

# Algorithm 1: Screening, diagnostic assessment, risk assessment and life-stage

## Step 1: Irregular cycles + clinical hyperandrogenism

(exclude other causes)\* = diagnosis

## Step 2: If no clinical hyperandrogenism

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

## Step 3: If ONLY irregular cycles OR hyperandrogenism

Adolescents ultrasound is not indicated = consider at risk of PCOS and reassess later

Adults - request ultrasound for PCOM, if positive (exclude other causes)\* = diagnosis

\* Exclusion of other causes requires TSH, Prolactin levels, FSH and if clinical status indicates other causes need to be excluded (e.g. CAH, Cushings, adrenal tumours etc)

## Diagnostic Criteria

### Irregular menstrual cycles

- normal in the first year post menarche = pubertal transition.
- > 1 to < 3 years post menarche: < 21 or > 45 days.
- > 3 years post menarche to perimenopause: < 21 or > 35 days or < 8 cycles per year.
- > 1 year post menarche > 90 days for any one cycle.
- Primary amenorrhoea by age 15 or > 3 years post thelarche (breast development).

With irregular cycles, PCOS should be considered and assessed according to the guidelines.

Ovulatory dysfunction can still occur with regular cycles. If anovulation suspected test progesterone levels.

### Clinical hyperandrogenism

Comprehensive history and physical examination for clinical hyperandrogenism. Adults: acne, alopecia and hirsutism and in adolescents severe acne and hirsutism.

Be aware of potential negative psychosocial impact of clinical hyperandrogenism. Perception of unwanted face and body hair and/or alopecia are important, regardless of apparent clinical severity.

Standardised visual scales are preferred when assessing hirsutism such as the modified Ferriman Gallway score (mFG). A cut-off score of  $\geq 4$ -6 indicates hirsutism, depending on ethnicity. It is acknowledged that self-treatment is common and can limit clinical assessment.

The Ludwig visual score is preferred for assessing the degree and distribution of alopecia.

Hirsutism prevalence is same across ethnicities. mFG cut-offs for hirsutism and severity, vary by ethnicity.

Only terminal hairs relevant in pathological hirsutism (untreated > 5 mm long, variable shape and pigmented).

### Biochemical hyperandrogenism

Use calculated free testosterone, free androgen index or calculated bioavailable testosterone in diagnosis.

Androstenedione and dehydroepiandrosterone sulfate (DHEAS) have limited role in PCOS diagnosis.

High quality assays needed for most accurate assessment. Direct free testosterone assays not preferred. Interpretation of androgen levels should be guided by the reference ranges of the laboratory used.

Reliable assessment of biochemical hyperandrogenism not possible on hormonal contraception. Consider withdrawal for  $\geq 3$  months before testing, advising non-hormonal contraception during this time.

In diagnosis, biochemical hyperandrogenism most useful when clinical hyperandrogenism is unclear.

Where levels are well above laboratory reference ranges, other causes should be considered. History of symptom onset and progression is critical in assessing for neoplasia, however, some androgen-secreting neoplasms may only induce mild to moderate increases in biochemical hyperandrogenism.

### Ultrasound and polycystic ovarian morphology (PCOM)

Ultrasound should not be used for the diagnosis of PCOS in those with a gynaecological age of < 8 years (< 8 years after menarche), due to the high incidence of multi-follicular ovaries in this life stage.

The transvaginal ultrasound approach is preferred in the diagnosis of PCOS, if sexually active and if acceptable to the individual being assessed.

Using endovaginal ultrasound transducers with a frequency bandwidth that includes 8MHz, the threshold for PCOM should be a follicle number per ovary of  $\geq 20$  and/or an ovarian volume  $\geq 10$ ml on either ovary, ensuring no corpora lutea, cysts or dominant follicles are present.

If using older technology, the threshold for PCOM could be an ovarian volume  $\geq 10$ ml on either ovary.

In patients with irregular menstrual cycles and hyperandrogenism, an ovarian ultrasound is not necessary for PCOS diagnosis; however ultrasound will identify the complete PCOS phenotype.

Transabdominal ultrasound should primarily report ovarian volume with a threshold of  $\geq 10$ ml, given the difficulty of reliably assessing follicle number with this approach.

## Ethnic variation

Consider ethnic variation in PCOS including:

- relatively mild phenotypes in Caucasians.
- higher BMI in Caucasians, especially North America and Australia.
- more severe hirsutism in Middle Eastern, Hispanic and Mediterranean women.
- increased central adiposity, insulin resistance, diabetes, metabolic risks and acanthosis nigricans in South East Asians and Indigenous Australians.
- lower BMI and milder hirsutism in East Asians.
- higher BMI and metabolic features in Africans.

## Anti-müllerian hormone (AMH)

Serum AMH levels should not yet be used as an alternative for the detection of PCOM or to diagnose PCOS.

## Cardiovascular disease risk and weight management

All with PCOS should be offered regular monitoring for weight change and excess weight, in consultation with and where acceptable to the individual. Monitoring could be at each visit or at a minimum 6-12 monthly, with frequency planned and agreed between the health professional and the individual.

Weight, height and ideally waist circumference should be measured and BMI calculated.

- BMI categories and waist circumference should follow World Health Organisation guidelines also noting ethnic and adolescent ranges.
- Consideration for Asian and high risk ethnic groups including monitoring waist circumference.

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

If screening reveals CVD risk factors including obesity, cigarette smoking, dyslipidemia, hypertension, impaired glucose tolerance and lack of physical activity, women with PCOS should be considered at increased risk of CVD.

Overweight and obese women with PCOS, regardless of age, should have a fasting lipid profile (total cholesterol, low density lipoprotein cholesterol, high density lipoprotein cholesterol and triglyceride level at diagnosis). Thereafter, measurement should be guided by the results and the global CVD risk.

All women with PCOS should have blood pressure measured annually.

CVD risk in women with PCOS remains unclear pending high quality studies, however prevalence of CVD risk factors is increased, warranting awareness and consideration of screening.

## Gestational diabetes, impaired glucose tolerance and type 2 diabetes

Regardless of age, gestational diabetes, impaired glucose tolerance and type 2 diabetes (5 fold in Asia, 4 fold in the Americas and 3 fold in Europe) are increased in PCOS, with risk independent of, yet exacerbated by obesity.

Glycaemic status should be assessed at baseline in all with PCOS and thereafter, every one to three years, based on presence of other diabetes risk factors.

In high risk women with PCOS (including a BMI > 25kg/m<sup>2</sup> or in Asians > 23kg/m<sup>2</sup>, history of abnormal glucose tolerance or family history of diabetes, hypertension or high risk ethnicity) an oral glucose tolerance test (OGTT) is recommended. Otherwise a fasting glucose or HbA1c should be performed.

An OGTT should be offered in all with PCOS when planning pregnancy or seeking fertility treatment, given increased hyperglycaemia and comorbidities in pregnancy.

If not performed preconception, an OGTT should be offered at < 20 weeks gestation, and all women with PCOS should be offered the test at 24-28 weeks gestation

## Obstructive sleep apnea (OSA)

Screening should only be considered for OSA in PCOS to identify and alleviate related symptoms, such as snoring, waking unrefreshed from sleep, daytime sleepiness, and the potential for fatigue to contribute to mood disorders. Screening should not be considered with the intention of improving cardiometabolic risk, with inadequate evidence for metabolic benefits of OSA treatment in PCOS and in general populations.

A simple screening questionnaire, preferably the Berlin tool, could be applied and if positive, referral.

A positive screen raises the likelihood of OSA, however it does not quantify symptom burden and alone does not justify treatment. If women with PCOS have OSA symptoms and a positive screen, they should ideally be referred to a specialist centre for further evaluation.

## Endometrial cancer

Health professionals and women with PCOS should be aware of a two to six fold increased risk of endometrial cancer, which often presents before menopause; however absolute risk remains relatively low.

Health professionals should have a low threshold for investigation of endometrial cancer in PCOS, with transvaginal ultrasound and/or endometrial biopsy recommended with persistent thickened endometrium and/or risk factors including prolonged amenorrhea, abnormal vaginal bleeding or excess weight. Routine ultrasound screening of endometrial thickness in PCOS is not recommended.

Optimal prevention for endometrial hyperplasia and endometrial cancer is not known. A pragmatic approach could include COCP or progestin therapy in those with cycles longer than 90 days.

## Algorithm 2: Prevalence, screening, diagnostic assessment and treatment of emotional wellbeing

| Psychological domains                         | Screening protocol / tools   | Intervention  |
|---|--|---|
| <b>Quality of life (QoL)</b>                  | Lower QoL scores in general and PCOS specific tools such as the modified PCOSQ tool.   | Capture and consider women's perceptions of their symptoms, impact on their QoL and priorities.<br>Target treatment to areas of greatest concern to those with PCOS.  |
| <b>Anxiety and depressive symptoms</b>        | High prevalence of moderate to severe anxiety and depressive symptoms in adults; and a likely increased prevalence in adolescents.<br>Routine screening for all at diagnosis and subsequently based on clinical judgement, considering risk factors, comorbidities and life events.<br>Suggested screening based on regional guidelines OR initial questions could include:<br>Over the last 2 weeks, how often have you been bothered by the following problems: <ul style="list-style-type: none"> <li>• Feeling down, depressed or hopeless?</li> <li>• Little interest or pleasure in doing things?</li> <li>• Feeling nervous, anxious or on edge?</li> <li>• Not being able to stop or control worrying?</li> </ul> <p>* Factors including obesity, infertility, hirsutism need consideration along with use of hormonal medications in PCOS, which may independently exacerbate depressive and anxiety symptoms and other aspects of emotional wellbeing.</p> | <b>If responses to initial screening questions positive:</b><br>Assess risk factors and symptoms using age, culturally and regionally appropriate tools, such as the Patient Health Questionnaire (PHQ) or the Generalised Anxiety Disorder Scale (GAD7) and/or refer to an appropriate professional for further assessment. <ul style="list-style-type: none"> <li>• If treatment is warranted, psychological therapy and/or pharmacological treatment should be offered to women with PCOS, informed by regional clinical practice guidelines.</li> </ul> <b>Pharmacological treatment:</b><br>Avoid inappropriate treatment with antidepressants or anxiolytics and consider impact on weight. Where mental health disorders are clearly documented and persistent, or if suicidal symptoms are present, treatment of depression or anxiety should be informed by clinical regional practice guidelines. |
| <b>Psychosexual dysfunction</b>               | Decreased scores on sexual function screen.<br>If concerns identified, screen adult women with PCOS.<br><b>Note:</b> Obesity and infertility are common in PCOS and also impact sexual function.   | If psychosexual dysfunction is suspected, further assessment, referral or treatment should follow as appropriate.   |
| <b>Body Image</b>                             | Negative body image has been described in PCOS and can be screened based on regional guidelines or by a stepped approach.<br>Initial questions could include: <ul style="list-style-type: none"> <li>• Do you worry a lot about the way you look and wish you could think about it less?</li> <li>• On a typical day, do you spend more than 1 hour per day worrying about your appearance?</li> <li>• What specific concerns do you have about your appearance?</li> <li>• What effect does it have on your life?</li> <li>• Does it make it hard to do your work or be with your friends and family?</li> </ul>  | Consider the impact of PCOS features such as hirsutism, acne, and weight gain in assessing and addressing body image in PCOS.   |
| <b>Eating disorders and disordered eating</b> | High prevalence of eating disorders and disordered eating has been described and can be screened based on regional guidelines or by using the following stepped approach.<br>Initial screening questions can include: <ul style="list-style-type: none"> <li>• Does your weight affect the way you feel about yourself?</li> <li>• Are you satisfied with your eating patterns?</li> </ul> <p>Or the SCOFF tool can be used.</p>   | If concerns are identified, further screening should involve: <ul style="list-style-type: none"> <li>• Assessment of risk factors and symptoms using age, culturally and regionally appropriate tools.</li> <li>• Referral to an appropriate health professional for further mental health assessment and diagnostic interview. If this is not the patient's usual healthcare provider, inform.</li> </ul>  |

# Algorithm 3: Lifestyle

## Lifestyle

### Effectiveness of lifestyle interventions

Healthy lifestyle behaviours (healthy eating and regular physical activity) should be recommended in all women with PCOS including those with excess weight, to achieve and/or maintain healthy weight and to optimise health, and quality of life across the life course. Ethnic groups at high cardiometabolic risk require more consideration.

Achievable goals such as 5% to 10% weight loss in those with excess weight yields significant clinical improvements and is considered successful weight reduction within six months. Ongoing monitoring is important in weight loss and maintenance. Consider referral to a professional to assist with healthy lifestyle.

SMART (Specific, Measurable, Achievable, Realistic and Timely) goal setting and self-monitoring can enable achievement of realistic lifestyle goals.

Psychological factors such as anxiety and depressive symptoms, body image concerns and disordered eating need consideration to optimise healthy lifestyle engagement.

All patient interactions should be patient-centred and value women's individualised healthy lifestyle preferences and cultural, socioeconomic and ethnic differences.

Adolescent and ethnic-specific body mass index and waist circumference categories should be considered when optimising lifestyle and weight.

### Behavioural strategies

Lifestyle interventions (may also include cognitive behavioural interventions) could include goal-setting, self-monitoring, stimulus control, problem solving, assertiveness training, slower eating, reinforcing changes and relapse prevention, to optimise weight management, healthy lifestyle and emotional wellbeing in women with PCOS.

### Dietary intervention

General healthy eating principles should be followed for all women with PCOS across the life course, with no one dietary type recommended in PCOS.

To achieve weight loss in those with excess weight, an energy deficit of 30% or 500 - 750 kcal/day (1,200 - 1,500 kcal/day) could be prescribed for women, also considering individual energy requirements, body weight, food preferences and physical activity levels and an individualised approach.

### Exercise intervention

Health professionals should encourage and advise the following for prevention of weight gain and maintenance of health:

- in adults from 18-64 years, a minimum of 150 min/week of moderate intensity physical activity or 75 min/week of vigorous intensities or an equivalent combination of both including muscle strengthening activities on 2 non-consecutive days/week.
- in adolescents, at least 60 minutes of moderate to vigorous intensity physical activity/day including those that strengthen muscle and bone at least 3 times weekly.
- activity be performed in at least 10 minute bouts or around 1000 steps, aiming to achieve at least 30 minutes daily on most days.

Health professionals should encourage and advise the following for modest weight-loss, prevention of weight-regain and greater health benefits including:

- a minimum of 250 min/week of moderate intensity activities or 150 min/week of vigorous intensity or an equivalent combination of both, and
- muscle strengthening activities involving major muscle groups on 2 non-consecutive days/week and minimised sedentary, screen or sitting time.

Physical activity can be incidental or structured. Self-monitoring, including with fitness tracking devices and technologies, could support and promote active lifestyles.

### Obesity and weight assessment

Women with PCOS have higher weight gain and obesity which can impact health and emotional wellbeing. In addressing this, consider related stigma, negative body image and/or low self-esteem by use of a respectful and considerate approach, considering personal sensitivities, marginalisation and potential weight-related stigma.

Prevention of weight gain, monitoring of weight and encouraging evidence-based and socio-culturally appropriate healthy lifestyle is important in PCOS from adolescence.

# Algorithm 4: Pharmacological treatment for non-fertility indications

**Off label prescribing:** COCPs, metformin and other pharmacological treatments are generally off label in PCOS, as pharmaceutical companies have not applied for approval in PCOS. However, off label use is predominantly evidence-based and is allowed in many countries. Where it is allowed, health professionals should inform women and discuss the evidence, possible concerns and side effects of treatment.

In those with a clear PCOS diagnosis or in adolescents at risk of PCOS (with symptoms)

## Education + lifestyle + first line pharmacological therapy for hyperandrogenism and irregular cycles

### COCP First line

Use lowest effective estrogen dose (20-30 micrograms ethinyl oestradiol or equivalent)

Consider natural estrogen preparations balancing efficacy, metabolic risk profile, side effects, cost and availability

Follow WHO COCP general population guidelines for relative and absolute contraindications and risks

35 micrograms ethinyl oestradiol plus cyproterone acetate not first line in PCOS due to increased adverse effects

Hirsutism requires COCP and additional cosmetic therapy for at least 6 months

Consider additional PCOS related risk factors such as high BMI, hyperlipidemia and hypertension

### Note:

Other contraceptives don't suppress hepatic SHBG production with limited efficacy for hyperandrogenism

## Second line pharmacological therapies

### COCP + lifestyle + metformin

No COCP preparation is superior in PCOS.

Should be considered in women with PCOS for management of metabolic features, where COCP + lifestyle does not achieve goals.

Could be considered in adolescents with PCOS and BMI  $\geq 25\text{kg/m}^2$  where COCP and lifestyle changes do not achieve desired goals.

Most beneficial in high metabolic risk groups including those with diabetes risk factors, impaired glucose tolerance or high-risk ethnic groups.

### COCP + anti-androgens

Evidence in PCOS relatively limited.

Anti-androgens must be used with contraception to prevent male fetal virilisation.

Can be considered after 6/12 cosmetic treatment + COCP if they fail to reach hirsutism goals.

Can be considered with androgenic alopecia.

### Metformin + lifestyle

With lifestyle, in adults should be considered for weight, hormonal and metabolic outcomes and could be considered in adolescents.

Most useful with BMI  $\geq 25\text{kg/m}^2$  and in high risk ethnic groups.

Side-effects, including GI effects, are dose related and self-limiting.

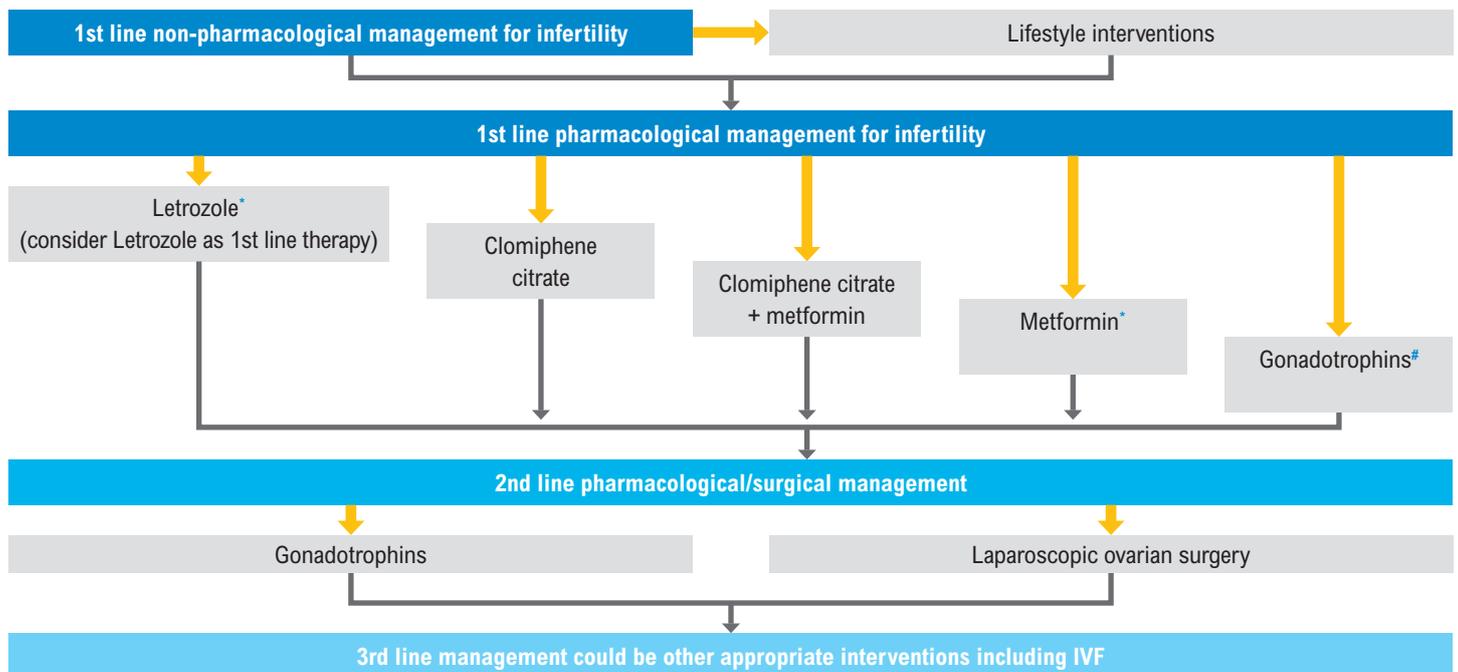
Consider starting low dose, with 500mg increments 1-2 weekly.

Metformin appears safe long-term. Ongoing monitoring required and has been associated with low vitamin B12.

**Anti-obesity medications can be considered with lifestyle as per general population guidelines, considering cost, contraindications, side effects, availability and regulatory status and avoiding pregnancy when on therapy.**

**Inositol (in any form) should currently be considered experimental in PCOS, with emerging evidence of efficacy highlighting the need for further research.**

# Algorithm 5: Assessment and treatment of infertility



\* **Off label prescribing:** Letrozole, COCPs, metformin and other pharmacological treatments are generally off label in PCOS, as pharmaceutical companies have not applied for approval in PCOS. However, off label use is predominantly evidence-based and is allowed in many countries. Where it is allowed, health professionals should inform women and discuss the evidence, possible concerns and side effects of treatment.

## Assessment and treatment of infertility

### Assessment of factors that may affect fertility, treatment response or pregnancy outcomes

Factors such as blood glucose, weight, blood pressure, smoking, alcohol, diet, exercise, sleep and mental, emotional and sexual health should be optimised in women with PCOS, to improve reproductive and obstetric outcomes, aligned with recommendations in the general population.

Refer to the International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018 available at: [www.monash.edu/medicine/sphpm/mchri/pcos](http://www.monash.edu/medicine/sphpm/mchri/pcos)

Monitoring during pregnancy is important for women with PCOS, given increased risk of adverse maternal and offspring outcomes.

For women with PCOS and infertility due to anovulation alone with normal semen analysis, the risks, benefits, costs and timing of tubal patency testing should be discussed on an individual basis.

Tubal patency testing should be considered prior to ovulation induction for women with PCOS where there is suspected tubal infertility.

### Ovulation induction principles

The use of ovulation induction agents, including letrozole, metformin and clomiphene citrate is off label in many countries\*.

Pregnancy should be excluded prior to ovulation induction.

Unsuccessful, prolonged use of ovulation induction agents should be avoided, due to poor success rates.

### Letrozole

Letrozole should be considered first line pharmacological treatment for ovulation induction in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation, pregnancy and live birth rates.

Where letrozole is not available or use is not permitted or cost is prohibitive, health professionals should use other ovulation induction agents.

Health professionals and women should be aware that the risk of multiple pregnancy appears to be less with letrozole, compared to clomiphene citrate.

### Clomiphene citrate and metformin

Clomiphene citrate could be used alone in women with PCOS with anovulatory infertility and no other infertility factors to improve ovulation and pregnancy rates.

Metformin could be used alone in women with PCOS, with anovulatory infertility and no other infertility factors, to improve ovulation, pregnancy and live birth rates, although women should be informed that there are more effective ovulation induction agents.

Clomiphene citrate could be used in preference, when considering clomiphene citrate or metformin for ovulation induction in women with PCOS who are obese (BMI is  $\geq 30$  kg/m<sup>2</sup>) with anovulatory infertility and no other infertility factors.

If metformin is being used for ovulation induction in women with PCOS who are obese (BMI  $\geq 30$ kg/m<sup>2</sup>) with anovulatory infertility and no other infertility factors, clomiphene citrate could be added to improve ovulation, pregnancy and live birth rates.

Clomiphene citrate could be combined with metformin, rather than persisting with clomiphene citrate alone, in women with PCOS who are clomiphene citrate-resistant, with anovulatory infertility and no other infertility factors, to improve ovulation and pregnancy rates.

The risk of multiple pregnancy is increased with clomiphene citrate use and therefore monitoring needs to be considered.

## Gonadotrophins

Gonadotrophins could be used as second line pharmacological agents in women with PCOS who have failed first line oral ovulation induction therapy and are anovulatory and infertile, with no other infertility factors.

# Gonadotrophins could be considered as first line treatment, in the presence of ultrasound monitoring, following counselling on cost and potential risk of multiple pregnancy, in women with PCOS with anovulatory infertility and no other infertility factors.

Gonadotrophins, where available and affordable, should be used in preference to clomiphene citrate combined with metformin therapy for ovulation induction, in women with PCOS with anovulatory infertility, clomiphene citrate-resistance and no other infertility factors, to improve ovulation, pregnancy and live birth rates.

Gonadotrophins with the addition of metformin, could be used rather than gonadotrophins alone, in women with PCOS with anovulatory infertility, clomiphene citrate-resistance and no other infertility factors, to improve ovulation, pregnancy and live birth rates.

Either gonadotrophins or laparoscopic ovarian surgery could be used in women with PCOS with anovulatory infertility, clomiphene citrate-resistance and no other infertility factors, following counselling on benefits and risks of each therapy.

Where gonadotrophins are prescribed, the following should be considered:

- cost and availability
- expertise required for use in ovulation induction
- degree of intensive ultrasound monitoring required
- lack of difference in clinical efficacy of available gonadotrophin preparations
- low dose gonadotrophin protocols optimise monofollicular development
- risk and implications of potential multiple pregnancy

Gonadotrophin induced ovulation should only be triggered when there are fewer than three mature follicles and should be cancelled if there are more than two mature follicles with the patient advised to avoid unprotected intercourse.

## Anti-obesity agents

Pharmacological anti-obesity agents should be considered an experimental therapy for women with PCOS for the purpose of improving fertility, with risk to benefit ratios currently too uncertain to advocate this as fertility therapy.

## Laparoscopic ovarian surgery

Laparoscopic ovarian surgery could be second line therapy for women with PCOS, who are clomiphene citrate resistant, with anovulatory infertility and no other infertility factors.

Laparoscopic ovarian surgery could potentially be offered as first line treatment if laparoscopy is indicated for another reason in women with PCOS with anovulatory infertility and no other infertility factors.

Risks should be explained to all women with PCOS considering laparoscopic ovarian surgery.

Where laparoscopic ovarian surgery is to be recommended, the following should be considered:

- comparative cost
- expertise required for use in ovulation induction
- intra-operative and post-operative risks are higher in women who are overweight and obese
- there may be a small associated risk of lower ovarian reserve or loss of ovarian function
- periadnexal adhesion formation may be an associated risk

## Bariatric Surgery

Bariatric surgery should be considered an experimental therapy in women with PCOS, for the purpose of having healthy baby, with risk to benefit ratios currently too uncertain to advocate this as fertility therapy.

If bariatric surgery is to be prescribed, the following should be considered:

- comparative cost
- the need for a structured weight management program involving diet, physical activity and interventions to improve psychological, musculoskeletal and cardiovascular health to continue post-operatively
- perinatal risks such as small for gestational age, premature delivery, possibly increased infant mortality
- potential benefits such as reduced incidence of large for gestational age fetus and gestational diabetes
- recommendations for pregnancy avoidance during periods of rapid weight loss and for at least 12 months after bariatric surgery with appropriate contraception

If pregnancy occurs, the following should be considered:

- awareness and preventative management of pre- and post-operative nutritional deficiencies is important, ideally in a specialist interdisciplinary care setting
- monitoring of fetal growth during pregnancy

## In-vitro fertilisation (IVF)

In the absence of an absolute indication for IVF ± ICSI, women with PCOS and anovulatory infertility could be offered IVF third line where other ovulation induction therapies have failed.

In women with anovulatory PCOS, the use of IVF is effective and when elective single embryo transfer is used, multiple pregnancies can be minimised.

Women with PCOS undergoing IVF ± ICSI therapy should be counselled prior to starting treatment, including on:

- availability, cost and convenience
- increased risk of ovarian hyperstimulation syndrome
- options to reduce the risk of ovarian hyperstimulation

Urinary or recombinant follicle stimulation hormone can be used in women with PCOS undergoing controlled ovarian hyperstimulation for IVF ± ICSI, with insufficient evidence to recommend specific FSH preparations.

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.

A gonadotrophin releasing hormone antagonist protocol is preferred in women with PCOS undergoing an IVF ± ICSI cycle, over a gonadotrophin releasing hormone agonist long protocol, to reduce the duration of stimulation, total gonadotrophin dose and incidence of ovarian hyperstimulation syndrome (OHSS).

Human chorionic gonadotrophins should be used at the lowest doses to trigger final oocyte maturation in women with PCOS undergoing an IVF ± ICSI cycle to reduce the incidence of OHSS.

Triggering final oocyte maturation with a GnRH agonist and freezing all suitable embryos could be considered in women with PCOS having an IVF/ICSI cycle with a GnRH antagonist protocol and at an increased risk of developing OHSS or where fresh embryo transfer is not planned.

In IVF ± ICSI cycles in women with PCOS, consideration should be given to an elective freeze of all embryos.

Adjunct metformin therapy could be used before and/or during follicle stimulating hormone ovarian stimulation in women with PCOS undergoing IVF ± ICSI therapy with a gonadotrophin releasing hormone agonist protocol, to improve the clinical pregnancy rate and reduce the risk of OHSS.

In a gonadotrophin releasing hormone agonist protocol with adjunct metformin therapy, in women with PCOS undergoing IVF ± ICSI treatment, the following could be considered:

- metformin commencement at the start of gonadotrophin releasing hormone agonist treatment
- metformin use at a dose of between 1000mg to 2550mg daily
- metformin cessation at the time of the pregnancy test or menses (unless the metformin therapy is otherwise indicated)
- metformin side-effects (refer to the International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018 available at: [www.monash.edu/medicine/sphpm/mchri/pcos](http://www.monash.edu/medicine/sphpm/mchri/pcos))

In IVF ± ICSI cycles, women with PCOS could be counselled on potential benefits of adjunct metformin in a gonadotrophin releasing hormone antagonist protocol to reduce risk of ovarian hyperstimulation syndrome (refer to the International evidence-based guideline for the assessment and management of polycystic ovary syndrome 2018 available at: [www.monash.edu/medicine/sphpm/mchri/pcos](http://www.monash.edu/medicine/sphpm/mchri/pcos)).

The term in vitro maturation (IVM) treatment cycle should be applied to “the maturation in vitro of immature cumulus oocyte complexes collected from antral follicles” (encompassing both stimulated and unstimulated cycles, but without the use of a human gonadotrophin trigger).

In units with sufficient expertise, IVM could be offered to achieve pregnancy and live birth rates approaching those of standard IVF ± ICSI treatment without the risk of OHSS for women with PCOS, where an embryo is generated, then vitrified and thawed and transferred in a subsequent cycle.