PRIMARY CARE
WOMEN'S HEALTH FORUM

Polycystic ovary syndrome: a long-term condition

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Session overview

Using cases typically seen in primary care to:

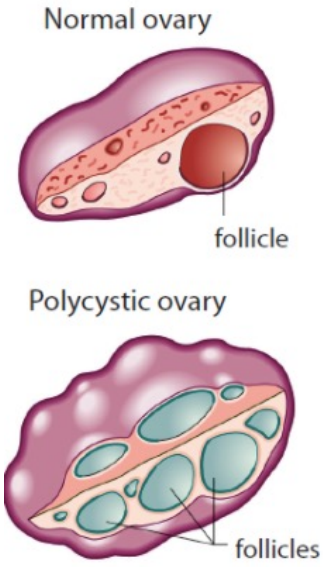
- Gain an understanding of the pathophysiology of PCOS
- Appreciate need for personalised management of:
  - Short term effects
  - Fertility concerns
  - Psychological impact
  - Long-term health risks

Question - PCOS

- What is the estimated prevalence of PCOS in the UK?

  - 2%
  - 5%
  - 10%
  - 20%
  - 30%

'Diabetes of bearded women'



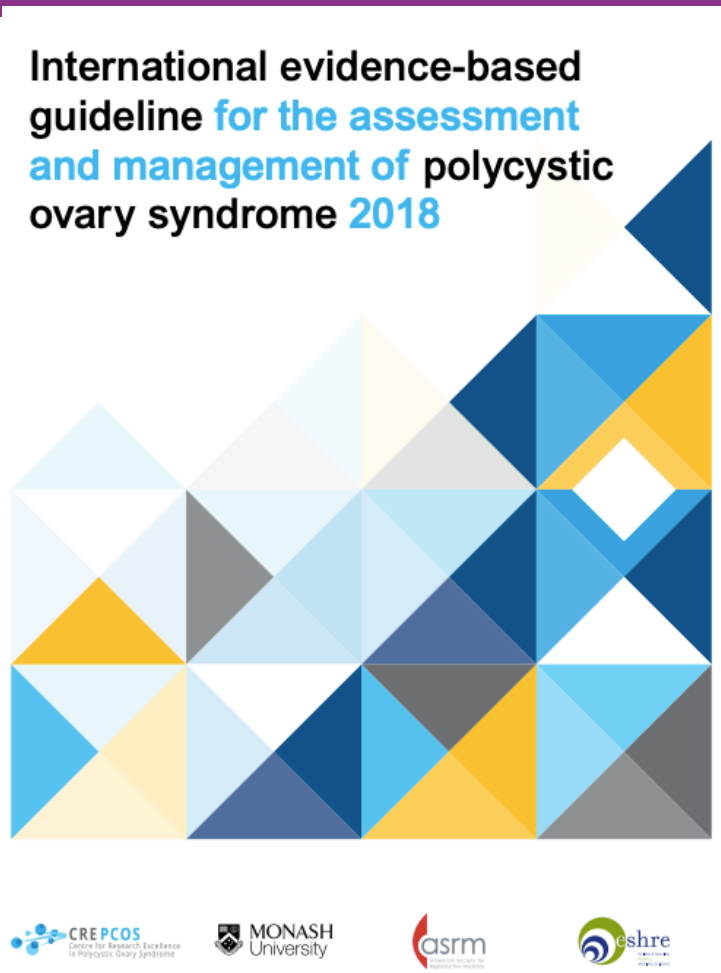
Rotterdam Criteria[3] requires 2 of 3 key features to be present for diagnosis of PCOS:

- Oligo and/or anovulation
- Hyperandrogenism (clinical and/or biochemical)
- Polycystic ovaries on USscan, (presence of > 20 follicles per ovary +/- ovarian volume >10ml)

AFTER THE EXCLUSION OF OTHER AETIOLOGIES

PCOS

- Commonest endocrine disorder of women of reproductive age.
- Affecting up to 8-13% of women in the UK, with up to 70% undiagnosed[1]
- A complex, long-term condition with metabolic, reproductive and psychological sequelae [2]
- Key feature is insulin resistance causing hormonal dysfunction
- Personalised care required to manage concerns



https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Polycystic-Ovary-Syndrome.aspx

PCOS

Reproductive

- Menstrual disturbance
- Hirsuitism & Acne
- Infertility
- Pregnancy complications
- Endometrial cancer

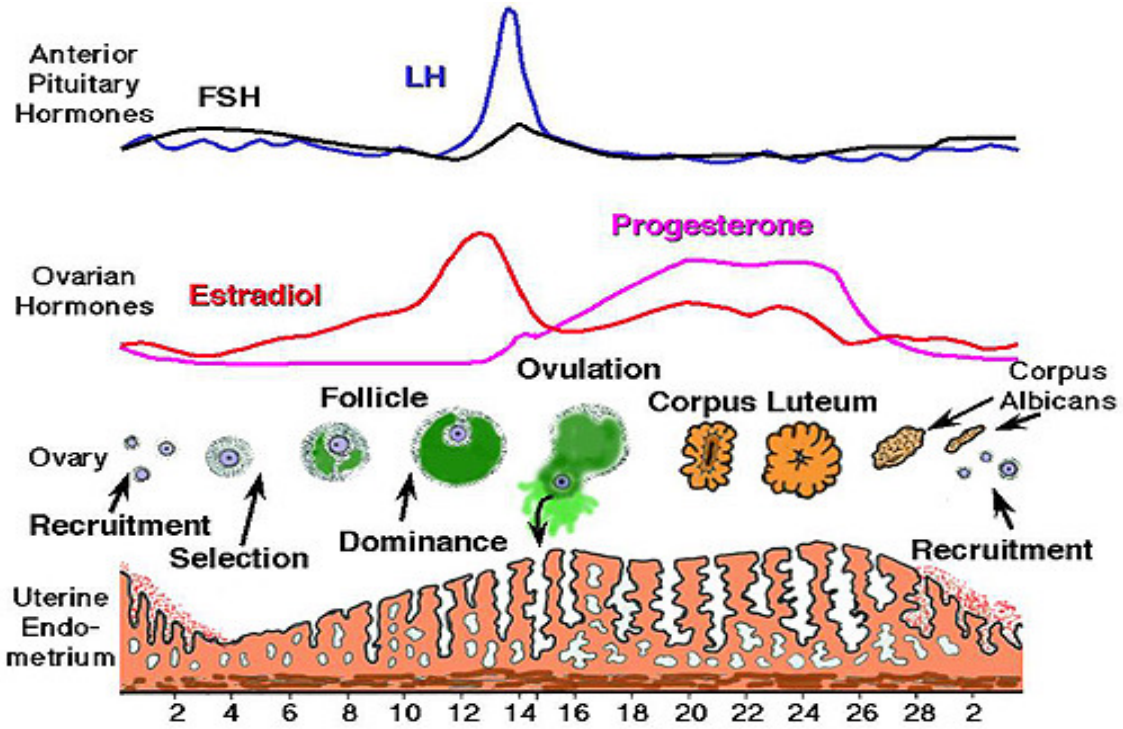
Metabolic

- Insulin resistance
- Metabolic Syndrome
- Type 2 diabetes
- Cardiovascular disease

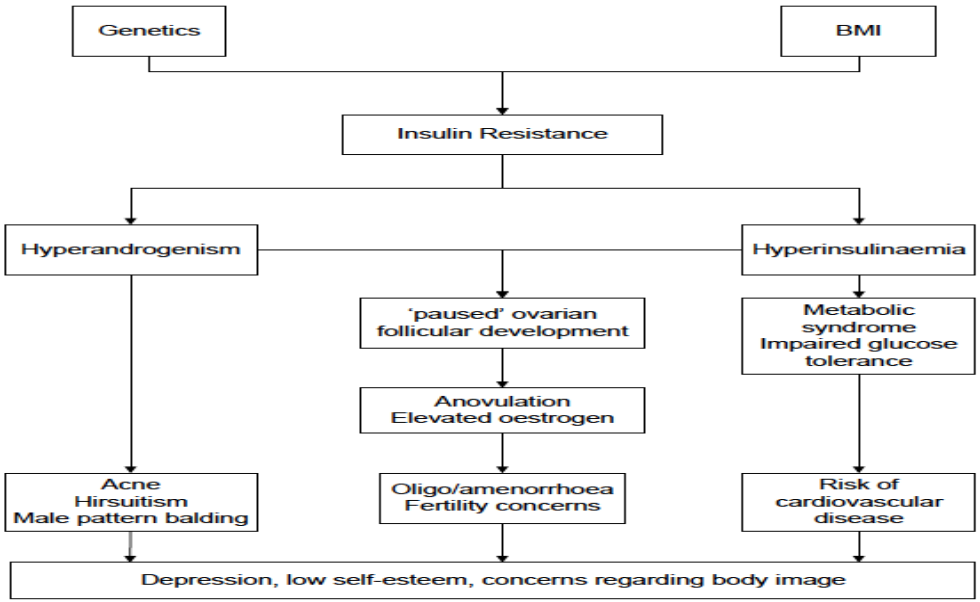
Psychological

- Anxiety
- Depression
- Body image concerns

Back to the class-room



PCOS – endocrine disorder



Ayesha

Ayesha is a 23 year old who phones for an appointment. She is concerned about recent increase in facial spots and facial hair.

She had acne a few years ago when she was at school, 'same as her friends' but this had improved. She has noticed more over the last few months and now the hair on her chin is becoming more of a problem.

Her weight has increased over the past 2 years since she finished college and has been working from home.

Her periods started when she was 13. They were irregular for the first few years, became regular 4-5/31 for a few years but she has noticed that she has 'missed a few' recently.

She denies any pregnancy risk – no sexual partner.

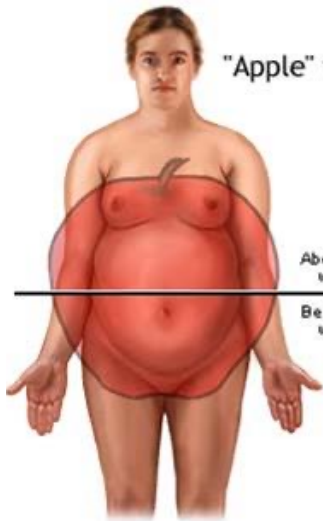
Hyper-androgenism in PCOS

Which of the following is not a feature of the hyper-androgenism classically seen in women with PCOS?

- Late onset acne
- Clitoral hypertrophy
- Hirsuitism
- Male pattern balding

Short term features of PCOS

- Classic “apple-shape” distribution of adipose tissue
- Oligo-/ amenorrhoea (70%)
- Acne (30%)
- Hirsutism (60-70%)
- Acanthosis nigricans (1-3%)
- Depression
- Infertility



Menstrual disturbance

- Primary amenorrhea > age 15 or 3 years post thelarche
- **Any menstrual pattern normal** in 1st year
- Abnormal cycles:
  - years 2 & 3 < 21 days or > 45 days
  - > 3 years < 8 bleeds per year or < 21 days or > 35 days
  - Or **menstrual chaos**

Differential diagnosis

Oligomenn (or amenn)

- Thyroid disease
- Hyperprolactinimea
- Non-classic congenital adrenal hyperplasia

Amenn

- Hypogonadotropic hypogonadism
- Cushings disease
- Androgen secreting tumours

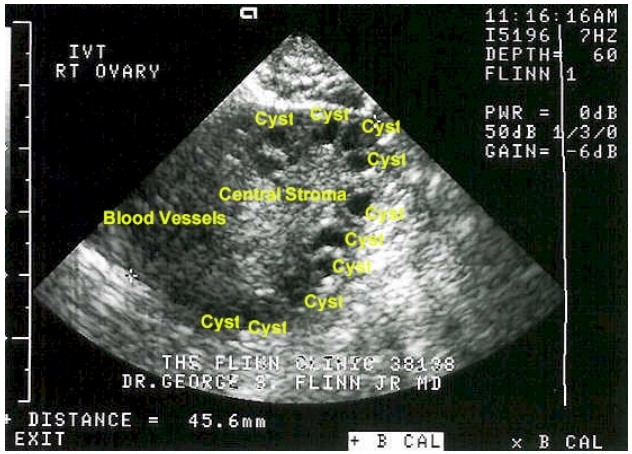
Biochemistry

- Day 2-5 (if possible) LH/FSH
- Testosterone
- Sex Hormone Binding Globulin (SHBG)
- Free Androgen Index = total testosterone/SHBG x 100

- Prolactin/TFTs

- If BMI >25 in caucasian women/>23 in S.Asian women
  - HbA1c (every 1-3 years) or OGTT
  - Lipid profile
  - LFTs

Ultrasound findings



- Ideally transvaginal scan
- If only TA possible, ovarian volume > 10ml diagnostic
- Remember multicystic ovaries
- Do not scan for PCO in women less than 8 years after menarche

- NOT necessary for diagnosis
- 50% South Asian women have **PCO**
- Ultrasound features alone don't warrant diagnosis but might mean increased lifetime risk of PCOS

Management of short-term problems

- Aim to reduce circulating free androgens:
  - Weight reduction increases levels of SHBG.
  - Any ethinyl-oestradiol (EE) product increases levels of SHBG.
  - Anti-androgen therapies include cyproterone acetate either alone or in combination with EE (Dianette)
  - EE plus drosperinone (Yasmin)

- Or/and
  - Typical acne treatments (antibiotics/roaccutane)
  - Hirsuitism treatments, i.e. laser, waxing

Lifestyle recommendations – weight reduction

- Obesity is a modifying rather than a causal factor for PCOS[5]
- Obesity increases insulin resistance and resulting hyperinsulinaemia causes adipogenesis and decreases lipolysis
- Influences the phenotypic expression of PCOS, exacerbating metabolic, reproductive and psychological features.
- Lipid abnormalities are increased independently in PCOS and exacerbated by excess weight
- Central obesity is associated with more severe metabolic disturbance
- Prevalence of impaired glucose tolerance and DM is further increased in women with PCOS with excess weight, especially in high risk ethnic groups.

- Weight loss reduces abdominal fat and insulin resistance and improves clinical features of PCOS

Psychological morbidity

- Anxiety (OR 2-5)[6]
- Depression (OR 2-4)[7]
- Psychosexual disorders
- Body image
- Eating disorders

Challenge diagnosing PCOS in adolescents

- Irregular menses and anovulatory cycles are typical during puberty transition
- High androgen levels and acne are common in teen years[8]

But if symptoms this suggests increased risk of PCOS

- Re-evaluate 8 years after menarche[9]
- Weight gain in early adulthood is significantly associated with symptoms[10]

'I can't get pregnant Doc'

Gemma, a 27 year old classroom assistant, phones for an appointment. She is upset because she can't get pregnant again.

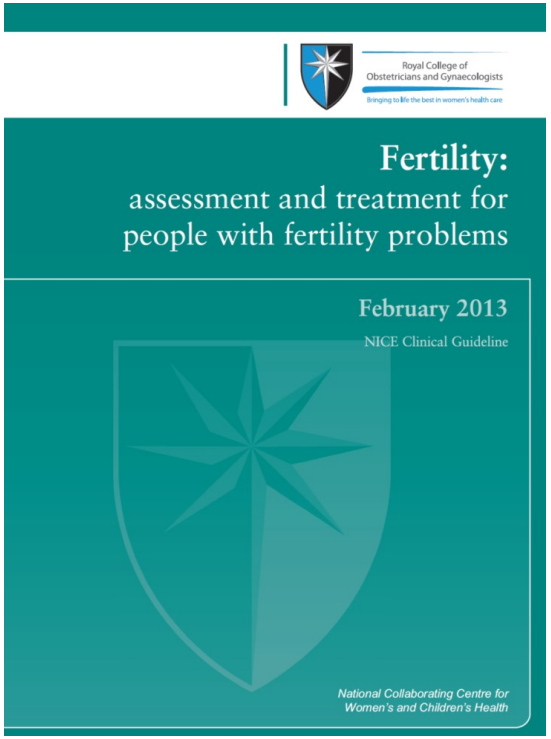
She has one child, Imogen, who is now aged 3, from her first and only pregnancy. Her husband, Dave, a bus driver, is the father of her daughter.

On further questioning Gemma reports that she's upset because her periods have become less frequent. The gap between her periods is now between 2 and 6 months.

She does frequent home pregnancy tests in the hope that the delayed period is caused by pregnancy.

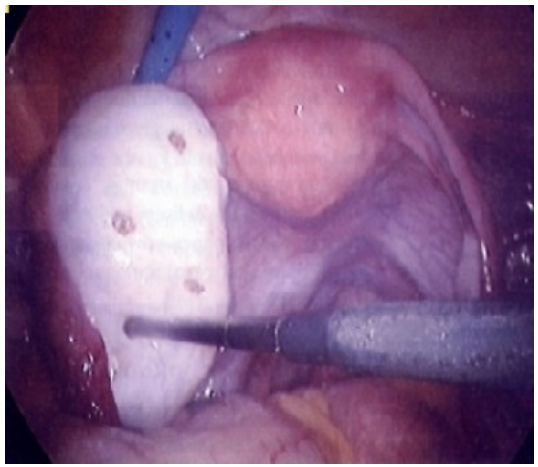
Causes of infertility

Male factor	30%
Ovulatory	25%
Tubal damage	20%
Uterine or peritoneal	10%
Unexplained	25%
Both male and female factors	40%
PCOS accounts for up to 70% of patients with anovulatory subfertility[11].	



https://www.nice.org.uk/guidance/CG156

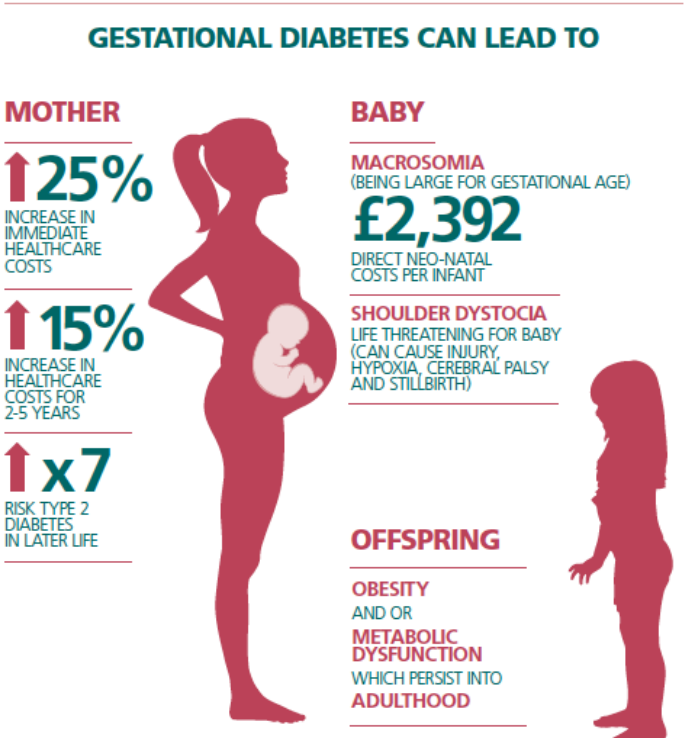
Fertility management



- **Weight reduction**
- **Preconception care – including 5mgs folic acid**
- Routine investigations (including semen analysis)
- **Consider** referral for ovulation induction with clomifene citrate.
- ? + metformin
- Laparoscopic ovarian drilling
  - Reduces circulating androgen levels
  - Indirect effect on pituitary gland - reduce LH and increase FSH
- Finally additional ovarian induction – assisted conception

Pregnancy & PCOS

- Risks to overweight women with PCOS in pregnancy[12]:
  - Gestational Diabetes Mellitus
  - Increased risk of PCOS in offspring
  - 14% will have a major pregnancy complication:
    - Risk of hypertension
    - Risk of VTE increased
    - >50% of maternal deaths obese or overweight
    - Increase in congenital malformations
    - Stillbirth & Neonatal death increased if BMI >30
    - Increase in operative delivery rate



Akelia

- *Akelia is a 46 year old woman who works in the local supermarket.*
- *She is well-known to the practice because of her regular attendance at the diabetic clinic and dietician. Her last recorded BMI is 42*
- *She has recently started having very heavy erratic periods.*
- *It is embarrassing for her at work as she now needs regular breaks to change her pad and has 'flooded' a few times when working on the checkout.*

Diabetes

PCOS – insulin resistance

4 times relative risk of diabetes (BMI matched)[13]

- Presents earlier
- 47% South Asian PCOS IGT or DM2 by age 41[14]
- Check HbA1c or OGTT every 3 years
- Separate risk factor for gestational diabetes mellitus

- **Beware** if long intermenstrual interval, low SHBG or acanthosis nigricans
- Note Family History

Endometrial risk

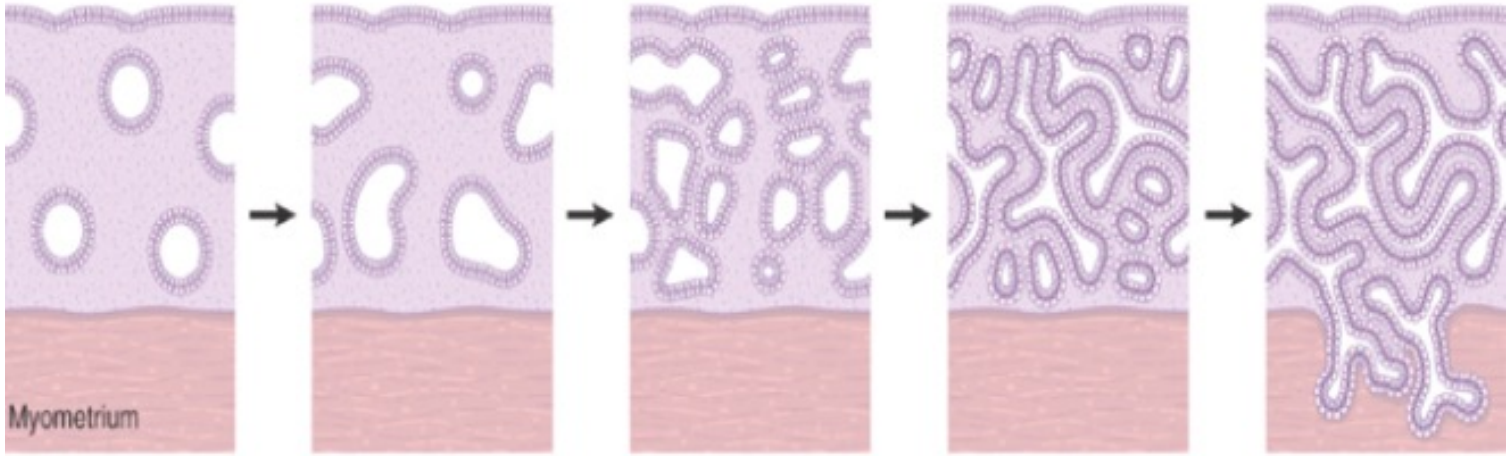
- Which of the following is not a risk factor for endometrial hyperplasia:

  - Combined hormonal contraception
  - Obesity
  - PCOS
  - Diabetes
  - Estrogen only HRT

Endometrial hyperplasia

Definition:

Irregular proliferation of endometrial glands with an increase in the gland to stroma ratio when compared with proliferative endometrium

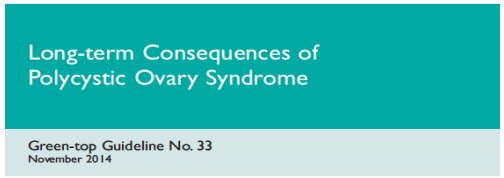


Endometrial hyperplasia

- Develops when oestrogen excess is unopposed by progesterone.

- Risk factors:
  - Increased BMI with excessive peripheral conversion of androgens in adipose tissue to oestrogen.
  - Anovulation associated with peri-menopause or PCOS.
  - Oestrogen- secreting ovarian tumours (e.g. granulosa cell tumours)
  - Drug-induced endometrial stimulation (systemic ERT or Tamoxifen in post-menopausal women)

Endometrial risk and PCOS



- Oligo/amenorrhoea with pre-menopausal oestrogen levels can cause endometrial hyperplasia and cancer.
- Women with PCOS have a 2 - 6 x increased risk of developing endometrial cancer.
- Intermenstrual intervals of > 3 months are associated with endometrial hyperplasia.
- Regular induction with at least 12 days progestogens, oral contraceptives or LNG-IUS is recommended.
- No increased risk of breast cancer in women with PCOS. No additional screening recommended

Long-term monitoring

- Screening for cardio-vascular disease
- Screening for diabetes.
- Prevention of endometrial hyperplasia
  - LNG containing intra-uterine system
  - Combined hormonal contraception
  - Induced withdrawal bleeds using medroxy-progesterone acetate (MPA) 10mgs daily for 12-14 days every 3-4 months (after excluding pregnancy).

Tips for PCOS

- This is a common long-term condition
- No referral needed. Manage in primary care
  - **Weight reduction**
  - Personalised symptom management
  - Psychological support
  - Refer for fertility advice when BMI < 30
  - Longer-term disease prevention
    - Manage complications of insulin resistance
    - Provide endometrial protection

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Thank you

Any Questions?

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