# Polycystic Ovarian Syndrome in Adolescents: Characterising the Clinical Phenotype and the Role of Precision Medicine

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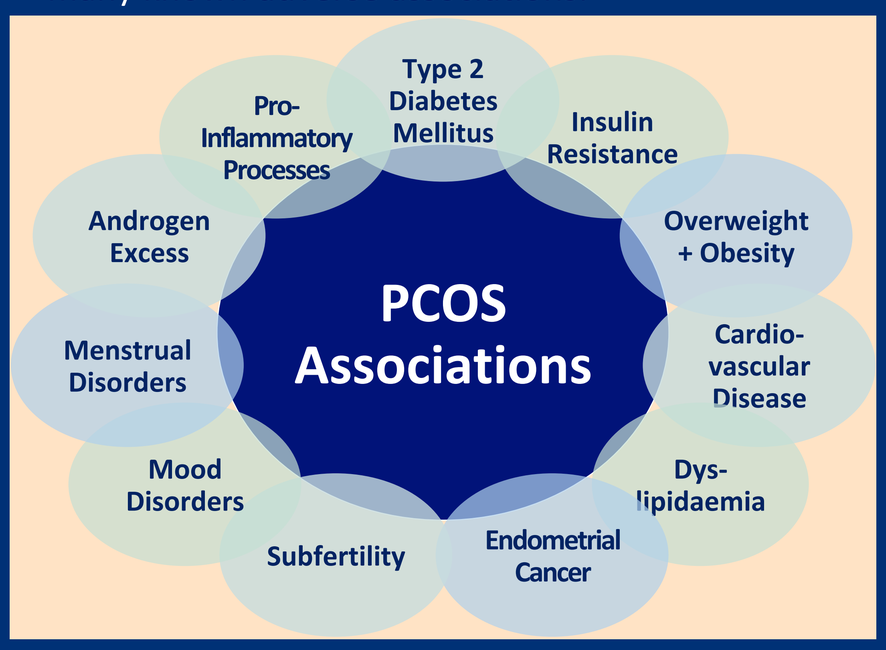
## Introduction

- Polycystic ovarian syndrome (PCOS) is the most common hormone disorder in adolescent and young adult females, affecting 4-20% of the population.
- Historically diagnosed during reproductive years, it is increasingly diagnosed and managed in paediatric and adolescent settings.
- PCOS is poorly understood in adolescents, but has many known adverse associations.




- Early diagnosis can reduce these long-term sequelae.
- However, diagnosing PCOS in adolescents is challenging as clinical signs of hyperandrogenism (acne, increased body hair), anovulatory cycles and poly/multicystic ovarian morphology are common.

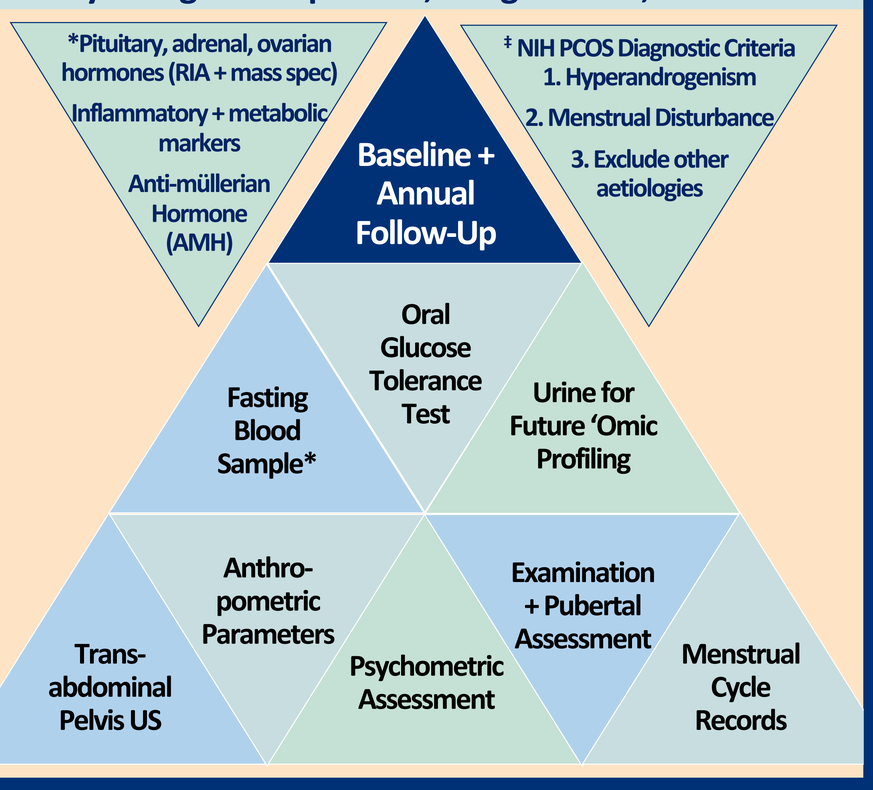
## Objectives

- To better understand the clinical phenotype of PCOS in adolescents.
- To plan future discovery (untargeted) proteomic and metabolomic ('omic) profiling of urine to identify novel non-invasive biomarkers of PCOS.

### Participant Selection Criteria

Females aged 12-19 yrs → Adolescent Endocrine or Gynaecology Clinics → Meeting NIH PCOS Criteria‡

### Study Design: Prospective, Longitudinal, Multicentre

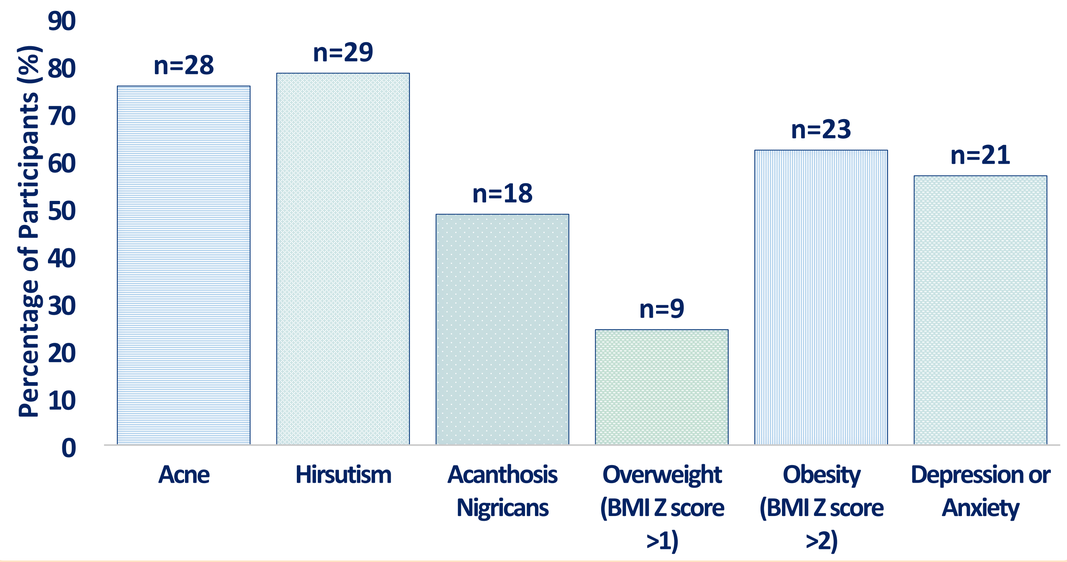



## Results

- To date, 37 participants have been recruited and 22 have completed their 12 month follow-up (FU).
- Median age at recruitment was 15.0 years (range 12.6-18.3 years).
- Mean age at menarche was 10.9 years (SD 1.38).
- Tanner stage was IV (n=17) and V (n=20).

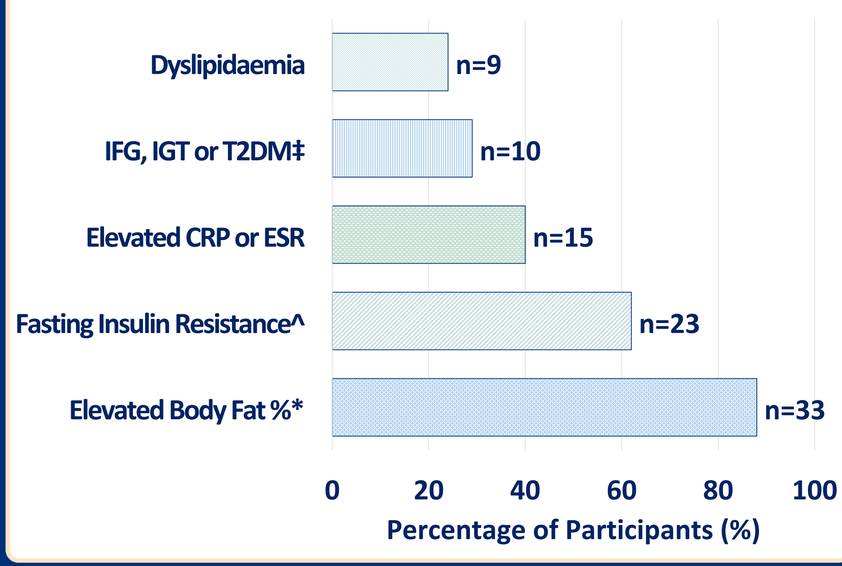
- **At Presentation** (Fig. 1), 92% participants (n=34) had clinical signs of hyperandrogenism (acne or hirsutism).
- The majority had evidence of metabolic dysfunction; 87% were overweight or obese and 49% had acanthosis nigricans.
- Anxiety and depression were common (57%) but less than half were known to mental health services (27%; n=10).

**Figure 1: Clinical Signs at Presentation (n=37)**




- **Family History** of the following was noted: 84% overweight/obesity (n=31), 81% type 2 diabetes (T2DM) (n=30), 62% hypertension (n=23), 51% cardiovascular disease, dyslipidaemia and PCOS (n=19 each), 41% female infertility (n=15) and 28% maternal gestational diabetes (n=11).

**Figure 2: Metabolic Dysfunction at Presentation**




- **High prevalence of metabolic dysfunction at baseline (Fig 2).**

‡IFG=Impaired Fasting Glucose (n=5), IGT= Impaired Glucose Tolerance (n=4), T2DM (n=1)

^Fasting insulin resistance defined as insulin >20mIU/l or >139pmol/l

*Body composition measured using body impedance analysis (normal range 16.9-29.9%)

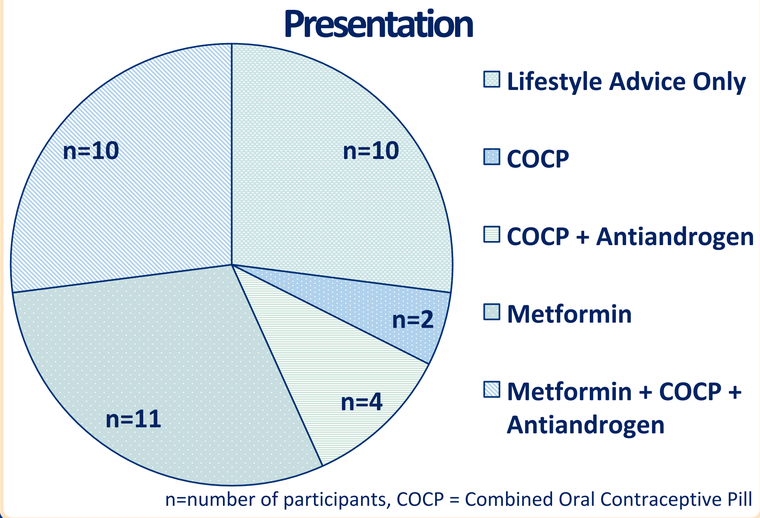
- **Changes from baseline → 12 month follow-up**
- Median FAI significantly improved; baseline 6.7% [IQR 4.6-12.0%], FU 2.6% [IQR 0.5-5.7], ($p$=0.002).
- Prevalence of IFG/IGT fell from 24% (n=9) at baseline to 5% (n=1) at FU.
- Median fasting insulin concentrations remained unchanged; baseline 153pmol/l [IQR 151-229], FU 157pmol/l [IQR 103-194] ($p$=0.554).
- Median BMI centile did not improve significantly; baseline 98.0 [IQR 91.6-99.1], FU 96.5 [IQR 91.9-99.4] ($p$=0.854).

## Future Directions

- We are undertaking discovery (untargeted) proteomic and metabolomic profiling of urine, using electrospray-ionisation quadrupole-time-of-flight mass spectrometry.
- **We aim to:**
  1. **Better understand PCOS molecular pathways.**
  2. **Identify novel non-invasive biomarkers.**
  3. **Translate these findings into a clinical useful assay to aid PCOS diagnosis and management.**

- **Hormonal abnormalities were common**
- Biochemical androgen excess as indicated by an elevated free androgen index (FAI >5%) was identified in 68% participants (n=23).
- Elevated AMH (>4ng/ml or >28pmol/l) was identified in 65% participants (n=20 of 31), median AMH 34pmol/l [IQR 18-48 pmol/l).
- **Pelvic ultrasound diagnosis of PCOS**
- Only three participants had ultrasonographic evidence of PCOS and a further quarter had equivocal results.

**Figure 3: Intervention Following Baseline Presentation**




n=number of participants, COCP = Combined Oral Contraceptive Pill

## Conclusions

- **PCOS in adolescence is associated with many comorbidities, particularly metabolic disease and mental health disorders.**
- **As such, accurate diagnosis and early intervention are imperative.**
- **However, diagnosing PCOS in adolescents remains challenging.**
- **Current management strategies are limited.**

## Acknowledgements

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**Harriet Gunn previously held the Marie Bashir Fellowship for Clinical Research in Adolescent Health (Australia). She now holds the UCL Clinical Academic Training Fellowship in Child and Adolescent Health (UK).**

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Sex differentiation, gonads and gynaecology or sex endocrinology

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