.	

No. Living#	Type	Recommendation	Grade/ Quality
4.4		**Metformin and combined oral contraceptive pills**	
4.4.1	**EBR**	COCP could be used over metformin for management of hirsutism in irregular menstrual cycles in PCOS.	❖❖❖ ⊕◯◯◯
4.4.2	**EBR**	Metformin could be used over COCP for metabolic indications in PCOS.	❖❖❖ ⊕◯◯◯
4.4.3	**EBR**	The combination of COCP and metformin could be considered to offer little additional clinical benefit over COCP or metformin alone, in adults with PCOS with a BMI ≤30 kg/m².	❖❖❖ ⊕◯◯◯
4.4.4.	**PP**	In combination with the COCP, metformin may be most beneficial in high metabolic risk groups including those with a BMI > 30 kg/m², diabetes risk factors, impaired glucose tolerance or high-risk ethnic groups.	
4.4.5	**PP**	Where COCP is contraindicated, not accepted or not tolerated, metformin may be considered for irregular menstrual cycles. For hirsutism, other interventions may be needed.	
4.5		**Anti-obesity pharmacological agents**	
4.5.1	**CR**	Anti-obesity medications including liraglutide, semaglutide, both glucagon-like peptide-1 (GLP-1) receptor agonists and orlistat, could be considered, in addition to active lifestyle intervention, for the management of higher weight in adults with PCOS as per general population guidelines.	❖❖❖
4.5.2	**PP**	Healthcare professionals should ensure concurrent effective contraception when pregnancy is possible, for women who take GLP-1 receptor agonists, as pregnancy safety data are lacking.	
4.5.3	**PP**	Gradual dose escalation for GLP-1 receptor agonists is recommended to reduce gastrointestinal adverse effects.	
4.5.4	**PP**	Shared decision making, when discussing GLP-1 receptor agonist use with women with PCOS, needs to consider side-effects, and the potential need for long-term use in weight management, given the high risk for weight regain after discontinuation, and the lack of long-term safety data.	
4.6		**Anti-androgen pharmacological agents**	
4.6.1	**EBR**	In combination with effective contraception, anti-androgens could be considered to treat hirsutism in women with PCOS, if there is a suboptimal response after a minimum of six months of COCP and/or cosmetic therapy.	❖❖❖ ⊕◯◯◯

No. Living#	Type	Recommendation	Grade/ Quality
4.6.2	CR	Given the negative psychological impact of female pattern hair loss, anti-androgens in combination with COCP could be trialed, acknowledging the lack of evidence in the PCOS population.	❖❖❖
4.6.3	PP	Whenever pregnancy is possible, healthcare professionals must educate and counsel women and adolescents, parents/s or guardian/s, regarding the risks of incomplete development of external genital structures of male fetuses (undervirilisation) when anti-androgens are used. To prevent this, women who can get pregnant should be strongly counseled to use effective contraception (e.g. intrauterine device or COCPs).	
4.6.4	PP	Anti-androgens could be considered to treat hirsutism, in the presence of another effective form of contraception, for women with contraindications for COCP therapy or when COCPs are poorly tolerated.	
4.6.5	PP	When prescribing anti-androgens, based on general population recommendations, healthcare professionals should consider that: • spironolactone at 25-100 mg/day appears to have lower risks of adverse effects • cyproterone acetate at doses ≥ 10 mg is not advised due to an increased risk including for meningioma • finesteride has an increased risk of liver toxicity • flutamide and bicalutamide have an increased risk of severe liver toxicity. The relatively limited evidence on anti-androgens in PCOS needs to be appreciated with small numbers of studies and limited numbers of participants.	
4.7		**Inositol**	
4.7.1	EBR	Inositol (in any form) could be considered in women with PCOS based on individual preferences and values, noting limited harm, potential for improvement in metabolic measures, yet with limited clinical benefits including in ovulation, hirsutism or weight.	❖❖❖ ⊕○○○
4.7.2	EBR	Metformin should be considered over inositol for hirsutism and central adiposity, noting that metformin has more gastrointestinal side-effects than inositol.	❖❖❖ ⊕○○○
4.7.3	PP	Women taking inositol and other complementary therapies are encouraged to advise their health professional.	
4.7.4	PP	Specific types, doses or combinations of inositol cannot currently be recommended in adults and adolescents with PCOS, due to a lack of quality evidence.	
4.7.5	PP	Shared decision making should include discussion that regulatory status and quality control of inositol in any form (like other nutrient supplements) can differ from those for pharmacological products and doses and qualities may vary.	
4.7.6	PP	Policy makers and healthcare professionals have a responsibility to ensure women have access to unconflicted, evidence-based information to inform shared-decision making, whilst also acknowledging and respecting individual values and preferences, including for complementary therapies.	

No. Living#	Type	Recommendation	Grade/ Quality
4.8		**Mechanical laser and light therapies for hair reduction**	
4.8.1	**EBR**	Mechanical laser and light therapies should be considered for reducing facial hirsutism and for related depression, anxiety and quality of life in women with PCOS.	❖❖❖ ⊕○○○
4.8.2	**EBR**	A greater number of laser treatment sessions may be required in women with PCOS, compared to women with idiopathic hirsutism, to achieve hair reduction.	❖❖❖ ⊕○○○
4.8.3	**CR**	Adverse effects appear limited in the hands of experienced and suitably qualified providers, and women should be encouraged to seek hair reduction therapies from such providers.	❖❖❖❖
4.8.4	**PP**	Where laser hair removal is prescribed, the following need to be considered: • Wavelength and delivery of laser treatment varies by skin and hair colour. • Laser is relatively ineffective in women with blond, grey or white hair. • The addition of COCP, with or without anti-androgens, to laser treatment may provide greater hair reduction and maintenance compared to laser alone. Low and high fluence laser appear to have similar efficacy in reducing facial hair, while low fluence laser has reduced associated pain.	
4.8.5	**PP**	Mechanical hair removal with Intense Pulse Light (IPL) could be considered, albeit benefits may be less pronounced compared to laser treatment. There is no evidence to support the efficacy of home-based IPL kits.	
4.8.6	**PP**	Policy makers should consider funding this evidence-based effective therapy for women with PCOS to alleviate distressing symptoms of hirsutism, and related negative impact on quality of life, body image and psychological health.	
4.9		**Bariatric/metabolic surgery**	
4.9.1	**CR**	Bariatric/metabolic surgery could be considered to improve weight loss, hypertension, diabetes (prevention and treatment), hirsutism, irregular menstrual cycles, ovulation and pregnancy rates in women with PCOS.	❖❖❖
4.9.2	**CR**	Bariatric/metabolic surgery in women with PCOS should be informed by general population guidelines.	❖❖❖❖
4.9.3	**CR**	PCOS is a metabolic condition and could be considered an indication at a lower BMI threshold for bariatric/metabolic surgery similarly to other metabolic conditions including diabetes.	❖❖❖
4.9.4	**CR**	Women should be strongly counseled on the likelihood of rapid return of fertility and the need to commit to effective contraception, ideally prior to surgery. Even when pregnancy is desired, contraception should be continued until a stable weight is achieved, usually after one year, to avoid significantly increased risk of growth restriction, prematurity, small for gestational age, pregnancy complications and prolonged hospitalisation of the infant.	❖❖❖❖

No. Living#	Type	Recommendation	Grade/ Quality
4.10		**Pregnancy outcomes**	
4.10.1	**EBR**	Women with PCOS have higher risk pregnancies, and healthcare professionals should ensure that PCOS status is identified during antenatal care, and appropriate monitoring and support is provided.	❖❖❖❖ ⊕◯◯◯
4.10.2	**EBR**	Healthcare professionals should recognise that pregnant women with PCOS have an increased risk of: • higher gestational weight gain • miscarriage • gestational diabetes • hypertension in pregnancy and preeclampsia • intrauterine growth restriction, small for gestational age babies and low birth weight • preterm delivery • caesarean section.	❖❖❖❖ ⊕◯◯◯
4.10.3	**EBR**	Assisted reproductive technology in women with PCOS should be considered as not conferring additional risk of miscarriage, preterm birth, impaired fetal growth and caesarean section, over that observed in women without PCOS.	❖❖❖ ⊕◯◯◯
4.10.4	**EBR**	Women with PCOS should be considered as not having an increased risk of large for gestational age babies, macrosomia and instrumental delivery.	❖❖❖ ⊕◯◯◯
4.10.5	**PP**	Early lifestyle intervention should be offered to pregnant women with PCOS, given the risk of higher baseline weight, excess gestational weight gain and pregnancy complications.	
4.10.6	**PP**	Blood pressure measurement should be performed when planning pregnancy or seeking fertility treatment, given the high risk of hypertensive disorders in pregnancy and the associated comorbidities in women with PCOS.	
4.10.7	**PP**	An OGTT should be offered to all women with PCOS when planning pregnancy or seeking fertility treatment, given the high risk of hyperglycaemia and the associated comorbidities in pregnancy. If not performed in the preconception phase, an OGTT should be offered at the first antenatal visit and repeated at 24-28 weeks gestation.	

No. Living#	Type	Recommendation	Grade/ Quality
4.11		**Metformin in pregnancy**	
4.11.1	**EBR**	Healthcare professionals should be aware that metformin in pregnant women with PCOS has not been shown to prevent: • gestational diabetes • late miscarriage (12 weeks +1 day to 21 weeks +6 days gestational age) • hypertension in pregnancy • pre-eclampsia • macrosomia or birthweight ≥ 4000 g.	❖❖❖❖ ⊕⊕◯◯
4.11.2	**EBR**	Metformin could be considered in some circumstances (e.g. risk for preterm birth), to reduce preterm delivery and limit excess gestational weight gain, in pregnant women with PCOS.	❖❖❖ ⊕⊕⊕◯
4.11.3	**PP**	Women should be counselled that the consequences of metformin exposure on long-term offspring health remain unclear and there is a suggestion of increased childhood weight, although causality is not certain.	
4.11.4	**PP**	Side-effects of metformin are mostly mild, transient gastrointestinal symptoms and are not worse in pregnancy.	
5		**Assessment and treatment of infertility**	
		General principles	
	PP	All fertility treatment in PCOS should be guided by the fertility management algorithm.	
	PP	Those with PCOS should be reassured that pregnancy can often be successfully achieved either naturally or with assistance.	
	PP	Prenatal vitamins supplementation should be commenced with ovulation induction therapy aligned to routine preconception care.	
	PP	Pregnancy should be excluded prior to ovulation induction therapy.	
	PP	The use of ovulation induction agents, including letrozole, metformin and clomiphene citrate is off-label in many countries. Where off-label use of ovulation induction agents is allowed, healthcare professionals need to inform women and discuss the evidence, possible concerns and side-effects.	
	PP	There should be ongoing monitoring of patients for adverse effects and infants for congenital anomalies in all studies conducted with ovulation induction agents and these should be reported in any published papers.	

No. Living#	Type	Recommendation	Grade/ Quality
5.1		**Preconception risk factors**	
5.1.1	**EBR**	Women with PCOS should be counseled on the adverse impact of excess weight on clinical pregnancy, miscarriage and live birth rates, following infertility treatment.	❖❖❖❖ ⊕◯◯◯
5.1.2	**CR**	Consistent with routine preconception care, in women with PCOS planning pregnancy, weight, blood pressure, smoking, alcohol, diet and nutritional status, folate supplementation (higher dose in those with BMI > 30), exercise, sleep and mental, emotional and sexual health should be considered and optimised to improve reproductive and pregnancy outcomes and overall health.	❖❖❖❖
5.1.3	**PP**	A reproductive life plan and age appropriate education on optimising reproductive health, is recommended in adolescents and women with PCOS, including healthy lifestyle, prevention of excess weight gain, and optimising preconception risk factors.	
5.1.4	**PP**	Healthcare professionals are encouraged to seek permission and if given, to assess weight and body mass index and initiate a dialogue on the importance of weight and lifestyle on women's health before pregnancy. This requires caution to avoid weight stigma and needs to consider the cultural, social and environmental determinants of health (see 3.6).	
5.1.5	**PP**	Chronic conditions such as diabetes, high blood pressure, anxiety, depression and other mental health conditions, should be optimally managed and women should be counseled regarding the risk of adverse pregnancy outcomes.	
5.2		**Tubal patency testing**	
5.2.1	**CR**	In women with PCOS and infertility due to anovulation alone with normal semen analysis, the risks, benefits, costs and timing and techniques of tubal patency testing in relation to the cost and complexity of the treatment, should be considered on an individual basis, depending on personal history and population prevalence, prior to starting ovulation induction with timed intercourse or intrauterine insemination.	❖❖❖
5.3		**Letrozole**	
5.3.1	**EBR**	Letrozole should be the first-line pharmacological treatment for ovulation induction in infertile anovulatory women with PCOS, with no other infertility factors.	❖❖❖❖ ⊕⊕⊕⊕
5.3.2	**PP**	The use of letrozole is still off-label in many countries. Where it is not allowed, clinicians should use other ovulation induction agents.	
5.3.3	**PP**	Letrozole should not be given where there is any possibility of a pre-existing pregnancy, though there is no evidence for increased teratogenicity compared to other ovulation induction agents.	

No. Living#	Type	Recommendation	Grade/ Quality
5.4		**Clomiphene citrate and metformin**	
5.4.1		**Metformin versus placebo**	
5.4.1.1	**EBR**	Metformin could be used alone, in women with PCOS with anovulatory infertility and no other infertility factors, to improve clinical pregnancy and live birth rates, whilst informing women that there are more effective ovulation agents.	❖❖❖ ⊕⊕◯◯
5.4.1.2	**PP**	Women should be counseled as to potential mild gastrointestinal side-effects with metformin.	
5.4.1.3	**PP**	Healthcare and resource burden including monitoring, travel and costs are lower with metformin.	
5.4.1.4	**PP**	Consideration of age and screening for other fertility factors needs to be discussed before prescribing metformin.	
5.4.2		**Clomiphene citrate versus metformin**	
5.4.2.1	**EBR**	Clomiphene citrate could be used in preference to metformin in women with PCOS with anovulatory infertility and no other infertility factors, to improve ovulation, clinical pregnancy and live birth rates.	❖❖❖ ⊕⊕◯◯
5.4.2.2	**PP**	The risk of multiple pregnancy is increased with clomiphene citrate use (alone or in combination with metformin) and therefore clomiphene cycles may require ultrasound monitoring.	
5.4.3		**Clomiphene citrate and metformin versus clomiphene citrate alone**	
5.4.3.1	**EBR**	Clomiphene citrate combined with metformin could be used rather than clomiphene citrate alone in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation and clinical pregnancy rates.	❖❖❖ ⊕⊕◯◯
5.4.4		**Clomiphene citrate and metformin versus metformin alone**	
5.4.4.1	**EBR**	Clomiphene citrate combined with metformin could be used rather than metformin alone in women with PCOS with anovulatory infertility and no other infertility factors to improve live birth rates.	❖❖❖ ⊕⊕◯◯
5.4.4.2	**PP**	Monitoring of combined cycles will need to be equivalent to clomiphene citrate alone.	
5.4.5		**Clomiphene citrate versus Letrozole**	
5.4.5.1	**EBR**	Letrozole should be used rather than clomiphene citrate in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation, clinical pregnancy, and live birth rates.	❖❖❖❖ ⊕◯◯◯
5.4.5.2	**PP**	Current evidence demonstrates no difference in fetal abnormality rates between letrozole or clomiphene citrate ovulation induction or natural conception.	

No. Living#	Type	Recommendation	Grade/ Quality
5.5		**Gonadotrophins**	
5.5.1	**EBR**	Gonadotrophins alone could be considered rather than clomiphene citrate in therapy naïve women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation, clinical pregnancy and live birth rates (refer to PP 5.5.6).	❖❖❖ ⊕⊕◯◯
5.5.2	**EBR**	Gonadotrophins alone could be used over gonadotrophins combined with clomiphene citrate in women with PCOS who are anovulatory and infertile with clomiphene citrate resistance or failure, and no other infertility factors.	❖❖❖ ⊕⊕◯◯
5.5.3	**EBR**	Gonadotrophins could be considered rather than the combination of clomiphene citrate and metformin in women with PCOS who are anovulatory and infertile, with clomiphene citrate-resistance and no other infertility factors.	❖❖❖ ⊕◯◯◯
5.5.4	**EBR**	Either gonadotrophins or laparoscopic ovarian surgery could be used in women with PCOS who are anovulatory and infertile, with clomiphene citrate-resistance and no other infertility factors, following counselling on higher live birth rate and higher multiple pregnancy rates with gonadotrophins.	❖❖ ⊕⊕◯◯
5.5.5	**EBR**	Gonadotrophins could be second-line pharmacological therapy for women with PCOS who are anovulatory and infertile, with no other infertility factors and who have failed first-line oral ovulation induction.	❖❖❖ ⊕⊕◯◯
5.5.6	**PP**	Where gonadotrophins are to be prescribed, the following should be considered: • Cost of the intervention for ovulation induction. • Expertise required for the use of the intervention for ovulation induction. • The degree of intensive ultrasound monitoring that is required. • A low dose step-up gonadotrophin protocol should be used to optimise the chance of monofollicular development. • Implications of potential multiple pregnancy.	
5.5.7	**PP**	There appears to be no difference in the clinical efficacy of the available gonadotrophin preparations.	
5.5.8	**PP**	When using gonadotrophins, best clinical practice is to avoid multiple pregnancy. Considerations here include cancelling cycles when there is more than a total of two follicles greater than 14 mm in diameter and advising avoidance of unprotected intercourse.	
5.5.9	**PP**	Live birth rate, clinical pregnancy rate per patient and ovulation rate per cycle are higher with gonadotrophins than with clomiphene citrate.	
5.5.10	**PP**	A low dose gonadotrophin protocol should be used to optimise the chance of monofollicular growth and minimise multiple pregnancy.	
5.5.11	**PP**	Cycle monitoring and drug costs coupled with multiple injection will influence choice in gonadotrophin use.	

No. Living#	Type	Recommendation	Grade/ Quality
5.6		**Laparoscopic ovarian surgery**	
5.6.1	**EBR**	Laparoscopic ovarian surgery could be second-line therapy for women with PCOS who are anovulatory and infertile, with clomiphene citrate resistance and no other infertility factors.	❖❖❖ ⊕⊕◯◯
5.6.2	**PP**	When using laparoscopic ovarian surgery, the following should be considered: • Comparative cost of the intervention for ovulation induction. • Expertise required for the safe use of the intervention for ovulation induction. • Both intraoperative and postoperative risks, which are higher in women who are above healthy weight.	
5.7		**In vitro fertilisation and in vitro maturation**	
5.7.0.1	**CR**	In the absence of an absolute indication for in vitro fertilisation (IVF)/intracytoplasmic sperm injection (ICSI), IVF could be offered in women with PCOS and anovulatory infertility, if first- or second-line ovulation induction therapies have failed.	❖❖❖
5.7.0.2	**PP**	In women with anovulatory PCOS, the use of IVF is effective and when elective single embryo transfer is used, multiple pregnancies can be minimised.	
5.7.0.3	**PP**	Women with PCOS undergoing IVF/ICSI treatment should be counselled prior to starting treatment about the increased risk of ovarian hyperstimulation syndrome and options to reduce the risk should be offered.	
5.7.1		**Gonadotrophin releasing hormone protocol**	
5.7.1.1	**PP**	Gonadotrophin releasing hormone protocol (GnRH) antagonist protocol cannot be recommended over GnRH agonist long protocol for women with PCOS undergoing IVF/ICSI to improve clinical pregnancy or live birth rate.	
5.7.1.2	**PP**	The use of a GnRH antagonist protocol for women with PCOS undergoing IVF/ICSI is recommended as it enables the use of an agonist trigger, with the freezing of all embryos generated if required, without compromising the cumulative live birth rate, to reduce the risk of significant ovarian hyperstimulation syndrome.	
5.7.2		**Trigger type**	
5.7.2.1	**CR**	Triggering final oocyte maturation with a GnRH agonist and freezing all suitable embryos is recommended, in an IVF/ICSI cycle with a GnRH antagonist protocol, where a fresh embryo transfer is not intended or where there is an increased risk of ovarian hyperstimulation syndrome.	❖❖❖❖
5.7.3		**Choice of follicle stimulating hormone**	
5.7.3.1	**CR**	Either urinary or recombinant follicle stimulating hormone (FSH) could be used in women with PCOS undergoing (controlled) ovarian (hyper) stimulation for IVF/ICSI, with insufficient evidence to recommend a particular type of FSH preparation.	❖❖

No. Living#	Type	Recommendation	Grade/ Quality
5.7.4		**Exogenous luteinising hormone**	
5.7.4.1	**CR**	Exogenous recombinant luteinising hormone treatment should not be routinely used in combination with follicle stimulating hormone therapy in women with PCOS undergoing controlled ovarian hyperstimulation for IVF/ICSI.	❖
5.7.5		**Adjunct metformin**	
5.7.5.1	**EBR**	Adjunct metformin therapy could be used before and/or during FSH ovarian stimulation in women with PCOS undergoing IVF/ICSI treatment with GnRH agonist long protocol, to reduce the risk of developing ovarian hyperstimulation syndrome and miscarriage.	❖❖❖ ⊕⊕◯◯
5.7.5.2	**PP**	Good practice in PCOS and IVF is the use of a GnRH antagonist protocol as it gives the flexibility of using a GnRH agonist trigger, freeze all strategy to reduce the risk of ovarian hyperstimulation syndrome. However, if using a GnRH agonist long protocol then metformin could be considered. If using metformin, the following could be considered: • Commence metformin at the start of GnRH agonist treatment. • Gradually titrate metformin up to a dose of between 1000 mg to 2500 mg daily in order to minimise side-effects. • Stopping metformin therapy at the time of the pregnancy test or period, unless the metformin therapy is otherwise indicated.	
5.7.6		**In vitro maturation**	
5.7.6.1	**EBR**	The use of in vitro maturation (IVM) and ICSI could be considered in women with PCOS, as an alternative to a stimulated IVF/ICSI cycle, where an embryo is frozen and replaced in a subsequent embryo transfer cycle, acknowledging there is no risk of ovarian hyperstimulation syndrome, but a lower cumulative live birth rate.	❖❖❖ ⊕⊕◯◯
5.7.6.2	**CR**	The use of IVM and ICSI could be considered prior to stimulated IVF/ICSI cycles acknowledging both benefits and limitations.	❖❖
5.7.6.3	**PP**	IVM should only be considered in services with sufficient expertise, and advocacy is needed for regional or national centres of expertise.	
5.7.6.4	**PP**	IVM could be offered as an option in women with prior severe ovarian hyperstimulation syndrome and where the risk of severe ovarian hyperstimulation syndrome is deemed unacceptably high, provided that expertise in IVM techniques exists.	
5.7.6.5	**PP**	Evidence suggests that IVM/ICSI is less effective than standard IVF/ICSI in terms of clinical pregnancy per patient and live birth rate per patient.	

No. Living#	Type	Recommendation	Grade/ Quality
5.8		**Inositol**	
5.8.1	**EBR**	Inositol in any form alone, or in combination with other therapies, should be considered experimental therapy in women with PCOS with infertility, with benefits and risks currently too uncertain to recommend the use of these agents as fertility therapies.	❖❖❖ ⊕◯◯◯
5.8.2	**PP**	There is limited evidence with uncertain results, on the effect of inositol on ovulation, clinical pregnancy and live birth rates.	
5.8.3	**PP**	Side-effects and safety are not known for inositol.	
5.8.4	**PP**	Women need to be aware that these agents can have limited regulation with variable dose, quality, consistency and combination with other agents.	
5.8.5	**PP**	Women's personal goals and preferences should be considered when discussing complimentary therapies.	
5.9		**Anti-obesity pharmacological agents**	
5.9.1	**CR**	We recommend using anti-obesity agents in PCOS for reproductive outcomes only in research settings to establish the efficacy and safety.	❖