POLYCYSTIC OVARIAN SYNDROME IN ADOLESCENTS:
DISCOVERY PROTEOMICS AND THE SEARCH FOR NOVEL NON-INVASIVE BIOMARKERS

1 2 3 HM Gunn*, 3 4 VS Forsyth, 1 J Häblqvist, 2 R Viner, 1 K Milb, 3 4 KS Steinbeck.
1 Translational Mass Spectrometry Research Group, UCL Great Ormond Street Institute of Child Health, London, UK; 2 Population, Policy and Practice Programme, UCL Great Ormond Street Institute of Child Health, London, UK; 3 Academic Department of Adolescent Medicine, Sydney Children’s Hospital Network, Sydney, Australia; 4 Discipline of Child and Adolescent Health, The University of Sydney, Sydney, Australia

Background Polycystic ovarian syndrome (PCOS) is common, affecting up to one-fifth of females and is associated with significant morbidity. Despite this, it is poorly understood, and diagnosis and management remain challenging in adolescents. Proteomics enables the better understanding of disease mechanisms and facilitates the identification of novel biomarkers.

Objectives To describe the clinical phenotype of PCOS in adolescents and undertake discovery proteomic urine profiling using ultra-performance liquid chromatography-mass spectrometry (UPLC-MS/MS) to identify novel non-invasive biomarkers of PCOS.

Method This prospective longitudinal study recruited adolescent females meeting NIH diagnostic criteria for PCOS. The following were measured at baseline and annual follow-up: hormonal and metabolic markers including an oral glucose tolerance test, psychological, pubertal and anthropometric parameters, and pelvic ultrasounds. We have undertaken UPLC-MS/MS and developed new methods for discovery proteomic profiling of urine in an attempt to identify new disease mechanisms, drug targets and potential biomarkers.

Results We recruited 40 participants (median age 15.0 years, range 12.5-18.3), with two-thirds completing annual follow-up. Clinical signs at presentation included acne (89%), hirsutism (78%) and acanthosis nigricans (49%). Two-thirds of participants had depressive or anxiety symptoms yet only one-third were known to mental health services. Metabolic dysfunction was common at baseline; overweight/obesity (86%), elevated body fat (88%) and dyslipidaemia (35%). These parameters persisted at follow-up. Insulin resistance was almost universal at baseline and follow-up (91%). Impaired glucose metabolism was common but improved from baseline (29%) to follow-up (10%; p=0.11). Over two-thirds had elevated anti-Müllerian hormone, three-quarters had an elevated free androgen index. Raised inflammatory markers (CRP/ESR) were present in 40% participants. Only three participants had definitive ultrasonographic evidence of PCOS. Interventions included lifestyle advice (27%), combined oral contraceptive pill (COCP) ± anti-androgen (16%), metformin (30%) or metformin + COCP ± anti-androgen (27%).

Conclusion and future directions Adolescents with PCOS are at high risk of metabolic dysfunction, inflammation and mental health disorders. Therefore, early diagnosis and intervention are imperative. However, current diagnostic and surveillance methods are suboptimal. We have used urinary proteomics to study metabolic pathways affected in PCOS and aim to identify novel non-invasive biomarkers. Subsequently, we will create a clinically translatable assay to aid diagnosis and stratify management of this common adolescent condition.

YOUTH GAMBLING AND MENTAL HEALTH- A POPULATION STUDY

1 A Emond*; 2 M Griffiths; 3 L Hollen. 1 Centre for Academic Child Health, Bristol Medical School, Bristol, UK; 2 International Gaming Research Unit, Nottingham Trent University, Nottingham, UK

Aims To investigate gambling behaviour in youth aged 17-24 and explore the associations with mental health and wellbeing.

Methods A large contemporary UK cohort study, the Avon Longitudinal Study of Parents and Children (ALSPAC), was used to collect the data. Young adult participants completed computer-administered gambling surveys in research clinics, on paper and online. Depression, anxiety and wellbeing scores, and drug and alcohol usage, were collected by self-completion questionnaires. The sample sizes were 3566 at age 17 years, 3940 at 20 years, and 3841 at 24 years. Multiple imputation techniques were utilised to adjust for missing data, and multivariable models created using the imputed data set.

Results Participation in gambling in the last year was reported by 54% of 17-year-olds, rising to 68% at 20 years, and 66% at 24 years, with little overall variance. Regular (weekly) gambling showed a strong gender effect, increasing from 13% at 17 to 17% at 24 years. The commonest forms of gambling were playing scratchcards, playing the lottery, and private betting with friends. The only activity which increased markedly between 17 and 24 years was gambling on activities via the internet, especially in males.

Problem gambling was measured at each age using the Problem Gambling Severity Index (PGSI), and responses categorised into ‘no problem’ ‘low risk gambling’ (16-21%) and ‘moderate risk/problem gambling’ (6-7%). At risk gamblers had shown higher hyperactivity scores and conduct problems on the SDQ at 16 years. Between 17 and 24