Methods We obtained nasal AECs by brush sampling from children with severe atopic asthma (AA) and healthy controls (HC) (n=3–6). Cells were cultured in the presence/absence of the predicted drugs amitriptyline and prednisone and stimulated with lipopolysaccharide (LPS, 10 μg/mL, 0–24h), to mimic a bacterial infection. A20 and p65 mRNA and the release of pro-inflammatory cytokines from AEC cultures were determined.

Results AEC basal A20 was lower in AA compared to HC (p<0.05). LPS stimulation induced A20 in HC rapidly (peak at 1h LPS, p<0.05) and the elevated levels were maintained for up to 4 hours. In AA, LPS also caused an increase in A20 mRNA (lower than in HC) and found to be only elevated at 4h. NF-κB p65 significantly increased 1h after LPS stimulation in HC and 4h after LPS in AA cells (both p<0.05).

Amitriptyline (effective concentration 10 μM), increased A20 levels in both HC and AA epithelial cells. HC responded with a peak expression at 1h LPS (p<0.05), while in AA cells, we observed a steady increase in A20 for up to 24h LPS. Prednisone (10^{-3} μM) induced A20 with a peak expression at 4h in AA and HC, but the increase was significantly higher in HC epithelial cells.

The increase in A20 mRNA was paralleled by a significant decrease in p65 mRNA in amitriptyline and prednisone-treated cells and a decrease in IL-8 release.

Conclusion ScsMap predicted drugs that successfully induced the anti-inflammatory protein A20 in AECs, which resulted in a reduced inflammatory response to bacterial stimulation (LPS). Although the anti-inflammatory effect of prednisone is well established, we here add that this is mediated through the induction of A20. Furthermore, the application of amitriptyline as an anti-inflammatory medication may need further investigation. This proof of concept study using bioinformatics could be used to identify other drugs that could be repositioned as anti-inflammatory treatment in asthma.

OC43 IMPACT OF FLASH AND CONTINUOUS GLUCOSE MONITORING ON QUALITY OF LIFE AND DISEASE BURDEN IN CHILDREN WITH DIABETES MELLITUS AND THEIR FAMILIES

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Introduction/Background Flash and continuous glucose monitoring technology has revolutionised the management of diabetics, particularly in paediatric populations. Recent government funding for flash glucose monitoring devices has enabled widespread usage in children and adolescents in the Republic of Ireland. We examined the impact of this novel technology on the lives of children with diabetes and their parents through the use of age modified questionnaires.

Design/Methods Qualitative research was carried out using anonymised ‘Quality of Life’ questionnaires. All children and adolescents and their families attending the diabetes service in Children’s University Hospital were eligible for the study and were invited to contribute at routine outpatient visit. Those using the technology were divided into three groups; preschool, primary school and secondary school. Together, children and their parents answered questions relating to ease of use, impact on schooling, independence, parent-child relationships and subjective burden of disease. Some sections were specific to the particular form of glucose monitoring (flash or continuous); but those regarding impact on day-to-day management of diabetes and impact on quality of life were common to all. A separate questionnaire was used for patients not using either technology and explored the factors that influenced that decision.

Results Preliminary data (n=39) shows that patient and parent experiences with flash and continuous glucose monitoring technology have been overwhelmingly positive. 90% of children surveyed are using one of these devices. Across all age groups, 100% of those using the technology reported subjective improvement in glycaemic control. All adolescents reported increased confidence in their ability to manage diabetes and a greater degree of personal independence. Parents reported significant reduction in frequency of hypoglycaemic events and >80% reported reduction in anxiety surrounding hypoglycaemia. >85% of both patients and parents found a significant reduction in the day-to-day burden of diabetes. Those not using glucose-monitoring devices listed parental concern regarding device accuracy and attachment of the device on the skin as the major deterring factors.

Conclusions This data demonstrates a positive impact of flash and continuous glucose monitoring on quality of life for children with diabetes mellitus. Government funding since 2018 has enabled equal access for all paediatric patients (over 4 years old) to this life-impacting technology which should now be offered to all children and adolescents, to include those with Type 2 Diabetes and other rarer sub-types, and those under 4 years old.

OC44 OPTIMIZATION OF DIAGNOSTICS FOR CARBOHYDRATE MECHANISM DISORDER IN CHILDREN WITH CYSTIC FIBROSIS

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Aim To study the incidence and optimize diagnostics of carbohydrate mechanism disorder in children with cystic fibrosis (CF).

Materials and methods We have examined 43 patients with cystic fibrosis. All the patients were subject to the following tests: blood chemistry, HbA1c, insulin, C-peptide ELISA assay, antibodies to ICA, IAA, GAD in order to rule out other forms of diabetes mellitus, oral glucose tolerance test (GTT). Carbohydrate mechanism disorders were diagnosed according to the WHO criteria (ISPAD 2018). In order to assess tissue sensitivity to insulin, Homa and Caro indices were calculated during the study. Additionally, 31 patients (including 15 children aged 3–11, others were adolescents) underwent Continuous Glucose Monitoring System (CGMS) test with the help of MiniMed Paradigm 722. All the children were given a molecular genetic test in order to detect various GFTR mutations.

Results The oral glucose tolerance test revealed carbohydrate metabolism disorders in 28% of the case, CF-associated diabetes mellitus was diagnosed in 19% of the case. Impaired glucose tolerance was diagnosed in 9% patients. Carbohydrate metabolism disorders among adolescents were distributed as
follows: impaired glucose tolerance (19%) and CF-associated diabetes mellitus (43%). Calculated indices of insulin resistance (Homa and Caro) showed that 71% of patients with carbohydrate metabolism disorders had a decrease in Caro (<0,332) on the 120th minute of the oral glucose tolerance test, which indicated insulin resistance.

The average HbA1c levels in children with CF-associated diabetes mellitus were 7,3±3,4%, children with glucose tolerance – 6,3±0,4% and in children with normal carbohydrate metabolism – 5,8±0,3%.

The CGMS assessment detected hyperglycemia in 81% patients, while carbohydrate metabolism disorders were diagnosed only in 28% of the cases. Stable postprandial hyperglycemia was detected with CGMS in 91% children aged ≥11 and 64% in group 3–11.

The 74,4% patients had delF508 mutations (homozygous-32%). All the cases of CF-associated diabetes mellitus were diagnosed in these patients.

Conclusions The incidence of carbohydrate metabolism disorders in CF-children was reliably higher than in overall population (28%). Carbohydrate metabolism disorders and CF-associated diabetes were reliably more frequent in children over 11 years of age.

Insulin resistance must be the most likely cause of carbohydrate metabolism disorders.

CGMS in patients with cystic fibrosis helps to detect hidden hyperglycemia that cannot be detected with the help of standard methods.

Carbohydrate metabolism disorders and CF-associated diabetes mellitus are more frequent in patients with delF508 mutation.

**OC45**

**POLYCYSTIC OVARIAN SYNDROME IN ADOLESCENTS: UTILISING DISCOVERY PROTEOMICS TO IDENTIFY NOVEL NON-INVASIVE BIOMARKERS**

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Background Polycystic ovarian syndrome (PCOS) is the most common hormone disorder in females, affecting 4–20% of the population. PCOS is associated with metabolic dysfunction, pro-inflammation and mood disorders. Despite this, it is poorly understood, and diagnosis and management remain challenging in adolescents. Proteomics enables a better understanding of disease mechanisms and facilitates the identification of novel biomarkers.

Aims

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

Method In this prospective longitudinal study, females aged 12–19 years meeting NIH diagnostic criteria for PCOS were recruited from adolescent endocrine and gynaecology clinics. At baseline and annual follow-up, the following were measured: pituitary, adrenal and ovarian hormones, anti-Müllerian hormone, inflammatory and metabolic markers including an oral glucose tolerance test, psychometric questionnaires, menstrual records, pubertal assessment, anthropometric parameters and pelvic ultrasounds. We have undertaken UPLC-MS/MS and developed new methods for discovery proteomic profiling of urine samples in an attempt to identify new disease mechanisms, drug targets and potential biomarkers.

Results To date, 37 participants have been recruited (median age 15.0 years, range 12.6–18.3), and 22 have completed annual follow-up. Clinical signs at presentation included acne (89%), hirsutism (78%), acanthosis nigricans (49%) and overweight/obesity (81%). Two-thirds of participants had depressive or anxiety symptoms. Only one-third were known to health services. Metabolic dysfunction was common; elevated body fat (88%), dyslipidaemia (24%), insulin resistance (62%), and impaired fasting glucose, impaired glucose tolerance or type 2 diabetes (40%). AMH was elevated in one-third of participants and three-quarters had an elevated free androgen index. Elevated inflammatory markers (CRP/ESR) were present in 40% participants. Only three participants had definitive ultrasonographic evidence of PCOS. Interventions included lifestyle advice only (27%), combined oral contraceptive pill (COCP) ± anti-androgen (16%), metformin (30%) or metformin + COCP ± anti-androgen (27%).

Conclusion and Future Directions Diagnosing PCOS in adolescents remains challenging; acne and irregular menstrual cycles are common and ultrasonographic diagnosis of PCOS is suboptimal. Given the high prevalence of metabolic and mental health disorders, early diagnosis and intervention are imperative. We describe the use of urinary proteomics to study metabolic pathways affected in PCOS and the potential identification of novel non-invasive biomarkers. Subsequently, we will use this hypothesis-generating data-set to create a non-invasive and clinically translatable assay to aid diagnosis and stratify management of this common adolescent condition.

**OC46**

**THE POPULATION INCIDENCE OF CHILDHOOD GONADOBLASTOMA OVER 20 YEARS IN THE REPUBLIC OF IRELAND**

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Background Gonadoblastoma (GB) is a rare tumour of the gonads presenting in childhood or adolescence. It is a lesion composed of a mixture of germ cells at different stages of maturation, with low malignant potential. It is associated with disorders of sex development, most commonly Turner mosaic syndrome with Y chromosome material (TMSY), and 46XY gonadal dysgenesis (GD). Little is known about the natural history and incidence, however prophylactic gonadectomy is recommended.

Objectives To determine the incidence and clinical features of GB presenting in childhood in the Irish Republic (ROI) from 1999–2018 inclusive.

Methods A retrospective review of children and adolescents with a diagnosis of GB was undertaken using the records of the National Cancer Registry Ireland (NCRI) and the National Diabetes Registry (NDR)