

# *Polycystic ovarian syndrome – an update for GPs*

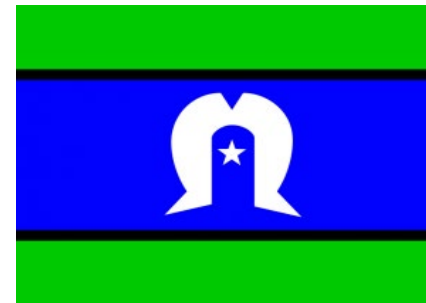
**Wednesday 19 June 2024**

*The content in this session is valid at date of presentation*

# *Acknowledgement of Country*

North Western Melbourne Primary Health Network would like to acknowledge the Traditional Custodians of the land on which our work takes place, The Wurundjeri Woi Wurrung People, The Boon Wurrung People and The Wathaurong People.

We pay respects to Elders past, present and emerging as well as pay respects to any Aboriginal and Torres Strait Islander people in the session with us today.



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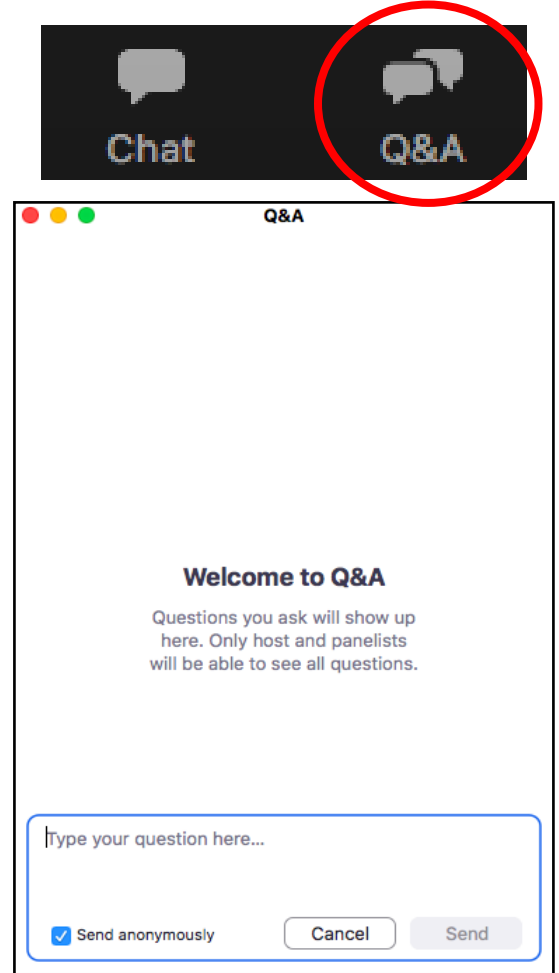
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# ***Polycystic Ovarian Syndrome – an update for GPs***

*19 June 2024*





**Pathways are written by GP clinical editors with support from local GPs, hospital-based specialists and other subject matter experts**



- **clear and concise, evidence-based medical advice**
- **Reduce variation in care**
- **how to refer to the most appropriate hospital, community health service or allied health provider.**
- **what services are available to my patients**

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[Polycystic Ovarian Syndrome \(PCOS\)](#)

[Postcoital Bleeding](#)

[Pruritus Vulvae](#)

[Sub-fertility](#)

[Pelvic Organ Prolapse](#)

[Ovarian Cancer - Established](#)

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# Speaker

## Dr Samina Ahmed - Joan Kirner Western Health

- Samina is a highly skilled gynaecologist and obtained her Fellowship from the Royal College of Obstetrics and Gynaecology Australia and New Zealand (RANZCOG) in 2016.
- She has specialty appointments at Geelong University Hospital, Joan Kirner Women's and Children's Hospital, Sunshine Private Hospital and St Vincent's Werribee as a specialist obstetrician and gynaecologist.
- She also holds a fertility sub-specialist appointment at Joan Kirner Western Health. In this role she assists couples to produce an offspring through assisted reproductive techniques (ART/IVF).
- In addition, Samina holds senior academic appointments at Deakin University Geelong and the University of Melbourne. She is also Supervisor at RANZCOG.
- She can speak English, Hindi, Urdu and Punjabi.
- She provides a broad range gynaecological services in a friendly and comprehensively informative manner. She is experienced in managing Infertility, ovulation induction, assisted reproductive techniques, menstrual abnormalities, endometriosis and pelvic pain, fibroids, ovarian cysts, pelvic organ prolapse with urinary incontinence, abnormal cervical cancer screening results and colposcopy.
- Samina has expertise in a wide range of surgical procedures, including hysterectomy, hysteroscopy, Mirena , contraception (IUD/sterilisation), suction D&C, endometrial ablation, colposcopy, and laparoscopy.
- As a medical professional her philosophy and motive is to give the maximum possible care with competence and passion.

Further reinforcement of this topic.

**Feel free to sign up with Jean Hailes, Managing polycystic ovary syndrome e-Learning course.**

This course aims to help general practitioners improve their knowledge and understanding of PCOS, its diagnosis, and key management principles.

Although the course has been designed for general practitioners, other health professionals are welcome to participate.

## e-Learning

### Managing polycystic ovary syndrome



#### Registration

Cost: \$75

Scan the QR code to register:



#### CPD information

RACGP activity ID: 383757

ACRRM activity ID: 28145

#### General information

The course is self-paced and online.

The expected duration is five and a half hours.

Access is unlimited for three months from registration date.

This course aims to help general practitioners improve their knowledge and understanding of PCOS, its diagnosis, and key management principles.

Although the course has been designed for general practitioners, other health professionals are welcome to participate.

#### Learning outcomes

At the end of this course, participants will be able to:

- identify the signs and symptoms of PCOS
- apply the current diagnostic criteria to diagnose PCOS
- outline management options for PCOS, including medical, nutritional and lifestyle advice
- identify the potential impacts of PCOS on psychological health and wellbeing.



RACGP CPD Accredited Activity		
Educational Activities	Measuring Outcomes	Reviewing Performance
4.5 hours	00 hours	1.0 hours

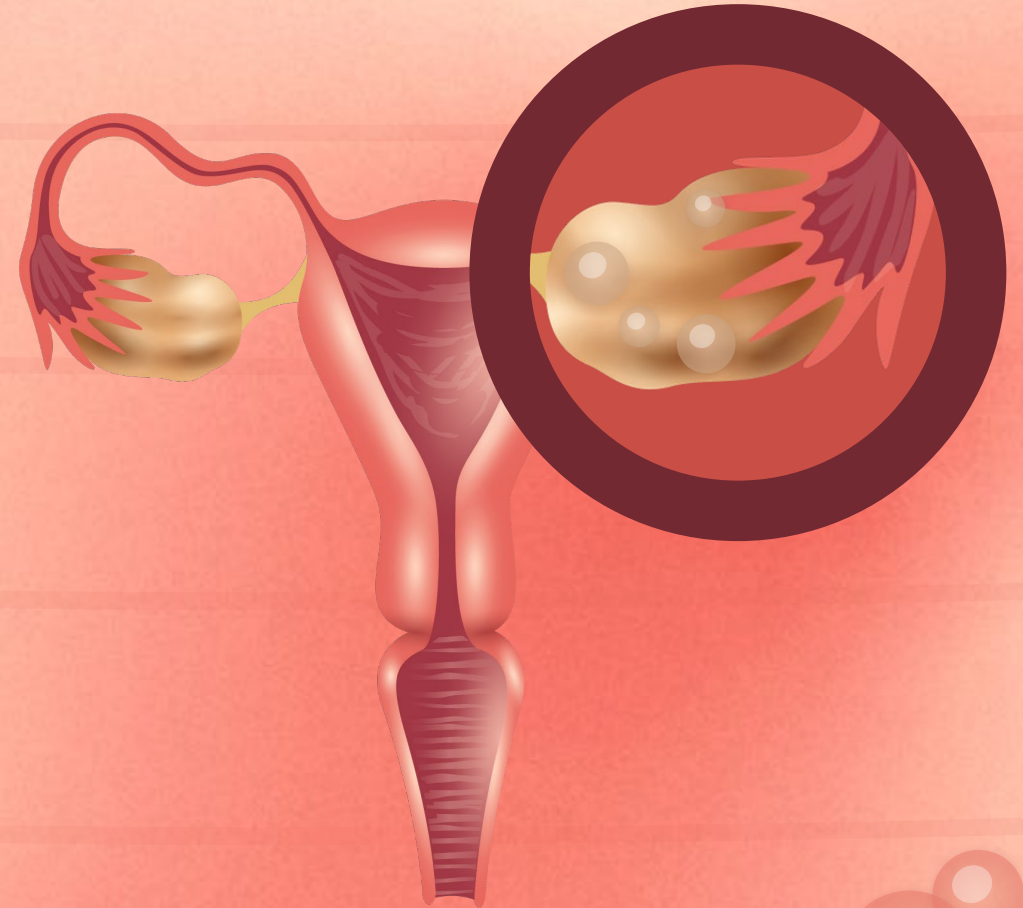
# POLYCYSTIC OVARY SYNDROME

An Update for GP's

Dr Samina Ahmed

Gynaecologist & Fertility Specialist

MBBS,FCPS,FRANZCOG,MastRepMed



# Objectives

01

## Introduction

PCOS a Heterogeneous Syndrome

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## Clinical Sequels

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Dermatological  
Reproductive  
Metabolic & Late Sequels

06

## Take Home

Evidence Based Target Approach to  
Manage PCOS Related Health Issues



# Introduction

## Other names

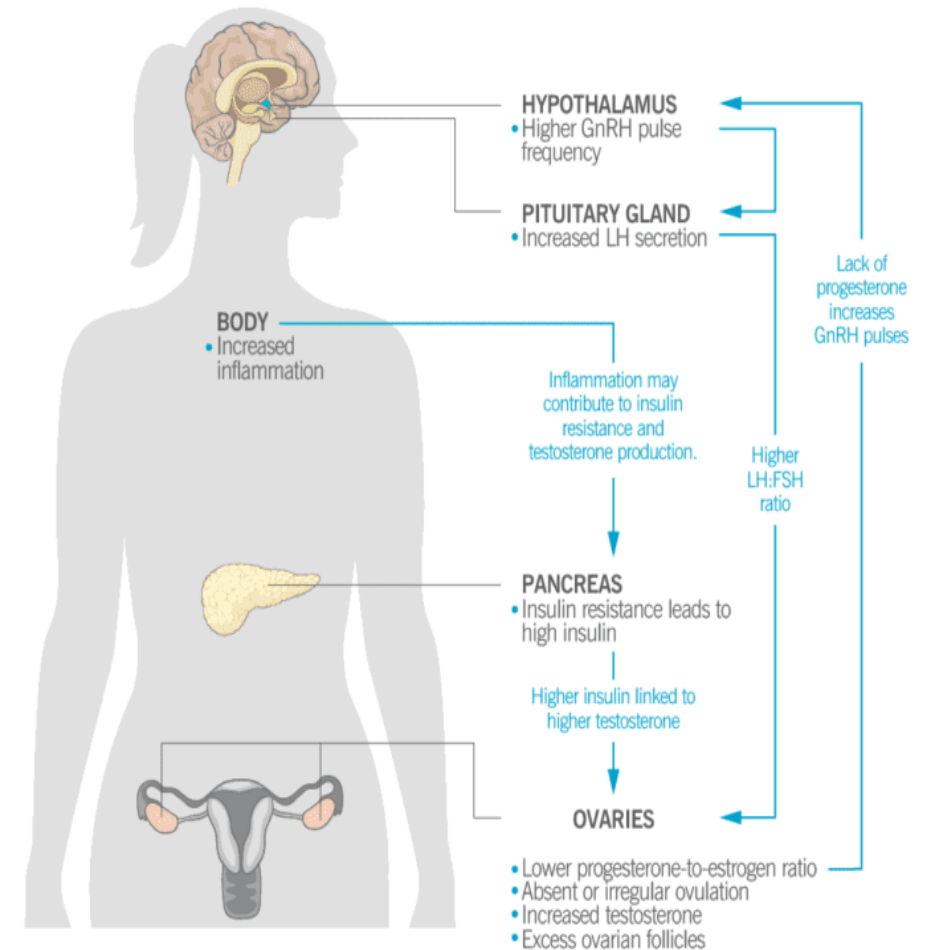
- Polycystic ovary disease
- Functional ovarian hyperandrogenism
- Ovarian hyperthecosis
- Sclerocystic ovary syndrome
- Stein-Leventhal syndrome

First described in 1935 by the American gynaecologists Irving F Stein and Michael L Leventhal

Polycystic ovary syndrome (PCOS) is the most common heterogeneous endocrine disorder of reproductive-age women around the world and is defined by a combination of signs and symptoms of androgen excess and ovarian dysfunction with the clinical manifestations of menstrual irregularities, subfertility, hyperandrogenism and long-term metabolic syndrome.<sup>1</sup>

## THE PCOS HORMONAL LANDSCAPE

Women with PCOS experience altered hormone levels compared to other women of reproductive age. However, this is still being researched, and may vary between individuals.



Adapted from: Azziz, R., Carmina, E., Chen, Z. et al. Polycystic ovary syndrome. Nat Rev Dis Primers 2, 16057 (2016).

# WHAT IS PCOS?

Polycystic ovary syndrome (PCOS) is a serious genetic, hormone, metabolic and reproductive disorder that affects women. It is the leading cause of female infertility. PCOS can lead to life-long complications and other serious conditions including severe anxiety and depression, obesity, endometrial cancer, type 2 diabetes, liver disease and cardiovascular disease.

## PCOS AFFECTS 1-IN-10 WOMEN



## COMMON SIGNS AND SYMPTOMS

irregular periods   excess facial and body hair   severe acne   small cysts in ovaries  
insulin resistance   anxiety and depression   infertility   weight gain   male pattern hair loss





## Pathophysiology

Underlying cause is unknown<sup>2,3</sup>

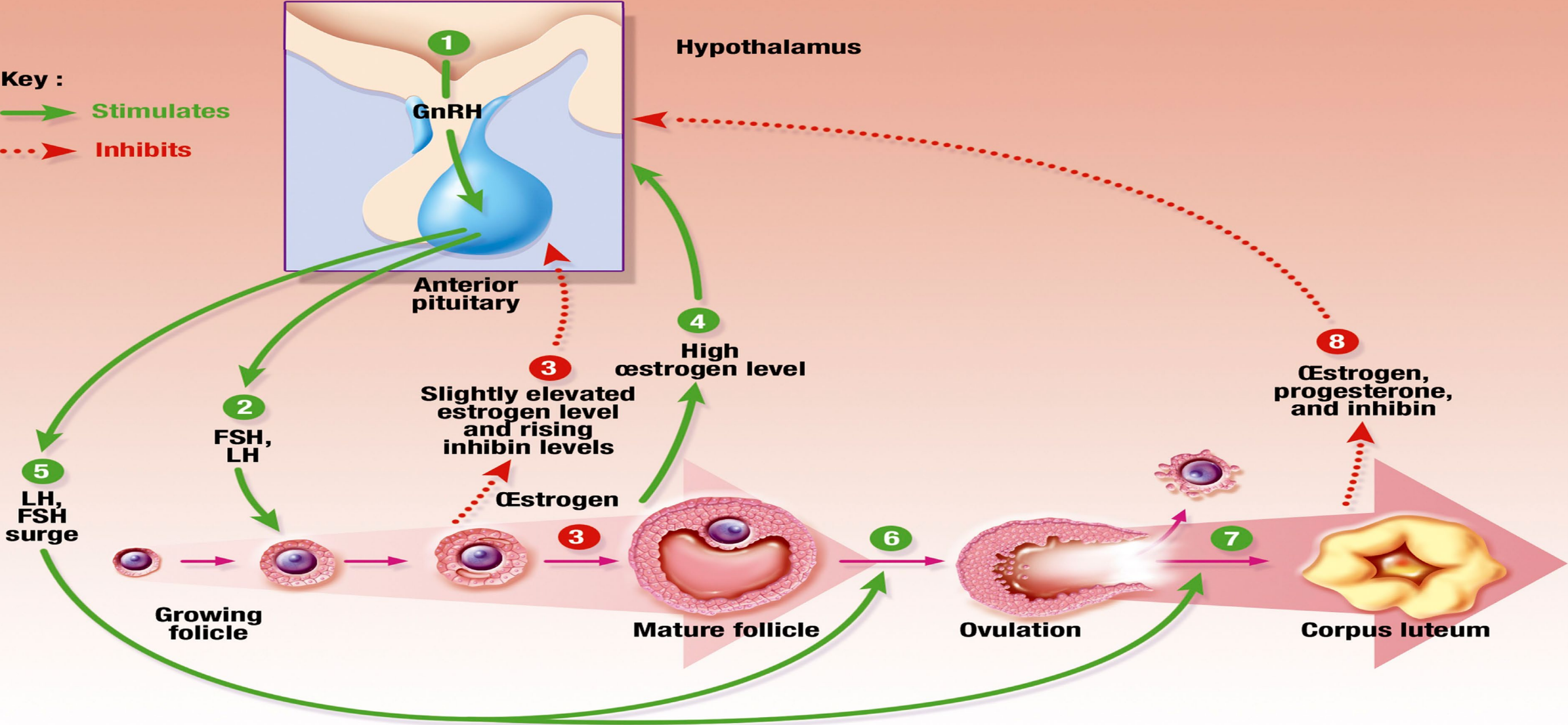
Genetic basis being suspected including:

- Dysregulation of CYP 11a gene
- Upregulation of other enzymes in androgen synthesis pathway
- Insulin receptor gene on chromosome 19p13.2
- Decreased sex hormone-binding globulin.

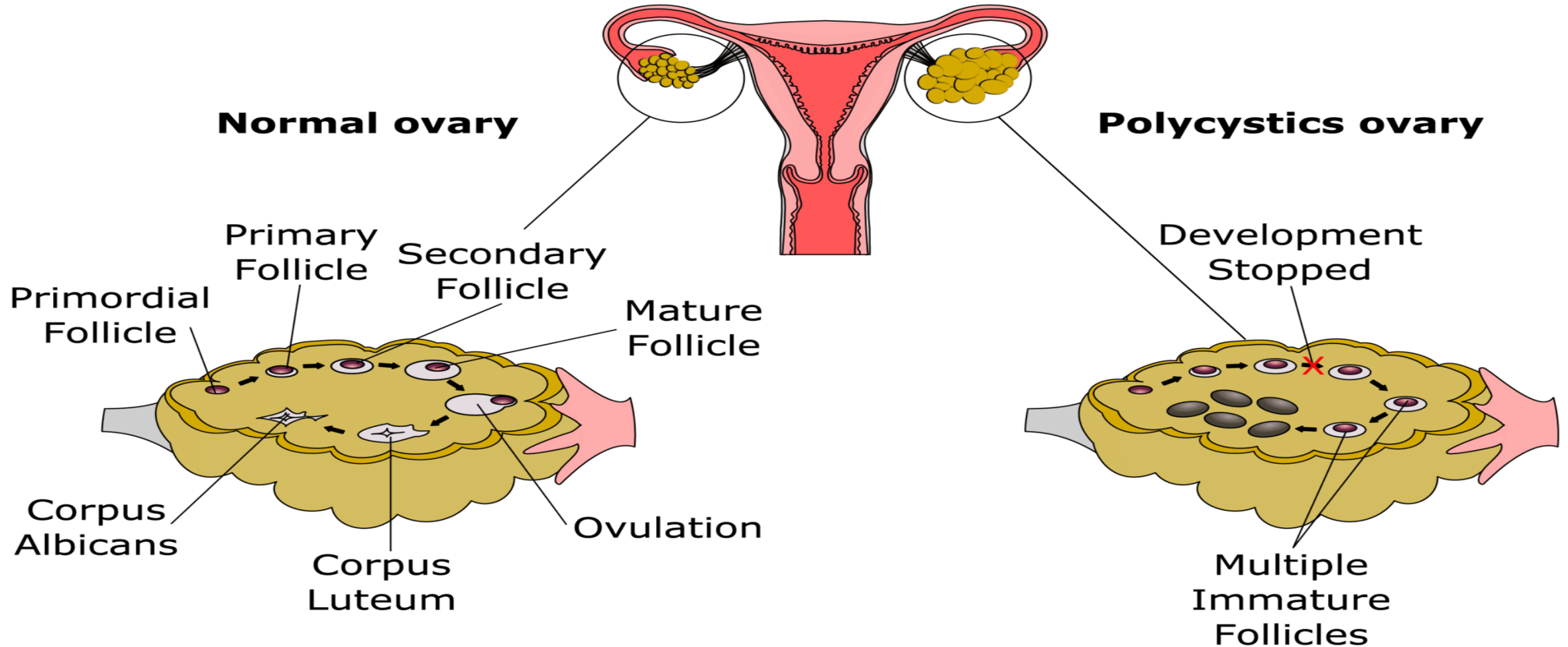
Others (predisposing factors)<sup>2,3</sup>

- Family history of PCOS
- High maternal androgen
- Onset of type 1 diabetes mellitus before menarche
- Insulin resistance
- Obesity

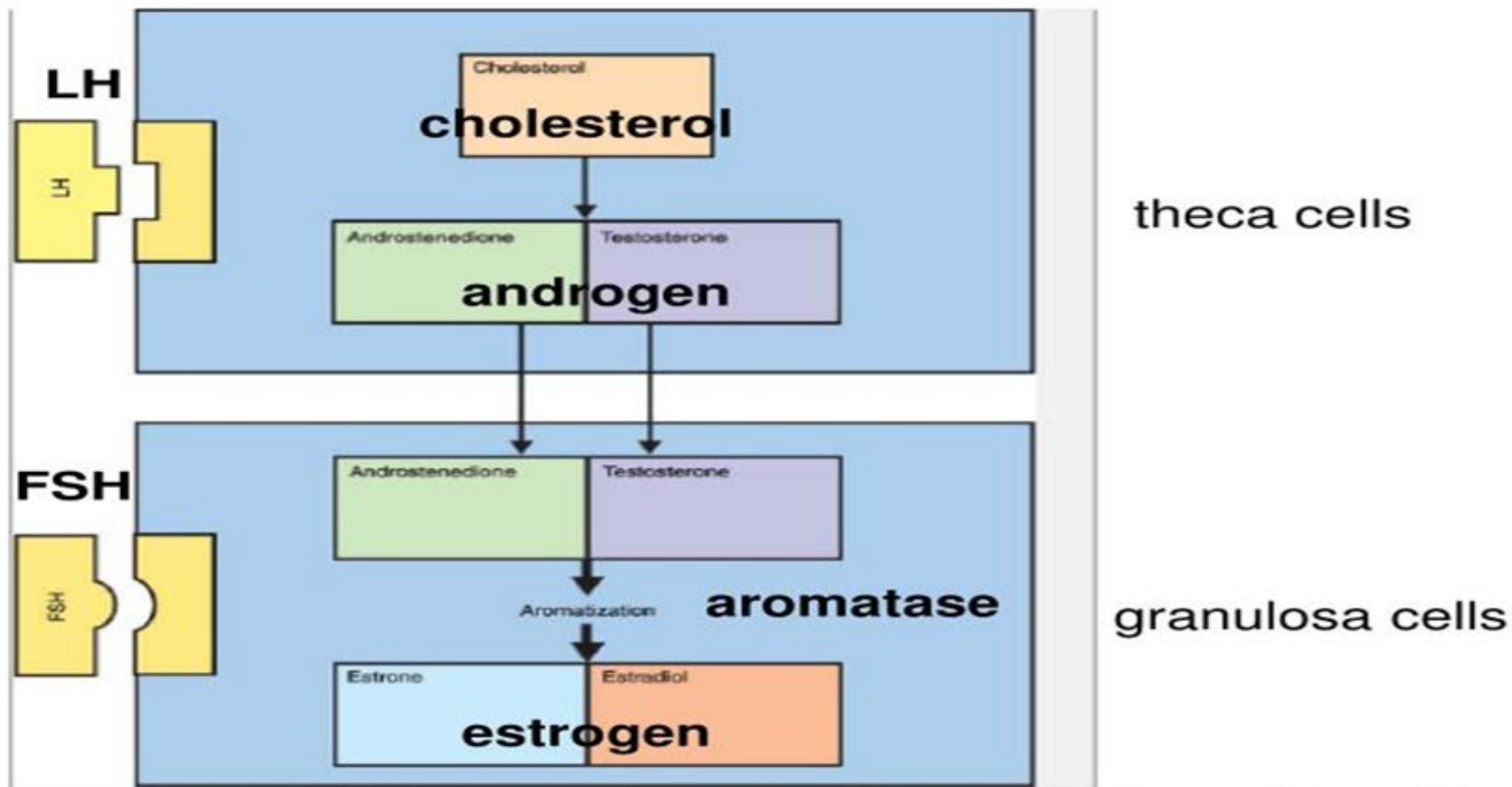
# Menstrual Cycle Physiology



# POLYCYSTIC OVARY SYNDROME



# Two-cell Two-gonadotropin Theory



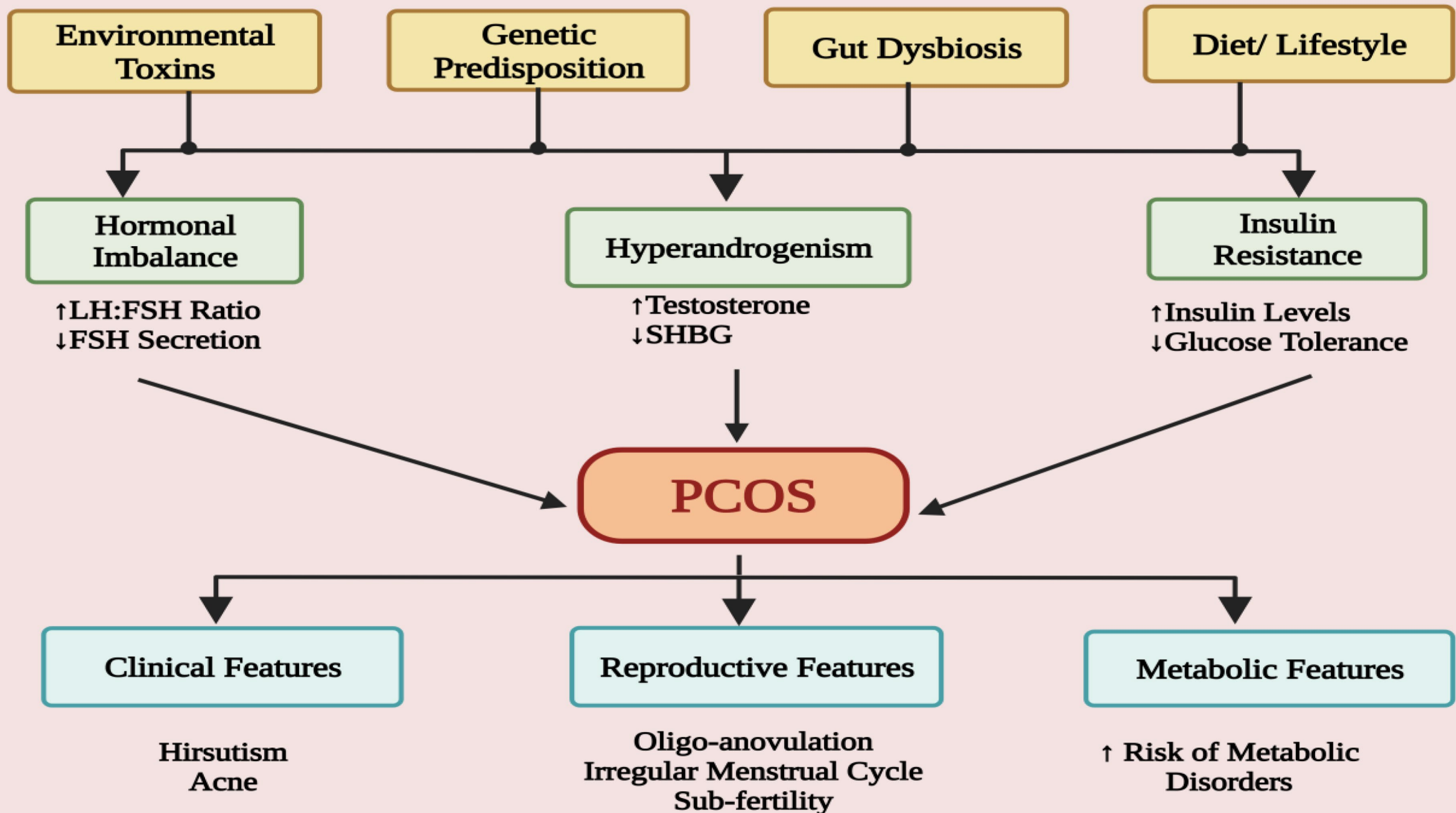
there is a subdivision and compartmentalization of steroid hormone synthesis activity in the developing follicle





## Clinical Sequels

- **Psychological**
  - Anxiety
  - Depression
  - Behavioural Changes
- **Dermatological**
  - Features of hyperandrogenism
  - Hirsutism /Acne /Androgenic alopecia
  - Acanthosis nigricans
- **Reproductive**
  - Menstrual dysfunction
  - Infertility/miscarriages
- **Metabolic & Late Sequels**
  - Endocrine dysfunction
  - Insulin resistance/diabetes mellitus
  - Obesity
  - Obstructive sleep apnoea
  - Metabolic syndrome
  - Endometrial Hyperplasia



A solid red circle is positioned on the left side of the slide, containing the word 'Diagnosis' in white text.

## Diagnosis

Controversies on what constitute PCOS

It is a diagnosis of **exclusion**<sup>3</sup>



## **ESHRE/ASRM (Rotterdam criteria) 2003**

Includes 2 out of the following 3

- Oligo- or anovulation
- Clinical and/or biochemical signs of hyperandrogenism
- Polycystic ovaries

## **NIH, 1990**

Includes both of

- Oligo-ovulation
- Hyperandrogenism and/or hyperandrogenemia (with exclusion of related disorders)

## **AE-PCOS, 2009**

- Hyperandrogenism: hirsutism and/or hyperandrogenaemia
- Ovarian dysfunction: oligo-anovulation and/or polycystic ovaries, and
- Exclusion of the other androgen-excess or related disorders

**RCOG recommends the use of Rotterdam criteria<sup>5</sup>**

## Differential Diagnosis

- Hyperthyroidism
- Hypothyroidism
- Hyperprolactinaemia
- Hypogonadotropic hypogonadism
- Primary ovarian failure
- Acromegaly
- Late onset CAH
- Androgen secreting ovarian tumour
- Androgen secreting adrenal tumour
- Cushing syndrome
- Exogenous androgen use<sup>6</sup>



## Investigations

- FSH, LH
- Testosterone – total and free, FAI
- DHEAS
- Thyroid function tests
- Serum prolactin
- Blood sugar test (2hr GTT)
- Fasting insulin level
- Fasting lipid profile
- 17 $\alpha$ hydroxyprogesterone 19
- Cortisol
- Ultrasound Pelvis<sup>7</sup>

# Hyperandrogenism (Biochemical Investigations)

- Total and free testosterone to assess biochemical hyperandrogenism in the diagnosis of PCOS
- Free testosterone can be estimated by the calculated free androgen index (FAI)
- If testosterone or free testosterone is not elevated, consider measuring androstenedione and dehydroepiandrosterone sulfate (DHEAS) (Taking into account their poor specificity and advancing age association with decreasing DHEAS)
- Patients with irregular menstrual cycles and hyperandrogenism, an AMH level is not necessary for PCOS diagnosis.
- Both clinical and biochemical hyperandrogenism persist in the postmenopausal women with PCOS. Postmenopausal hyperandrogenism symptoms should be taken care of unless other causes of hyperandrogenism like androgen secreting tumours etc have been excluded<sup>5</sup>

# Features of Hyperandrogenism (Clinical Assessment)

- **Hirsutism**
  - A modified Ferriman Gallwey score should be used to detect hirsutism, depending on ethnicity
  - Severity of hirsutism may vary by ethnicity, but the prevalence of hirsutism appears similar across ethnicities.
- **Acne**
- **Androgenic alopecia**
- **Acanthosis nigricans**





# PCOM on Ultrasound

- Follicle count  $\geq 20$  per ovary of 2-9 mm or OV 10cm<sup>3</sup> in adults<sup>7</sup>
- Ovarian volume (OV)  $\geq 10$  ml or follicle number per section  $\geq 10$  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 definitive criteria to define PCOM on ultrasound in adolescents, hence it is not recommended
- In presence of menstrual irregularities and clinical /biochemical hyperandrogenism, ultrasound is not necessary for PCOS diagnosis.<sup>7</sup>



## Clinical Approach & Treatment

- No universal treatment for PCOS is available
- Treatment is individualized, based on:
  - Woman's goal
  - Severity of symptoms
  - SDM (*Shared Decision Making*)
  - SMART Goals (*Specific, Measurable, Achievable, Realistic & Timely*)
- Modalities include
  - Conservative
  - Interdisciplinary Medical Team
  - Surgical



# Psychological Screening & Models of care

- Prevalence, screening and management of psychological features and models of care are common and important component of PCOS
- Women with PCOS should be asked about their perception of PCOS related symptoms, impact on quality of life, key concerns and priorities for management.
- High prevalence of moderate to severe depressive symptoms and depression in adults and adolescents with PCOS is noted and should be screened for by using regionally validated screening tools and refer appropriately
- Screening for mental health disorders comprises assessment of risk factors, symptoms, and risk of self-harm and suicidal intent <sup>8,10</sup>

# Psychosexual function and Body Image

- Permission to discuss psychosexual function should be sought noting that the diagnosis of psychosexual dysfunction requires both low psychosexual function, combined with related distress.
- PCOS can hurt body image that contributes to above
- Eating disorders should be considered in PCOS, regardless of weight, especially in the context of weight management and lifestyle interventions
- If disordered eating or eating disorders are suspected, appropriately qualified practitioners including Dietitians, Psychologists and other allied health practitioners should be taken on board<sup>9</sup>

# SMART

- Interventions to optimize healthy lifestyle and emotional well-being in PCOS patients by utilizing SMART goals (Specific, Measurable, Achievable, Realistic, and Timely) have been proven quite beneficial in achieving and retaining required targets.
- The above behavioural strategies include
  - Goal-setting
  - Self-monitoring
  - Problem-solving
  - Assertiveness training
  - Reinforcing changes
  - Relapse prevention

## Dietary interventions

- There is no evidence to support any one type of diet composition over another for anthropometric, metabolic, hormonal, reproductive or psychological outcomes.
- Any diet composition consistent with healthy eating will have health benefits, and professionals should advise sustainable healthy eating to individuals in accordance to their preferences and goals.<sup>10,11</sup>



# Weight Management

- Anti-obesity medications including liraglutide, semaglutide (Ozempic), both glucagon-like peptide-1 (GLP-1) receptor agonists and orlistat, could be considered, in addition to active lifestyle intervention for weight management<sup>20</sup>
- Ensure concurrent effective contraception is on board in reproductive age women as pregnancy safety data is lacking for these agents<sup>10,11</sup>

## Weight Management (Continued)

- Inositol<sup>19,21</sup>
  - Limited harm
  - Potential for improvement in metabolic measures
  - limited clinical benefits including in ovulation, hirsutism or weight
  - SDM should include discussion that regulatory status and quality control of inositol in any form can differ
  - Inositol alone, or in combination with other therapies is still experimental and benefits /risks currently too uncertain to recommend their use as fertility therapies.

**Specific types, doses or combinations of inositol cannot currently be recommended in adults and adolescents with PCOS, due to a lack of quality evidence**

## Weight Management (Continued)

- Metformin<sup>17,18</sup>
  - should be considered over inositol for hirsutism and central adiposity
  - Has more gastrointestinal side-effects than inositol.
  - Metformin alone should be considered in adults with PCOS and a BMI  $\geq 25$  kg/m<sup>2</sup> for anthropometric, and metabolic outcomes including insulin resistance, glucose, and lipid profiles.
  - Suggested maximum daily dose is 2.5 g in adults and 2 g in adolescents starting with low dose of 500 mg with gradual increase over the weeks
- Bariatric/metabolic surgery could be considered to improve weight loss, hypertension, diabetes, hirsutism, irregular menstrual cycles, ovulation and pregnancy rates<sup>25</sup>



# Dealing with Hyperandrogenism

Common Sequels of hyperandrogenism are :

- Hirsutism /Acne /Androgenic alopecia
- Acanthosis nigricans

Self-administered and professional cosmetic therapy is first line (laser is recommended)

Eflornithine cream can be added and may induce a more rapid response

Pharmacological Therapy<sup>11,21,22</sup>

- Consider if there is patient concern or if cosmetic treatment is ineffective/inaccessible/unaffordable
- Should be trialled for at least 6 months before making changes in dose or medication
- Primary therapy is the COCP (monitor glucose tolerance in those at risk of diabetes)
- Anti-androgen monotherapy (eg. aldactone or cyproterone acetate) should not be used without adequate contraception and for women with contraindications for COCP therapy or when COCPs are poorly tolerated
- Combination therapy – if COCP is ineffective, add anti-androgen to COCP

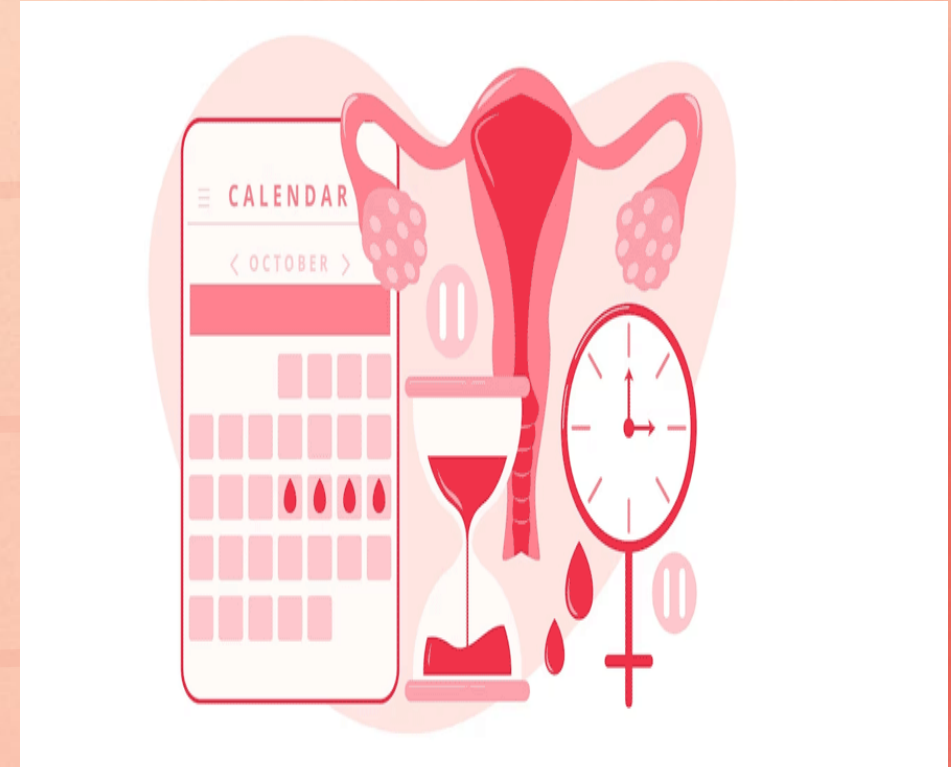
## **Antiandrogens (Continued)**

- Spironolactone at 25-100 mg/day appears to have lower risks of adverse effects
- Cyproterone acetate at doses  $\geq 10$  mg is not advised due to an increased risk including for meningioma
- Finasteride 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<sup>20</sup>**

# Menstrual Irregularities

- Lifestyle change (5–10% weight loss + structured exercise)
- COCP can be used in reproductive age adults with PCOS for management of irregular menstrual cycles and hirsutism<sup>22</sup>
- There is no clinical advantage of using high dose ethinylestradiol ( $\geq 30 \mu\text{g}$ ) vs low dose ethinylestradiol ( $< 30 \mu\text{g}$ )
- 35  $\mu\text{g}$  ethinyl estradiol plus cyproterone acetate preparations should be considered as second-line therapy over other COCPs
- Progestin only oral contraceptives may be considered for endometrial protection<sup>19</sup>
- SDM is critical while prescribing COCP to treat PCOS. Accurate information and reassurance on the efficacy and safety of COCP should be provided to improve chances of desired outcome<sup>7,21</sup>



## Menstrual Irregularities (Continued)

- COCP in conjunction with metformin may be most beneficial in high metabolic risk groups including those with a BMI > 30 kg/m<sup>2</sup>, diabetes risk factors, impaired glucose tolerance or high-risk ethnic groups<sup>9</sup>
- Where COCP is contraindicated, not accepted or not tolerated, metformin may be considered for irregular menstrual cycles. For hirsutism, other interventions may be needed<sup>11</sup>
- Combination with the COCP, metformin may be most beneficial in high metabolic risk groups including those with a BMI > 30 kg/m<sup>2</sup>, diabetes risk factors, impaired glucose tolerance or high-risk ethnic groups<sup>5</sup>



## Reproductive Outcome

# PCOS Related Pregnancy Risks

- Pregnant women with PCOS have an increased risk of<sup>18,28</sup>
  - Higher gestational weight gain
  - Miscarriage
  - Gestational diabetes
  - Hypertension in pregnancy and preeclampsia
  - Intrauterine growth restriction, small for gestational age
  - preterm delivery
  - caesarean section
  - Prenatal depression





## **Reproductive Outcome**

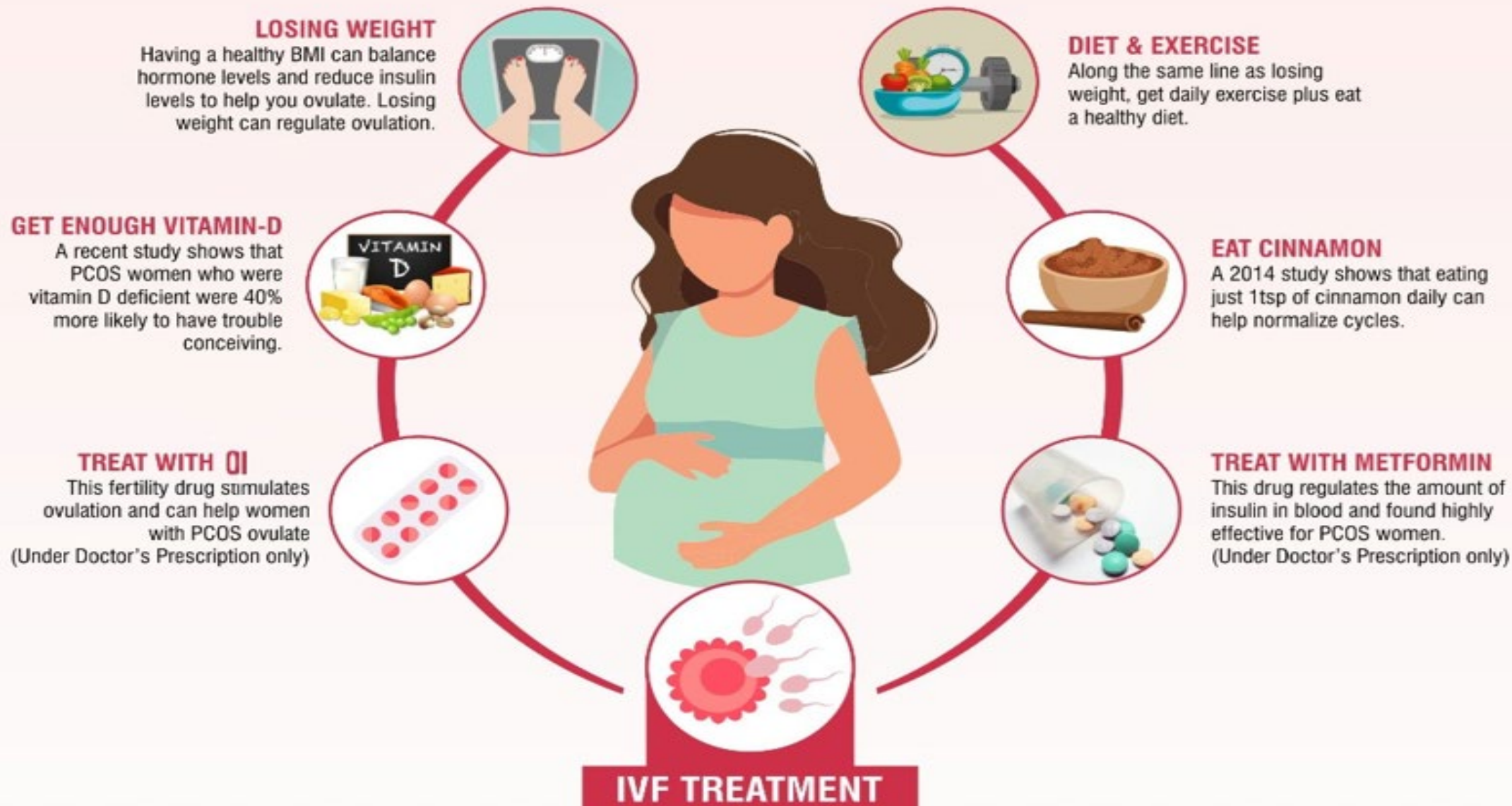
### **PCOS Related Pregnancy Risks**

- Advise prenatally about smoking cessation, optimal weight, exercise and folate supplementation<sup>28</sup>
- Perform OGTT antenatally early & in 2<sup>nd</sup> trimester to rule out Gestational/Type 2 DM , if not performed prenatally <sup>20</sup>
- Advice regarding the age-related decline in fertility to allow optimal timing of family planning<sup>28</sup>

## Reproductive Outcome (Continued)

- Metformin in pregnant women with PCOS has not been shown to prevent<sup>18</sup>
  - Macrosomia
  - Gestational diabetes
  - Late miscarriage
  - Hypertensive disorders in pregnancy
- Metformin can be considered in some circumstances during pregnancy to reduce risk for preterm birth and excess gestational weight gain
- Women should be informed that long term consequences of metformin exposure on the offspring is unclear and there is a theoretical risk of increased childhood weight, though not substantial evidence .
- Side-effects of metformin are mostly mild, transient GI symptoms and are not worse in pregnancy.

# PCOS & GETTING PREGNANT





# Reproductive Outcome PCOS & Infertility

- Most women with PCOS can achieve a natural pregnancy with lifestyle modifications & younger patients can be reassured but approximately 40% of women with PCOS need infertility assistance<sup>29</sup>
- Age related fertility discussion and plan is highly important<sup>29</sup>
- Letrozole is an Aromatase inhibitors (AI) which is proven effective as ovulation-inducing agent and being mostly used for this purpose<sup>30</sup>
- AI prevent the aromatase-induced conversion of androgens to estrogens, including in the ovary. This mechanism though not fully elucidated but results in increased secretion of FSH, stimulating ovarian follicle development and maturation leading to pregnancy<sup>7,30</sup>

# Reproductive Outcome PCOS & Infertility

- Clomiphene citrate versus Letrozole<sup>30</sup>
  - Evidence has shown that 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.
  - Current evidence demonstrates no difference in fetal abnormality rates between letrozole or clomiphene citrate ovulation induction or natural conception.



# Reproductive Outcome PCOS & Infertility

- IVF vs OI<sup>7,9,29</sup>
  - IVF can be considered PCOS Patients with anovulatory infertility, if first- or second-line ovulation induction therapies have failed.
  - In anovulatory PCOS, IVF is found to be effective .
  - Risk of multiple pregnancies can be minimised by performing single embryo transfer
  - Women with PCOS are at increased risk of OHSS due to pathophysiology of the pre-existing syndrome and should be counselled prior to starting treatment about the additional risk and options to reduce the risk should be discussed.
  - Risk for OHSS can be reduced by using appropriate dosage of gonadotrophins and prompt monitoring in accordance with their AMH, BMI, age & response to the treatment.

# Public Fertility Care

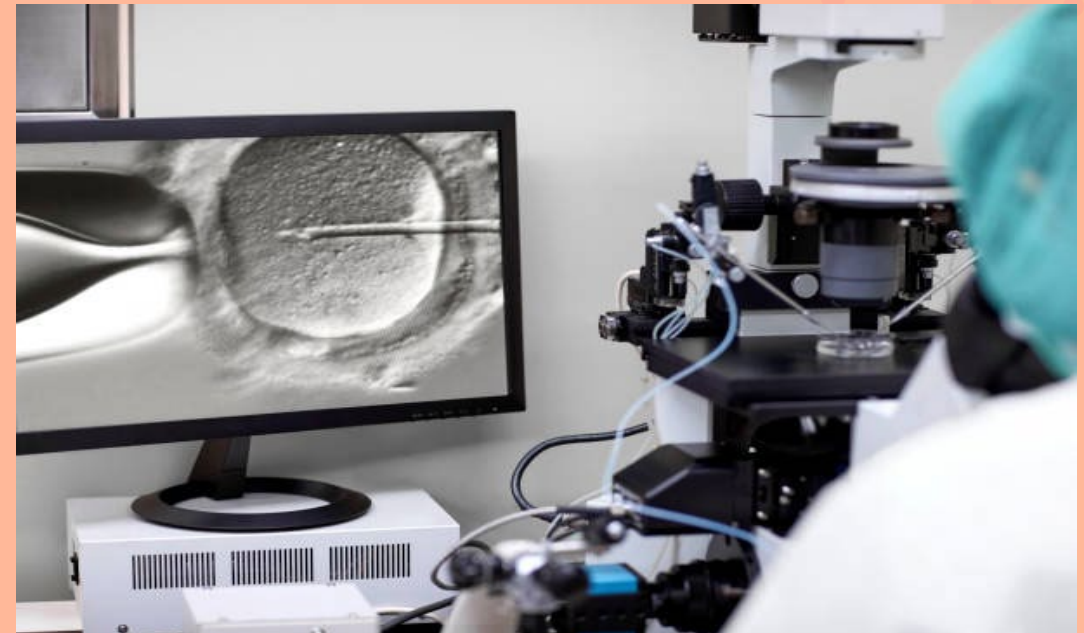
- Provides 2 x stimulation cycles per person at **no cost** & use of all frozen embryos created
- Minimal cost for medication & screening tests
- Must complete screens at GP & attached results to referral
- All referrals from the North West Victoria region sent to Royal Women's Hospital



Oct 2022, Government Announcement

## Eligibility Criteria

- Maximum egg age is 42 years at time of treatment
- Victorian Resident
- Medicare Card



# Public Fertility Care

## Services currently include

Fertility assessment and management

IVF/ICSI

IUI

Ovulation Induction

Frozen embryo transfers

Donor sperm & egg programs

Medical fertility preservation

## To be introduced in 2024 / 25

Altruistic surrogacy program

Genetic testing of embryos for Monogenic conditions (PGT-M)

Donor embryo program

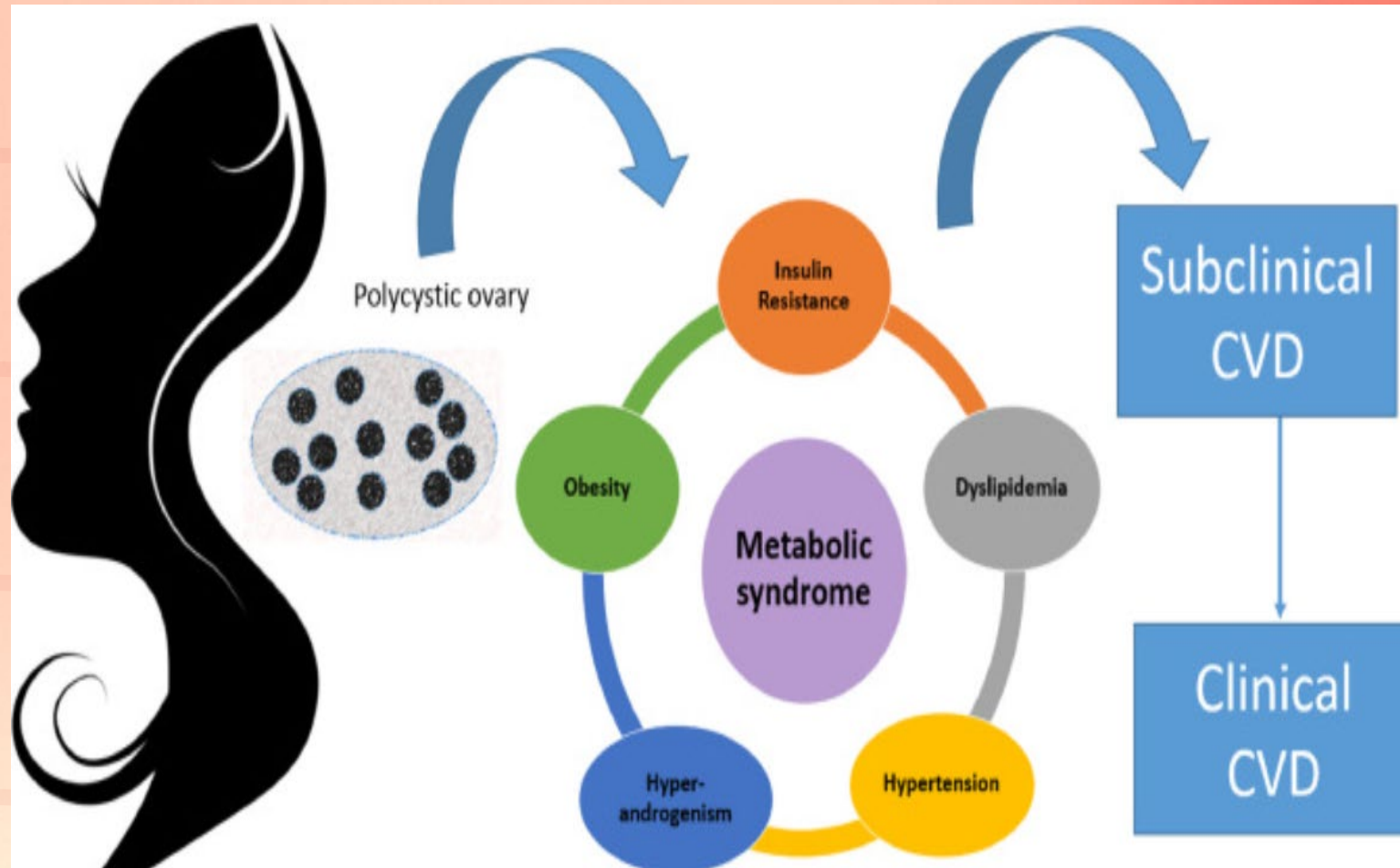
## Services not offered

Elective egg freezing

Reversal of sterilisation procedures

## Cardiometabolic risk

- PCOS patients have an increase in cardiometabolic risk factors. Indigenous women have a higher prevalence of these risk factors and are more prone to encounter PCOS related complications at much younger age than non-Indigenous women.
- 75% of Lean-body women with PCOS will have insulin resistance and ~50% can develop metabolic syndrome



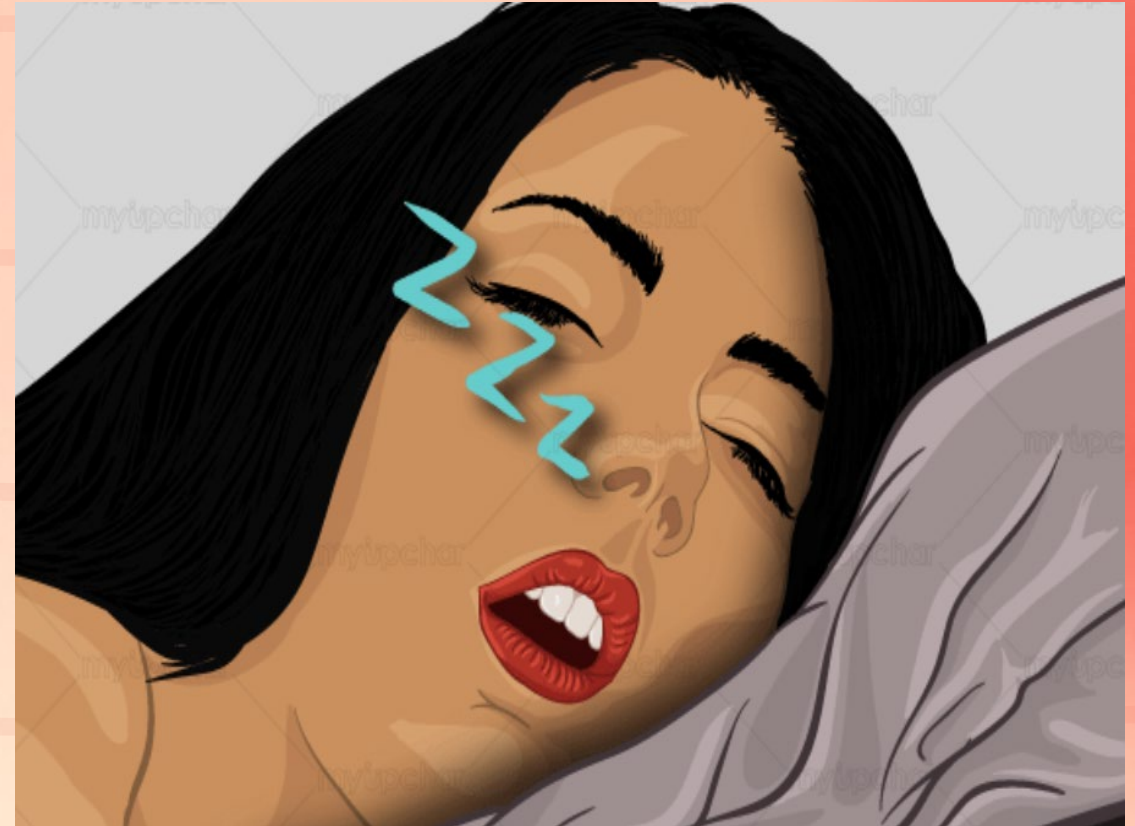


## Cardiometabolic risk (Continued)

- Lifestyle change with a >5% weight loss in those who are overweight reduces diabetes risk by ~50–60% in high risk groups<sup>11</sup>
- Metformin\* reduces the risk of diabetes by ~50% in adherent high-risk groups<sup>27</sup>
- The COCP is indicated for contraception and metformin for diabetes. Their combine use is supported by evidence and is recommended by international and national specialist societies and is evidence based to combat insulin resistance & hyperandrogenism in patients with PCOS<sup>22,27</sup>

## Obstructive Sleep Apnea

- PCOS patients have significantly higher prevalence of OSA compared to women without PCOS, independent of BMI<sup>23</sup>
- PCOS patients should be assessed for symptoms if present, screen with validated tools or refer to Respiratory Physicians for further evaluation<sup>24</sup>
- Berlin questionnaire is a validated tool in general population and can be used in PCOS patients as well<sup>7</sup>
- Formal diagnosis requires a Sleep Study<sup>7</sup>
- Treatment should be tailored according to individual needs & goals<sup>24</sup>



## Endometrial hyperplasia & Cancer

- PCOS patients have higher risk of developing endometrial hyperplasia and endometrial cancer<sup>26</sup>
- 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<sup>7</sup>
- Overall chance of developing endometrial cancer is low, therefore routine screening is not recommended in PCOS patients<sup>25</sup>
- Preventative measures including lifestyle modification, cycle regulation and progestogen therapy can reduce the risks<sup>29</sup>
- When increased endometrial thickness is detected, consider a histological diagnosis in the form of biopsy<sup>26</sup>

### Causes, Symptoms & Treatment



Endometrial hyperplasia is a condition that can lead to endometrial cancer if left untreated.

Talk to your doctor to learn more about Endometrial hyperplasia

## Take Home

- Polycystic ovarian syndrome is one of the most important endocrine disorders that affects females in the reproductive age and may lead to serious complications.
- Further studies are needed to determine the exact aetiology of PCOS, methods of prevention and proper management.
- PCOS is an endocrine disorder associated with hormonal and menstrual abnormalities
- It may be associated with short- and long-term complications
- Diagnosis involves clinical, laboratory, and radiological methods
- Treatment depends on the needs of the patient and the severity of the symptoms
- Treatment can be conservative, medical or surgical incorporating SDM & SMART approach



Q&A

## References

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A large red circle is positioned on the left side of the slide, containing the word 'Resources' in white text.

## Resources

- [Evidence-Based-Guidelines-2023.pdf \(monash.edu\)](#)
- Jean Hailes for Women's Health: [www.managingpcos.org.au](http://www.managingpcos.org.au)
- National Health and Medical Research Council. Evidence-based guideline for the assessment and management of polycystic ovary syndrome: [www.nhmrc.gov.au/guidelines/publications/ext0002](http://www.nhmrc.gov.au/guidelines/publications/ext0002)
- Teede HJ, Misso ML, Deeks AA, et al. [Assessment and management of polycystic ovary syndrome: summary of an evidence-based guideline.](#) Med J Aust 2011;195(Suppl)65–112.

# Session Conclusion

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